Journal of Basic & Clinical
PATHOPHYSIOLOGY

Vol. 7, Supplement 1, Autumn-Winter 2019-2020
p-ISSN: 2322-1895 e-ISSN: 2345-4334

Proceedings of

24th Iranian and 3rd International Congress of

Physiology and Pharmacology

(FAOPS Satellite Congress)

30 Oct - 01 Nov 2019

Shahed University, Tehran, Iran

A Semiannual Publication of
Shahed University

In the Name of GOD

24th Iranian 3rd International Congress of Physiology and Pharmacology

2019 FAOPS Satellite Congress

30 Oct- 01 Nov 2019

Tehran, Iran

Organized by: Shahed University in collaboration with Iranian Society of Physiology and Pharmacology

Content

Sponsors

Nourophysiology Research Center
Shahed University

Federation of the Asian and Oceanian
Physiological Society

Iranian Neuroscience
Society

Cell Injury and Regeneration
Association

Iranian Society of Toxicology

Iranian Scientific Association of Clinical Laboratory

Iranian Society
for Immunology and Allergy

Biochemical Society of Iran

Iranian Laboratory Hematology Association

Iranian Society of Blood Transfusion

Neuroscience Research Center
University of Medical Sciences

Message of the President of the Congress

It is a privilege and an honor to host the 24th Iranian Congress of Physiology and Pharmacology in 2019 in Tehran.

On behalf of the organizers, I am excited to greet and invite you great scientists, academics, and students in all diverse field of medical science; especially physiology and pharmacology, to attend this congress and share your insights into the recent researches and cutting edge technologies by your active and exuberant presence throughout the programmed sessions.

I sincerely hope that the conference will have significant impacts on unveiling the novel developments in science as well as improving public health.

Also, I invite you to use this opportunity to visit some of the numerous historical, art, and cultural attractions of Tehran.

We are looking forward to meeting you in Tehran in October 2019.

Dr. Zahra Kiasalari

Message of the Scientific Secretary of the Congress

The 24th Iranian Congress of Physiology and Pharmacology will be held in October 2019 in Tehran. This congress offers unique opportunity for academics, researchers and young intellectuals in various fields of medical science; specially physiology and pharmacology to gather, exchange and share their experiences and new finding as well as overview latest research developments.

It is a great pleasure to welcome all participants and especially the International guests to enhance the scientific program of the congress.

We look forward to meet you in Tehran the capital city of ancient Iran.

International Invited Speakers

Ishikawa Yoshihiro

Professor of Pharmacology

Cardiovascular Research Institute, Yokohama City University, School of Medicine,Yokohama, Japan

Title of Presentation: Heart Failure and more; from the bed to the benchtop

Anand Ashima

Professor of Physiology

Chair, IUPS Ethics Committee, Council Member,International Union of Physiological Sciences, India

Title of Presentation: Promoting Research Integrity : a Matrix of Merits and Metrics

Iezhitsa Igor

Associate Professor of Pharmacology

Universiti Teknologi MARA, Faculty of Medicine, Sungai Buloh, Malaysia

Title of Presentation: Meeting the Challenge of Glaucoma: Is Magnesium Acetyltaurate an Option to Consider?

Scientific Committee

Scientific Committee

Last Name	First Name	Last Name	First Name
Abdollahi	Mohammad	Mahmoudi	Mitra
Abedini	Mohammad Reza	Malekinejad	Hassan
Ahangarpour	Akram	Mesdaghinia	Azam
Ahmadi	Slahadin	Minaiyan	Mohsen
Ahmadi Asl	Nasser	Mirkhani	Hossein
Ahmadiani	Abolhassan	Mirnajafi-Zadeh	Javad
Akbari	Esmaeil	Mirzaii Dizgah	Iraj
Alaei	Hojatallah	Moallem	Seyed Adel
Alipour	Mohammad Reza	Moazedi	Ahmad Ali
Alipour	Mohsen	Moezi	Leila
Alizadeh	Alimohamad	Moghadamnia	Ali Akbar
Allahtavakoli	Mohammad	Mohaddes	Gisou
Arzi	Ardeshir	Mohammad Sharifi	Ali
Ashraf Pour	Manouchehr	Mohammad Zadeh	Mohammad
Azhdari Zarmehri	Hassan	Mohammadi	Jamshid
Azizi	Ebrahim	Mohammadi	Mostafa
Babaei	Hossein	Mohammadi	Jamshid
Babaei	Parvin	Mombeini	Tajemah
Babapour	Vahab	Motamedi	Fereshteh
Babri	Shirin	Mousavizadeh	Kazem
Badvi	Mohammad	Nabavizadeh	Fatemeh
Baharvand	Hossein	Naderi	Nima
Bahrami	Gholamreza	Naghdi	Naser
Baluchnejadmojarad	Tourandokht	Najafipour	Hamid
Banafshe	Hamid Reza	Najafzadehvarzi	Hossein
Baskabadi	Mohamad Hosein	Narenjkar	Jamshid
Bohlooli	Shahab	Naseri	Mohsen
Changizi- Ashtiyani	Saeed	Nasri	Sima
Cheraghali	Abdolmajid	Nassiri Asl	Marjan
Dargahi	Leila	Niknahad	Hossein
Dehghan	Gholam Abbas	Oryan	Shahrbanoo
Dehpour	Ahmad Reza	Ostad	Seyed Nasser
Delfan	Bahram	Palizvan	Mohammad Reza
Eghbal	Mohammad Ali	Panahpour	Hamdollah
Eidi	Akram	Panjeshahin	Mohammad Reza
Ejtemaei Mehr	Shahram	Pipelzadeh	Mohammad Hasan

Eliassi	Afsaneh	Pourahmad Jaktaji	Jalal
Emamghoreishi	Masoumeh	Pourkhalili	Khalil
Erfani	Hossein	Pourmotabbed	Ali
Esmaeili	Mohammad Hossein	Pourshanazari	Ali Asghar
Faghihi	Mahdiyeh	Rabbani	Mohammed
Fahanik-babaei	Javad	Rahmati	Batool
Faizi	Mehrdad	Rasekh	Hamid Reza
Farzin	Davood	Rashidypour	Ali
Fathi Moghaddam	Hadi	Rasoulian	Bahram
Fatholahi	Yaqob	Rastegar	Hossein
Foadoddini	Mohsen	Rezayat Sorkhabadi	Seyed Mahdi
Ghadiri Soufi	Farhad	Rezayof	Ameneh
Ghahremani	Mohammad Hossein	Rezvani	Mohammad Ebrahim
Gharib Naseri	Mohammad Kazem	Roghani	Mehrdad
Ghasemi	Asghar	Sabetkasaei	Masoumeh
Ghazi Khansari	Mahmoud	Saboory	Ehsan
Goudarzvand	Mahdi	Sabzevari	Omid
Habibi Asl	Bahlool	Sadeghi Mansourkhani	Hossein
haeri	Ali	Sadeghipour	Hamid Reza
Haghjooy Javanmard	Shaghayegh	Sadr	Seyed Shahabeddin
Haghparast	Abass	Sahraei	Hedayat
Hajhashemi	Valiollah	Salami Zavareh	Mahmoud
Hajzadeh	Mousa Reza	Salehi	Iraj
Hasanzadeh	Kambiz	Samarghandian	Saeid
Hassanpour Ezati	Majid	Sarihi	Abdolrahman
Hatam	Masoumeh	Sarkaki	Alireza
Heydari	Mahmood reza	Sattari Ghandforoush	Mohammad Reza
Hoseinzadeh	Hossein	Sayyah	Mohammed
Imen Shahidi	Mohsen	Semnanian	Saeed
Jafari	Mohammad Reza	Sepehri	Gholamreza
Jafari	Fariba	Sepehri	Hamid
Jamshidzadeh	Akram	Sepehri	Houri
Janahmadi	Mahyar	Shahidi	Siamak
Javan	Mohammad	Shamsizadeh	Ali
Jorjani	Masoumeh	Sharaki	Mohammad Reza
Kadkhodaei	Mehri	Shardi Manaheji	Homa
Kafashian	Mohamadreza	Sharifi	Reza
Kaidi	Ayat	Sharifzadeh	Mohammed
Kalantari	Heibatullah	Sheibani	Vahid
Karami	Mohammad	Shid-Moosavi	Mostafa
Karami	Manijeh	Shojaiefard	Manzar Banoo

Karimi	Gholamreza	Slotani Tehrani	Bahram
Karimian	Seyed Morteza	Sobhani	Abdolrasoul
Keshavarz	Mansoor	Soltani	Nepton
Keshavarzi	Zakiye	Tabaei	Soheila
Keyhanmanesh	Rana	Vaez Mahdavi	Mohammad Reza
Khaksari	Mehdi	Vafaei	Abbas Ali
Khaksari Haddad	Mohammad	Vahdati-Mashhadian	Naser
Khalili	Mohsen	Vakili	Abedin
Khameneh	Saeed	Varedi	Masoumeh
Khazaei	Majid	Vatanpour	Hossein
Kiasalari	Zahra	Yaghmaei	Parichehr
Komaki	Alireza	Yazdanpanah	Hassan
Komeili	Gholamreza	Zarifkar	Assadollah
Kouhpayeh	Seyed Amin	Zarrindast	Mohammad Reza
Maghsoudi	Maryam	Zeraati	Fatemeh

Executive Committee

کمیته اجرایی	
سمت	**نام و نام خانوادگی**
دبیر اجرایی	دکتر مهرداد روغنی
مدیر اجرایی	دکتر رضا محمدصالحی
کمیته دانشجویی	دکتر محمدرضا جلالی ندوشن
سمپوزیوم‌ها	دکتر محسن خلیلی
کارگاه‌های اقماری	دکتر مجید حسن‌پور عزتی
امور بین الملل	دکتر جواد میرنجفی‌زاده
بازآموزی	دکتر لطفعلی جباری
مسئول دبیرخانه الکترونیک	مریم قاسم پور
امور مالی	محمدرضا تفتیان
امور پشتیبانی	عبدالخالق همتی
فناوری اطلاعات	مهندس وحید حقیقت‌دوست
انتظامات و تشریفات	حامد اسدی
روابط عمومی و تبلیغات	سعید صادقی

همکاران اجرایی	
بهمن اسماعیلی	سمیه محب اسلامی
فریبا زند	سکینه محمودی
سید مجتبی حسینی	محمد ملک پور
اشرف درویش	منصور موگویی
معصومه روحانی	ولی نایبی
ناصر ریاحی	زیبا یزدانی
داود زاویه	
سیدامیر زعیم زاده	
حسین سالاری	
رضا شاکری	
محمدهادی شعاعی پی	
منصوره طوماری	
پژمان کریمی	
فاطمه کریمی جم	

کمیته بخش دانش آموزی	کمیته دانشجویی
Dr. Javad Fahanik Babaei	Dr. Javad Fahanik Babaei
Dr. Salmani	Vahid Khodashenas
Dr. Reza Bandali	Fatemeh Nabi
Mina Godarzi	Leila Nasiri
Dr. Ekram Mohamadi	Reyhaneh Ghasemi
Dr. Raheleh Gholamzadeh	Elham Smaeel Hamaat
Dr. Behnaz Rahimi	Amir Rostami
Vahid Khodashenas	Ashkan Sanaei
Dr. Freshteh Dalouchi	Elham Zahedi
	Mahdi Alizadeh
	Mohamad Hossein Akhbari
	Fatemeh Lak Zaee
	Mohamad Reza Khajevand Khazhei
	Fatemeh Tale Ahmad
	Sepideh Salari
	Marzieh Fakoor
	Amir Baratlou
	Maryam Nazarei
	Donya Nazarinia
	Mina Godarzi
	Mahsa Tashakorei
	Zahra Behrozei
	Negin Saeedi
	Somayeh Ahmadi
	Marjan Nikbakht Zadeh
	Arash Abdi
	Banafsheh Bagheri
	Faezeh Ghozatlo
	Samira Ahmadi

Scientific Program

A: Plenary Lecturers Schedule

First Day (Wednesday, 30 Oct 2019) Main Hall		
Speaker	**Title of Presentation**	**Presentation Time**
Fathollahi Yaghoub	3rd Millennium Science	11:45 - 12:30
Ahmadiani Abolhassan	Personalized Medicine, How and Why?	13:30 – 14:15
Zarrindast Mohammad Reza	Genetics and Addiction	14:15 – 15:00
Second Day (Thursday, 31 Oct 2019) Main Hall		
Speaker	**Title of Presentation**	**Presentation Time**
Igor Iezhitsa	Meeting the Challenge of Glaucoma: Is Magnesium Acetyltaurate an Option to Consider?	08:00 – 08:50
Dehpour Ahmad Reza	The Phytohormone Receptors	08:50 – 09:45
Ishikawa Yoshihiro	Heart Failure and More; From the Bed to the Benchtop	13:30 – 14:15
Anand Ashima	Promoting Research Integrity : a Matrix of Merits and Metrics	14:15 -15:00
Third Day (Friday, 1 Nov 2019) Main Hall		
Speaker	**Title of Presentation**	**Presentation Time**
Motamedi Fereshteh	Preconditioning and Neuroprotection	08:00 –08:50
Mohammad Hossein Pourgholami	Hypoxia-Inducible Factor	08:50- 09:45

B: Symposium Oral Presentation Schedule

First Day (Wednesday, 30 Oct 2019)			
Morning Session (8:00 – 9:45) Hall: 3			
Title of Panel: In Vitro Generation of Human Cardiac Muscle Cells by Cardiogenic Differentiation of Pluripotent Stem Cells and Their Biomedical Application Presidium: Sara Pahlavan, Sarah Rajabi, Mohammad Javan, Vahid Khori			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S083101-1	Comprehensive in vitro proarrhythmia assay (CiPA) using cardiomyocytes differentiated from pluripotent stem cells	Sara Pahlavan	08:00 - 08:30
S083101-2	Cardiac tissue engineering as a promising approach to advance mechanistic studies and drug screening	Sarah Rajabi	08:30 – 09:00
S083101-3	Generation of cardiac organoid for *in vitro* physiological and pharmacological studies	Fahimeh Varzideh	09:00 – 09:20
S083101-4	The path through bio-banking cardiac progenitor cells	Sadaf Vahdat	09:20 – 09:40

First day (Wednesday, 30 Oct 2019)			
Morning Session (8:00 – 9:45) Hall: 2			
Title of Panel: Challenges and Benefits of Mathematical Biology Presidium: Majid Hassanpour-Ezatti, Behrouz Raesi, Hamidreza Navidi, Abolfazl Tarri, Mohammad Sayyah			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S082102-1	Differential transform method for solving the model describing biological species living together	Abolfazl Tarri	08:00 - 08:25
S082102-2	Applications of comparative and non-comparative game models in bioinformatics	Hamidreza Navidi	08:25 – 08:50
S082102-3	Classification of Global Phase Portraits of Morris-Lecar Model for Spiking Neuron	Behrouz Raesi	08:50 – 09:15
S082102-4	Mathematical perspectives in the biology and medicine	Majid Hassanpour-Ezatti	09:15 – 09:40

First day (Wednesday, 30 Oct 2019)			
Morning Session (8:00 – 9:45) **Hall: 1**			
Title of Panel: The Role of Micrornas in the Central Nervous System Function Presidium: Ameneh Rezayof, Ehsan Arefian, Maryam Ghasemi-Kasman, Maryam Zahmatkesh			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S081103-1	Inhibitory role of microRNAs in glioblastoma	Ehsan Arefian	08:00 - 08:20
S081103-2	miRNAs in diagnosis and treatment of the Parkinson's disease	Azita Parvaneh Tafreshi	08:20 – 08:40
S081103-3	The role of microRNAs in reprogramming of somatic cells into neurons	Maryam Ghasemi-Kasman	08:40 – 09:00
S081103-4	The role of microRNAs in the future multiple sclerosis cell therapy	Fatemeh Kouhkan	09:00 – 09:20
S081103-5	MicroRNAs: Key Regulators in synaptic plasticity	Ameneh Rezayof	09:20 – 09:40

First day (Wednesday, 30 Oct 2019)			
Morning Session (8:00 – 9:45) **Hall: 4**			
Title of Panel: General Symposium Presidium: Leila Dargahi, Ali Reza Mohajjel Nayebi, Saeed Semnanian, Fatemeh Goshadrou			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S084104	Ustokhoddus and epilepsy in Iran	Batool Rahmati	08:00 -0 8:10
S084105	The therapeutic potential of interferon beta in Alzheimer's disease	Leila Dargahi	08:10 –0 8:20
S084106	Survey on the effects of diosmin on learning and memory following the use of paraquat herbicide poisoning in the animal model of rat	Ali Shahraki	08:20 –08:30
S084107	Environmental enrichment treatment restores spatial learning and memory deficits induced by prenatal noise stress	Sayyed Alireza Talaei	08:30 –08:40
S084108	Effect of silymarin on the tolerance to analgesic effects of morphine in mice with skin cancer	Ali Reza Mohajjel Nayebi	08:40 – 08:50
S084109	Role of Ghrelin in Alzheimer's disease: Metabolomics Studies based on 1H-NMR Technique in a rat model	Fatemeh Goshadrou	08:50 – 09:00
S084110	In vivo and in vitro evaluation of neuroprotective effect of Doxycycline through downregulation of activity and expression of NMDA/nitric oxide and CREB signaling pathway.	Faiza Mumtaz	09:00 – 09:10
S084111	Adolescent morphine exposure alters the neuronal responses of lateral paragigantocellularis nucleus to naloxone in adult morphine dependent rats	Sara Sabuee	09:10 – 09:20
S084112	Estradiol affects on microglia reactivity and functional recovery following central pain syndrome	Kobra Naseri	09:20 – 09:30
S084113	Auraptene mitigates migration, invasion and metastatic behavior of human malignant glioblastoma invitro	Amir Reza Afshari	09:30 – 09:40

First day (Wednesday, 30 Oct 2019)			
Morning Session (8:00 – 9:45) Hall: 5			
Title of Panel: General Symposium Presidium: Alireza Garjani, Hamid Najafipour, Mona Salimi, Hassan Malekinejad			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S085114	Interaction between hyperglycemia and autophagy in human umbilical vein endothelial cells	Alireza Garjani	08:00 - 08:10
S085115	Dose-dependent effects of long-term administration of hydrogen sulfide on myocardial ischemia-reperfusion injury in male Wistar rats	Sajad Jeddi	08:10 –08:20
S085116	The latest uncovered molecular pathways in the pathophysiology of atherosclerosis and therapeutic effects of Cynodon dactylon hydroalcoholic extract on experimentally-induced atherosclerosis in rats	Hassan Malekinejad	08:20 – 08:30
S085117	Gallic acid improves cardiovascular disorders by MicroRNA-24 and 126 and antioxidant effects in diabetes	Fatemeh Ramezani Aliakbari	08:30 –0 8:40
S085118	HTLV-1 infection affected lipid profile, CCR1, CCR2, CXCR2, eNOS, iNOS genes expression and oxidative stress in aorta of HTLV-1 infected BALB/c male mice	Mahdiyeh Hedayati Moghadam	08:40 –08:50
S085119	Cardioprotective Effect of Ethanolic Leaf Extract of Melissa Officinalis L Against Regional Ischemia-Induced Arrhythmia and Heart Injury after Five Days of Reperfusion in Rats	Afshin Nazari	08:50 –09:00
S085120	Exploration of saliva proteomics as a potent non-invasive and painless gateway to study neurological diseases	Arun Pratap Sikarwar	09:00 – 09:10
S085121	Pharmacological effects of targeted treatment of human metastatic breast cancer cells (SKBR3) through Docetaxel and cMET siRNA	Naime Majidi Zolbanin	09:10 – 09:20
S085122	Metformin enhances the sensitivity of multidrug resistant ovarian cancer cells to cisplatin	Vahid Shafiei-Irannejad	09:20 – 09:30
S085123	Gamma-Aminobutyric acid plus magnesium sulfate improves insulin sensitivity in type 2 diabetic rat model	Shahla Sohrabipour	09:30 – 09:40

First day (Wednesday, 30 Oct 2019)			
Morning Session (8:00 – 9:45) Hall: 6			
Title of Panel: General Symposium Presidium: Asghar Ghasemi, Tajemah Mombeini, Afsaneh Eliassi, Homeira Zardooz			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S086124	Evaluation of ischemia reperfusion-induced acute kidney injury by salivary assessment of renal function, apoptosis, oxidative stress and inflammation in male rats.	Arash Abdi	08:00 - 08:10
S086125	Crocin Ameliorates IL-18, p53 and Nox-4 Expression Levels and Prevent Diabetic Nephropathy	Habib Yaribeygi	08:10 – 08:20
S086126	Remote limb ischemic preconditioning accelerates recovery of renal function following ischemia-reperfusion injury: the possible role of lactate as a mediator	Zahra Akbari	08:20 – 08:30
S086127	Mas receptor antagonist (A799) alters the renal hemodynamics responses to angiotensin II administration after renal moderate ischemia/reperfusion in rats: gender related differences	Maryam Maleki	08:30 – 08:40
S086128	Evaluation of the protective effect of crocin on bleomycin-induced pulmonary fibrosis in rats	Alireza Malayeri	08:40 – 08:50
S086129	Expression level of endoplasmic reticulum stress genes in the lung tissue of obese male and female ovalbumin sensitized rats	Mohammad Reza Aslani	08:50 – 09:00
S086130	Inhibition of angiotensin II type I pathway ameliorate fibrosis and inflammation associated with colorectal cancer	Fereshteh Asgharzadeh	09:00 – 09:10
S086131	Molecular Evaluation of Doxorubicin and Quercetin on Apoptosis and Drug Resistance of HT29 Cancer Stem and non- Stem Cells	Shekufeh Atashpour	09:10 –0 9:20
S086132	Exercise training mitigates the heart dysfunction and lung inflammatory response induced by exposing to waterpipe tobacco smoke	Siyavash Joukar	09:20 – 09:30
S086133	The effect of rat cardiac extract with different ages on differentiation neonatal rat bone marrow mesenchymal stem cells into cardiomyocyte	Fatemeh Jamalzadeh	09:30 – 09:40

First day (Wednesday, 30 Oct 2019)			
Morning Session (8:00 – 9:45) **Hall: 7**			
Title of Panel: General Symposium Presidium: Mohammad Khaksari, Zahra Soltani, Hossein Azizi, Ali Rashidy-pour			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S087134	Lack of weight loss and reduced food intake of tamoxifen or estrogen in aging animals compared with young mice: Leptin sensitivity	Mohammad Khaksari	08:00 - 08:10
S087135	Effect of extraction of focus fig leaf on carbohydrate metabolism and insulin secretion from pancratic isolated islets in adult male diabetic rats	Hamid Farahani	08:10 – 08:20
S087136	Beneficial effects of tamoxifen on leptin sensitivity in young mice fed a high fat diet: Role of brain's neuropeptides and estrogen receptor α	ZeinabFarhadi	08:20 –08:30
S087137	High calorie diet induced insulin resistance and obesity upregulates the expression and secretion of Irisin peptide in adipose tissue of mice	Shokooh Salimi Moghadam	08:30 – 08:40
S087138	Clinical Pharmacology of Iranian Propolis on Type 2 Diabetes Mellitus: A Randomized Double-Blind Clinical Trial.	Ali Asghar Hemmati	08:40 –08:50
S087139	Exercise training improves angiogenesis through alterations in the expression levels of miR-503 and CDC25 in the heart tissue of diabetic rats	Gonja Javani	08:50 – 09:00
S087140	Progesterone Eliminates Estrogen-Mediated Cardioprotection Against Diabetic Cardiomyopathy in Ovariectomized Rats	Hossein Azizian	09:00 – 09:10
S087141	Oleopein protect myocardium in type 2 diabetic rats: role of inflammatory cytokines	Mohammad Shahbazian	09:10 – 09:20
S087142	The comparison of antioxidant effect of aspirin, metformin, atorvastatin and captopril co-administration in the heart and kidney tissues of diabetic rats	Maryam Paseban	09:20 –09:30
S087143	Magnesium pathway on decreasing of blood glucose and insulin resistance in type 1 and two diabetes in different kinds of animal models and type 2 and non-insulin resistance patients	Nepton Soltani	09:30 – 09:40

First day (Wednesday, 30 Oct 2019)			
Afternoon Session (16:00 – 17:45) **Hall: 3**			
Title of Panel: Nitric Oxide Donors and Type 2 Diabetes: Translation from Basic Science to Clinical Implications Presidium: Asghar Ghasemi, Batool Rahmati, Azhdar Heydari, Esmaeil Akbari			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S083144-1	The role of nitric oxide in pathophysiology of type 2 diabetes	Asghar Ghasemi	16:00-16:20
S083144-2	Potential targets of nitric oxide system for therapeutic interventions in type 2 diabetes	Azhdar Heydari	16:20–16:40
S083144-3	Beneficial effects of nitrate and nitrite in type 2 diabetes: A nutritional perspective	Zahra Bahadoran	16:40–17:00
S083144-4	Nitric oxide donors: New generation of anti-diabetic drugs**?**	Hamid Reza Banafshe	17:00–17:20
		Common Debate	17:20–17:40

First day (Wednesday, 30 Oct 2019)			
Afternoon Session (16:00 – 17:45) **Hall: 6**			
Title of Panel: Cardioprotection against Ischemia-Reperfusion Injury: Translation from The Experimental Setting to the Clinical Arena Presidium: Reza Badalzadeh, Abedin Vakili, Hamid Soraya, Mohammad Hossein Boskabady			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S086145-1	Pathophysiology of myocardial ischemia-reperfusion injury	Mansour Esmailidehaj	16:00-16:20
S086145-2	Cardioprotection: protective conditionings and interaction of cardiovascular co-morbidities and risk factors with conditioning interventions	Khalil Pourkhalili	16:20–16:40
S086145-3	Cardioprotection: new therapeutic targets and mediators	Hamid Soraya	16:40–17:00
S086145-4	Combination therapies, multi-targeted therapeutic approaches and practical guidelines for preclinical and clinical studies	Reza Badalzadeh	17:00–17:20
		Common Debate	17:20–17:40

First day (Wednesday, 30 Oct 2019)			
Afternoon Session (16:00 – 17:45) Hall: 1			
Title of Panel: Current Perspective of Ocular Pharmacology: Focus on Glaucoma and Retinopathy Presidium: Igor Iezhitsa, Javad Mirnajafi-zadeh, Norhafiza Razali, Ali Khoshbaten			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S081146-1	The Role of Inhibitors of the Renin-Angiotensin System in the Attenuation of Dexamethasone-induced Remodeling in the Trabecular Meshwork	Anna Krasilnikova	16:00-16:20
S081146-2	The discovery of a novel series of benzimidazoles as a new prospective class of ocular hypotensive agents	Igor Iezhitsa	16:20–16:40
S081146-3	Protective effect of palm oil tocotrienol-rich fraction against experimental model of diabetic retinopathy.	Nurul Alimah Abdul Nasir	16:40–17:00
S081146-4	Mechanisms of regulation of aqueous humour dynamics by trans-resveratrol in steroid-induced oculohypertensive rat model.	Norhafiza Razali	17:00–17:20
S081146-5	Correction of experimental retinal ischemia by L-isomer of ethylmethylhydroxypyridine malate	Anna Peresypkina	17:20–17:40

First day (Wednesday, 30 Oct 2019)			
Afternoon Session (16:00 – 17:45) Hall: 2			
Title of Panel: Computational Thinking and Education Presidium: Mohammad Reza Raoufy, Alireza Asgary, Hamid Gholamipour, Mahyar Janahmadi			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S082147-1	Convergence of knowledge, technology and society	Yaghoub Fathollahi	16:00-16:25
S082147-2	Computational physiology in other countries	Alireza Asgary	16:25–16:50
S082147-3	The application of computational physiology to bedside	Abdol-Hossein Vahabie	16:50–17:15
		Common Debate	17:15–17:40

First day (Wednesday, 30 Oct 2019)			
Afternoon Session (16:00 – 17:45) Hall: 5			
Title of Panel: Particulate Matter and Health Presidium: Mahin Dianat, Alireza Sarkaki, Mohammad Badavai, Mohammad Reza Shahraki			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S085148-1	The Association of Ambient Particulate Matter with Cardiovascular Dysfunction: A Focus on Natural Antioxidants	Mahin Dianat	16:00-16:20
S085148-2	Spatial memory and brain hippocampus electrical activity impair following prolonged exposure to ambient dust storm in rats	Alireza Sarkaki	16:20–16:45
S085148-3	How Does Ambient Particulate Matter Air Pollution Affect the Respiratory System? In Vivo and in Vitro Evidence	Maryam Radan	16:45–17:05
S085148-4	Effects of Gallic acid on behavioral and electrophysiological alterations induced by cerebral ischemia/reperfusion followed by exposure to ambient dust storm in rats	Kosar Bavarsad	17:05–17:25
S085148-5	Evaluation of the preventive effects of Gallic acid on blood brain barrier function and oxidative stress of brain caused by cerebral ischemia/ reperfusion following exposure to amient particulate matter in rats	Hamzeh Mirshekari Jahangiri	17:25–17:40

First day (Wednesday, 30 Oct 2019)			
Afternoon Session (16:00 – 17:45) Hall: 4			
Title of Panel: Stem Cells and Regenerative Medicine Presidium: Ali Mohammad Sharifi, Nahid Abootaleb, Abolhassan Ahmadiani, Hossein Baharvand			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S084149-1	Role of " Pharmacological conditioning" in regenerative medicine	Ali Mohammad Sharifi	16:00-16:20
S084149-2	The Amniotic Membrane Mesenchymal Stem Cell Derived Conditioned Medium Exerts Neuroprotection Against Cerebral Ischemia	Nahid Abootaleb	16:20–16:40
S084149-3	Restoring the IL-1β/NF-κB-induced impaired chondrogenesis by using di allyl disulfide	Kobra Bahrampour	16:40–17:00
S084149-4	In vivo reprogramming as a new avnue to regenerative therapies in neurodegenerative diseases	Mohammad Javan	17:00–17:20
S084149-5	Applications of microfluidics in regenerative pharmacology	Mohammad Adel Ghiass	17:20–17:40

First day (Wednesday, 30 Oct 2019)

Afternoon Session (16:00 – 17:40) Hall: 7			
Title of Panel: Student Symposium Presidium:			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S087150	Mirror neuron functions, mechanisms and model	Pouria Bandali	16:00-16:10
S087150	Detecting Human Emotions Using Electroencephalography(EEG) using Dynamic Programming Approach	Soheil Bandali	16:10–16:20
S087150	AIDS	Avin Samadi	16:20–16:30
S087150	A study on relationship between blood group and personality	Skekoofa Rouzbeh	16:00–16:40
S087150	An Interface for IoT: Feeding Back Health-Related Data to Parkinson's Disease Patients	Saba Sabohi	16:40–16:50
S087150	A study on relationship between blood group and personality	Bahare Salajegheh	16:50–17:00
S087150	A study on relationship between blood group and personality	Parvin Jandaghi	17:00–17:10
S087150	Is early and fast blood pressure control important in hypertension management?	Raha Rezaee	17:10–17:20
		Common Debate	

Second day (Thursday, 31 Oct 2019)			
Morning Session (10:45 – 12:30) Hall: 1			
Title of Panel: Future of Physiology and Pharmacology in the Artificial Inteligent Age Presidium: Masoumeh Jorjani, Seyed Ali Ziai, Mir Shahram Safari, Majid Nili Ahmadabadi			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S091151-1	Impact of Artificial Inteligent on Physiology and Pharmacology	Masoumeh Jorjani	10:45-11:05
S091151-2	Pharmacogenomics and personalized medicine	Seyed Ali Ziai	11:05–11:25
S091151-3	Translational pharmacology: it is time to shift the paradigm	Hassan Niknejad	11:25–11:45
S091151-4	Virtual neurophysiology	Mir Shahram Safari	11:45–12:05
S091151-5	Microfluidics & microfabrication in self-organization of hepatocyte morphogenesis	Mohammad Ajodanian	12:05–12:25

Second day (Thursday, 31 Oct 2019)			
Morning Session (10:45 – 12:30) Hall: 2			
Title of Panel: Traumatic Brain Injury: Therapeutic Strategies Based on Neurological, Electrophysiological and Immunological Findings Presidium: Mohammad Sayyah, Narges Hosseinmardi, Fereshteh Motamedi, Mohammadreza Palizvan			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S092152-1	Electrophysiological basis of neural epileptiform activity after traumatic brain injury	Mahyar Janahmadi	10:45-11:00
S092152-2	Role of glia in traumatic brain injury-induced electrophysiological and behavioral deficits	Narges Hosseinmardi	11:00–11:15
S092152-3	The neuroprotective effects of erythropoietin on the neurological scores, brain edema and blood brain barrier permeability after severe traumatic brain injury in male rats: the role of AMPK	Ali Siahposht-Khachaki	11:15–11:30
S092152-4	Investigating the effect of oral mucosa mesenchymal stem cells treatment on brain edema and behavioral and cognitive outcome caused by experimental traumatic brain injury	Zahra Soltani	11:30–11:45
S092152-5	Adjuvant therapy in prevention of post-traumatic epilepsy	Mohammad Sayyah	11:45–12:00
		Common debate	12:00–12:25

Second day (Thursday, 31 Oct 2019)			
Morning Session (10:45 – 12:30) Hall: 3			
Title of Panel: Deep Brain Stimulation and Brain Disorders Presidium: Javad Mirnajafi-Zadeh, Mohammad Mohammad-Zadeh, Mohammad Rostampour, Esmail Riahi			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S093153-1	Deep brain stimulation in movement disorders	Mohammad Rohani	10:45-11:10
S093153-2	Deep brain stimulation as a promising intervention for treatment- refractory obsessive-compulsive disorder	Mohammad Ghadirivasfi	11:10–11:35
S093153-3	Deep brain stimulation of the orbitofrontal cortex prevents relapse to morphine seeking	Esmaeil Riahi	11:35–12:00
S093153-4	Effect of deep brain stimulation on seizure and synaptic transmission	Javad Mirnajafi-Zadeh	12:00–12:25

Second day (Thursday, 31 Oct 2019)

Morning Session (10:45 – 12:30) Hall: 4			
Title of Panel: Brain Reward Pathways and Interaction with other Neuronal Systems Presidium: Abdolrahman Sarihi, Reza Arezoomandan, Hojatallah Alaei, Hedayat Sahraei			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S094154-1	Stress and addiction: biological mechanisms	Abdolrahman Sarihi	10:45-11:05
S094154-2	A modulatory/regulatory role(s) for oxytocin in rewarding circuits; focus on dopaminergic activities in striatum and amygdala	Amir-Hossein Bayat	11:05–11:25
S094154-3	Evaluation of the Effect of Sex reward and Sexual Deprivation on Morphine Acquisition, Extinction, and Reinstatement	Reza Arezoomandan	11:25–11:45
S094154-4	Measurement of the c-fos Protein Level and pCREB/CREB Ratio in the Ventral Tegmental Area in the Reinstatement Phase of Morphine-induced Conditioned Place Preference Confirmed the Modulatory Role of the Nucleus Accumbens CB1 Receptor	Hossein Khaleghzadeh-Ahangar	11:45–12:05
S094154-5	Limbic Structures and Fear Memory Extinction: A decade of study	Abbas Ali Vafaei	12:05–12:25

Second day (Thursday, 31 Oct 2019)			
Morning Session (10:45 – 12:30) Hall: 5			
Title of Panel: Pharmacoepigenetics Presidium: Seyed Ali Ziai, Davood Farzin, Nima Naderi, Gholamreza Sepehri			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S095155-1	The role of pharmacoepigenetics in personalized therapy: promises and opportunities	Zahra Fazeli Attar	10:45–11:15
S095155-2	Treatment response prediction in obsessive-compulsive disorder: The application of data minig methods	Sare Asadi	11:15–11:45
S095155-3	Role of pharmacogenetics on drug metabolism	Zeynab Cheraghi	11:45–12:15
S095155-4	Implementation of nextgeneration sequencing testing in a clinical pharmacogenmic	Sayyed Mohammad Hossein Ghaderian	12:15–12:30

Second day (Thursday, 31 Oct 2019)			
Morning Session (10:45 – 12:30) Hall: 6			
Title of Panel: Generan Symposium Presidium: Mahmoud Ghazykhansari, Mehri Kadkhodaei, Seyed Morteza Karimian, Gisou Mohaddes			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**

S096156	Traumatic brain injury causes behavioral deficits accompanied by synaptic plasticity changes in rat	Seyed Asaad Karimi	10:45-10:55
S096157	Effect of neck dry cupping on thyroid factors in patients with hypothyroidism	Sheida Kolahi Jahromi	10:55–11:05
S096158	The effect of Allium jesdianum hydroalcoholic extract on sleeping time and the level of anxiety in mice	Fatemeh Mahan	11:05–11:15
S096159	Analysis of Biochemical Parameters in Animals under Radiation Emitted from Wi-Fi and Jammer	ManzarBanoo Shojaeifard	11:15–11:25
S096160	Flaxseed Oil Supplementation Improve Gene Expression Levels of PPAR γ, LP(a), IL 1 and TNF α in Type 2 Diabetic Patients with Coronary Heart Disease	Elmira Akbari	11:25–11:35
S096161	Metformin via activation of AMPK inhibits inorganic polyphosphate-induced inflammation in local, systemic short- and long-term mice models	Maryam Fakhraei	11:35–11:45
S096162	Comparison the effect of propofol and isoflurane on hemodynamic parameters and stress response hormones during Laparoscopic Cholecystectomy surgery	Nima Bakhtiari	11:45–11:55
S096163	The effect of acute Taxus Baccata on electrocardiogram activity in the rat	Yousef Panahi	11:55-12:05
S096164	Cytotoxicity evaluation of novel acetophenonic isoxazolin derivatives on MCF7 and HT29 cancerous cell lines	Hoda Abolhasani	12:05-12:15
S096165	Xanthomicrol retards tumor growth and progression in a mouse melanoma (B16F10) allograft model	Foad Ghazizadeh	12:15-12:25

Second day (Thursday, 31 Oct 2019)

Morning Session (10:45 – 12:30) Hall: 7

Title of Panel: Graduate Student Symposium

Presidium:

Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S097166	Pharmacopia products from animal	Fahanik Babaei Javad	10:45-10:55
S097166	Gut microbiota and neurodegenarative diseases	Negin Saeedi	10:55–11:05
S097166	Interactions between gastrointestinal microbiota and probiotics in the treatment of epileps	Fatemeh Zarei	11:05–11:15
S097166	Lead, intoxication, risks, prevention, diagnosis and treatment	Abdollah Abdollahpour	11:15–11:25
S097166	Human Hunger For S pace Exploration, but How About Human Biology In Space?	Arun Pratap Sikarwar	11:25–11:35
S097166	Effect of colors on body physiology, diseases, cognitive, learning and memory	Raheleh Gholamzadeh	11:35–11:45
S097166	Prospect of mesenchymal Stem Cell Conditioned Medium in Regenerative Medicine: is a new hope for treatment of stroke?	Donya Nazari Nia	11:45–11:55
		Common debate	

Second day (Thursday, 31 Oct 2019)

Afternoon Session (16:00 – 17:45) Hall: 1

Title of Panel: The Place of Social Justice in Biopsychosocial Processes Leading to Health and Behavior

Presidium: Mohammad Reza Vaez-Mahdavi, Somayyeh Heisiat-talab, Firouz Ghaderi, Mohammad Taher Moazedi

Presentaion Code	Title	Speaker	Presentation Time
S091167-1	Bayesian brain (updating of past experiences)	Mohammad Reza Vaez-Mahdavi	16:00-16:20
S091167-2	Early life stress effects on addictive behavior is related to changes in Opioid receptors in rat brain	Nayere Askari	16:20–16:35
S091167-3	Evaluation and Comparison of Effects of Different Types of Social Stress on Immune Response Regulation	Tooba Ghazanfari	16:35–16:50
S091167-4	Social Inequality May Affect on Animal Health; an Experimental Study	Fatemeh Heidari	16:50–17:05
S091167-5	Effect of melatonin treatment on epididymal sperm parameters, testis structure, apoptosis and oxidative stress after inequality in rats	Shiva Nasiraei Moghadam	17:05–17:20
S091167-6	Food Intake Inequality, Deprivation, and Intermittent Fasting Effect on Oxidative Balance of the Brain and Liver, and Anxiety Behavior	Saeedeh Rezaei	17:20–17:40

Second day (Thursday, 31 Oct 2019)

Afternoon Session (16:00 – 17:45) Hall: 3

Title of Panel: Cardiac Symposium
Presidium: Ali Khoshbaten, Ashima Anand, Mahin Dianat, Mahnaz Kessmati

Presentaion Code	Title	Speaker	Presentation Time
S093168-1	Heart failure and more: from the bed to the benchtop	Yoshihiro Ishikawa	16:00-16:20
S093168-2	Congential Cardiac disease: Factors Underlying exercise limitation and dyspnea	Ashima Anand	16:20–16:40
S093168-3	Lavender oil and probiotics protect heart against injury in myocardial infarction induced by Isoprenaline in rats: a hemodynamic, biochemical, and histopathological evaluation	Abedin Vakili	16:40–17:00
S093168-4	Oxytocin and Cardioprotection	Ali Mohammad Alizadeh	17:00–17:20
S093168-5	The effect of high intensity interval training on cardioprotection against ischemia-reperfusion injury	Ali Khoshbaten	17:20–17:40

Second day (Thursday, 31 Oct 2019)

Afternoon Session (16:00 – 17:45) Hall: 4

Title of Panel: From Persian Medicine Manuscript to New Physiological and Pharmacological Evidence
Presidium: Mohsen Naseri, Elham Emaratkar, Seyyed Ali Mozaffarpur, Mohammadreza Esmaeili Dooki

Presentaion Code	Title	Speaker	Presentation Time
S094169-1	From traditional medicine manuscript to the prevention of relapse in opioid-dependent patients	Mohsen Naseri	16:00-16:20
S094169-2	Report on activity and researches were performed in the department of Traditional Medicine, Shahed University based on breastfeeding as personalized medicine in Iranian Traditional Medicine	Elham Emaratkar	
S094169-3	Report on activity and researches were conducted in school of Traditional Medicine, Iran University of Medical Sciences based on recommended foods and remedies in Iranian traditional medicine for the treatment of different diseases	Amir Hossein Jamshidi	16:20–16:40
S094169-4	Report on activity and researches were performed in a school of Traditional Medicine, Shahid Beheshti University of Medical Sciences based on pulmonary phlegm and its association with mucus from the perspective of Iranian traditional medicine and its laboratory evidence	Rasool Choopani	16:40–17:00
S094169-5	Clinical trials for controlling cancer complications based on principles of Persian medicine	Ghazaleh Heidari Rad	
S094169-6	Evaluation of Effects of Food Products Based on Traditional Persian Medicine on Hemorheology in Polycythemia	Mahdi Yousefi	17:00–17:20
S094169-7	The Effect of Citrullus on Neuronal Conduction Velocity, Memory and Thyroid Function in Rats	Mousa Reza Hajzadeh	
S094169-8	Cassia fistula emulsion comparing with mineral oil on pediatric functional constipation	Mohammadreza Esmaeili Dooki	
S094169-9	Report on activity and researches were performed in the school of Traditional Medicine, Babol University of Medical Sciences based on standardizing personalized viewpoint of Persian Medicine (Mizaj) and some RCTs on Herbal drugs	Seyyed Ali Mozaffarpur	

Second day (Thursday, 31 Oct 2019)

Afternoon Session (16:00 – 17:45) Hall: 5			
Title of Panel: Convergence in New Sciences and Technologies (NBICS) Presidium: Moslem Bahadori, Seyed Mahdi Rezayat, Soheila Fazli Tabaei, Abbas Haghparast			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S095170-1	Perspective and Strategic plan of convergence in Medical Sciences	Seyed Mahdi Rezayat	16:00-16:20
S095170-2	Structures of science convergence in Medical Sciences Universities	Soheila Fazli Tabaei	16:20–16:40
S095170-3	Fourth industrial revolution and Medical Sciences	Alireza Hamzehei	16:40–17:00
S095170-4	The Role of Converging Technologies in Promoting Health and Human Empowerment	Ashkan Zolriasatein	17:00–17:20
		Common Debate	17:20–17:40

Second day (Thursday, 31 Oct 2019)			
Afternoon Session (16:00 – 17:45) Hall: 6			
Title of Panel: Advanced Technologies in Neurophysiology Presidium: Mohammad Ismail Zibaii, Amir-Mohammad Alizadeh, Abbas Haghparast, Hamid Latifi			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S096171-1	Fiber optic probe and nanomaterial mediated Optogenetics: Current and Future opportunities	Mohammad Ismail Zibaii	16:00-16:20
S096171-2	Use of Neuroimaging Techniques in Neuroscience	Reza Khosrowabadi	16:20–16:40
S096171-3	Multi-electrode array systems; costs and benefits for Iranian researchers	Amir-Mohammad Alizadeh	16:40–17:00
S096171-4	Applications of in vivo whole cell patch-clamp in neurophysiology	Mir-Shahram Safari	17:00–17:20
S096171-5	Virtual Reality In Neuroscience: Applications and Future	Mohammad Reza Abolghasemi	17:20–17:40

Second day (Thursday, 31 Oct 2019)

Afternoon Session (16:00 – 17:45) Hall: 7			
Title of Panel: Physical Activity, Enriched Environment and their Effects on Brain Functions in Normal and Pathological Conditions Presidium: Ali Rashidy-Pour, Alireza Komaki, Gholam ali Hamidi, Naser Naghdi			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S097172	Physical activity and brain plasticity and functions	Ali Rashidy-Pour	16:00-16:20
S097172	Environmental enrichment and Addiction-related behavior disorders	Hossein Miladi-Gorji	16:20–16:40
S097172	Role of Endocannabinoid system in the antidepressant and anxiolytic effects of exercise	Ali Ahmadalipour	16:40–17:00
S097172	Neurodegenerative diseases and oxidative stress: Physical exercise as a preventive or disease-modifying treatment	Iraj Salehi	17:00–17:20
S097172	Therapeutic Effects of Exercise against PTSD	Sakineh Shafia	17:20–17:40

Second day (Thursday, 31 Oct 2019)			
Afternoon Session (16:00 – 17:45) Hall: 2			
Title of Panel: Therapeutic Art Presidium: Naser Naghdi, Reza Dehqani, Shadmehr Rastin, Abdolrahman Najl Rahim			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S092173-1	Art-Health Relation Methodology	Reza Dehqani	16:00-16:25
S092173-2	Cinema and Movie Therapy	Shadmehr Rastin	16:25–16:50
S092173-3	The Impact of Teaching Acting on Amateur Actors and its Relation with Behavioral Therapy	Amir Sharifi	16:50–17:15
S092173-4	Revealing the Hidden World of the Brain; Note and Music	Abdolrahman Najl Rahim	17:15–17:40

Third day (Friday, 1 Nov 2019)			
Morning Session (10:45 – 12:30) **Hall: 2**			
Title of Panel: Orexinergic System and Brain Cognitive Functions Presidium: Mahmoud Elahdadi Salmani, Saeed Semnanian, Tajemah Mombeini, Ameneh Rezayof			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S102174-1	Orexin-mediated modulation of opioid dependence	Saeed Semnanian	10:45–11:10
S102174-2	Brain Orexinergic System and Reward-related Behaviors	Abbas Haghparast	11:10–11:35
S102174-3	Brain Orexinergic system and stress pathophysiology	Mahmoud Elahdadi Salmani	11:35-12:00
S102174-4	The Orexinergic (Hypocretin) System and Nociception: An Update to Supraspinal Mechanisms	Hassan Azhdari Zarmehri	12:00-12:25

Third day (Friday, 1 Nov 2019)			
Morning Session (10:45 – 12:30) **Hall: 5**			
Title of Panel: Kidney, from Physiology to Clinic Presidium: Seyed Mostafa Shid Moosavi, Mehdi Nematbakhsh, Behjat Seifi, Mehri Kadkhodaei			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S105175-1	Comparison of ischemic acute kidney injury induced by clamping renal arteries, veins, or pedicles	Seyed Mostafa Shid Moosavi	10:45–11:05
S105175-2	Angiotensin 1-7 and Renal Circulation	Mehdi Nematbakhsh	11:05–11:25
S105175-3	Regenerative medicine and stem cell in kidney: A novel approach	Abolfazl Khajavi Rad	11:25-11:45
S105175-4	Interrelationship between multiple gasotransmitter systems in acute and chronic renal injuries	Behjat Seifi	11:45-12:05
S105175-5	Therapeutic Effect of Adipose-derived Mesenchymal Stem Cells on Renal Function and Histopathology in Ischemia-Reperfusion Acute Kidney Injury	Saeed Changizi Ashtiyani	12:05-12:25

Third day (Friday, 1 Nov 2019)			
Morning Session (10:45 – 12:30) **Hall: 4**			
Title of Panel: Hypertension; Systemic and Pulmonary: Role of Oxidative Stress Presidium: Hamid Najafipour, Mohammad Badavi, Siyavash Joukar, Masoud Haghani			
Presentaion Code	**Title**	**Speaker**	**Presentation Time**
S104176-1	Vascular oxidative stress: the link between diabetes and cardiovascular diseases	Mohammad Badavi	10:45–11:05

S104176-2	Apelin and blood pressure: role of oxidative stress	Yaser Azizi	11:05–11:25
S104176-3	Aging and hypertension: role of oxidative stress	Nasser Ahmadiasl	11:25-11:45
S104176-4	Pulmonary arterial hypertension and role of oxidative stress	Hamid Najafipour	11:45-12:05
S104176-5	Effect of acute hypertension induced by aortic constriction on the brain and heart infarction: role of oxidative stress	Mohammad Taghi Mohammadi	12:05-12:25

Third day (Friday, 1 Nov 2019)

Morning Session (10:45 – 12:30) **Hall: 6**

Title of Panel: Physiology of Gastrointestinal System
Presidium: Fatemeh Nabavizadeh, Parvin Zareian, Gholamreza Komeili, Aminollah Bahaoddini

Presentaion Code	Title	Speaker	Presentation Time
S106177-1	Effect of hydrogen sulfide on the induction and treatment of diabetic enteropathy	Seyed Ali Mard	10:45–11:10
S106177-2	Protective effects of isoflavones against non-alcoholic fatty liver disease: mechanism of action	Mohammad Reza Alipour	11:10–11:35
S106177-3	Influence of Sleep Deprivation on the 24-Hour Ghrelin Secre tion Pattern	Parvin Zareian	11:35-12:00
S106177-4	Targeted drug delivery of capecitabine to mice xenograft gastric cancer by PAMAM dendrimer nanocarrier	Fatemeh Nabavizadeh	12:00-12:25

Third day (Friday, 1 Nov 2019)

Morning Session (10:45 – 12:30) **Hall: 7**

Title of Panel: Lipid, Lipoprotein in Atherosclerosis
Presidium: Behshid Ghadrdoost, Abbas Pousti, Yaser Azizi, Javad Fahanik-Babaei

Presentaion Code	Title	Speaker	Presentation Time
S107178-1	Lipids and lipoprotein metabolism -recent progress	Behshid Ghadrdoost	10:45–11:10
S107178-2	Cholesterol efflux and reverse cholesterol Transport	Yaser Azizi	11:10–11:35
S107178-3	Dynamic Macrophages: Mechanisms of Activation in Atherosclerotic Vascular Disease.	Kamran Rakhshan	11:35-12:00
S107178-4	Novel risk markers - what do they tell us?	Sedigheh Saedi	12:00-12:25

Third day (Friday, 1 Nov 2019)

Morning Session (10:45 – 12:30) **Hall: 3**

Title of Panel: General Symposium
Presidium: Mahin Ganjkhani, Manijeh Motevalian, Mohammad Rostampour, Vahid Sheibani

Presentaion Code	Title	Speaker	Presentation Time
S103179	Effects of Melatonin on Calcium Action Potential of Helix aspersa Neurons in a Pentylenetetrazol Induced Epileptic Model: Experimental and Theoretical Studies	Mahin Ganjkhani	10:45–10:55
S103180	Role of vitamin D3 in memory improvement and nitric oxide level in demyelinated hippocampus of rat	Mahdi Goudarzvand	10:55–11:05
S103181	The Role of Glial Cells in Spatial Working Memory Deficits in a Rat Model of Traumatic Brain Injury (TBI)	Amir Rezagholizadeh	11:05-11:15
S103182	The role of hippocampal glial glutamate transporter (GLT-1) on synaptic dysfunction in morphine dependent rats.	Negin Saeedi	11:15-11:25
S103183	Intra-BLA administration of L-arginine and L-NAME dose not reduce the acquisition of nicotine-induced place preference in the rats	Hedayat Sahraei	11:25-11:35
S103184	The effect of ghrelin on the MK801- induced memory impairment	Mohammad Rostampour	11:35- 11:45
S103185	The role of 5-HT1A receptors and neuronal nitric oxide synthase on the neuronogenesis of dentate gyrus in seizure- induced kindling model in rat	Mohammad MohammadZadeh	11:45- 11:55
S103186	The interplay between angiotensin II and vasopressin receptors in parvocellular portion of the paraventricular nucleus of hypothalamus on the cardiovascular response: effects on hypovolemia hypotension	Masoumeh Hatam	11:55- 12:05
S103187	Molecular, histological and behavioral evidences for neuroprotective effects of minocycline against nicotine-induced neurodegeneration and cognition impairment: possible role of CREB-BDNF signaling pathway	Manijeh Motevalian	12:05- 12:15
S103188	Is there any relevance between serum heavy metals concentration and BBB leakage in Multiple sclerosis patients?	Mehdi Aliomrani	12:15- 12:25

C: Poster Presentation Schedule

First Day (Wednesday, 30 Oct 2019)			
Morning Session (9:45 – 10:45)			
Neurosiences, Regenerative Medicine, Clinical Physiology			
Poster presentation board code	**Abstract title**	**Presenter**	**Specific theme**

P-101	The role of dopamine D2-like receptors on the inhibitory effects of low frequency electrical stimulation in perforant path kindling in rat	Mahmoud Rezaei	Neurosiences
P-102	Sanguinarine reverses cisplatin resistance in multidrug resistant ovarian cancer cells	Morteza Molaparast	Biomedicine
P-103	Effect of oxytocin on brain edema and aquaporin-4 in an experimental model of stroke	Azam Abareshi	Neurosiences
P-104	The role of mGluR4 receptors within the nucleus accumbens in the expression of morphine-induced conditioned place preference in male rat	Zahra Ebrahimi Farzad	Neurosiences
P-105	Betulinic acid attenuated motor, cognitive and globus pallidus electrical power deficits in animal model of Parkinson's disease.	Maryam Abrishamdar	Neurosiences
P-106	Effect of Cerebrolysin on the structural change of the bladder wall and spinal cord in the animal model of spinal cord injury	Nasrin Abolhasanpour	Neurosiences
P-107	Blockade of Glutamate Receptors within the Prelimbic Cortex Attenuate Concentration of Excitatory Amino Acids in the Morphine Self-administration in Rats	Fateme Aboutalebi	Neurosiences
P-108	Possible interaction of the Nucleus accumbens shell endocannabinoid system and GABA (A) system on locomotor activity in Male rats.	Hatam Ahmadi	Neurosiences
P-109	effects of vanillic acid on learning and memory in male rats with Alzheimer's disease induced by β-amyloid	Nesa Ahmadi	Neurosiences
P-110	Increases in the expression of MIAT1 and BC1 lncRNAs in rat hypothalamus are related to the gene expression of inflammatory cytokines and their receptors in morphine-tolerant rats	Shamseddin Ahmadi	Neurosiences
P-111	Low-frequency electrical stimulation reduces the impairment in synaptic plasticity following epileptiform activity in rat hippocampal slices through α1, but not α2 adrenergic receptors	Nooshin Ahmadirad	Neurosiences
P-112	Possible Involvement of Opioidergic Mechanisms and L-arginine/NO/cGMP/KATP channel pathway in Antinociceptive Effects of Cnicus benedictus L. and cnicin in Male Rat	Davoud Ahmadimoghaddam	Neurosiences
P-113	Investigating the activity of the pyramidal neurons of the CA1 area following the administration of lovastatin in male intact rat	Azade Eskandary	Neurosiences
P-114	The effect of Lipopolysaccharide (LPS) pretreatment on hippocampal apoptosis in traumatic rats	Mansoureh Eslami	Neurosiences
P-115	Diabetic encephalopathy affects mitochondria and axonal transport proteins	Maryam Eslami Gharaati	Neurosiences
P-116	The effect of nanocurcumin on the threshold of clonic seizures induced by intravenous penthylenetetrazol	Zahra Esmaili	Neurosiences
P-117	Study of the effect of intracerebroventricular injection of kaempferol and its intraction with type B GABA recrptor on pain in male rat	Maryam Esmaeili Salem	Neurosiences
P-118	Protective Role Of Luteolin Against Memory Impairment Induced By Traumatic Brain Injury(TBI) In The Male Rats	Zeinab Ashaari	Neurosiences
P-119	Ischemic post-conditioning improved neuronal cytoskeletal markers against ischemic brain injury in the hippocampus of young adult but not aged rats	Ghorbangol Ashabi	Neurosiences
P-120	The effect of isoflavones on epilepsy disorder in ovariectomized rats	Nastaran Afsordeh	Neurosiences

P-121	Preventive effects of Brassica nigra against the memory deterioration in the kindled male wistar rats	Fatemeh Aghaie	Neurosciences
P-122	Investigation of the Antioxidant Activity of Curcumin against b-amyloid Induced Cell Damage in SH-SY5Y Cells	Leila Elyasi	Neurosciences
P-123	Effect of ceftriaxone on synaptic plasticity of hippocampal dentate gyrus neurons in OKA-induced model of Alzheimer disease in rats	Mohammad Amani	Neurosciences
P-124	Hepatoprotective effect of estrogen receptors against liver injury induced by traumatic brain injury in male rats: oxidative stress role	Sedigheh Amiresmaili	Neurosciences
P-125	Formulation and characterization of Rosa damascena extract nanoniosome as an herbal neutral adjuvant for topical ophthalmic drugs	Zeinab Amiri	Neurosciences
P-126	Overexpression of Protein Kinase Mζ in the Hippocampus Improves Cognitive Performance in a Rat Model of Alzheimer's Disease	Niloufar Amini	Neurosciences
P-127	N-acetyl cysteine treatment protects brain mitochondria in hyperammonemic mice	Ahmadreza Aminian	Neurosciences
P-128	The Effect of 40-Hz Light Therapy on learning and memory impairment in STZ-induced dementia rats	Mozhdeh Anjomani	Neurosciences
P-129	Protective effect of crocin, an active constituent of saffron, against 6- hydroxydopamine neurotoxicity in SH-SY5Y cells as a model of Parkinson's disease	Fariba Ansari	Neurosciences
P-130	Monitoring of molecular factors of STIM1, STIM2 and cell death in the striatum of male rats in neurotoxic model of Huntington disease	Nazila Iranipour	Neurosciences
P-131	Study the interaction effect of the intracerebroventricular injection of the Apelin and the agonist and antagonist of Vanilloid type 1 receptor on pain in male Wistar rat.	Zohre Izdi	Neurosciences
P-132	Crocin as an active ingredient of saffron attenuates cognitive deficits due to intracerebroventricular injection of colchicine in the rat	Ensie Azadi Ahmadabadi	Neurosciences
P-133	orexin is involved in naloxone induced hyperactivity of locus coeruleus in morphine dependent rats	Niloofar Aghajani	Neurosciences
P-134	Effect of sodium nitroprusside on lipopolysaccharide-caused spatial memory and synaptic plasticity impairment in rats	Akbar Anaei Goudari	Neurosciences
P-135	Evaluating the role of astrocytes on progesterone control of seizures in a pilocarpine epileptic model	Effat Baran	Neurosciences
P-136	Neuroprotection of Iranian Brown Propolis on ischemic neuronal damage in mice: a potential antioxidant property	Gholamreza Bazmandegan	Neurosciences
P-137	Effects of Lavandula officinalis hydroalchoholic extract on mouse reserpine induced depression	Banafsheh Bagheri	Neurosciences
P-138	Respiratory-related evoked potential in emotional contexts by automated stimulation inspiratory apparatus	Sobhan Bamdad	Neurosciences
P-139	Evaluation effects of Toxoplasma gondii infection on motor dysfunction and striatal histological alterations in experimental rat model of Parkinson	Zahedeh Bavandi	Neurosciences
P-140	The effect of hippocampal cis-p tau injection in learning and memory and synaptic plasticity	Fatemeh Bakhtiarzadeh	Neurosciences
P-141	Study the effect of Ultra-low dose naloxone on KCC2 cotransporter expression in morphine tolerant and hyperalgesic rats	Mozhgan Baratzadeh	Neurosciences

P-142	Isoniazid prevents the acquisition of morphine dependence: a study using naloxone-induced withdrawal behaviors in morphine-dependent mice	Amir Abbas Barzegari	Neurosiences
P-143	Morphine consumption during pregnancy exacerbates neonatal Hypoxia-Ischemia injury in rat through enhancing inflammation, oxidative stress and reducing BDNF	Morad Bornavard	Neurosiences
P-144	Administration of levothyroxine on behavior and cognitive decline in rat model of multiple sclerosis: a biochemical study	Elham Basiratnia	Neurosiences
P-145	Bilateral intra-hippocampal infusion of Modafinil prevented chronic sleep deprivation – induced spatial memory retention deficits in Morris Water Maze in male rats	Maryam Belaran	Neurosiences
P-146	Ferulic acid through attenuation of oxidative stress and neuro-immune response exerts antinociceptive effect in mouse model of formalin test	Shima Balali Dehkordi	Neurosiences
P-147	Spinal cell death fluctuations are potentially responsible for variation in hyperalgesia during persistent peripheral inflammation	Mansoureh Baniasadi	Neurosiences
P-148	Hippocampal orexin infusion develops anxiety behaviors	Saeedeh Bahramzadeh Zoeram	Neurosiences
P-149	The effect of stress on sleep alterations after learning and the role of Cinnamaldehyde on this interaction in rat	Farideh Bahrami	Neurosiences
P-150	The effect of platelet-rich plasma on neuropathic pain induced by spinal cord injury in male rats	Zahra Behroozi	Neurosiences
P-151	Protective effects against brain tissues oxidative damage as a possible mechanism for learning and memory improving effects of captopril in scopolamine treated rats	Farimah Beheshti	Neurosiences
P-152	The effects of Nigella sativa extract on Cell survival rate of Dorsal Root Ganglion (DRG) sensory neurons after axotomy	Belal Pashaie	Neurosiences
P-153	Antidepressant effects of ethanolic extract of Propolis using mice model of depression induced by reserpine	Rahmatollah Parandin	Neurosiences
P-154	Early suppression of NMDA receptor function improves autistic-like behaviors in adult rats prenatally exposed to valproic acid	Mahdieh Parvan	Neurosiences
P-155	Neuroprotective and antioxidant effects of Carvacrol in the ketamine- induced model of mania in the rat	Marzieh Pashmforosh	Neurosiences
P-156	A conditioned place preference study of isoniazid influence on the expression of morphine rewarding properties	Ali Pourahmadi	Neurosiences
P-157	Arbutin Improves Functional Recovery in LPC-induced demyelition model in rat optic chiasm through Regulation of Inflammatory and Oxidative processes	Fereshte Pourabdolhossein	Neurosiences
P-158	Effects of Intracerebroventricular and Intra-Arcuate Nucleus Injection of Ghrelin on Pain Behavioral Responses and Met-Enkephalin and β-Endorphin Concentrations in the Periaqueductal Gray Area in Rats	Samaneh Pirzadeh	Neurosiences
P-159	Bilateral intra-hippocampal infusion of Modafinil prevented chronic sleep deprivation – induced spatial learning impairments in Morris Water Maze in male rats	Kaveh Tabrizian	Neurosiences
P-160	Intranasal insulin effects on brain insulin level and peripheral glucose and insulin concentrations in type 2	Nihad Torabi	Neurosiences

	diabetes		
P-161	The effect of safranal in prevention of cognitive decline in intracerebroventricular streptozotocin model of Alzheimer's disease in the rat	Shahram Jalalzadeh	Neurosiences
P-162	Therapeutic effects of Levodopa/Carbidopa on olfactory function, depression-like and anxiety like behaviors in 6-OHDA- induced Parkinson,s disease in rats	Maryam Sadat Jalali	Neurosiences
P-163	The effect of intracerebroventricular infusion of Neuregulin1β on spatial memory in sporadic dementia model of Rats	Mazieh Jalilzad	Neurosiences
P-164	Effect of acute administration of quinidine, dextromethorphan and combination of dextromethorphan/quinidine on pentylenetetrazole (PTZ)-induced clonic and tonic seizure thresholds in mice	Hassan Jamali	Neurosiences
P-165	Evaluation molecular profile in the CA1 region following microinjection of amyloid-beta in to the entorhinal cortex in the rats; Protective role of calcium channel blockers	Marzieh Joneidi	Neurosiences
P-166	Evaluation and In vitro imaging of Amyloid-β Plaques in the Brain Sections of Alzheimer's Patients Using a Novel Peptide Radiotracer	Safura Joker	Neurosiences
P-167	Evaluating the Effects of Chronic Administration of Natural Honey on the Development of Morphine Dependence in Rats	Mohammad Charkhpour	Neurosiences
P-168	Investigating the anxiety like behaviour and Nrf2 gene expression during crystal meth addiction in male rats who were under treatment with buprenorphine	Homeira Hatami	Neurosiences
P-169	Anti-nociceptive and anti-inflammatory effects of Ferulago angulata	Valiollah Hajhashemi	Neurosiences
P-170	The effects of thymoquinone on cognitive and hippocampal long-term potentiation in thioacetamide - induced hepatic encephalopathy in rat	Somayeh Hajipour	Neurosiences
P-171	Changed Evoked Excitability of CA1 Pyramidal Neurons of Hippocampus in the Valproic Acid Rat model of autism	Razieh Hajisoltani	Neurosiences
P-172	Effects of lithium carbonate and ceftriaxone on recovery after spinal cord injury in rats	Bohloul Habibi Asl	Neurosiences
P-173	Irisin and neural differentiation in rat model of Parkinson's disease	Hossein Hassanpour	Neurosiences
P-174	Activation of 5-HT1A receptors modulates hippocampal theta activity: Relevance to Alzheimer's disease	Soheila Hosseinzadeh	Neurosiences
P-175	Co administration effects of the cisplatin and vitamin E on anxiety behavior in male rats	Masoud Hoseinzadeh	Neurosiences
P-176	Comparison of duration time effects of systemic hypoxia on the hypoxic brain in rats	Fezzeh Hosseinzadeh	Neurosiences
P-177	The effect of cerebrolysin on recognition memory impairment and oxidative stress in D-galactose-Induced Senescence in Mice	Leila Hosseini	Neurosiences
P-178	Combination of muscimol and endomorphin-1 following spinal cord injury in rats	Marjan Hosseini	Neurosiences
P-179	The effects of propranolol on cold allodynia, anxiety and nerve conductive velocity following L5 spinal nerve ligation in rats	Mahdi Hosseini	Neurosiences
P-180	The effects of crocin on long-term potentiation of the CA1 of hippocampus in rats under chronic restraint	Azadehalsadat Hosseini Dastgerdi	Neurosiences

	stress		
P-181	The effect of crocin and exercise on long term potentiation in rats under chronic unpredicted stress	Hajaralsadat Hosseini Dastgerdi	Neurosiences
P-182	The effect of Acetyl L-Carnitine on ultrastructure of motoneuron synapses in adult rats with compressive spinal cord injury	Marjan Heshmati	Neurosiences
P-183	Dexmedetomidine attenuates the induction and reverses the progress of 6-hydroxydopamine- induced Parkinsonism; involvement of KATP channels, alpha 2 adrenoceptors and anti-inflammatory mechanisms	Hashem Haghdoost-Yazdi	Neurosiences
P-184	Hepatocyte growth factor attenuates the severity of status epilepticus in kainic acid-induced model of temporal lobe epilepsy by targeting apoptosis and astrogliosis	Sobhan Haghani	Neurosiences
P-185	Okadaic acid attenuates short-term and long-term synaptic plasticity of hippocampal dentate gyrus neurons in rats	Nasrin Hamidi	Neurosiences
P-186	Cobalamin modulate neurotoxic effects of trimethyltin chloride on hippocampus neural cells and cognitive function	Zeinab Hamidizad	Neurosiences
P-187	The role of orexin receptor 1 of basolateral nucleus of amygdala in the orexin-induced analgesia	Roghaieh Khakpay	Neurosiences
P-188	Investigating the effects of estrogen on physical or psychological stress-induced learning and memory impairments, explorative and anxiety like behaviours in female rats	Mina Khaleghi	Neurosiences
P-189	Nicotine administration during adolescence alters the pain perception and neural response of ventrolateral periaqueductal gray matter to formalin injection	Fatemeh Khaluzade	Neurosiences
P-190	The anti- inflammatory effects of Saliva macrosiphon methanol extract in experimental model of acute inflammation	Sara Khani	Neurosiences
P-191	The analgesic effects of Saliva macrosiphon methanol extract in presence and absence of Atropine & Naloxone in male rat	Arian Khani	Neurosiences
P-192	ANRIL potentially regulates NTF3 expression level in hypoxia	Fatemeh Khani-Habibabadi	Neurosiences
P-193	The effect of nobiletin on behavioral and histological alterations in a model of Parkinson's disease induced by intranigral injection of lipopolysaccharide in the rat	Maryam Khorasani	Neurosiences
P-194	Potential role of intra-accumbal orexin-1 receptors in the acquisition of methamphetamine-induced conditioned place preference in the rats	Elahe Khosrowabadi	Neurosiences
P-195	Current trends of Mesenchymal Stem Cells in regenerative medicine; an efficacious treatment	Mahsa Bazargan	Regenerative Medicine
P-196	The effect of ointment containing Honey and Achillea millefolium and Nigella sativa oil on the process of treatment of wound and scald	Sina Jamali	Regenerative Medicine
P-197	Wound healing potency of PCL/GEL nanofibers containing biologically produced Te NPs	Mohsen Doostmohammadi	Regenerative Medicine
P-198	Trigonelline ameliorates liver dysfunction and neutrophil infiltration following a challenge of carbon tetrachloride in the mouse	Amir Rostami	Regenerative Medicine
P-199	Use of Mesenchymal Stem Cells as a suitable model for tissue engineering of rat kidney	Samira Shahraki	Regenerative Medicine
P-200	Evaluation of antioxidant potential and wound healing activity of topical formulation of Heliotropium bacciferum extract in rat	Hadis Fathalipour	Regenerative Medicine

P-201	Effect of Caw vitreous humour on wound healing in diabetic wistar rat	Sara Mohammadimehr	Regenerative Medicine
P-202	The efficacy of a traditional medicine preparation on second-degree burn wounds in rats	Nasser Ebrahimpoor	Clinical Physiology
P-203	The Combination of ATP and Trolox Improves human Sperm Quality after Cryopreservation	Bahareh Ebrahimi	Clinical Physiology
P-204	The antidiabetic activities of new 1,2,3 triazol compounds as dipeptidyl peptidase-4 (DPP4) inhibitor in a rat diabetes model	Melika Ebrahimi	Clinical Physiology
P-205	Modification of curcumin by lysine amino acid and encapsulation in nano-niosomes for its use in cancer treatment	Najmeh Alsadat Abtahi	Clinical Physiology
P-206	Effect of Losartan as AT1-Angiotensin II receptor antagonist on renal function and tissue changes after renal ischemia reperfusion in male and female rats.	Saeedeh Ahmadi Jokani	Clinical Physiology
P-207	Effects of Nitroglycerin on Renal Ischemia-Reperfusion Injury in adult male Rats	Fateme Ahmadi	Clinical Physiology
P-208	The Effect of Sodium Cromoglycate on Acetic Acid-induced Ulcerative Colitis in Rats	Sara Assadpour	Clinical Physiology
P-209	Introducing a new protocol for immunofluorescence imaging of islets and Akt-2 and cAMP assay of beta cells in mice	Ali Ashrafian	Clinical Physiology
P-210	The effects of morphine on cultured mouse Sertoli cells: A possible mechanism of infertility in addicted men.	Fatemeh Asgharzadeh	Clinical Physiology
P-211	Bee venom derived BBB shuttle and its correlation with oligodendrocytes proliferation markers in mice model of multiple sclerosis	Fatemeh Emami	Clinical Physiology
P-212	The protective and anti-apoptotic effects of zinc on morphine induced-Sertoli cells apoptosis: A probable therapeutic role for zinc	Mohammad Amini	Clinical Physiology
P-213	Effects of Injections of Loratadine and Steroid Hormones into Hippocampus on Learning and Passive Avoidance Memory in the Rats	Zahra Azardar	Clinical Physiology
P-214	Neuroprotective effects of clarithromycin on the neurological scores, brain edema and blood brain barrier disruption after severe traumatic brain injury in male rats: a behavioral and biochemical study	Farahnaz Babayan Mashhadi	Clinical Physiology
P-215	Effects of Green Tea Catechin, Doxorubicin and their combination on Human Neuroblastoma Cell Line BE(2)C cell cycle progression	Zahra Bakhtiarie	Clinical Physiology
P-216	Role of the Ventromedial Hypothalamic D2 Receptor Antagonist (sulpiride) In Regulation Of Food Intake In 24 Hours Food Deprived Rat	Shiva Bakhshi	Clinical Physiology
P-217	The effect of oral administration of hydroalcoholic extract of quercus, crisium vulgare and falcaria vulgaris on preventing gastric ulcer induced by ethanol on inflammatory parameters in rat	Ali Mohammad Basatinya	Clinical Physiology
P-218	Evaluation of skin absorption of the Citrullus colocynthis in treatment of Type II diabetic patients	Rafie Belali	Clinical Physiology
P-219	Expression changes of TLR-2 and TLR-4 in gentamicin induced nephrotoxicity in rats	Zahra Pakfetrat	Clinical Physiology
P-220	Effects of trans-anethole on serum homocysteine and histological changes of ovary, uterus and adrenal in estradiol valerate induced-PCOS rat model	Zahra Peyravi	Clinical Physiology
P-221	Impact of chronic administration of orexin type 1 receptor antagonism on hematologic parameters in morphine dependent rats	Zahra Piri	Clinical Physiology

P-222	Study the effects of hydroalcholic extract of Arum orientale on hemodynamics and neutrophil's activity in isoproterenol-induced myocardial infarction in rats	Asal Javidmehr	Clinical Physiology
P-223	Study the effect of Gensing extract following epilepsy model induction by Penicillin on cognitive behaviour in adult male rat.	Sanaz Janati	Clinical Physiology
P-224	The role of G-protein receptor 30(GPR30) in spatial learning and memory task in aged female rats receiving marijuana	Mohadeseh Chahkandi	Clinical Physiology
P-225	Cytotoxic effects of Hesperidin, hesperidin/carvacrol nanoemulsion and hesperidin/carvacrol combination on human breast cancer cellular model	Sara Hadidi	Clinical Physiology
P-226	Protective effect of crocin the paracetamol-induced renal toxicity in rats	Jalal Hassanshahi	Clinical Physiology
P-227	The antidiabetic activities of a newly synthesized quinazoline compound with dipeptidyl peptidase-4 (DPP-4) inhibitor activity in a murine diabetes model	Samaneh Hosseinpoor	Clinical Physiology
P-228	Exposure to cell phone radiofrequency changes corticotrophin hormone level and histology of brain and adrenal gland in male Wistar rat	Seyed Maedeh Hoseinnezhad Darzi	Clinical Physiology
P-229	Protective effect of melatonin against chemicals-induced cardiotoxcity	Fatemeh Sadat Heydari Yazdi	Clinical Physiology
P-230	The protective effect of voluntary exercise on type 2 diabetes-induced alteration of sperm parameters	Uldouz Kharazi	Clinical Physiology
P-231	Olanzapine prevents chemotherapy induced nausea and vomiting in patients with cancer : A randomized clinical trial	Atefeh Khani	Clinical Physiology
P-232	In vitro effects of Capparis spinosa extract on sperm function, DNA fragmentation, and oxidative stress in normozoospermia	Motahareh Khojasteh	Clinical Physiology
P-233	The high risk of hydration process with saline-furosemide, dextrose and mannitol in female gender in cisplatin induced nephrotoxicity rat model	Mohammad Sedigh Khosravi	Clinical Physiology
P-234	The beneficial effects of progesterone on electrophysiological alterations is mediated through GABA-A receptor in a chronic constriction injury model of neuropathic pain in rats	Soheila Khajemahalle	Clinical Physiology
P-235	Beta Boswellic Acid enhances spatial learning and memory by reduction of tau phosphorylation level in the hippocampus regions of Alzheimer's model	Marzieh Dehghan Shasaltaneh	Clinical Physiology
P-236	Effect of radio frequency wave (900 MHz) on brain serotonin levels and homocysteine in sreum and some of the tissues in rats	Fateme Radmard	Clinical Physiology
P-237	Evaluation of xanthine oxidase (XOX) in patients with arrhythmia in hospitals of Abadan city	Esmat Radmanesh	Clinical Physiology
P-238	Long noncoding RNAs XIST and MEG3 are dysregulated in rituximab treated Pemphigus patients	Mahbubeh Rojhannezhad	Clinical Physiology
P-239	Synthesis and Optimization of nano-niosome for Targeted delivery of Trachyspermum (Ajowan) with aim the Treatment of Fungal Infections	Fardin Rahimi	Clinical Physiology
P-240	Effects of Injections of Oxybutynin and Steroid Hormones into Hippocampus on Learning and Passive Avoidance Memory in Rats	Mostafa Rahimi Nasrabad	Clinical Physiology
P-241	Metronidazole consumption is associated with reduced progeny production and development in Drosophila melanogaster	Zahra Rostami	Clinical Physiology
P-242	Anxiolytic Effect of Hyssopus officinalis L.	Maryam Rashidi	Clinical

	Hydroalcoholic Extract on Ovariectomized Wister Rats		Physiology
P-243	Dose prepregnancy chronic valproate administration affect offspring electrophysiological properties of hippocampus	Tina Rahjoo	Clinical Physiology
P-244	Effects of Injections of Pramipexole and steroid Hormones in to Hippocampus on passive avoidance learning and memory in male Rats	Marzieh Zaferani	Clinical Physiology
P-245	In vitro Antibacterial Effects of Aqueous Extracts of Pistacia Vera L. Hulls on Gram–Positive and Gram–Negative Bacteria of Upper respiratory tract Diseases	Malek Zarei	Clinical Physiology
P-246	Does the oxidant-antioxidant status affect suicide behavior?	Sajjad Salari	Clinical Physiology
P-247	Cyanidine 3 glucoside attenuates oxidative stress in a model of acute kidney injury induced by lipopolysaccharide in the mouse	Sepideh Salari	Clinical Physiology
P-248	The effects of honey syrup and mixture of Cyperus rotundus, Crocus sativus L, Piper nigrum and Boswellia Serrata on memory impairment and oxidative stress parameters in hypothyroid rats	Shiva Saeri	Clinical Physiology
P-249	The effects of injection of Amlodipine and Steroid Hormone into Hippocampus on Learning and passive Avoidance memory in the rats	Hossein Salmani	Clinical Physiology
P-250	The effect of methadone and haloperidol combination on anxiety induced by morphine withdrawal in male mice	Ashkan Sanaie Rad	Clinical Physiology

First day (Wednesday, 30 Oct 2019)			
Afternoon Session (15:00 – 16:00)			
Cardiovascular, Exercise, Respiratory, Traditional Medicine			
Poster presentation board code	**Abstract title**	**Presenter**	**Specific theme**
P-251	Resveratrol attenuates angiotensin II–induced interleukin-6 expression through activation of sirtuin1 in hypertrophied H9c2 cells	Fariba Akhondzadeh	Cardiovascular

P-252	Maintaining of plasma lysyl oxidase level in patients with atherosclerosis following by MgSo4 treatment	Fariba Azarkish	Cardiovascular
P-253	Does increased Nitric Oxide production and oxidative stress due to high fat diet affect cardiac function after myocardial infarction?	Marjan Aghajani	Cardiovascular
P-254	The effects of oral administration of beetroot juice on blood pressure and its interaction with adrenergic system of male hypertensive rat	Zahra Aghaei Fard	Cardiovascular
P-255	Effect of Ischemic Postconditioning on Myocardial Function and Infarct Size Following Reperfusion Injury in Diabetic Rats Pretreated With Vildagliptin.	Goltaj Bayrami	Cardiovascular
P-256	Cytoprotective and antioxidant effects of Evolocumab against H2O2-induced oxidative stress in human endothelial cells (HUVECs)	Shahryar Bahrizade	Cardiovascular
P-257	Anti-arrhythimic effects of the potassium channel blocker, dalfampridine in isolated rat atria	Azam Bakhtiarian	Cardiovascular
P-258	The influence of intermittent fasting on expression of antiaging proteins and blood pressure in rats of different ages	Firuzeh Badreh	Cardiovascular
P-259	Evaluating the effects of Silybum marianum extract on cardiac expression of Farnesoid-X receptor (fxr), ucp2 and ucp3 genes in the rat model of cirrhosis	Gholamreza Bayat	Cardiovascular
P-260	Perillyl alcohol regresses monocrotaline-induced pulmonary arterial hypertension in rats	Ahmad Beik Khormizi	Cardiovascular
P-261	Central GABA-A receptors are involved in cardioprotection against ischemia/reperfusion injury	Hoda Parsa	Cardiovascular
P-262	Pretreatment with vildagliptin boosts ischemic-postconditioning effects on experession levels of Micro_RNA's in rats with type 2 diabet following in-vitro myocardial ischemic reperfusion injury	Lale Pirzeh	Cardiovascular
P-263	Cardioprotective effects of memantine " an NMDA receptor antagonist" in myocardial infarction in rats	Kosar Jannesar	Cardiovascular
P-264	Protective effects of Ferula Assa-Foetida on myocardial ischemic-reperfusion injury in diabetic rats	Faezeh Jafarynezhad	Cardiovascular
P-265	Computational prediction of microRNAs targets for Myocardial Infarction Associated Transcript (MIAT) long non-coding RNA	Saeideh Jafarinejad	Cardiovascular
P-266	Combined effect of exercise and genistein on expression of miR-29, miR-133, Igf-1, and bcl-2 in the heart of ovariectomized diabetic rats	Parisa Habibi	Cardiovascular
P-267	The relationship between heart rate variability and metabolic alterations in conscious rats with hemorrhagic shock	Fateme Khodadady	Cardiovascular
P-268	p- Coumaric acid protects cardiac function against LPS-induced acute lung injury by attenuation of oxidative stress	Maryam Kheiry	Cardiovascular
P-269	Investigation of the effect of resveratrol on serum and cardiac levels of angiotensin II and its receptors transcription in the rat cardiac hypertrophy model	Fahimeh Dorri Mashhadi	Cardiovascular
P-270	Crocin attenuates oxidative stress and inflammation in myocardial infarction induced by isoprenaline via the PPARγ pathway in diabetic rats	Neda Dashtbozorgi	Cardiovascular

P-271	Ellagic Acid Improves Testis Weight Following Isoproterenol-Induced Myocardial Infarction in Diabetic Male Rats	Ali Rajabimohammadabad	Cardiovascular
P-272	Effects of hydroalcoholic extract of Rosa damascena mill on the cardiac angiogenesis in diabetic male rats	Mohammad Zarei	Cardiovascular
P-273	Hepcidin Peptide Inhibitor as Cardioprotection by Targeting Oxidative Stress and Inflammation in Type 1 Diabetic	Motahareh Zeinivand	Cardiovascular
P-274	Ferula assa-foetida gum attenuates ischemia/reperfusion-induced arrhythmias in type 2 diabetic rats	Mahdieh Salari	Cardiovascular
P-275	Role of LAMP2 and PCNA genes in patients with type 2 diabetes and coronary artery disease	Seyedeh Fatemeh Sajadi	Cardiovascular
P-276	Effect of aqueous fraction of Ziziphus jujuba on cardiovascular responses in Goldblatt hypertensive rats	Mohammad Naser Shafei	Cardiovascular
P-277	The effect of nesfatin-1 on the fibrosis in the rat model of the cardiac ischemia-reperfusion injury	Masoumeh Sharifi	Cardiovascular
P-278	Curcumin coated gold nanoparticles attenuates Doxorubicin Induced Cardiotoxicity via improved cardiac function	Zeynab Sharifiaghdam	Cardiovascular
P-279	Investigation on combination effects of gallic acid and cyclosporine A during ischemia/ reperfusion on rat electrocardiogram parameters and arrhythmia	Najmeh Sadeghi	Cardiovascular
P-280	In vitro proangiogenic activity of evolocumab as a PCSK9 inhibitor	Leila Safaeian	Cardiovascular
P-281	Study of Gallic Acid Effects on Serum Parameters of Streptozotocin-Nicotinamide Diabetic Male (Animal Model of Type 2 Diabetes)	Hassanali Abedi	Cardiovascular
P-282	Memantine, an NMDA receptor antagonist, attenuates cardiac remodeling, lipid peroxidation and neutrophil recruitment in heart failure	Samin Abbaszadeh	Cardiovascular
P-283	Toxic effects of aluminum chloride on viability and membrane integrity of human lymphocytes	Mahmood Alidadi	Cardiovascular
P-284	A Comparative study on the equine and camelid antivenoms upon cardiovascular changes induced with Hemiscorpius lepturus venom in rats	Hossein Fatemikia	Cardiovascular
P-285	The investigation of gallic acid on electrophysiology parameters in STZ- nicotinamide induced diabetic rats	Farzaneh Faraji	Cardiovascular
P-286	Mercury and Atherosclerosis: Cell Biology, Pathophysiology, and Epidemiological Studies	Tahereh Farkhondeh	Cardiovascular
P-287	Effect of Enalapril on myocardial capillary density in male diabetic rats	Ali Reza Fallahzadeh	Cardiovascular
P-288	Cerebrolysin Ameliorates Isoproterenol-Induced Myocardial Injury in Male Rats	Gholamreza Ghavipanjeh	Cardiovascular
P-289	Cerebral Ischemia/Reperfusion Injury in the Hypothyroid Rat	Somayeh Keshavarz	Cardiovascular
P-290	Therapeutic effects of Ferula Assa-Foetida on metabolic parameters and cardiovascular disorders in type 2 diabetic rats	Mahboobe Kahtenaroon	Cardiovascular
P-291	The Effect of Hydro-Alcoholic Extract of Ginger (Zingiber Officinale Roscoe) on Diabetic Cardiomyopathy in Streptozotocin-Induced Diabetic Rats	Maryam Mahmoudabady	Cardiovascular

P-292	Effect of human amniotic membrane mesenchymal stem cells-condition medium on myocardial ischemia reperfusion injury in rats	Behnaz Mokhtari	Cardiovascular
P-293	The effect of different digoxin concentrations on heart tissue and antioxidant status in iron-overloaded rats	Yaser Masoumi	Cardiovascular
P-294	Effect of Fish and Flaxseed Oil Supplementation on Isoprenaline-Induced Myocardial Infarction in Rats: Inhibition of Mitochondrial Permeability Transition Pore Opening	Maryam Moghimian	Cardiovascular
P-295	Toxic effects of cadmium chloride on viability and membrane integrity of human lymphocytes	Mona Sadat Mirkamali	Cardiovascular
P-296	Reveratrol decreases Interleukin-6 and soluble glycoprotein130 during mal-adaptive phase of cardiac hypertrophy in rats	Razieh Najjari	Cardiovascular
P-297	Comparison selective phosphodiesterase 3 inhibitor and non-selective phosphodiesterase inhibitor effects on cardiac remodeling and hemodynamic parameters of heart failure in rat animal	Mohammad Mahdi Vahedi	Cardiovascular
P-298	The effect of Astragaloside IV on myocardial infarction in rats	Haleh Veaz	Cardiovascular
P-299	The Effect of 4-phenylbutyric acid on hemodynamic parameters on isoproterenol induced myocardial infarction in rat.	Fatemeh Vatankhah	Cardiovascular
P-300	The role of Atrial natriuretic peptide and Nitric oxide on antiarrhythmic effect of Oxytocin in rat	Fariba Houshmand	Cardiovascular
P-301	The prevalence and 5-year incidence of low physical activity in 10,000 urban population in Kerman, Iran: Relationship with other cardiovascular risk factors	Mahboobeh Yeganeh	Cardiovascular
P-302	The Effect of Salvia Extract Supplementation on serum C-reactive protein following Eccentric Exhaustive Exercise in non-Athlete Women	Saeed Takhti	Exercise
P-303	The effect of voluntary exercise on function and morphological structure of Leydig cells in type 2 diabetic rats	Hamed Heydari	Exercise
P-304	Effects of Immediate and Delayed Exercise on Motor disorder & Brain Edema in the Experimental Traumatic Brain Injury	Forouzan Rafie	Exercise
P-305	Effects combined exercise training on levels of chemerin, omentin and insulin resistance in men with type 2 diabetes	Mehdi Zarei	Exercise
P-306	Therapeutic effects of physical activity against juvenile stress induced anxiety or depression like behaviors and BDNF levels in the prefrontal cortex of adult female rats.	Mohammad Saeedi	Exercise
P-307	Comparing the Effect of Air Pollution on Salivary Malondialdehyde and Total Antioxidant Capacity Response to a Semi-Soccer Protocol in Indoor Vs. Outdoor Environment	Ali Samadi	Exercise
P-308	The effects of exercise on hippocampal inflammatory cytokine levels, brain oxidative stress markers and memory impairments induced by lipopolysaccharide in rats	Zahra Gholamnezhad	Exercise
P-309	Effects of L-citrulline supplementation on blood pressure response to an exhaustive exercise in healthy women	Atefeh Fereidooni	Exercise
P-310	The Effects of Glycyrrhiza glabra L. extract Use with Aerobic Training on Inflammatory Factors	Mohammad-Ali Kohanpour	Exercise

	and Cognitive state in Elderly with Mild Cognitive Impairment		
P-311	Influence of maternal high intensity training in preconception and pregnancy periods on the cardiac oxidative stress of adult male offspring	Reyhane Mohamadkhani	Exercise
P-312	Systemic introduction of mesenchymal stem cells conditioned media in repeated doses modified tracheal responsiveness and lung pathology in asthmatic rats	Mahdi Ahmadi	Respiratory
P-313	The effect of aqueous-alcoholic extract of Berberis integerrima Bge on the basic tension of the isolated smooth muscle and its interaction of the adrenergic system	Mahya Sadat Afrazian	Respiratory
P-314	Systemic and lung changes due to inhaled parquet in rat	Fatemeh Amin	Respiratory
P-315	Anti-inflammatory and anti-remodeling effects of myrtenol in the lungs of asthmatic rats: Histopathological and biochemical findings	Mohammad Abbas Bejeshk	Respiratory
P-316	Nasal breathing enhances resting-state frontal and temporal lobes activity	Tannaz Parsazadegan	Respiratory
P-317	Evaluation of the protective effects of curcumin and nanocurcumin against paraquat-induced lung injury in rats: the role of oxidative stress and gene expression	Asieh Hosseini	Respiratory
P-318	The role of endothelin-1 receptors on pulmonary hemodynamic in rats subjected to liver dysfunction	Maryam Khoramzadeh	Respiratory
P-319	The effects of carvacrol hematological parameters, oxidative stress and pulmonary function tests in patients exposed with sulfur mustard	Mohammad Reza Khazdair	Respiratory
P-320	Genistein preserves the lungs of ovariectomized diabetic rats: addition to apoptotic and inflammatory markers in the lung	Faeze Daghigh	Respiratory
P-321	Evaluation of the Effect of Human Amniotic Membrane Mesenchymal Stem Cells Conditioned Medium (hAM-MSCs-CM) on Ovalbumin-Induced Asthma in BALB/c Mouse Model	Fereshteh Dalouchi	Respiratory
P-322	Allergen induces anxiety-like behavior and enhances activity of amygdala in rat model of asthma	Kolsoum Dehdar	Respiratory
P-323	Anti-inflammatory and anti-oxidative effects of Myrtenol in the rats with allergic asthma	Mohammad Amin Rajizadeh	Respiratory
P-324	Perillyle alcohol ameliorates monocrotaline-induced pulmonary arterial hypertension with through PARP1-mediated miR-204 and its downstream pathway in rats	Soodeh Rajabi	Respiratory
P-325	The effect of quercetine on expression of miR-204 and its targets in monocrotaline induced pulmonary arterial hypertension in rats	Majid Askaripour	Respiratory
P-326	Overactivation of resting brain networks is associated with lung function impairment in patients with asthma	Leila Gholami Mahtaj	Respiratory
P-327	Muscarinic receptors blockade and nitric oxide production contribute in the relaxant effect of Berberis vulgaris extract on rat tracheal smooth muscle	Seyedeh Zahra Ghasemi	Respiratory
P-328	Relaxant effect of Urginea maritima through the beta-2 adrenergic, calcium and potassium channels pathway on the tracheal smooth muscle	Hamideh Kazemirad	Respiratory

P-329	Serum Levels of Visfatin, Sirtuin-1, and Interleukin-6 in Stable and Acute Exacerbation of Chronic Obstructive Pulmonary Disease	Sara Mokhtari	Respiratory
P-330	Carvacrol Affected lung injury induced by inhaled paraquat	Arghavan Memarzia	Respiratory
P-331	Study of Microscopic Effect of Palmatine on Diabetic Wound Healing of Male wistar Rats	Amirhosein Toozandeh Jani	Traditional Medicine
P-332	Green Synthesis, production of Gold Nanoparticles Using Extract of Shilajit	Mandana Jafari	Traditional Medicine
P-333	Antioxidant effect of Hyssopus officinalis leaves extract in the model of Salmonella colitis.	Hadi Cheraghi	Traditional Medicine
P-334	The effect of Buxus hyrcana on learning and memory and oxidative stress in the epileptic model of memory impairment in the rat	Abdolkarim Hosseini	Traditional Medicine
P-335	Investigation on the effect of hydroalcoholic extract of plantago lanceota leaf Compared to Phenytoin on wound healing on Diabetes rats whit streptozotocin	Hoda Haghshenas	Traditional Medicine
P-336	Evaluating the effect of Silybum marianum seed and Cichorium intybus root extracts on hepatic gene expression of Farnesoid X Receptors (FXR) in rat model of acetaminophen-induced hepatotoxicity	Azadeh Khalili	Traditional Medicine
P-337	In vitro evaluation of Cholinesterase inhibitory effects and metal chelating abilities of Asarum europaeum	Arezoo Rastegari	Traditional Medicine
P-338	Inhibition of Cyclooxygenase 2 in Breast Cancer Cell Line by Pistacia Atlantica Extract	Alireza Rafati	Traditional Medicine
P-339	Evaluation of anti-inflammatory, antioxidant, and antibacterial effect of fractions of Punica granatum var. pleniflora extract	Mahboobeh Raeiszadeh	Traditional Medicine
P-340	Protective effect of Silybum marianum L. on liver toxicity And tissue changes induced by acetaminophen	Mostafa Salari	Traditional Medicine
P-341	Protective effects of Resveratrol against Bisphenol A induced Hepatotoxicity in rats	Fatemeh Soleymani	Traditional Medicine
P-342	Clinical trials for controlling cancer complications based on principles of Persian medicine	Sajjad Sadeghi	Traditional Medicine
P-343	The effects of different doses of Nepeta menthoides in mice reserpine-induced depression	Sedighe Talebi	Traditional Medicine
P-344	Effect of nettle (Urtica Dioica) on quality of sleep in hemodialysis patients: A randomized clinical trial	Khadije Alizade	Traditional Medicine
P-345	Pancreatic lipase inhibitory activity of Burdock (Arctium lappa L.) extract	Narjes Farzin	Traditional Medicine
P-346	Lupeol-containing Hawthorn hydroalcoholic extract regulated the polycystic ovarian syndrome-upregulated androgen receptors in rats	Faezeh Malekinejad	Traditional Medicine

Second day (Thursday, 31 Oct 2019)			
Morning Session (9:45 – 10:45)			
Neurosiences, Biomedicine, Clinical Physiology, others			
Poster presentation	**Abstract title**	**Presenter**	**Specific theme**

board code			
P-347	Chrysin attenuates hippocampal inflammation, electrophysiological activity and memory deficits, in cerebral hypoperfusion and reperfusion in male rats	Maryam Khombi Shooshtari	Neurosiences
P-348	Effect of curcumin pretreatment on morphine-induced inhibitory memory impairment and nitric oxide in rat	Khatereh Kharazmi	Neurosiences
P-349	Protective effect of alpha-pinene on blood-brain barrier damage and brain edema in a rat model of focal cerebral ischemia	Mahdieh Khoshnazar	Neurosiences
P-350	Role of amygdala–medial prefrontal cortex circuitry in regulating the expression of fear memory extinction	Masoomeh Dadkhah	Neurosiences
P-351	to Consider the effect of Ritalin abuse on the changes of the enzyme dopamine Beta hydroxylase in prefrontal cortex and serum corticosterone and anxiety in adult male and female rats	Samira Danyali	Neurosiences
P-352	Could treadmill exercise and sex hormones treatment improve learning, memory and hippocampal BDNF level in transient congenital hypothyroid rats?	Leila Derafshpour	Neurosiences
P-353	Activation of hippocampal glial glutamate transporter (GLT-1) reduces the naloxone-induced withdrawal signs in morphine dependent rats	Mahgol Darvish	Neurosiences
P-354	Monophosphoryl lipid A inhibits accelerated epileptogenesis in traumatic rat once administered immediately after trauma	Mozhde Radpour	Neurosiences
P-355	Effects of carvacrol and physical exercise on motor and memory impairments associated with Parkinson’s disease	Ziba Rajaei	Neurosiences
P-356	Neuroprotective effects of morin in the 6-hydroxydopamine model of Parkinson's disease in rats	Hossein Rajabi Vardanjani	Neurosiences
P-357	Protective effects of against glutamate-induced oxidative stress and apoptosis in PC12 and N2a cells	Arezoo Rajabian	Neurosiences
P-358	Effects of Cepo-Fc on recognition memory impairment and pain behavioral responses during persistent peripheral inflammation	Nasser Rahmani	Neurosiences
P-359	Monoacylglycerol lipase inhibitor, JZL-184, like aspirin, has neuroprotective effects in the mice middle cerebral artery occlusion model of stroke	Mohammadreza Rahmani	Neurosiences
P-360	The intensity of LPGi neuronal responses to naloxone during the rest phase differs from the active phase	Fatemeh Rahmati Dehkordi	Neurosiences
P-361	Interaction between naloxone and silver nanoparticles in central amygdala	Mahnaz Rahimpour	Neurosiences
P-362	The effects of cinnamaldehyde on acute or chronic stress-induced anxiety-related behavior and locomotion in male mice	Razieh Rahimi Malek	Neurosiences
P-363	Effect of intracerebroventricular administration of MHY1485 and adiponectin on memory in experimental model of Alzheimer's disease	Samira Rashtiani	Neurosiences
P-364	Neuroprotective consequences of postconditioning on embolic model of cerebral ischemia in rat.	Hossein Rezazadeh Mehrizi	Neurosiences
P-365	The effect of Tanacetum polycephalum on passive avoidance learning and memory against the pentylenetetrazol-induced model of memory impairment in the rat	Farnoosh Rezaali	Neurosiences
P-366	Effect of chondroitinase ABC I immobilization on porous silicon nanoparticles in myelin repair	Safoura Rezaei	Neurosiences
P-367	The effect of sinomenine on intrahippocampal kainate-induced oxidative stress in the rat	Samira Ramazi	Neurosiences
P-368	The role of GABAB receptors in cardiovascular and single unit responses in posterior insular cortex	Afsaneh Ranjbar	Neurosiences
P-369	Dopamine modulates synaptic plasticity in hippocampal CA1 region in control and kindled mice	Nahid Roohi	Neurosiences
P-370	The effect of quinpirole on anxiety level and freezing behavior in rats.	Motahareh Rouhi Ardeshiri	Neurosiences

P-371	Interaction effects of intra-hippocampal injections of Escitalopram with estrogen and progesterone on conditional avoidance memory behavior in the male Wistar rats	Nazanin Zahra Roozkhosh	Neurosiences
P-372	Buprenorphine treatment changed the level of P2X4 receptor gene in the amphetamine addicted rats	Shima Roshani	Neurosiences
P-373	Can Irisin affect the motor dysfunction of the rat model of Parkinson Disease (PD)?	Moslem Riyahi	Neurosiences
P-374	Anti-cataleptic effect of L-Dopa is ameliorated by inactivation of Adenosine A2A receptors in 6-OH Dopamine lesioned rats	Siamak Reyhani Rad	Neurosiences
P-375	Effects of concurrent blockade of orexin receptor-2 and cannabinoid receptors-1 on the nicotine-induced enhancement of neuronal activity in the ventral tegmental area and the nucleus accumbens	Parham Reisi	Neurosiences
P-376	Effect of closed-loop low-frequency stimulation on seizure intensity and learning and memory impairment in pilocarpine model of epilepsy in rats	Meysam Zare	Neurosiences
P-377	The effect of low and high doses of lead over one and two months on spatial learning and memory	Fatemeh Zare Mehrjerdi	Neurosiences
P-378	Anticonvulsive effects of endocannabinoids; an investigation to determine the role of regulatory components of ndocannabinoid metabolism in the Pentylenetetrazol induced tonic- clonic seizures	Parisa Zareie	Neurosiences
P-379	Study of the effect of intracerebroventricular injection of kaempferol and its intraction with vanilloid type 1 receptor on pain in male rats	Mohamad Mahdi Zarei	Neurosiences
P-380	Investigating the effects of subchronic sesame and flaxseed oils consumption against seizure and depression in adult male mice	Raha Zalkhani	Neurosiences
P-381	Effects of Memantine and Docosahexaenoic acid on Learning and Spatial Memory in Adult Male Rats model of Alzheimer's disease	Nastaran Zamani	Neurosiences
P-382	Effects of Brief Electrical Stimulation on Regeneration of Transected Sciatic Nerve	Hosein Samaram	Neurosiences
P-383	Effects of ethanolic extract of Artemisia persica on scopolamine-induced cognitive impairment and anxiety in rats	Mahbubeh Setorki	Neurosiences
P-384	Motion sickness in pets: a clinical case report	Sina Salajegheh Tazerji	Neurosiences
P-385	Evaluation of low dose of methamphetamine in the Astrocyte Model of Alzheimer's Disease Induced by Aβ1-42	Bita Soltanian	Neurosiences
P-386	Thoracic Spinal Cord Injury Causes alterations in Oscillatory Activity and Dopaminergic Markers in Rat Primary Motor Cortex Associated with Deficit in Forelimb Motor Skills	Omid Salimi	Neurosiences
P-387	Impact of buprenorphine on learning and memory ability, oxidative status and inflammation in the hippocampus of rat	Saeed Samarghandian	Neurosiences
P-388	The role of 5-HT3 receptors Blockade in the entorhinal cortex on the Spontaneous Alternation of spatial memory in the electerical amygdala kindled rats	Zeinab Sayyahi	Neurosiences
P-389	Neuroprotective effects of thyroid hormones on methamphetamine–induced cell death in primary hippocampal neurons	Seyedeh Masoumeh Seyedhoseini Tamijani	Neurosiences
P-390	The relationship of GST-T1 and GST-M1 polymorphisms with oxidative stress in acetaminophen poisoned patients	Saeedeh Shojaeepour	Neurosiences
P-391	Isoniazid inhibits morphine-induced incentive sensitization in mice using a conditioned place preference paradigm	Kamran Shahabi	Neurosiences
P-392	Chronic early life maternal deprivation induced depressive like behavior in young adult male rats	Payam Shahsavar Kaleh Sar	Neurosiences

P-393	Pretreatment with crocin along with treadmill exercise ameliorates motor and memory deficits in hemiparkinsonian rats by anti-inflammatory and antioxidant mechanisms	Somayeh Shahidani	Neurosiences
P-394	The effects of frankincense on depression and anxiety-like behaviors induced by LPS in rats	Seyedeh Fatemeh Shahidpoor	Neurosiences
P-395	A new memory impairment model following hippocampal intracerebral hemorrhage	Shima Shirzad	Neurosiences
P-396	Evaluation of the alcoholic extract of Portulaca oleracea on modulation of neuropathic and acute pain in rats	Mehdi Sadeghi	Neurosiences
P-397	Ventra tegmental area microinjected-SKF38393 increases regular chow intake in 18 hours food deprived rats	Farzaneh Saebi Rad	Neurosiences
P-398	The effects of policosanol on learning and memory impairment and Malondialdehyde (MDA) in male rats with Alzheimer's disease induced by β-amyloid (1-40)	Samaneh Safari	Neurosiences
P-399	The effect of hydro-alcoholic extract of fumaria officinalis leaf on pain and seizure by pentylentetrazole-induced mice	Fatemeh Taleahmad	Neurosiences
P-400	The effect of oral administration of extraction of Cyperus rotundus rhizomes on elevated platform stress-induced memory impairment in Adult Mice	Dariush Taheri	Neurosiences
P-401	Protective effects of vitamin K2 against neurodegeneration	Zahra Tayarani-Najaran	Neurosiences
P-402	Quetiapine reverses paclitaxel-induced neuropathic pain in mice: Role of alpha2- adrenergic receptors	Alirez Abed	Neurosiences
P-403	Gallic Acid Nano phytosome Suppresses Excessive Self-Grooming in Autism-Like Rat Models	Haniyeh Abbasalipour	Neurosiences
P-404	• Evaluating the effect of Naringenin on Perphenazine induced catatonia in rats	Atefe Arab Firozjae	Neurosiences
P-405	Spatial learning paradigm can increase post-stress total time of REM sleep in immobilized rats	Fatemeh Erfani Sharifian	Neurosiences
P-406	Reinstatement of morphine seeking behavior by the forced swim stress and drug-priming: role of orexin receptor within the ventral tegmental area	Ronak Azizbeigi	Neurosiences
P-407	Central injection of neuropeptide Y modulates sexual behavior in male rats: interaction with GnRH and KNDy secreting neurons	Vahid Azizi	Neurosiences
P-408	Carvacrol and thymol attenuate cytotoxicity induced by amyloid β25-35 via activating protein kinase C and inhibiting oxidative stress in PC12 Cells	Zahra Azizi	Neurosiences
P-409	Selective alterations in purinergic P2X7 receptor expression during methamphetamine-induced addiction and withdrawal syndrome in the hippocampus of male rats	Hana Azizi Khoshsirat	Neurosiences
P-410	The conditioned medium of mesenchymal stem cells derived from human embryonic stem cells stimulates angiogenesis after ischemic stroke in rats	Afsaneh Asgari Taei	Neurosiences
P-411	Environmental enrichment treatment restore impaired hippocampal synaptic plasticity induced by prenatal noise stress	Fatemeh Aghighi Bidgoli	Neurosiences
P-412	Pre-/post-training morphine increases rat hippocampal miR33 expression	Behrang Alani	Neurosiences
P-413	Overexpression of Protein Kinase Mzeta in the hippocampal dentate gyrus maintains long term plasticity against entorhinal amyloidopathy in freely moving rats	Shayan Aliakbari	Neurosiences
P-414	The effect of hydro-alcoholic extract of Mentha pulegium on pain and seizure induced by pentylenetetrazol in male mice	Mahdi Alizadeh	Neurosiences
P-415	Effect of aerobic exercise on tolerance to morphine usage and pain modulation	Safoura Alizade	Neurosiences
P-416	Selegiline induces adipose tissue-derived stem cells into neuron-like cells through MAPK signaling	Maedeh Amalavar	Neurosiences

P-417	Recovery from stress-induced depression is impaired in aging possibly by altered expression levels of mir-101b, glutamate transporter SLC1A1 (EAAT3), and Rac1 in the prefrontal cortex of rat models	Arshad Ghaffari-Nasab	Neurosiences
P-418	The role of nitric oxide in anticonvulsant effect of aqueous extract of Hyssopus officinalis on seizures induced by pentylenetetrazole	Masoumeh Gholami	Neurosiences
P-419	Beneficial effect of carvacrol on spatial learning performances in Lipopolysaccharide-treated rats	Manizhe Gholami	Neurosiences
P-420	Improvement of stress-induced amnesia by probiotic treatment in rats: Implication of GABA-A receptors	Kimia Alizadeh	Neurosiences
P-421	Anti-aging Activities of Ceftriaxone in Mice Treated with D-galactose	Iman Fatemi	Neurosiences
P-422	Effect of cerebrolysin on memory impairment-induced by chronic alcohol consumption in rats: Role of oxidative stress and apoptosis	Fereshteh Farajdokht	Neurosiences
P-423	Effect of Syringic acid on pain, oxidative stress and pentylenetetrazole -induced seizure in male rats	Soroor Foroozan	Neurosiences
P-424	Portulaca oleracea, relieves neuropathic pain following chronic constriction sciatic nerve injury in rat: anti-inflammatory and antioxidant activity	Fatemeh Forouzanfar	Neurosiences
P-425	Menaquinone-4 effects on working memory impairment and anxiety behavior after transient cerebral ischemia/ reperfusion in male wistar rat	Bahram Farhadi Moghadam	Neurosiences
P-426	The effect of safranal on prevention of learning and memory deficits following intracerebroventricular injection of colchicine in the rat	Farzane Fereidooni	Neurosiences
P-427	The effect of nobiletin on inflammatory response, oxidative stress, cholinesterase, and apoptosis in amyloid beta-induced model of Alzheimer's disease in the rat	Reihane Ghasemi Tarei	Neurosiences
P-428	The effect of Thymus vulgaris on rotarod motor performance in the pentylenetetrazol kindled rats	Zahra Qods	Neurosiences
P-429	Simvastatin exerts antidepressant-like activity in mouse forced swimming test: Role of NO-cGMP-KATP channels pathway and PPAR-gamma receptors	Behnam Ghorbanzadeh	Neurosiences
P-430	Applying nasal airflow reduces mechanical ventilation-induced cognitive impairment	Sepideh Ghazvineh	Neurosiences
P-431	Intra-CA1 administration of L-arginine and L-NAME reduces the acquisition of nicotine-induced place preference in the rats.	Hassan Ghoshooni	Neurosiences
P-432	Effect of electroconvulsive therapy (ECT) on depressed male rats which were pre-induced with Alzheimer's disease	Faezeh Ghozatlu	Neurosiences
P-433	Zncl2 attenuates memory and motor activity impairment induced by hypoxia in rat	Zohreh Ghotbeddin	Neurosiences
P-434	Role of CB1 cannabinoid receptors in pentylenetetrazole seizure threshold in mice	Mohammadmahdi Ghanbari	Neurosiences
P-435	The side effect of maternal exposure to Nanoparticles on reflexive motor behaviors in mice offspring	Aazam Ghanbari	Neurosiences
P-436	Troxerutin exerts neuroprotection against lipopolysaccharide (LPS) induced oxidative stress and neuroinflammation through targeting SIRT1/SIRT3 signaling pathway.	Sedighe Kardgar	Neurosiences
P-437	Long-term cold water drinking induces dyslipidemia and liver fatty changes	Said Abdul Ghafour Saeedy	Biomedicine
P-438	Long-term drinking of cold water impairs spermatogenesis and testicular structure	Ahmad Faisal Faiz	Biomedicine
P-439	Investigating viability of human leukemia/lymphoma cells upon coadministration of umbelliprenin and radiotherapy	Keyhan Ebrahimi	Biomedicine

P-440	Anti-metastatic potential of crocin on triple negative breast cancer in mice model	Laleh Arzi	Biomedicine
P-441	Effects of morphine on serum reproductive hormone levels and the expression of genes involved in fertility-related pathways in male rats	Marziyeh Ajdary	Biomedicine
P-442	Ultrasensitive determination of metformin in real samples using a Ag FRET based nanosensor	Sina Azarian Moghaddam	Biomedicine
P-443	Combinatorial effects of ionizing radiation and 7-geranyloxycoumarin on leukemia/lymphoma cells	Ramin Bagheri	Biomedicine
P-444	Application of Nanoparticles in the drug delivery system associated with central nervous system cancer	Mohammad Ali Pahlevan Neshan	Biomedicine
P-445	In vitro wound healing activity of Scrophularia striata hydroalcoholic extract	Pari Tamri	Biomedicine
P-446	Application of Monoclonal Anti Bodies Enhances the Cytotoxicity of Natural Killer Cells in Breast Cancer	Arsalan Jalili	Biomedicine
P-447	Testosterone and Voluntary Exercise Decrease Apoptosis in the Pancreas of Castrated Diabetic Rats	Leila Chodari	Biomedicine
P-448	In vitro release of Levonorgestrel from reservoir solution core (RSC) rings	Fateme Hosseinzade	Biomedicine
P-449	Effect of TAT-Signaling Fusion System Along with GroEL/ES Chaperones Co-expression on Secretory Expression of Somatropin	Mohammad Rabbani	Biomedicine
P-450	Application of microporous scaffolds in continues drug delivery of Clindamycin	Maryam Rezaei	Biomedicine
P-451	Cancer cell migration and invasion research based on gradient microfluidic chip	Laleh Rafiee	Biomedicine
P-452	Investigation of the estrogen effects and determine the role of its classical receptors on liver damage caused by Traumatic brain injury in male rats.	Nader Shahrokhi	Clinical Physiology
P-453	The effect of carvacrol on hippocampal damage caused by chronic cerebral hypoperfusion	Azadeh Shahrokhi Raeini	Clinical Physiology
P-454	Investigation of level of substanceP and CGRP in brain and spinal cord in experimental endometriose in rat and therapetic effect of royal jelly on them	Hossein Shahrokhi Sardo	Clinical Physiology
P-455	Effect of topical ointment formulation of Urtica dioica extract in the treatment acid burn in mice	Sara Shojaeizad	Clinical Physiology
P-456	Medication errors reduction in cancer patients: the role of the clinical pharmacologist	Hamdollah Sharifi	Clinical Physiology
P-457	Protective effects of long term testosterone administration on epididymal sperm parameters in experimental varicocele male rats	Anahid Shafie	Clinical Physiology
P-458	Investigation the effects of Iranian snake, Naja naja oxiana venom on the level of blood glucose of experimental diabetic rats	Shiva Shahdadi	Clinical Physiology
P-459	The effect of ghrelin intrahippocampal injection on avoid memory in rat	Vahideh Sahraiian	Clinical Physiology
P-460	The effects of Sitagliptin on the serum and ovarian inflammatory mediators of rats with polycystic ovary syndrome	Azadeh Safaeian	Clinical Physiology
P-461	Behavioral effect of yettrium oxide nanoparticle on spatial memory imporovement in cholestatic male wistar rats	Sima Samady	Clinical Physiology
P-462	The nephron-protective role comparison between saline, mannitol, ringer and saline-furosemide hydration process in cisplatin induced nephrotoxicity in male rats	Alireza Samimiat	Clinical Physiology
P-463	Biological therapies, effective medical disciplines for patients with nonsmall cell lung carcinoma	Saba Talebian	Clinical Physiology
P-464	The protective effect of coadministration of Melatonin and Atorvastatin on semen parameters in male rats	Ehsan Aali	Clinical Physiology
P-465	Methotrexate through pro-inflammatory cytokines reductions could ameliorate sepsis Complications in LPS-induced mice.	Azita Alijamaat	Clinical Physiology

P-466	The study of treadmill exercise on the cardiac injury and behavioral deficits induced by methadone maintenance treatment and brain BDNF changes in behavioral sensitization phenomenon in morphine withdrawn rats	Maryam Alizadeh	Clinical Physiology
P-467	The effect of oral administration of hydroalcoholic extract of quercus, crisium vulgare and falcaria vulgaris on preventing gastric ulcer induced by ethanol on antioxidant parameters in rats	Abolfazl Farahi	Clinical Physiology
P-468	Comparison between the Effects of Hydroalcoholic Extract of Dill and Statins on Lipid Profile	Zahra Forouzandeh	Clinical Physiology
P-469	The effect of nobiletin on behavioral function in plus elevated and forced swim tests in amyloid beta-induced model of Alzheimer's disease in the rat	Marzeih Fakour	Clinical Physiology
P-470	Evaluation of antiviral properties of Yarrow alcoholic extract in ovo inoculation of Newcastle disease virus	Adel Feizi	Clinical Physiology
P-471	Influence of Morphine on TLR 4-MyD 88-NF-κB Signal Transduction Pathway of MCF-7 Cell Line	Ahmad Ghasemi	Clinical Physiology
P-472	Search for and evaluation of pharmacodynamic and pharmacokinetic parameters of selective blocker of TRPA1 ion channels	Evgeniya Beskhmelnitsyna	others
P-473	N-acetyl cysteine and estrogen treatment can improve ovarian function after cryopreserved ovary transplantation	Fatemeh Ebrahimi	others
P-474	Evaluation and comparison of protective effects of Curcumin and vitamin E against acrylamide induced oxidative stress and cytotoxicity	Sanam Ashrafi	others
P-475	Effect of Thioflavin-T on the levels of Leptin, Adiponectin, Insulin and histological examination of the liver on male NMRI with high fat diet	Nafiseh Amaniekhtesar	others
P-476	Phytochemical analysis and protective effects of date palm pollen extract in gentamicin induced nephrotoxicity	Neda Omidian	others
P-477	Improved spatial long-term memory, behavioral outcomes, and neuroprotective effect after progesterone administration in rat with traumatic brain injury: role of progesterone classic receptors	Ladan Amirkhosravi	others
P-478	The evaluation of VEGF and HIF-1α genes polymorphisms and multiple sclerosis susceptibility	Arian Amirkhosravi	others
P-479	Impact of acute psychological stresses and CRH administration into PVN and CeA nuclei on food intake and serum leptin level in adult male rats	Mina Sadat Izadi	others
P-480	The efficiency of magnetic Nanoparticles functionalized by gallic acid in crossing the Blood-Brain barrier in Listeriosis Infection in rats	Mehrdad Azarmi	others
P-481	The protective effect of melatonin on benzo(α)pyrene-induced neurotoxicity in mice	Samira Barangi	others
P-482	Safety assessment of a new strain of native Iranian Lactobacillus pentosus (IBRC=11143) in male Wistar rats	Saba Bahrevar	others
P-483	synthesis of 1,4- dihydropyridines from benzalldehyde and 2-chloro benzaldehyde, 4-methylbenzaldehyde, 5-bromo, 2-hydroxybenzaldehyde and cinnamaldehyde using diethyl ammonium nitrate ionic liquid catalyst and iron magnetic nanoparticles and their medical usage in medicine	Shahin Papi	others
P-484	Investigating the effect of Busulfan on Leydig cell maturation in testicular tissue of male wistar rats	Sajad Talkhabi	others
P-485	The effects of chronic Pistacia vera seed oil treatment on working memory and spatial learning and memory	Mahsa Hassanipour	others
P-486	Survey of Protective Effects of Vitamin E and cerium Oxide Nanoparticles on Chlorpyrifos-Induced Oxidative Stress on the Liver enzymes	Mohammad Reza Khaksar	others
P-487	Anticancer properties of fruits mentioned in the Holy Quran	Layasadat Khorsandi	others

P-488	Evaluation the effect of Combination of Gundelia tournefortii, Echinops percicusl and Althaea officinaalis extracts on Wound Healing in lab Rabbit	Mohammad Darvishpour	others
P-489	Assessment of follicular development of immature mouse ovarian tissue encapsulated in sodium alginate grafted under the kidney capsule: An Experimental study	Maryam Dehghan	others
P-490	investigation the effects of honey and nitroglycerin on wound healing in male rats	Alireza Raji-Amirhasani	others
P-491	The effects of electromagnetic field and N-acetyl cysteine on ovarian function after ovary transplantation in mice	Khadijeh Rasayi Far	others
P-492	The Prevalence and Predictors of Overweight and Obesity and their five-year incidence in a General Population: A Community-based Study in Southeastern Iran (KERCADR Study, Phase 2)	Farzaneh Rostamzadeh	others
P-493	The effects of swimming exercise and Nepeta menthoides on depression like behavior induced by reserpine	Faezeh Rezaei	others
P-494	Probiotic treatment improves the impaired spatial cognitive performance and restores synaptic plasticity in an animal model of Alzheimer's disease	Zahra Rezaeiasl	others
P-495	Effects of prenatal exposure to chrysotile asbestos on hippocampal cell proliferation, astrogliosis and long-term behavioral changes in adult male rat offspring.	Ehsan Raeis-Abdollahi	others
P-496	The protective effect of troxerutin on plasma level of testosterone and total Leydig cells in type 1 diabetic rats	Zohreh Zavvari Oskuye	others

Second day (Thursday, 31 Oct 2019)
Afternoon Session (15:00 – 16:00)
Educational Physiology and Pharmacology, Endocrionology, Renal, Gastroinstinal, Stem Cells and Cell Therapy

Poster presentation board code	Abstract title	Speaker	Specific theme
P-497	Protective effects of tannic acid administration on sepsis-induced male infertility in rats	Fatemeh Pourmirzaei	Educational Physiology and Pharmacology
P-498	Effect of dipeptide Noopept on spinal neuron apoptosis and pain behavioral responses during persistent peripheral inflammation	Mona Taghizadeh	Educational Physiology and Pharmacology
P-499	Atorvastatin reduces depressive-like behavior through inhibiting nitric oxide pathway in ovariectomized mice.	Samane Jahanabadi	Educational Physiology and Pharmacology
P-500	The effect of application of logbook practical physiology in the learning of medical and pharmacy students Ramsar Campus, Mazandaran University of Medical Sciences in 1997	Fatemeh Hosseinzadeh Dogolsar	Educational Physiology and Pharmacology
P-501	Neurocognitive manifestationofovariectomized mice attenuated by hydroalcholic extract of pistachio	Elham Hakimizadeh	Educational Physiology and Pharmacology
P-502	The analgesic activity of imidazopyridine compounds as potential inhibitors of cyclooxygenase	Fatemeh Khademabbasi Ardakani	Educational Physiology and Pharmacology
P-503	Implementation of Interprofessional Education (IPE) in improvement of learning and professional competency in postgraduate students	Majid Khazaei	Educational Physiology and Pharmacology
P-504	Educational puzzle for understanding thyroid gland physiology	Milad Mohammadzadeh	Educational Physiology and Pharmacology
P-505	The effectiveness of game-based pharmacology training on learning outcomes in nursing students	Khadijeh Moradbeygi	Educational Physiology and Pharmacology
P-506	Beneficial effects of tamoxifen and raloxifene or their combination with estrogen on cardiovascular indices in postmenopausal diabetic animals	Mohammad Navid Ebrahimi	Endocrionology
P-507	The effect of testosterone enanthate on Liver tissue in adult male rats	Fereshte Ebrahimian	Endocrionology
P-508	Relationship between adipokines and cardio vascular disease risk factors with Normal-Weight Obesity Syndrome in women	Saeedeh Ahmadi Jokani	Endocrionology
P-509	Effect of topical nitrite administration on excisional wound healing in type 2 diabetic male rats	Hamideh Afzali	Endocrionology
P-510	The effect of Myricitrin and Vitamin E on insulin resistance, lipid profiles and hepatic enzymes in aging mice induced by D-galactose.	Mina Omidi	Endocrionology
P-511	Study of Self-Renewal Genes of OCT4, SOX2 and NANOG in Pancreatic Cancer	Golzar Amiri	Endocrionology
P-512	Investigation of rs4986938 G/A Polymorphism in ERβ Gene and its Relationship with Breast Cancer Susceptibility in West of Mazandaran Province, Iran	Nematollah Ahangar	Endocrionology
P-513	Protective effect of Myricitrin on nephropathy of aging model induced by D-galactose in female mice	Akram Ahangarpour	Endocrionology
P-514	Effect of Hydroalcoholic Extract of Artemisia turanica on Biochemical Parameters in Streptozotocin-Induced Diabetic Rats.	Hassan Bagheri Yazdi	Endocrionology
P-515	Menstrual cycle effects on voice characteristics in Iranian women	Faeze Toozandejani	Endocrionology
P-516	The effects of combined vitamin D and estrogen on traumatic brain injury in male rats	Nazanin Sabet	Endocrionology

P-517	The impact of Noise and Vibration exposure on urine catecholamine metabolites of male subjects	Ameneh Jari	Endocrionology
P-518	Study of the effect of saffron and fluoxetine on depression and endocrine profiles in adult men and women	Zahra Javid	Endocrionology
P-519	Berberin impact the cognitive and brain electrical activity complications in thioacetamide- induced hepatin encephalopathy in rats.	Alireza Sarkaki	Neurosiences
P-520	The evaluation of the nicotine effect on the H.P.A axis in male rats	Negar Rahimi Monjezi	Endocrionology
P-521	The roles of autophagy in the formation and differentiation of pancreatic beta cells	Fatemeh Rezaei	Endocrionology
P-522	Anti-apoptotic and anti-inflammatory effects of Stachys schtschegleevii methanolic extract in the liver of type 2 diabetic rats	Reza Rezaie	Endocrionology
P-523	Environmental exposure to bisphenol A and toxicity of reproductive system	Zohreh Zare	Endocrionology
P-524	Gamma-Aminobutyric acid plus magnesium sulfate improves insulin sensitivity in type 2 diabetic rat model	Shahla Sihrabipour	Endocrionology
P-525	Effect of long-term nitrate administration on protein levels of nitric oxide-producing enzymes in liver, adipose tissue, and skeletal muscle in type 2 diabetic male rats	Majid Shokri	Endocrionology
P-526	The effect of adulthood psychological stress on number or area of Langerhans islets and pancreatic glut2 levels in rats exposed to early life stress	Forouzan Sadeghimahalli	Endocrionology
P-527	Effect of hypothyroidism protein levels of nitric oxide-producing enzymes in cardiovascular system in male rats	Roghaieh Samadi	Endocrionology
P-528	The Effect of Fennel on Lipid Profile of Streptozotocin-induced Diabetes Rats	Zahra Samadi Noshahr	Endocrionology
P-529	The impact of oral adminstration of the walnut leaf (Juglans regia L.) extracts and the activity and distribution of aldose reductase in diabetic rat testis	Zahra Abbasi	Endocrionology
P-530	Antioxidant effect of the methanol extract of soybean seeds (Glycine max L.Merr.) on oxidative stress in in rats with Esteradiol Valerate -induced Polycystic Ovary Syndrome	Sanaz Alivandi Farkhad	Endocrionology
P-531	Administration of Ziziphus Jujuba during neonatal and juvenile growth period improved liver oxidative damage of propylthiouracil- induced hypothyroid rats	Vajiheh Alikhani	Endocrionology
P-532	N-acetylsysteine increases mortality rate at aluminum phosphide poisoning rats	Khadije Farrokhfall	Endocrionology
P-533	Evaluation of serum CMPF level in pre-diabetes patients compared to normal people	Shohreh Fardipour	Endocrionology
P-534	Effect of crocin combined with voluntary exercise on TNF-α and IL-6 of HFD/STZ induced type 2 diabetic rats	Vajihe Ghorbanzadeh	Endocrionology
P-535	Contribution of nitric oxide synthases in impaired cardiac function in male rats with transient congenital hypothyroidism	Mahboubeh Ghanbari	Endocrionology
P-536	Vitamin C supplementation by preserving the survival of pancreatic beta cells through a miRNA- related signaling pathway ameliorate metabolic disorder in type 2 diabetes	Rafighe Ghiasi	Endocrionology
P-537	High-fat feeding before, during and after pregnancy affects HPA axis activity in rats	Roxana Karbaschi	Endocrionology
P-538	Platelet rich plasma (PRP) improve impaired glucose	Narges Karbalaei	Endocrionology

	hemostasis, disrupted insulin secretion and pancreatic oxidative stress in streptozotocin-induced diabetic rat	Harofteh	
P-539	Effects of IMODTM on oxidative stress and histological alterationsin the heart of diabetic male rats	Ahad Karimzadeh Kalkhoran	Endocrionology
P-540	L-arginine low dose can elevate menopausal estrogen	Fatemeh Lakzaei	Endocrionology
P-541	Diabetes Induced by Methylglyoxal and Endoplasmic Reticulum Stress Stop by Gallic Acid and L-glutamine In Male Mice	Shahnaz Mojadami	Endocrionology
P-542	Hepatoprotective effect of Descorainia sophia ethanolic extract on antioxidant enzymes activity against carbon tetrachloride induced damage in Wistar rats	Mahboubeh Mahlouji	Endocrionology
P-543	The Effect of Estradiol Against Tributyltin Toxicity in Rat Pancreatic Islets	Perham Mohammadi	Endocrionology
P-544	Effect of high dose of testosterone enanthate on the blood cells and RBC index in male rats	Sahar Mohamadi Vala	Endocrionology
P-545	Effect of Capparis Spinosa Alcoholic Extract on the Isolated Rat Pancreatic Islets	Sara Mostafalou	Endocrionology
P-546	The effects of tropisetron on liver injury in streptozotocin-induced diabetic rats	Roya Naderi	Endocrionology
P-547	PIH improves pancreatic islet function and survival in vitro and in vivo	Marzieh Nemati	Endocrionology
P-548	Normobaric oxygen therapy improves glucose metabolism in obese male rats	Reza Norouzirad	Endocrionology
P-549	The effect of exenatide, a glucagon like peptide 1, on anthropometric indices (body weight, WHR, ovary weight) in rats with poly cystic ovarian syndrome	Asma Vatankhah	Endocrionology
P-550	The expression of SIRT1, inflammatory proteins, and tissue injury in pancreas of ovariectomized diabetic rat: Beneficial effect of swimming exercise	Hadi Yousefi	Endocrionology
P-551	Remote limb ischemic preconditioning accelerates recovery of renal function following ischemia-reperfusion injury: the possible role of lactate as a mediator	Zahra Akbari	Renal
P-552	The Effect of Plantago Major on Kidney Function in Adriamycin Induced Nephrotoxicity	Mahnaz Allahyari	Renal
P-553	The renoprotective effects of naringin and trimetazidine through inhibition of apoptosis and downregulation of micoRNA-10a in renal ischemia/reperfusion injury model	Negin Amini	Renal
P-554	Effect of gender difference on brain and kidney tissue alteration after different reperfusion times from renal ischemia – reperfusion in rats.	Fakhri Armin	Renal
P-555	Protective effect of Rheum turkestanicum against gentamicin-induced nephrotoxicity	Mohammad Taher Boroushaki	Renal
P-556	The Reno-Protective Role of Angiotensin 1-7 in Cisplatin Induced Nephrotoxicity	Zahra Pezeshki	Renal
P-557	Cisplatin Alters Sodium Excretion and Renal Clearance in Rats: Gender and Drug Dose Related	Sima Jilanchi	Renal
P-558	Cyclosporine-A induced nephrotoxicity in male and female rats: Is zinc a suitable protective supplement?	Samira Choopani	Renal
P-559	Nephroprotection of Long-term exercise is mediated through H2S in 5/6 nephrectomized rats	Mahdi Hajiaqaei	Renal
P-560	Evaluation of Rheum turkestanicum in Hexachlorobutadien-Induced Renal Toxicity	Azar Hosseini	Renal
P-561	Thymoquinone ameliorates kidney fibrosis in a rat model of unilateral ureteral obstruction	Sara Hosseinian	Renal

P-562	Stem Cell Therapy Ameliorate Ischemia-Reperfusion of Kidney After 24 h Reperfusion	Leila Hafazeh	Renal
P-563	the impact of different time of renal ischemia-reperfusion on lung histological change in male and female rats.	Aghdas Dehghani	Renal
P-564	Comparison of systemic and centrally erythropoietin administration on kidney protection during severe hemorrhagic shock in rats	Mina Ranjbaran	Renal
P-565	Study the role of gender in the effect of sodium hydrogen sulfide on renal damage induced by ischemia reperfusion injury in rats	Shadan Saberi	Renal
P-566	The effect /of angiotensin1-7 and losartan on renal ischemic/reperfusion injury in male rats	Tahereh Safari	Renal
P-567	Evaluating the effect of chronic Ethanol consumption on alteration of glomerular filtration barrier proteins genes expression and matrix metalloproteinases 2 and 9 activity in the kidney of male rats.	Mahrokh Samadi	Renal
P-568	Dextrose Hydration May Promote Cisplatin-induced Nephrotoxicity in Rats:Gender-related Difference	Farzaneh Karimi	Renal
P-569	Eugenol effects on metabolic-syndrome renal damages	Fatemeh Kourkinejad Gharaei	Renal
P-570	Induction of acute kidney injury in rats by low dose glycerol	Negin Givechian	Renal
P-571	The effect of estrogen on renin-angiotensin system receptors (Mas, At1) in kidney damage induced by ischemia / reperfusion in ovariectomized female rats	Halimeh Lakzaei	Renal
P-572	Effect of Sesame Oil Against Kidney Damage in Doxorubicin-Induced Nephrotic Rat	Somayyeh Mahzari	Renal
P-573	P-coumaric acid pretreatment attenuate cisplatin induced renal and hepatic functional disturbances, oxidative stress and tissue damages	Zeynab Mohamadi Yarijani	Renal
P-574	Non-protective effect of alcohol in cisplatin induced nephrotoxicity rat model	Fatemeh Moslemi	Renal
P-575	Zinc and ischemia preconditioning in renal ischemia/reperfusion	Bahar Mazaheri	Renal
P-576	Learning and memory performance and synaptic plasticity in CA1 hippocampal neurons following acute kidney injury and estradiol replacement in ovariectomized rats	Maryam Malek	Renal
P-577	Effect of troxerutin on expression of miRNA192, TGF-β and SIP1 levels of kidney tissue in type 1 diabetic male rats	Fariba Mirzaei Bavil	Renal
P-578	Maternal ethanol exposure during pregnancy and lactation impairs the kidney of male offspring through alteration of podocyte proteins genes expression, Matrix Metalloproteins (MMPs) and inflammatory stress: a 3- month follow-up	Faride Nezamimajd	Renal
P-579	Bilateral renal denervation prevents induction of hypertension by long-term feeding moderately high-fat diet in obesity-prone rats	Somayeh Nazari	Renal
P-580	The effect of estrogen on renal ischemic-reperfusion-induced kidney injury in ovariectomized rats	Samin Nahavandi	Renal
P-581	The effect of zinc sulfate on miR-122, miR-34a, antioxidants, biochemical and histopathological parameters following hepatic ischemia/reperfusion injury in rats	Ghaidafeh Akbari	Gastroinstinal

P-582	Cannabinoids reduced human colorectal cancer cell proliferation and migration through CB2 receptors	Aylar Alenabi	Gastroinstinal
P-583	The effects of alpha7 nicotinic acetylcholine receptors gene suppression on nicotine-induced apoptosis and cell cycle arrest of human hepatoma HepG2 cells	Khalil Hajiasgharzadeh	Gastroinstinal
P-584	The effect of low-fructose diet on serum adiponectin and TNFα levels and some parameters of non-alcoholic fatty liver disease due to high fat diet in the Sprague-Dawley rat	Babak Hassankhan	Gastroinstinal
P-585	The protective effect of acetyl-L-carnitine in carbon tetrachloride-induced model of acute liver injury in the mouse.	Vahid Khodashenas	Gastroinstinal
P-586	Dapsone reduced acetic acid-induced inflammatory response in rat colon tissue through inhibition of NF-kB signaling pathway	Asma Rashki Ghalehno	Gastroinstinal
P-587	Effects of single and double therapy with 17-AAG, Capecitabine and Irinotecan on proliferation and oxidative stress status of HT-29 colorectal carcinoma cells	Shima Zeynali-Moghaddam	Gastroinstinal
P-588	Evaluation of the therapeutic potential effect of Fas receptor gene Knockdown in experimental model of Non-Alcoholic Steatohepatitis	Feryal Savari	Gastroinstinal
P-589	Gastroprotective Effect of Zingerone on Ethanol-Induced Gastric Ulcers in Rats	Neda Sistani Karampour	Gastroinstinal
P-590	Expression of MT1 receptor in patients with gastric adenocarcinoma and its relationship with clinicopathological features	Ramin Ataee	Gastroinstinal
P-591	Butyrate and deoxynivalenol: Challenges and beneficial effects for intestinal barrier	Arash Alizadeh	Gastroinstinal
P-592	The modulation effects of Shilajit on serum levels of cytokines and adipokines in rats with the non-alcoholic fatty liver disease	Baran Ghezelbash	Gastroinstinal
P-593	Therapeutic effects of Tumor Necrosis Factor-α (TNF-α) on Gastric cancer in the in-vitro model	Mohammad Hosein Gheini	Gastroinstinal
P-594	Chronic psychological stress and non-alcoholic fatty liver disease	Elham Karimi-Sales	Gastroinstinal
P-595	In all 3,4-methylenedioxymethamphetamine (MDMA) decrease regional blood flow and induce necrosis in the rat liver	Ravieh Golchoobian	Gastroinstinal
P-596	study of diosgenin effects on acute liver failure induced by LPS/D-Gal in male c57 BL/6 mice	Seyed Mahdi Mohamadi Zarch	Gastroinstinal
P-597	An imidazoline receptor1 (IR1) agonist alleviated the ER stress induced genes expression in the mice liver	Azam Moslehi	Gastroinstinal
P-598	Complex interactions of heavy metals and Metallothioneins in colorectal cancer: a review of experimental and clinical evidences	Fatemeh Maghool	Gastroinstinal
P-599	Protective effects of metadoxine and montelukast against acetaminophen-induced liver injury in mice	Mohsen Minaiyan	Gastroinstinal
P-600	CDK9 has a crucial role in cardiac differentiation by modulating of DNA methylation profile in myomiRs promoter	Leila Abkhooie	Stem Cells and Cell Therapy
P-601	Effect of triplet therapy with stem cells plus triiodothyronine plus exercise on brain damage in a middle-aged rodent model of stroke	Kobra Akhoundzadeh	Stem Cells and Cell Therapy
P-602	Mesenchymal stem cell-derived endometrium promote neurogenesis and motor function recovery in a mouse model of Parkinson's disease	Saeid Bagheri-Mohammadi	Stem Cells and Cell Therapy

P-603	leukemia inhibitory factor (LIF) over expression protect adipocyte derived mesenchymal stem cells against oxidative and serum deprivation strress in vitro	Mohammad Reza Tabandeh	Stem Cells and Cell Therapy
P-604	In vivo cytokinesis blocked micronucleus assay with cytochalasin B in the Balb/c mouse Bone Marrow stem cells	Romina Javaheri	Stem Cells and Cell Therapy
P-605	The effect of Cytochalasin B and TIO2 Nanoparticles in the Balb/c mouse Bone Marrow stem cells in vivo	Rahele Javaheri	Stem Cells and Cell Therapy
P-606	Differentiation of Rat bone marrow Mesenchymal stem cells with different ages into cardiomyocyte after treatment with neonatal rat cardiac extract	Fatemeh Halvaeipoor	Stem Cells and Cell Therapy
P-607	Sox2 mediated trans-differentiation of melanocytes toward neural progenitor cells, an approaches for application in neurodegenerative disorders	Samaneh Dehghan	Stem Cells and Cell Therapy
P-608	Human endometrial stromal cells protect against cisplatin-induced acute kidney injury by inhibiting cellular apoptosis	Hadis Zeinali	Stem Cells and Cell Therapy
P-609	Study the correlation between the mesenchymal bone marrow stem cells features and postoperation outcomes of patients with severe left ventricular dysfunction candidated for off-pump coronary bypass surgery	Zakieh Sadat Sheikhalishahi	Stem Cells and Cell Therapy
P-610	Conditioned Medium Derived from Hypoxic Adipose tissue Mesenchymal Stem Cells attenuated neuroinflammation on Alzheimer's disease model in rats	Shima Mehrabadi	Stem Cells and Cell Therapy
P-611	The role of mesenchymal stem cell-derived Exosomes in treatment of Cardial diseases	Sahar Hormozi	Stem Cells and Cell Therapy
P-612	Effects of Ischemic Renal Tissue as Conditioned Medium on Mesenchymal Stem Cell; an in vivo study in Acute Ischemic Kidney Injury model	Shahrzad Havakhah	Stem Cells and Cell Therapy

Third day (Friday, 1 Nov 2019)
Morning Session 0(09:45 – 10:45)
Neurosiences, Biomedicine, Clinical Physiology, others

Poster presentation board code	Abstract title	Presenter	Specific theme
P-613	Effect of Lycopene on serum antioxidant and inflammatory mediators in rat's model of experimental Multiple Sclerosis (MS)	Hossein Kargar Jahromi	Neurosiences
P-614	Effect of botulinum toxin type A injection on pain symptoms, quality of life and sleep quality of patients with diabetic neuropathy: A randomized double-blind clinical trial	Zahra Kamiab	Neurosiences
P-615	Effect of Oleuropein on Morphine-induced working Memory Impairments in Rats	Ayat Kaeidi	Neurosiences
P-616	Lead neurotoxic effects reverses by protective effects vitamin E in hippocampal synaptic plasticity in rats	Ruhollah Karamian	Neurosiences
P-617	Role of changes in cardiac metabolism following endotoxemia-induced cardiac dysfunction	Hamid Soraya	Cardiovascular
P-618	The effect of nobiletin on inflammatory response, oxidative stress, and apoptosis in a model of Parkinson's disease induced by intranigral injection of lipopolysaccharide in the rat	Sedigheh Keshtkarvanashi	Neurosiences
P-619	Protective effect of Nigella sativa on Cisplatin-induced memory impairment in male rats	Marzieh Kafami	Neurosiences
P-620	Upregulation of the hippocampal connexin43 during memory consolidation	Nazila Kooravand Bardpareh	Neurosiences
P-621	Homosynaptic and Heterosynaptic Plasticity in Visual Cortical Neurons	Masoumeh Kourosharami	Neurosiences
P-622	Evoluation the effect of chronic toxoplasmosis on synaptic plasticity in rat	Bahere Kiani	Neurosiences
P-623	Naloxone reversible effect of immobilization stress on learning and memory in rat	Mehdi Graily Afra	Neurosiences
P-624	Evaluation of anti-inflammatory effect of aqueous extract of Cuminum cyminum L. fruit with formalin-induced inflammatory model in male rats	Sahar Golabi	Neurosiences
P-625	Isorhamnetin exerts neuroprotective effects in STZ-induced diabetic rats via attenuation of oxidative stress, inflammation and apoptosis	Mina Goudarzi	Neurosiences
P-626	Involvement of the opioid receptors of cuneiform nucleus in regulation of cardiovascular responses during normal and hemorrhagic conditions	Reza Mohebbati	Neurosiences
P-627	Assessment of the protective effects of huperzine-A in a rat model of temporal lobe epilepsy induced by kainic acid	Parvaneh Mohseni Moghaddam	Neurosiences
P-628	Adjustment of mitochondrial dynamics by Mitochondrial ATP-sensitive potassium channel after temporal lobe epilepsy	Ali Mohammad Khanizadeh	Neurosiences
P-629	The effect of intraperitoneal injection of alpha-lipoic acid on memory deficit in the methamphetamine-induced neurotoxicity	Hossain Mohammad Pour Kargar	Neurosiences
P-630	Paraoxon-induced anxiolytic activity is associated with alterations in expression of apoptosis-related genes in rat hippocampus	Moslem Mohammadi	Neurosiences
P-631	Persistent peripheral inflammatory pain changes spatial memory via hippocampal neuronal apoptosis	Mola Mohammadi	Neurosiences
P-632	Peroxisome proliferator-activated receptor alpha (PPARα) activation by fenofibrate protects neurovascular functions and structure in pentylenetetrazole-induced kindling seizure in mice	Mohammad Taghi Mohammadi	Neurosiences

P-633	Involvement of nuclear transcription factors in rat hypothalamus in the development of morphine tolerance	Shiva Mohammadi Talvar	Neurosciences
P-634	Silk protein exhibits anti-depressant and anxiolytic properties through regulation of cerebral oxidative stress, neuroinflammation and apoptosis in a mouse model of spatial restraint stress	Javad Mahmoudi	Neurosciences
P-635	Amygdala – and serum – neurotrophic factor levels depend on rearing condition in male rats	Belal Mosaferi	Neurosciences
P-636	Effects of Achillea biebersteinii Hydro-Alcoholic Extract on Anxiety Like-Behavior and Reproductive Parameters in Rat Model of Chronic Restraint Stress	Sina Moshtagh	Neurosciences
P-637	The Effect of Intracerebroventricular Administration of Calcitonin Gene Related Peptide and Rat-Calcitonin on CGRP and rCT mRNA in Periaqueductal Gray Matter of Formalin Tested Healthy and Diabetic Rats	Oliya Moshiri	Neurosciences
P-638	Effect of scopolamine and mecamylamine on depressive-like behavior of rivastigmine in the tail suspension test	Azadeh Mesripour	Neurosciences
P-639	Morphine affects long term potentiation induced by different stimulation patterns at the Schaffer collateral-CA1 synapses of rat hippocampal slices	Masumeh Mosleh	Neurosciences
P-640	Behavioral effect of yttrium oxide nanoparticles on improved spatial memory deficits by amyloid beta in male Wistar rats	Marzieh Meyari	Neurosciences
P-641	Modified bilateral common carotid occlusion: A proper model for studying memory deficit?	Mehrnoush Moghaddasi	Neurosciences
P-642	The effects of mental exercise and Nepeta menthoides on depression like behavior induced by reserpine	Maryam Malakian	Neurosciences
P-643	The effect of rosmarinic Acid on Liposaccharide-induced memory deficit in rat	Tajmah Mombeini	Neurosciences
P-644	Minocycline mitigates tremor syndrome and defect of cognitive and balance induced by harmaline	Marzieh Maneshian	Neurosciences
P-645	Neuroprotective effect of sumac extract on recognition memory impairment in rat model of Alzheimer's disease	Marzie Mousavimehr	Neurosciences
P-646	Zinc supplementation during pregnancy improves working memory impairment and inflammatory response in an animal model of schizophrenia.	Ronak Mousaviyan	Neurosciences
P-647	Chronic administration of vitamin E ameliorate oxidative stress in the hippocampus of pups from alcoholic mothers	Rahebeh Mahdinia	Neurosciences
P-648	Protective effect of Hydralazine on a cellular model of Parkinson's disease: a 2 possible role of hypoxia-inducible factor (HIF)-1α	Mehrnaz Mehrabani	Neurosciences
P-649	Effect of clavulanic acid on memory dysfunction: In vitro and in vivo assay	Soghra Mehri	Neurosciences
P-650	Antagonism of the ghrelin receptor in the rat brain downregulate the hippocampal Htr1A receptors of serotonin	Atefe Mirzabeh	Neurosciences
P-651	Roles of GABA of the KF nucleus in generating the cardiovascular chemoreflex, a cardiovascular and single-unit study	Nafiseh Mirzaei Damabi	Neurosciences
P-652	The neuroprotective effect of Ketone body on a model of nervous lesion(M.S.) in the mice	Vahideh Mirzaei	Neurosciences
P-653	Changes in fatty acid composition in spinal cord of	Nafise Sadat	Neurosciences

	ethidium bromide-treated rats as a multiple sclerosis (MS) model; GC-MS evaluation	Mirshafieyan	
P-654	Anti-inflammatory effects of levothyroxine in a rat model of multiple sclerosis	Mohammad Ali Mirshekar	Neurosiences
P-655	In-vivo evaluation of some hybrid derivatives based on dimethyl fumarate-benzothiazole scaffold as candidates for Multiple Sclerosis (MS) treatment	Seyedeh Azin Mirmotahari	Neurosiences
P-656	A survey of the effects of diosmin on learning and memory following the use of paraquat herbicide poisoning in a model of rats	Somayeh Miri	Neurosiences
P-657	Paroxetine attenuates cerebral ischemia/reperfusion injury in rat via its anti-inflammatory and antioxidant effects	Yazdan Naderi	Neurosiences
P-658	effect of acute administration of caffeine and the role of nitric oxid pathway on neuropathic pain threshold in a rat model of chronic constriction injury	Monir Naderi Tehrani	Neurosiences
P-659	The effect of ethyl acetate extract of oleo-gum-resin of ferula assa-foetida L. on painful diabetic neuropathy in adult male rats	Samad Nazemi	Neurosiences
P-660	Protective effects of fullerene nanoparticles on learning and memory, histopathological changes of brain and genes expression of mTOR and HIF-1α in streptozotocin-induced experimental diabetes mellitus	Fariba Namdar	Neurosiences
P-661	The effect of hydro-alcoholic extract of Curcuma longa on pain and Pentylenetetrazol induced seizure mice	Fatemeh Nabi	Neurosiences
P-662	Tauopathy in spinal cord injury: a systematic review	Elnaz Nakhjiri	Neurosiences
P-663	Comparison the convulsive potential of pentylentetrazol and pilocarpine	Giti Nasudi	Neurosiences
P-664	Orexin 1 receptors in the nucleus accumbens' shell reversed the devastating effect of olanzapine on effort-based decision-making in the rat	Saeede Nasrollahi	Neurosiences
P-665	Effects of probiotic (combination of Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) on memory processes in LPS-induced rats	Marjan Nassiri-Asl	Neurosiences
P-666	Functional coupling of the brain mitochondrial ATP-sensitive large conductance Ca+2-activated K+ channel (mitoBKCa) to respiratory chain in amyloid-β Alzheimer model rats	Maryam Nazari	Neurosiences
P-667	Conditioned medium obtained from human amniotic mesenchymal stem cells attenuates focal cerebral ischemia/ reperfusion injury in rats	Donya Nazarinia	Neurosiences
P-668	Protective effect of piperine on hippocampal synaptic plasticity impairment in streptozotocin-induced model of Alzheimer's disease	Masoomeh Nazifi	Neurosiences
P-669	Neuroprotective effect of quercetin on oxidative stress and apoptosis of motor neurons in cultured spinal cord slices of adult mouse	Hamidreza Noghli	Neurosiences
P-670	Modulating proteoglycan receptor PTPσ using intracellular sigma peptide improves remyelination in demyelinated optic chiasm of mice	Parvin Niknam	Neurosiences
P-671	Effect of quercetin, ghrelin and exercise on the expression of genes BDNF, cytochrome b and caspase3 model of Parkinson in male mice MPTP-induced	Neda Nikokalam Nazif	Neurosiences

P-672	Effect of melatonin on diabetic retinopathy in rats	Vahid Nikoui	Neurosiences
P-673	Effect of acute L-Carnitine administration on pentylenetetrazole (PTZ) -induced clonic and tonic seizure thresholds in mice	Sayyed Morteza Vaghefi	Neurosiences
P-674	Dose-dependent anticonvulsant and protective effects of metformin in kainate induced temporal lobe epilepsy	Somayeh Vazifekhah	Neurosiences
P-675	Role of insulin-like growth factor 2 (IGF-2) in memory impairment following intracerebral hemorrhage	Farzaneh Vafaee	Neurosiences
P-676	The Effect of extract of Prangos Ferulacea on Behavioral, Motor and Cognitive Functions in Autistic Model Rats	Arefe Vafaeinezhad	Neurosiences
P-677	Effects of different addictive foods on memory in male rats	Ghazale Hadian	Neurosiences
P-678	Evaluation of the neuroprotective, anticonvulsant, and cognition improvement effects of apigenin in model of temporal lobe epilepsy: Involvement of the mitochondrial apoptotic pathway	Paria Hashemi	Neurosiences
P-679	Intra-hippocampal L-NAME low dose did not affect morphine antinociception in the rat formalin test	Mahboobeh Hashemi	Neurosiences
P-680	The effects of Lithium chloride and cathodal/anodal transcranial Direct Current Stimulation on the level of p-CREB/CREB in PFC of male NMRI mice	Mojgan Hamdami	Neurosiences
P-681	Opium protects brain against ischemic injury through reducing inflammation and enhancing antioxidant defense in male rat	Salimeh Yarahmadzehi	Neurosiences
P-682	Effect of betahistine on depression induced by PTZ in kindled mice	Azadeh Yazdi	Neurosiences
P-683	The effect of very low frequency electromagnetic waves on the formalin-induced pain in male rats	Elham Yousefhaghi	Neurosiences
P-684	The effect of repeated ICV injections on brain inflammation and anxiety	Shiba Yousefvand	Neurosiences
P-685	Evaluation of Anti-Fungal Activity of Two Species of Cousinia	Ebrahim Salimi Sabour	Biomedicine
P-686	Curcumin ameliorates methotrexate-induced testicular oxidative stress in the rat	Maryam Sharayeli	Biomedicine
P-687	Three Novel Candidates as Mu Opioid Receptor Antagonists: An In Silico Study	Hadis Shahriari	Biomedicine
P-688	Biofilm inhibition activity of CuO/ZnO nanoparticles by cold tolerant Microbacterium sp.	Bahar Shahnavaz	Biomedicine
P-689	Neopterin increase in Obstructive Sleep Apnea Patients	Samaneh Sheikhi Kouhsar	Biomedicine
P-690	Dermal and Ocular Safety Assessment of ordinary vs. Nano-form Titanium Dioxide (TiO2) in the Animal Models	Goudarz Sadeghi Hashjin	Biomedicine
P-691	Opium addiction during pregnancy through inflammation increases adverse pregnancy outcome	Hamed Fanaei	Biomedicine
P-692	Adjuvant therapy with memantine enhances the antiproliferative effects of doxorubicin in MCF-7 breast cancer cells	Maryam Kahyaei_Aghdam	Biomedicine
P-693	Adjuvant therapy with memantine enhances the sensitivity of A2780 ovarian cancer cells to cisplatin	Negin Mahboubi	Biomedicine
P-694	Elucidation of the mechanisms of Ciprofloxacin-induced myopathy	Mohammad Reza Neshat	Biomedicine

P-695	The effect of Zataria multiflora on pulmonary function tests, respiratory symptoms, bronchodilator drugs use and hematological parameters in chronic obstructive pulmonary disease	Vahideh Ghorani	Clinical Physiology
P-696	Anti-inflammatory effect of lycopene in lipopolysaccharide-induced model of acute kidney injury in C57BL/6 mouse	Atefeh Ghorbanpour	Clinical Physiology
P-697	Evaluation of the effect of oral administration of Quercus, Cirsium vulgare and Falcaria vulgaris hydroalcoholic extracts on prevention of gastric ulcer caused by ethanol by studying the levels of caspase 9, c-fos, c-myc and Bcl-2 in rats	Mahbobeh Kamrani Mehni	Clinical Physiology
P-698	The role of bone marrow mesenchymal stem cells in the expression of TLR2 and TLR4 in acute kidney injury induced by renal ischemia-reperfusion in rats	Zeinab Karimi	Clinical Physiology
P-699	The effect of maternal stress on pain in adult male rats and the possible effect of oxytocin treatment	Shima Karimi Afshar	Clinical Physiology
P-700	Bioinformatics studies of polyphenolic compounds of Pistacia and grapes to inhibit proteinase kinase BRAF in colorectal cancer	Ziba Karimi Sadr	Clinical Physiology
P-701	Effect of different dark chocolate diets on memory in chronic psychical stressed rats	Elham Kalantarzade	Clinical Physiology
P-702	Evaluation of the prescription pattern of proton pump inhibitors in a tertiary hospital	Zahra Kiani	Clinical Physiology
P-703	Combination of ascorbic acid and calcitriol attenuates airway remodeling in a murine model of chronic asthma	Farzaneh Kianian	Clinical Physiology
P-704	The effect of facilitatory kinesiotape on thoracic superficial erector spinae muscle activity in healthy men	Sakineh Goljaryan	Clinical Physiology
P-705	The protective effects of long term NaHS administration on sperm parameters, testicular morphometry, testicular H2S levels, oxidative stress markers in varicocele male rats	Keivan Lorian	Clinical Physiology
P-706	Evaluating the expression of ERα66 and its novel variant ERα36 in drug-resistant lactotroph pituitary adenomas by gender	Fatemeh Mahboobifard	Clinical Physiology
P-707	Regular exercise and psychosocial stress modulate angiogenesis in heart failure	Seyed Mohamad Mortazavi	Clinical Physiology
P-708	Association between frequency of early ovarian hyperstimulation syndrome (OHSS) and vitamin D levels in follicular fluid of non-obese PCOS and healthy women	Fatemeh Masjedi	Clinical Physiology
P-709	L-carnitine and cholesterol-loaded cyclodextrin attenuate vitrification induced reactive oxygen release in sheep epididymal sperm	Leili Mavalizadeh	Clinical Physiology
P-710	Effect of oxytocin on cerebral damage, spatial memory and apoptosis in a rodent model of cerebral stoke	Shahein Momenabadi	Clinical Physiology
P-711	The effect of methanolic extract of fenugreek on learning and memory in an experimental model of Alzheimer's disease in the rat	Leila Nasiri	Clinical Physiology
P-712	The Therapeutic Potential of Losartan in Colorectal Cancer	Seyedeh Elnaz Nazari	Clinical Physiology
P-713	Wound healing effects of topical Vitamin K: A randomized controlled trial	Gholamreza Houshmand	Clinical Physiology
P-714	Effects of Saffron Aqueous Extract on Hepatic Angiotensinogen Gene Expression and Insulin Resistance in Rats under Sub-chronic Stress	Yeganeh Yazdani	Clinical Physiology

P-715	Induction of cytotoxicity and apoptosis in FLT3 mutant expressing cells using novel pyrimido cyanoacrylates and quinoline derivatives	Mohammad-Ali Sobhanifar	others
P-716	Effect of vitamin D on severity of morphine dependence in the conditioned place preference model in rat	Mahbubeh Saeedfar	others
P-717	Experimental evaluation of mouse hind paw edema induced by Iranian Naja oxiana venom	Ramin Seyedian	others
P-718	Preparation of a soft contact lens model based on molecularly imprinted for timolol using computational method and experimental design	Faezeh Shakermahani	others
P-719	L-carnitine oral administration effects on genes expression in the liver and serum adiponectin levels in rat model of type 2 diabetes	Beydolah Shahouzehi	others
P-720	Both injection doses and slow release of progesterone are effective on histopathological changes after TBI.	Sara Shirazpour	others
P-721	Sub-chronic administration of brewed coffee on rat behavior and cognition and oxidative stress Alzheimer's disease model	Gohar Sedaghat	others
P-722	Oral administration of Auraptene and Umbelliprenin controls inflammation in a CFA-induced inflammatory rat model	Zhila Taherzadeh	others
P-723	The effect of methadone on blood glucose, lipids and glucose-modulating hormones in methadone-dependent Wistar rats	Zoya Tahergorabi	others
P-724	Effects of Pumpkin seed on sexual function, blood factors and sex hormones in male rats	Abdollah Abdollahpour	others
P-725	Gender-related relation between metabolic syndrome and S447X and HindIIIpolymorphisms of lipoprotein lipase gene in northern Iran	Elaheh Abdollahi	others
P-726	Survey on the anti-fungal activity of a synthetic econazole derivative in mice	Masoumeh Ezzati Givi	others
P-727	Hormetic Effect of some Phytochemicals in Myeloid Cell Leukemia Type-1 Gene Expression by overcompensation stimulation method	Omid Gholami	others
P-728	Evaluation of protective effects of methylene blue on testicular damage induced by cisplatin	Fatemeh Gholami Jourabi	others
P-729	Assessment of Protective effects of carvacrol and rutin on haloperidol-induced oxidative stress and genotoxicity, in peripheral blood lymphocytes	Seyede Hediye Fatemi	others
P-730	Learning to obtain food on specific time dramatically provokes plasma ghrelin-induced dopamine release in the hippocampus of adult male rats	Maedeh Ghasemi	others
P-731	The effect of selegiline on acute toxicity of aluminium phosphide in rats	Adeleh Maleki	others
P-732	The effect of maternal treatment of troxerutin during pregnancy on serum level of apelin and stereological structure of testis in male offspring with obese mother	Keyvan Mehri	others
P-733	The comparison of mice autologous serum and bovine BSA impact on on quality and 2PN embryos numbers of NMRI mice in IVF medium	Sima Nasri	others
P-734	The effect of troxerutin on caspase 3 and glucokinase expression of the liver in streptozotocin-induced hyperglycemic adult male rats	Azadeh Nochalabadi	others

P-735	Evaluation of the effects of using peroxisome proliferator-activated receptor alpha (PPARα) on brain infarction, brain swelling and edema in focal-transient cerebral ischemia in rat	Hadi Vahidi	others
P-736	Noscapine protects rat H9c2 cardiomyocytes against oxygen and glucose deprivation-reperfusion injury	Gelareh Vahabzadeh	others
P-737	Study of the effect of cisplatin on sperm parameters and testicular histology and supportive effects of propolis	Hadis Hashemi	others
P-738	Investigation of the hypoglycemic antioxidant effect of four rice bran species in Iran	Maryam Hemati	others
P-739	A practical guide for inducing a rat model of osteoporosis using ovariectomy	Nasibeh Yousefzadeh	others
P-740	Evaluation of antiviral properties of Yarrow alcoholic extract in ovo inoculation of Newcastle disease virus	Adel Feizi	Physiology and Pharmacology
P-741	The effect of testosterone enanthate on Liver tissue in adult male rats	Fereshte Ebrahimian	Endocrionology
P-742	The Protective Effect of Sesame Oil on Doxorubicin Induced Nephrotoxicity	Abolfazl Khajavi Rad	Renal
P-743	Efficacy of repetitive daily normobaric hyperoxia preconditioning against gentamicin-induced nephrotoxicity in rats	Khalil Pourkhalili	Renal
P-744	Effect of dietary nitrate or nitrite supplementation on PTZ- induced clonic seizure threshold in mice	Azhdar Heydari	Neurosiences
P-745	Study of the effect of intracerebroventricular injection of kaempferol and its intraction with type B GABA recrptor on pain in male rat	Maryam Esmaeili Salem	Neurosiences
P-746	Investigation of level of BDNF and NGF in brain and spinal cord in experimental endometrioses in rat and therapeutic effect of royal jelly on them	Fatemeh Dejam	Clinical Physiology and Pharmacology
P-747	Chlorogenic acid inhibited growth in 4T1 cancer cell line and induced apoptosis	Zahra Changizi	others
P-748	Effects of Montelukast Injection into Hippocampus on Memory Level and Passive Avoidance Learning Rats .	Sima Rabienezhadganji	Neurosiences
P-749	Effect of handling on migraine of mother-deprived neonatal rats.	Abbas Tajabadi	Clinical Physiology and Pharmacology
P-750	Effect of maternal stress and oxytocin treatment on anxiety-like behaviors.	Asma Alimolaie	Clinical Physiology and Pharmacology
P-751	The effect of oxytocin on maternal stress-induced impairment of spatial memory in adult rats	Fatemeh Ashrafganjoie	Neurosiences
P-752	The Protective Effects of Ginger (Zingiber officinale Roscoe) Extract on brain Toxicity Induced by Ethanol in Rat	Abolfazl Akbari	Traditional Medicine
P-753	The cardioprotective effects of aminoguanidine on lipopolysaccharide induced inflammation in rats	Ali Akbar Asghari	Cardiovascular
P-754	Investigating the effect of low frequency stimulation of olfactory bulb on seizure severity and working memory improvement in kindled rats	Marzieh Khodadadi	Neurosiences
P-755	Formability of prions and disease development mechanisms by PrPsc	Navid Shahbazi Shiran	Biomedicine
P-756	Comparison of inflammatory Response between low and high scored mustard gas injured victims in	Atefe Mirzaei	Others

	Sardasht		
P-757	The study of married and single females, received a training course on Principles of health maintenance based on Persian medicine, in terms of physical pain, social function and general health	Zakaria Rohani Yazdeli	Others
P-758	Effect of long term application of probiotics on brain damage and spatial learning and memory in a mouse model with cerebral hypoperfusion	Abedin Vakili	Neurosiences
P-759	To study and comparison effect of involuntary exercise on hippocampal BDNF in male and female PTSD rats	Sakineh Shafia	Neurosiences
P-760	Methadone affecting on lifespan and reproductive ability in Drosophila melanogaster	Majid Hassanpour-Ezatti	Biomedicine
P-761	Cardioprotective effects of nicotinamide-mononucleotide in combination with postconditioning modalities in aged rats: involvement of mitochondrial function and biogenesis	Reza Badalzadeh	Cardiovascular
P-762	Interaction of central nitrergic and oxytocinergic systems on food intake regulation in neonatal layer-type chickens	Anahita Vosughi	Others
P-763	Co-administration effects of nitrite and sodium hydrosulfide on oxidative stress in type 2 diabetic rats background and objective	Asghar Ghasemi	Clinical Physiology and Pharmacology
P-764	Effect of combination therapy on resistance and apoptosis of melanoma cancer cell (B16f10)	Marjan Hajimoradi Javarsiani	Others
P-765	The role of endocannabinoid system in the antidepressant and anxiolytic effects of exercise	Leila Hosseinzadeh Anvar	Neurosiences
P-766	Effects of Exendin-4 on Oxidative Stress and Metabolic Disorders Induced by Bisphenol A in Adult Male Mice	Golshan Afshari	Neurosiences
P-767	Early postnatal maternal deprivation affected maternal care and offspring body mass index	Homeira Zardooz	Others
P-768	Assessing the effect of valproate sodium on spatial learning and memory in morphine-tolerant rats	Seyed Hossein Marashi	Neurosiences

Notice:

The abstract published in this abstract book were not edited either scientifically or literary. The 24th Iranian and 3rd International Congress of Physiology and Pharmacology repudiate any error or incorrect statements made by the authors.

Oral Papers

S083101-1

Comprehensive in vitro proarrhythmia assay (CiPA) using cardiomyocytes differentiated from pluripotent stem cells Mohammad Javad Khodayar[1,2], Heibatullah

Sara Pahlavan

Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR

The generation of human induced pluripotent stem cells (iPSCs) from somatic cells of healthy individuals or patients with genetic diseases and their induction toward cardiac fate offers a unique opportunity for in vitro studies of human heart development, investigation of molecular mechanisms of cardiac diseases as well as drug discovery and toxicity testing. Cardiotoxicity is one of the major reasons for drug attrition from market which may impose tremendous costs to pharmaceutical companies. Drugs may impose side effects on structure or electrophysiology of cardiac myocytes. Comprehensive in vitro proarrhythmia assay (CiPA) using the iPSC-derived cardiomyocytes and multielectrode array (MEA) system have been proposed as a robust, efficient, and sensitive platform for electrophysiological cardiotoxicity screenings. While industry standard assays are based on using immortalized cell lines or animal models, CiPA takes the advantage of cardiomyocytes obtained from cardiogenic differentiation of iPSC, literally representing the most similar physiology to human heart. Therefore, this high throughput physiologically relevant platform for cardiotoxicity may provide an advanced complementary method with great potential for reducing the costs of drug development and cardiotoxicity-related drug attrition. However, the implementation of CiPA initiative is highly dependent on necessary adjustments to this technique including generation of mature iPSC-derived cardiomyocytes as well as standard culture, differentiation and assay methods. In this symposium, we will describe methods to induce cardiomyocytes differentiation in vitro, methods to enhance maturation of in vitro generated cardiomyocytes including tissue engineering approaches and cardiac organoid, and last but not least bio-banking of cardiac progenitor cells as a promising tool for large scale production of cardiomyocytes in vitro.

S083101-2

Cardiac tissue engineering as a promising approach to advanced mechanistic studies and drug screening

S Rajabi1, S Pahlavan2, S Abbasalizadeh2, M Kazemi Ashtiani1, H Baharvand2

1. Department of Cell Engineering, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran
2. Department of Stem Cell and Developmental Biology, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Millions of people worldwide suffer from cardiovascular diseases. Although current interventional and pharmacological approaches provide efficient therapies, curative treatment of end-stage heart failure is limited to heart transplantation. Bioengineering of whole hearts using human embryonic stem cells (hESCs)-derived cardiovascular progenitor cells (CPCs) and natural matrices is a promising approach to overcome organ donor shortage. Here, we developed a novel strategy for generation of heart constructs by repopulating engineered decellularized rat hearts using hESCs-derived CPCs. We modified decellularization protocol to improve efficacy which was confirmed by multiple tests including DNA content analysis as well as biochemical studies. The decellularized hearts were recellularized by hESC-derived CPCs, which were generated in a scalable suspension bioreactor system. We immobilized bFGF onto heart ECM prior to cell perfusion. At day 12 post seeding, functional studies were performed on recellularized hearts. The beating rhythm was evaluated using a multielectrode array system. Contraction motions were recorded using video microscopy and analyzed. qRTPCR, immunostaining and transmission electron microscopy (TEM). Our results demonstrated that perfusion-decellularization of whole heart allows the generation of a heart ECM scaffold with a perfusable vascular tree which acts as an efficient template to generate synchronously beating heart tissue. Comprehensive characterization of the decellularized heart matrix demonstrated preservation of complex ECM proteins, 3D spatial orientation and the micro-structure of native heart. Careful expansion of CPCs in a scalable stirred-suspension bioreactor combined with step-wise seeding onto decellularized hearts containing immobilized bFGF resulted in improved retention of CPCs and differentiation to cardiomyocytes, smooth muscle cells and endothelial cells as evaluated by immunohistochemistry and qRT-PCR. We observed spontaneous and synchronous contractions of humanized hearts after 12 days of perfusion as well as advanced alignment of myofilaments. Our study provides a robust platform for generation of artifcial human hearts and resolves major bottlenecks hindering further development of this technology. Bioengineered hearts might soon fnd their way toward clinical application.

S083101-3

Generation of cardiac organoid for in vitro physiological and pharmacological studies

Varzideh F[1], Ansari H1, Pahlavan S[1], Aghdami N[2], Baharvand H[1,3]

1. Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran
2. Department of Regenerative Medicine, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran
3. Department of Developmental Biology, University of Science and Culture, Tehran, Iran

Human cardiomyocytes (CM) differentiated from pluripotent stem cells (PSCs), by differentiation protocols display properties similar to fetal cardiac cells rather than adult CM. Immaturity of in vitro generated CM limited their application in physiological studies, drug screening and cell therapy. In this study, we examined the ability of (hESC)-derived cardiac progenitor cells (CPC) to develop into mature cardiomyocytes after formation of self-organized cardiac organoids (CO) and subsequent heterotopic transplantation into mice. We observed that the expression of genes coding for the cardiac contractile apparatus and ion channel genes was higher in the CO group compared to cultured CM. However, the number of proliferating Ki67+/TBX5+ cells and beating frequency was reduced in CO over in vitro culture. Also, intraperitoneal implantation of CO induced neovascularization and further enhanced maturation as indicated by gene expression changes, more developed CM ultrastructure and excitability pattern of working cardiomyocytes compared to in vitro CO and in vivo CM transplants. Human COs provide a heart micro-tissue with enhanced CM maturation by organoid transplants. These COs provide an appropriate tool for disease modeling, drug testing, and regenerative medicine.

S083101-4

The path through bio-banking cardiac progenitor cells

Sadaf Vahdat[1], Elena Mahmoudi[1], Maryam Barekat[1], Hossein Baharvand[1,2]

1. Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran.
2. Department of Developmental Biology, University of Science and Culture, Tehran, Iran

Cardiovascular progenitor cells (CPCs), the cardiac-committed proliferative cells with the potential to generate almost all cardiovascular lineages, are considered as invaluable cell sources for experimental and clinical studies in the cardiovascular field. CPCs can be generated *in vitro* through cardiogenic differentiation of human pluripotent stem cells (hPSCs); however, scalability and clinical-grade generation of hPSC-derived CPCs are as the proposed obstacles and requirements for their wide range of applications. Therefore, establishment of a culture system for large-scale expansion, maintenance and bio-banking of hPSC-derived CPCs is highly demanded. We have attempted to develop a simple, defined, and reproducible culture condition by chemical screening of signaling factors for expansion, maintenance, and storage of hPSC-derived CPCs. The characteristics of expanded CPCs including morphology, gene expression pattern, chromosomal stability, and *in vitro* differentiation propensity into major cardiac lineages were retained. Moreover, the safety and cardio-protective effect of expanded CPCs after transplantation into infarcted hearts of rat models were exhibited. Taken together, the expanded cells in our novel introduced culture system might ultimately be promising cell sources for commercialization, drug screening, developmental, tissue engineering, and cell-based clinical studies.

S082102-1

Differential transform method for solving the model describing biological species living together

A. Tari

Department of mathematics, Shahed University, Tehran, Iran

In this paper, the mathematical model of describing biological species living together is studied. Here, we extend the well-known differential transform (DT) method for finding the numerical solutions of this problem. To this end, we give some preliminary results of the DT and by proving some theorems, we show that the DT method can be easily applied to mentioned system. Finally, several test problems are given to show the accuracy of the proposed method and compared with other existing methods.

S082102-2

Applications of comparative and non-comparative game models in bioinformatics

H. Navidi[1], M. Hassanpour-ezatti[2]

1. Department of computer sciences, Shahed University, Tehran, Iran
2. Department of Biology, Shahed University, Tehran, Iran

Game theory is the mathematical study of interaction among independent, self-interested agents. The audience for game theory has grown dramatically in recent years, and now spans disciplines as diverse as political science, biology, psychology, economics, linguistics, sociology and computer science–among others. What has been missing is a relatively short introduction to the field covering the common basis that anyone with a professional interest in game theory is likely to require. Such a text would minimize notation, ruthlessly focus on essentials, and yet not sacrifice rigor. This Synthesis Lecture aims to fill this gap by providing a concise and accessible introduction to the field.

S082102-3

Classification of Global Phase Portraits of Morris-Lecar Model for Spiking Neuron

B. Raesi[1], M. Hassanpour-Ezatti[2], H. Zahmati[1]

1. Department of Mathematics, Basic Sciences School, Shahed University,
2. Department of Biology, Basic Sciences School, Shahed University

The Morris-Lecar model (ML model) is one of the most famous spiking neuron models. It was introduced in 1981 by Morris and Lecar while they studied on Barnacle giant muscle fiber. Today's, this model is considered as a conductance based model of spiking neurons. Neurons which are able to generate spike or action potential are called spiking neurons. The first mathematical neuronal model (HH model) that describes action potential mechanism, was introduced by Hodgkin and Huxley in 1952. In this paper all possible global phase portraits of the Morris-Lecar
Model with hyperbolic equilibrium points are classified. We use geometrical properties of nullclines and Poincar e-Bendixson theorem to omit impossible phase portraits. Finally some possible phase portraits for Morris-Lecar model are determined numerically.

S082102-4

Mathematical perspectives in the biology and medicine

M Hassanpour-ezatti[1], A. Tarri[2], H.R. Navidi[2], B. Raesi[2]

1. Department of Biology, Basic Sciences School, Shahed University
2. Department of Mathematics, Basic Sciences School, Shahed University

Like other experimental sciences in the first half of the 20th Century, biomedical science at the beginning of the 21st century, has reached the fundamental maturity of theory, empirical tools, and findings, thanks to its relatively safe cellular and molecular foundations. Indeed, the mathematician seeks patterns in number, in space, in science, in computers, and in imagination. Mathematical theories explain the relations among patterns; functions and maps, operators and polymorphism bind one type of pattern to another to yield lasting mathematical structures. Therefore, principal perspective for applications of mathematics in biomedicine could be presenting models for explanation and prediction of natural phenomena that fit the patterns. We will provide the basic principles of interactionism for the reader unfamiliar with the conceptual of the mathematical biology (MB) theory research method. We will discuss why MB is a fitting perspective for use in the study of biological phenomenon, physician and mathematician's perspectives, and MB products. We will conclude with a brief discussion of challenges to researchers maintaining the interaction perspective in biomathematics theory research. We emphasize the potential benefits of integrating biomedical finding into mathematical models for future basic and clinical experimental studies.

S081103-1

Inhibitory roles of microRNAs in glioblastoma

Ehsan Arefian

School of Biology, College of Science, University of Tehran, Tehran, Iran

Annually, 3.5 in 100,000 people are diagnosed with central nervous system (CNS) cancer. The most aggressive form of brain tumor is glioblastoma. This tumor has an extremely poor prognosis with a very low survival rate. Glioblastoma multiform (GBM) is the most malignant and the aggressive type of brain tumor with an average life expectancy of fewer than 15 months. This is mostly due to the highly mutated genome of GBM, which is characterized by the deregulation of many key signaling pathways involving growth, proliferation, survival, and apoptosis. Despite advances in surgery, radiotherapy, chemotherapy, and targeting therapy, the disease remains one of the most lethal malignancies in humans, and new approaches to improvement of the efficacy of anti-glioma treatments are urgently needed. The main cause of malignancy of GBM tumors are that they are within the CNS, leading to physical separation and delivery of the chemotherapy fails. A promising approach to cancer treatment is using microRNAs. MicroRNAs are closely associated with biological processes of tumor cells as the key regulators by recognizing specific mRNA targets, and further mediating posttranscriptional inhibition of tumor related genes. Each miRNA, by influencing many mRNAs, can control a wide range of biological functions including organ morphology, development, cell differentiation and proliferation, apoptosis and many signalling pathways. Several miRNAs are differentially expressed in a variety of malignancies compared to corresponding healthy tissue. Some of these miRNAs have been shown to modulate oncogenes and tumor suppressors, as is the case for GBM. Therefore, miRNAs could hold great potential for the future treatment of this disease.
Keywords: Glioblastoma multiform; gene therapy; microRNAs

S081103-2

miRNAs in diagnosis and treatment of the Parkinson's disease

Azita-Parvaneh Tafreshi

Department of Molecular Medicine, Faculty of Medical Biotechnology, Research Institute of Genetic Engineering and Biotechnology, Tehran, Iran.

Parkinson's disease (PD) is one of the incurable age related neurodegenerative diseases with unknown mechanisms which is partly due to genetic susceptibility and environmental factors involved in the disease. So far, no treatments are available for the disease, but just to decrease the motor symptoms. The ineffectiveness of the therapies is partly because most of the dopaminergic neurons are damaged in the diagnosed patients. In recent years, both small (microRNAs; miRNAs) and long non coding (LncRNAs) are of potential interests to unravel the underlying molecular mechanisms during the onset and progression of PD, to identify new targets and to develop novel strategies for the treatment of the disease. Non coding RNAs are considered as key regulators of gene expression in complex organisms. miRNAs as major regulators of the PD-related genes, have also potentially been considered as biomarkers at preclinical stage of the disease. The abundance of miRNAs in blood samples as well as the exosomes, makes them easily and cheaply extractable and analysable in patients for long periods. High throughput screenings of patients would unravel more candidate miRNAs and develop a simple and fast method for diagnosis and prognosis of PD disease in the near future. miRNA-based approaches have also been considered for the treatment of PD. miRNA-mimics and antago-miRs are used to regulate the miRNA levels inside the cells, which need to be delivered into the brain to target the disease. To transport to the brain and cross the blood brain barrier, exosomes might be considered as natural carriers for miRNA entrance and release into neurons and other brain cells. Altogether, the miRNA-regulated molecular mechanisms and therapeutic based strategies could therefore be translated into clinical approaches for PD as well as other neurodegenerative disorders.
Keywords: Parkinson's disease; micro RNAs; Diagnosis; Treatment

S081103-3

The role of microRNAs in reprogramming of somatic cells into neurons

Maryam Ghasemi-Kasman

Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran; Neuroscience Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

Glial activation is a common pathological process of brain injury and neurodegenerative disorders. Several approaches have been employed to reduce the number of activated astrocytes and microglia in the damaged area. In recent years, different types of somatic cells have been converted to desired cells in the lesion areas both in vitro and in vivo. Interestingly, internal glial cells including astrocytes and NG2 cells could be efficiently converted to the neuroblasts and neurons by overexpression of some transcription factors (TFs) or microRNAs (miRNAs). Notably, some specific subtypes of neurons have achieved by in vivo reprogramming and resulting cells could be successfully integrated into local neuronal circuits. However, direct reprogramming has revolutionized regenerative medicine by using patient's own internal cells, but there are some major obstacles that should be elucidated before application of induced cells in clinical therapies. Here, we aim to highlight the current studies on in vitro and in vivo reprogramming of somatic cells to neurons using miRNAs.
Keywords: Terminally differentiated cells; Neural repair; Direct reprogramming; Neuron

S081103-4

The role of miRNAs in the future of MS Cell Therapy

Fatemeh Kouhkan

Department of Molecular Biology and Genetic Engineering, Stem Cell Technology Research Center, Tehran, Iran

Multiple Sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS), which is often characterized by long-term neurological disabilities. The molecular root of MS is believed to be the hyperactivity of T cells which subsequently results in the autoimmune response against the CNS through the attack to myelin, oligodendrocytes, and neurons. To date, there is no certain cure for this disease, and the majority of approved therapy such asglatiramer acetate, interferon-beta (IFN-β), and mitoxantrone mainly target the immunological aspects of MS. A smart approach, referred to as cell therapy, has been recently introduced that uses stem cells from the patient and differentiates them to oligodendrocyte precursor cells (OPCs) in order to regenerate the damaged tissues. However, this method is not immune from challenges: Growth factors are usually used in order to induce a certain differentiation to stem cells. Growth factors are in general very expensive, and employing them to obtain differentiated cells is usually very time-consuming. These limitations have led scientists to look for a better understanding of the molecular mechanism of the differentiation pathways in order to find alternative approaches to rapidly induce the desired differentiation to stem cells. Regarding this, microRNAs have been reported to be able to get stem cells to differentiate relatively rapidly. microRNAs (miRNA) are potent regulators of molecular processes and have broad implications in all aspects of cell biology including OL differentiation. Over-expression or down-regulation of some miRNAs is sufficient to promote normal OPCs to differentiate into oligodendrocytes, both in vitro and in vivo. This presentation focuses on the role of miRNAs in oligodendrocyte development even in the absence of exogenous growth factors. Thus, providing insights into the molecular mechanisms underlying miRNA pathways, implying a unique role for miRNAs in cell fate determination of OL cells and propose a novel strategy to improve the efficacy of OL differentiation, with potential applications in cell-therapy for neurodegenerative diseases.
Keywords: Multiple sclerosis; NPCs; Oligodendrocytes; miRNAs

S081103-5

MicroRNAs: Key Regulators in synaptic plasticity

Ameneh Rezayof

Neuroscience Lab, Department of Animal Biology, School of Biology, College of Science, University of Tehran, Tehran, Iran

Synaptic plasticity, as a cellular mechanism for encoding and storing information in the different parts of brain, requires gene expression and new protein synthesis. MicroRNAs (miRNAs) are endogenous small non-coding RNAs which through post-transcriptional regulation of the gene silencing influence synaptic plasticity. miRNAs control synaptic transmission in both pre-synaptic and post-synaptic neurons by targeting multiple signaling pathways. It seems that synaptic plasticity relies heavily on proper miRNAs signaling pathways. A large body of evidence suggests the modulatory involvement of specific miRNAs in neuronal synaptogenesis to induce cognitive functions including learning and memory processes. Interestingly, spine formation, dendritic branching and growth was suggested to be regulated by miRNAs which implicated in synaptic efficacy and remodeling, long-term potentiation (LTP) and depression (LTD). Using animal models of hippocampus-dependent memory, the overexpression or inhibition of different kinds of miRNAs has been confirmed in memory consolidation and retrieval. The implication of corticolimbic miRNAs in the regulation of genes expression was also demonstrated in the synthesis of memory proteins including brain derived neurotrophic factor (BDNF) and cyclic AMP response element binding protein (CREB). It should be considered that the induction of synaptic plasticity following the acquisition of new information can change miRNAs abundance to regulate the synthesis of a wide variety of proteins. It seems that different brain regions utilize the different types of miRNAs to regulate their target genes in the cognitive functions. On the other hand, deregulation of the miRNAs was reported in the different neurodegenerative diseases such as Alzheimer's disease. Based on these findings, it can be concluded that miRNAs play a critical role in synaptic plasticity and cognitive functions.
Keywords: MicroRNAs; Synaptic plasticity; memory formation

S084104

Ustokhoddus and epilepsy in Iran

Batool Rahmati[1,2]

1. Neurophysiology Research Center, Shahed University, Tehran, Iran

2. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran

Background and Objective: Antiepileptic effects of Ustokhoddus have been explained in Iranian traditional medicine and it has been supported by scientific documents. But, it should be noticed that Lavandula officinalis and Lavandula dentata and also Nepeta menthoides all are called Ustokhoddus in Iran and sell under this label in the markets. Therefore, it is necessary to study antiepileptic effects of each plant in different animal models.
Materials and Methods: Extracts of mentioned plants were studied on Seizures induced by intraperitoneal (i.p) injection of pentylenetetrazol (PTZ), timed intravenous infusion of PTZ, PTZ kindling, maximal electro shock (MES), and also, Status Epilepticus (SE) induced by pilocarpine and kainic acid.
Results: Lavandula officinalis inhibited seizure induced by kindling, reduced duration and enhanced latency of seizures. On the other hands, Nepeta menthoides did not inhibit seizure factors induced by kindling. Nepeta menthoides not only failed to inhibit seizure but also intensified it in acute administration of PTZ and MES methods, and prevented antiepileptic effects of valproate and phenytoin. On the other hands, Lavandula dentata reduced seizure induced by pilocarpine but intensified kainic acid induced epilepsy. Lavandula dentata enhanced SE onset latencies and reduced total duration of seizures induced by pilocarpine and also reduced % of mortality. While speed up SE onset and also enhanced total duration and occurrence of SE induced by intrahippocampal administration of kainic acid.
Conclusion: We cannot nominate all these species as Ustokhoddus because they exhibited different effects on epilepsy.
Keywords: Epilepsy, Lavandula officinalis, Lavandula dentata, Nepeta menthoides, Ustokhoddus

S084105

The therapeutic potential of interferon beta in Alzheimer's disease

Leila Dargahi*, Sara Chavoshinezhad, Abolhassan Ahmadiani

Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Neuroinflammation, apoptosis and impaired hippocampal neurogenesis are major players in cognitive/memory dysfunctions including Alzheimer's disease (AD). Interferon beta (IFNβ) is a cytokine with anti-inflammatory, anti-apoptotic and neuroprotective effects on the central nervous system which also affects neural progenitor cells even in the adult brain. In this study, we examined the therapeutic potential of intranasal IFNβ in a rat model of AD.
Methods: AD model was induced by lentiviral-mediated overexpression of mutant APP in the hippocampus of adult rats. Intranasal (IN) administration of IFNβ (0.5µg/kg and 1µg/kg doses) was started from day 23 after virus injection and continued every other day to the day 50 of experiments. Memory performance was assessed using Y maze, Morris water maze and passive avoidance tests. The expression levels of APP, Aβ plaque burden, and markers of neuroinflammation, neurogenesis and apoptosis were evaluated as therapeutic outcomes.
Results: Our results showed that IFNβ treatment ameliorates spatial and passive avoidance learning and memory deficits induced by over-expression of mutant human APP gene in the hippocampus. Moreover, IFNβ reduced APP expression, Aβ plaque formation, gliosis and pro-inflammatory responses, apoptosis and ectopic neurogenesis in the CA1 and CA3 regions of the AD rat hippocampus. This is while, IFNβ increased neurogenesis in the dentate gyrus neurogenic niche.
Conclusion: IFNβ can be a promising therapeutic approach to improve cognitive performance in AD-like neurodegenerative context.
Keywords: Intranasal interferon beta; Alzheimer's disease; Learning and memory; Neuroinflammation; Neurogenesis; Apoptosis

S084106

Survey on the effects of diosmin on learning and memory following the use of paraquat herbicide poisoning in the animal model of rat

Mohammad Ali Mirshekar[1,2], Somayeh Miri[1], Ali Shahraki*[3]

1. Department of Physiology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
2. Clinical Immunology Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
3. Department of Biology, Faculty of Sciences, University of Sistan and Baluchestan, Zahedan, Iran;

Objective: Exposure to herbicide paraquat (PQT) is a potential risk factor for cognitive impairment. Many cognitive behaviors, including spatial memory, passive avoidance, balance, and motor performance, may be affected by PQT. This study aimed at determining cognitive behaviors, motor function, and malondialdehyde (MDA) content of the hippocampus after i.p. injection of PQT in rats and evaluating the effects of diosmin (DM) in preventing PQT effects on cognitive behaviors and MDA level in the hippocampus.
Methods: In this study, 32 male Wistar rats were divided randomly into four groups: control, PQT (4 ml/kg), DM (100 mg/kg), and DM+PQT. PQT (4 mg/kg, i.p.) was used three times a day for one week to develop a cognitive deficit model. The rats were pretreated using DM (100 mg/kg) for seven days before PQT administration. Passive avoidance task (PAT), rotarod test, and spatial memory tests were also performed. The MDA level was measured in the hippocampus of different groups to determine lipid peroxidation.
Results: Based on the findings, 100 mg/kg of DM increased the step-through latency, total time in the target quarter, and bar latency in the cognitive deficit model ($P<0.01$ and $P< 0.001$, respectively). The hippocampal concentration of MDA was significantly lower in the DM+PQT group, compared with the PQT group ($P<0.001$).
Conclusion: DM could effectively prevent cognitive deficits (spatial memory and passive avoidance) and motor dysfunctions induced by PQT administration. Also, MDA concentration reduced in the hippocampus induced by i.p. injection of PQT. The present study suggests DM as a suitable compound for memory restoration in cases of PQT poisoning.
Key words: paraquat, memory, learning, latency time

S084107

Environmental enrichment treatment restores spatial learning and memory deficits induced by prenatal noise stress

Sayyed Alireza Talaei*, Fatemeh Aghighi, Mahmoud Salami

Physiology Research Center, Institute for basic sciences, Kashan University of Medical Sciences, Kashan, I.R. Iran.

Background and Objective: Prenatal stress impairs spatial learning and memory of the offspring. On the other hand, it has been demonstrated that environmental enrichment improves spatial learning and memory performances. Effects of environmental enrichment in early postnatal periods on learning and memory deficits induced by prenatal noise stress are unknown.
Materials and Methods: Study was carried out on the male Wistar rats. Offspring were divided into four groups: control group (CON), control enriched animals (EE), stressed animals (PS) and stressed animals introduced to enrichment (SE). Prenatal stress was evoked by noise stress for 2 hrs/day during the last week of the pregnancy. After weaning at postnatal day 22, experimental offspring were given the environmental enrichment or standard housing condition for one month. Spatial learning was evaluated by the Morris water maze (MWM) at 3 consecutive days (3 trials/day). The rats' spatial memory retrieval was also estimated on the last day.
Results: Our results indicated that rats whose mothers received noise stress during pregnancy period spent more time and traveled more distance to find the hidden platform than the controls in the learning stage. Also, they spent less time and passed less distance in the target quadrant, in probe trial. However, spatial learning and memory deficits induced by prenatal noise stress were recovered by environmental enrichment treatment.
Conclusion: We concluded that EE can be successfully employed for recovery spatial learning and memory impairment induced by prenatal stress in rats.
Keywords: Prenatal noise stress, Environmental enrichment, Spatial learning and memory, Rats

S084108

Effect of silymarin on the tolerance to analgesic effects of morphine in mice with skin cancer

Alireza Mohajjel Nayebi1, Hassan Rezazadeh1, Afsaneh Veisee1, Kiarash Fekri1

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Morphine is the most widely used analgesic for management of pain in the patients suffering from cancer. Tolerance to its analgesic effects, is one of the challenges in chronic administration of this opioid. The aim of this study was to investigate the effect of silymarin on the tolerance to analgesic effects of morphine in mice with skin cancer.
Materials and Methods: Forty two cancerous male Albino-Swiss mice were divided into six groups. Two non-cancerous groups were also studied (one as the control group and the other received morphine). To induce skin tumor, a single dose of 7,12-Dimethylbenz[a]anthracene (DMBA) was applied topically. After 7 days, croton oil (1mg in 250µl acetone) was administered twice a week topically for 16 weeks. Pain latency time was assessed using hot-plate test and tumorigenesis was controlled daily for 30 weeks. The normal and cancerous mice were treated with morphine (20 mg/kg/day). The control groups received saline in the same manner. Three groups of mice received silymarin (50, 100, 150 mg/kg) in addition to morphine. The last group received polyethylene glycol as the solvent for silymarin.
Results: We observed that silymarin (100, 150 mg/kg) postponed the tolerance 7 and 12 days respectively.
Conclusion: Our data suggest that silymarin may be able to delay the morphine tolerance in skin-tumor bearing patients. Further clinical studies are required to prove this.
Keywords: Morphine, Pain, Tolerance, Skin Cancer, Silymarin

S084109

Role of Ghrelin in Alzheimer's disease: Metabolomics Studies based on 1H-NMR Technique in a rat model

Fatemeh Goshadrou[1], Afsaneh Arefi Oskouie[1], Maryam Eslami[2]

1. Department of Basic Sciences, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Physiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Background and Objective: Alzheimer's disease (AD) is the most common neurodegenerative disease of the central nervous system. The objective of this work is to investigate metabolic profiling in the serum of animal models of AD compared with healthy controls and then to peruse the role of ghrelin as a therapeutic drug for AD. Nuclear Magnetic Resonance (NMR) technique was used to identify metabolites.
Materials and Methods: Rats were randomly divided into five groups (n=8): control, sham-operated, ghrelin, Alzheimer group and ghrelin treated Alzheimer group. All groups surgically were cannulated in the lateral ventricular and received intracerebroventricular β-amyloid or saline. After a week of recovery, ghrelin or saline was injected for 14 days. Then they were evaluated by passive avoidance learning. Blood sampling was performed at the end of experiments. After centrifuging the collected serum was stored at − 80 °C until applied for NMR analysis
Results: Using multivariate statistical analysis, models were built and indicated. There are significant differences and high predictive power between AD and treated groups, the AUC of ROC curve and Q2 were 0.870 and 0.759, respectively. A biomarker panel consisting of 14 metabolites was identified to discriminate the AD group from the control group. Another panel of 12 serum metabolites was able to differentiate AD patients from treated subjects. Both panels had good agreements with clinical diagnosis.
Conclusion: Analysis of results displayed ghrelin improves memory and cognitive abilities and affected pathways by ghrelin includes oxidative stress, osteoporosis pathways, and vascular risk factors.
Keywords: NMR, Ghrelin, metabolomics, Alzheimer's disease

S084110

In vivo and in vitro evaluation of neuroprotective effect of Doxycycline through downregulation of activity and expression of NMDA/nitric oxide and CREB signaling pathway

Faiza Mumtaz [1,2], Hamed Shafaroodi[1,2],Fardad Pirri[1,2], Muhammad Zubair[3], Ahmad Reza Dehpour[1,2]

1. Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran
3. Key Laboratory of Integrated Management of Crop Diseases and Pests, College of Plant Protection, Nanjing Agriculture University, Nanjing, 210095, PR China

The neuroprotective effects of doxycycline in neurodegenerative diseases such as epilepsy need to explore. This study was designed to examine the underlying mechanisms for anticonvulsant activity and cerebellar protection of doxycycline on pentylenetetrazole (PTZ) induced seizures in mice and glutamate induced toxicity in cerebellar granular cells (CGN). The possible involvement of N-methyl-D-aspartate (NMDA) receptor and nitric oxide (NO), in neuroprotection of doxycycline was studied by using NMDA receptor antagonists and nitric oxide synthase inhibitor both in vivo and in vitro. Results showed that acute administration of doxycycline increased the seizure threshold. Furthermore, coadministration of subeffective doses of MK-801, Ketamine, L-NAME and 7-NI enhanced the anticonvulsant effect of subeffective dose of doxycycline (12.5 mg/kg). In addition, doxycycline significantly reversed the PTZ induced histopathological changes in mice brain. In cerebellar granule neurons (CGNs) culture studies on glutamate induced excite-toxicity were confirmed via cell viability studies. The nitrite assay and qRT-PCR had been carried out to find the role of NMDA /NO and CREB signaling in doxycycline neuroprotection. The level of NO was significantly reduced in coadministration of doxycycline with both PTZ and glutamate. Moreover, glutamate mediated mRNA expression of NR2A, NR2B, nNOS and cAMP response element-binding protein (CREB) genes in CGN were significantly attenuated by doxycycline. In conclusion, the involvement of NMDA receptors/NO and CREB pathway in the effects of doxycycline on PTZ induced seizure and cerebellar neurons have been shown. Inhibition of NMDA/NO and CREB signaling pathway may be reconsidered as a pharmacological mechanism for neuroprotection of doxycycline.
Keywords: Doxycycline; seizure; Pentylenetetrazole; Nitric oxide (NO), N-methyl-D-aspartate (NMDA), cAMP response element-binding protein (CREB), cerebellum

S084111

Adolescent morphine exposure alters the neuronal responses of lateral paragigantocellularis nucleus to naloxone in adult morphine dependent rats

Sara Sabuee[1], Hossein Azizi[1], S. Mohammad Ahmadi-soleimani[2], Saeed Semnanian[1]

1. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Neuroscience Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran

Background and Objective: Adolescence is a critical period during which environmental factors can affect the brain development and life-long behavioral manifestations. Recent evidence indicates an intense trend toward drug abuse in adolescents. Cellular mechanisms underlying persistent neurobehavioral effects of opiate exposure during this stage are remained largely unexplored. Lateral paragigantocellularis (LPGi) nucleus plays a pivotal role in opiate dependence. The present study examined the effect of adolescent morphine exposure on LPGi neuronal responses to naloxone in morphine dependent rats.
Method: Adolescent male Wistar rats (30 days old) received increasing doses of morphine (2.5 to 25 mg/kg, s.c.) every 12 h, for 10 days. Control rats received saline with the same protocol. Then, during adulthood (65 days old), animals were rendered dependent on morphine. Extracellular single-unit recording was used for investigating LPGi neuronal responses to naloxone in morphine-treated rats undergone adolescent morphine exposure.
Results: Results showed that adolescent morphine treatment significantly increases both the baseline activity and the number of LPGi excitatory responses to naloxone. However, the extent of excitatory responses was reduced in adult morphine-treated animals. It also changed the histogram pattern of inter-spike intervals in recorded signals.
Conclusion: Adolescence is a sensitive developmental stage during which chronic morphine treatment causes long-lasting neuro-adaptations in LPGi region and this may change future susceptibility for drug addiction.
Keywords: Adolescence; Morphine; Extracellular single unit recording; LPGi nucleus; Naloxone

S084112

Estradiol affects on microglia reactivity and functional recovery following central pain syndrome

Naseri Kobra[1, 2], Jorjani Masoumeh[2]

1. Birjand University of Medical Sciences, Birjand, Iran
2. Shahid Beheshti University of Medical Sciences, Neuroscience Research Center, Tehran, Iran

Background and Objective: Central pain syndrome (CPS) is a debilitating state that affects many patients with a primary lesion or dysfunction in the CNS. CPS as one of the consequences of spinal cord injury has many patho-physiological aspects that are not well documented. Since microglial cells have an important role in various types of pain, the interaction of them in pain processing on CPS condition could be helpful. In addition, estrogen is a multi-active steroid that has shown anti-inflammatory and neuroprotective effects, so it seems that this agent is effective in the treatment of CPS.
Materials and Methods: Male rats received a laminectomy at T8 and T9 and then unilateral electrolytic lesion centred on the spinothalamic tract (STT). Thermal pain, mechanical allodynia and locomotor function were assessed in days 0 and 3, 7, 14, 21 and, 28 post injury by tail flick, von Frey filament and open field tests respectively. Besides behavioral analysis, the effects of STT lesion on microglial cells expressing Iba1 were investigated by immunohistochemistry technique and western blotting.
Results: Data showed STT lesion significantly increased thermal pain at day 3 in comparison with sham group ($p<0.05$). Contra- and ipsi-lateral allodynia appeared at days 14 after spinal cord injury ($p<0.05$). Additionally unilateral electrolytic spinal lesion attenuated locomotor function of injured animals 7 days after surgery ($p<0.05$). In histological assessments, at site of lesion, microglias were substantially activated at day 3 and 7 post surgery. Alteration in Iba1 band density in western blot analysis were parallel to immunohistochemistry data and verified each other that microglia activation was important in early stage of pain progression. Surprisingly estradiol attenuated microglial level at both days 3 and 7 following injury.
Conclusion: STT lesion induced neuropathic pain expression 14 days after injury and data suggested estradiol could exert effective role via microglia in pain alteration at the first week following unilateral electrolytic spinal lesion.
Keywords: Central pain syndrome, Neuropathic pain, Microglia, Glia, Iba1 (ionized calcium binding adaptor molecule 1)

S084113

Auraptene mitigates migration, invasion and metastatic behavior of human malignant glioblastoma invitro

Mohammad Jalili-Nik[1], Arash Soltani[1], Seyed Mohamad Sadegh Modaresi[2], Mohammad Soukhtanloo[1], Elmira Mohtashami[3], Seyed Hadi Mousavi[4], Azar Hosseini[3], Hamid Mollazadeh[5], Amir R. Afshari[3,4,5] *

1. Department of Clinical Biochemistry, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. College of Pharmacy, University of Rhode Island, Kingston, USA
3. Pharmacological Research Center of Medicinal Plants, Mashhad University of Medical Sciences, Mashhad, Iran
4. Medical Toxicology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
5. Department of Physiology and Pharmacology, Faculty of Medicine, North Khorasan University of Medical Sciences, Bojnurd, Iran

Auraptene is a natural geranyloxycoumarin from Citrus species, which has been reported for its anti-invasion potential and anticancer activity in human cancer cells. Glioblastoma multiforme (GBM) demonstrates the well-known type of malignant brain tumor because of its aggressive growth behavior and exceedingly intrusive nature. We here investigated the anti-metastatic impacts of auraptene and its potential and probable mechanisms of action in GBM cells (U87) for the first time. Under sub-lethal concentrations (12.5 and 25 µg/mL), auraptene significantly mitigated cellular migration and invasion of U87 cells that were evaluated by scratch wound healing and Transwell assays, respectively. Gelatin zymography evaluation also exhibited that auraptene inhibits significantly MMP-2 and MMP-9 enzymatic activities in GBM cells 24 and 48 hours after treatment.
Moreover, a down-regulation in the expression of MMP-2, MMP-9, and VCAM-1 genes was observed. Western blot analysis affirmed that auraptene repressed crucial metastasis-related proteins, such as JNK, p-JNK, phospho-mTOR, and mTOR protein levels and indicated an up-regulation in NF-κB p65 protein expression. In agreement with our experimental results, molecular docking studies revealed that auraptene possessed high affinity toward MMP-2/9 and JNK1/2/3. Based on these findings, auraptene might be a promising potential novel candidate as an anti-metastatic agent of human malignant GBM in the future.
Keywords: Glioblastoma multiforme, Auraptene, Invasion, Metastasis, mTOR

S085114

Interaction between Hyperglycemia and Autophagy in Human Umbilical Vein Endothelial Cells

Alireza Garjani[1], Aysa Rezabakhsh[2], Reza Rahbarghazi[2], Hassan Malekinejad[3], Nasrin Maleki Dizaji[1], Hamid Soraya[3]

1. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran
2. Stem Cell Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
3. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran

Background: Many vascular injuries induced by diabetes, such as inefficient or aberrant neoangiogenesis, are caused by increased gloucose blood level. Autophagy represents a homeostatic cellular mechanism for the turnover of unfolds proteins and damaged organelles through a lysosome-dependent degradation manner. To better address whether stimulation or inhibition of autophagy could blunt or exacerbate cytotoxic effect of high glucose condition, two well-known autophagy modulators, namely rapamycin and hydroxychloroquine, were used in combination with 30 mM glucose condition on endothelial cells over course of 72 hour.
Materials and Methods: Cells viability were measured by MTT assay. We used Griess method and TBARS assay to monitor changes in the levels of nitric oxide and malondialdehyde followed by flow cytometric analysis of ROS using DCFDA. To investigate the role of rapamycin and hydroxychloroquin on migration and in vitro angiogenic properties, we used routine scratch test and tubulogenesis assay, respectively. The expression of autophagic modulators LC3, Becline-1 and P62 was measured by using western blotting.
Results: Our data showed that rapamycin increased cell survival in high glucose condition and hydroxychloroquine diminished it. Of interest, rapamycin significantly decreased the total levels of oxidative stress markers in both sets of environments. In contrast to hydroxychloroquin the stimulatory effects on cell migration and tubulogenesis were observed in all groups after exposure to rapamycin. Furthermore, autophagy flux was induced by rapamycin which blocked in presence of 3-Methyladenine.
Conclusion: Together, rapamycin could protect endothelial cells from damages caused by high glucose condition. This effect was mediated by autophagy-dependent manner.
Keywords: Autophagy, Rapamycin, High glucose, 3-Methyladenine, Endothelial Cells

S085115

Dose-dependent effects of long-term administration of hydrogen sulfide on myocardial ischemia-reperfusion injury in male Wistar rats

Sajad Jeddi[1], Sevda Gheibi[1,2], Khosrow Kashfi[3], Mattias Carlström[4], Asghar Ghasemi[1]

1. Endocrine Physiology Research Center, Research institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Maternal and Childhood Obesity Research Center, Urmia University of Medical Sciences, Urmia, Iran
3. Department of Molecular, Cellular and Biomedical Sciences, Sophie Davis School of Biomedical Education, City University of New York School of Medicine, New York, USA
4. Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

Background and Objective: Decreased circulating levels of hydrogen sulfide (H2S) is associated with higher mortality following myocardial ischemia. This study aimed at determining the long-term dose-dependent effects of sodium hydrosulfide (NaSH) on myocardial ischemia-reperfusion (IR) injury in male rats. Materials and Methods: Rats were divided into control and intervention groups. The intervention groups were intraperitoneally injected on a daily basis for 9 weeks with NaHS (0.28, 0.56, 1.6, 2.8, and 5.6 mg/kg); the control group received an equal volume of normal saline. At the end of the study, heart from all rats were isolated and hemodynamic parameters in LV were recorded. Heart levels of total antioxidant capacity (TAC), catalase (CAT) activity as well as infarct size of the hearts were measured at the end of study and the ratio of reduced to oxidized glutathione (GSH/GSSG) was calculated. Results: In heart tissue following ischemia, NaSH had the following effects: (a) at low doses (up to 1.6 mg/kg), it increased recoveries of hemodynamic parameters, decreased infarct size, and increased TAC, CAT activity, and GSH/GSSG ratio; (b) at high doses (2.8 and 5.6 mg/kg), it decreased recoveries of hemodynamic parameters, increased infarct size, and decreased TAC, CAT activity, and GSH/GSSG ratio. Conclusions: NaSH exhibited biphasic effects; at relatively low concentrations it had a protective effect against myocardial IR injury; whereas at higher concentrations, it exacerbated myocardial IR injury. These effects were partly due to increased and decreased in the anti-oxidant power of heart tissue following administration of low- and high-doses of NaHS, respectively.
Keywords: Hydrogen sulfide; Infarct size; Ischemia-reperfusion injury

S085116

The latest uncovered molecular pathways in the pathophysiology of atherosclerosis and therapeutic effects of Cynodon dactylon hydroalcoholic extract on experimentally-induced atherosclerosis in rats

Pashaie B[1], Hobbenaghi R[2*], Malekinejad H

1. Department of pathology, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran
2. Department of Pharmacology & Toxicology, School of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran

Backgrounds and aims: Atherosclerosis is characterized by inflammatory reactions, which results in increased generation of reactive oxygen species and ultimately endothelial dysfunction. Endothelium-dependent vasodilation, as a direct result of imbalance between the nitric oxide and reactive oxygen species production, is an important character of atherosclerosis-related endothelial dysfunction.
Methods: In this study in addition of highlighting some new molecular pathways of atherosclerosis pathophysiology including the role of oxidative/nitrosative stress imbalance, any alterations in cardiac-related CK-MB and LDH activities were analyzed. The expression of TLR-4 as one of the key player in innate immunity and inflammation was determined by means of q-PCR technique. Moreover, the production of proatherosclerotic metabolite, trimethylamine-N-oxide (TMAO) was also measured. The second part of study devoted to show any potential protective effects of Cynodon dactylon hydroalcoholic extract on experimentally-induced atherosclerosis damages in rats.
Results: the up-regulation of TLR-4 expression and elevation of TMAO production in the atherosclerotic tissues were highlighted. We found a remarkable protective effects of used extract on altered oxidative stressed status, histopathological injuries, up-regulated TLR-4 expression and elevated TMAO production.
Conclusions: Our data suggest novel therapeutic targets in atherosclerosis therapy and a marked and positive beneficial effects of Cynodon dactylon hydroalcoholic extract on experimentally-induced atherosclerosis in rodent model and these results may direct the further research to phase II and III medical trials.

S085117

Gallic acid improves cardiovascular disorders by MicroRNA-24 and 126 and antioxidant effects in diabetes

Fatemeh Ramezani-Aliakbari[1], Mohammad Badavi [1,2,3*], Mahin Dianat [1,2], Seyed Ali Mard [1,2], Akram Ahangarpour [1,2,4]

1. Dept. of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahwaz Iran
2. Ahvaz Physiology Research center, Ahvaz Jundishapur University of Medical Sciences, Ahwaz Iran
3. Atherosclerosis Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahwaz Iran
4. Diabetes Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahwaz, Iran

Background and Objective: Endothelial dysfunction and diabetic cardiomyopathy are critical complications of diabetes. Gallic acid (GA) plays a significant role in cardiovascular disorders result from diabetes. Increased miR-24, miR-126 plasma associated with endothelial dysfunction. This study was designed to assess the effects of GA on miR-24, miR-126 plasma and cardiomyopathy in the diabetic rats. Materials and Methods: Adult male Sprague-Dawley rats were divided into three groups (n=8): control (C), diabetic (D) and diabetic group treated with GA (D+G, 25 mg/kg, by gavage) for eight weeks. The blood glucose, body weight, lipid profile, blood pressure, miR-24 and miR-126 plasma, electrocardiographic and hemodynamic parameters, antioxidant and inflammatory biomarkers were measured. Results: The levels of miR-24, QRS complex voltage, miR-126, heart rate, body weight, high-density lipoprotein cholesterol (HDL-c), total anti-oxidant capacity (TAC), cardiac contractility (±dp/dt), and systolic blood pressure significantly reduced and blood glucose, total cholesterol (TC), triglycerides (TG), very low-density lipoprotein cholesterol (VLDL-c), malondialdehyde (MDA), interleukin-6 (IL-6), QT intervals, tumor necrosis factor-alpha (TNF-α) and low-density lipoprotein cholesterol (LDL-c) significantly elevated among the diabetic rats compared with the control group. However, GA restored body weight, blood pressure, TC, TG, VLDL-c, TNF-α, heart rate, QT intervals, miR-126, blood glucose, HDL-c, MDA, TAC, QRS complex voltage, miR-24, ±dp/dt and IL-6 among the GA treated rats compared with the diabetic group. Conclusion: The results propose that GA improves endothelial dysfunction and cardiomyopathy result from diabetes. These protective effects is probably mediated via increasing miR-24 and miR-126 plasma levels.

Key words: Diabetes, Endothelium, MicroRNA, Gallic acid, cardiomyopathy

S085118

HTLV-1 infection affected lipid profile, CCR1, CCR2, CXCR2, eNOS, iNOS genes expression and oxidative stress in aorta of HTLV-1 infected BALB/c male mice

Mahdiyeh Hedayati Moghadam[1], S.A Rahim Rezaee [2,3], Nema Mohamadian Roshan [4], Mohsen Ghoryani [5], Maryam Paseban [2], Saeed Niazmand [2]

1. Department of Physiology, School of Medicine, Jiroft University of Medical Sciences, Jiroft, Iran
2. Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3. Immunology Research Center, Inflammation and Inflammatory Diseases Division, Mashhad University of Medical Sciences, Mashhad, Iran
4. Department of Pathology, Ghaem Hospital, Mashhad University of Medical Sciences
5. Immunology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and objective: In the present study, the eNOS, iNOS, CCR1, CCR2, CXCR2 genes expression and oxidative stress were evaluated in the aorta of HTLV-1-infected male BALB/c mice.
Material and Methods: Twenty eight male BALB/c mice were divided into two groups: control and HTLV-1-infected. The mice in HTLV-1-infected group were inoculated with HTLV-1-infected cells. Two months later mice were deeply anaesthetized and aorta, spleen and mesenteric lymph nodes of the mice were removed. The extracted DNA of splenocytes, mesenteric lymph nodes and PBMCs obtained for the quantification of HTLV-1 proviral load by quantitative real time PCR, TaqMan method. Moreover, the oxidative stress markers (MDA and total thiol levels, SOD and CAT activity), as well as the eNOS, iNOS, CCR1, CCR2, CXCR2 genes expression were assessed in the homogenate aortic tissues.
Results: Real time analysis confirmed the mice who injected with MT-2 were infected to HTLV-1. Triglyceride plasma and aorta MDA levels in HTLV-1 infected group were significantly higher than control group while, the aorta total thiol levels and the activity of SOD and CAT were significantly lower compared to the control group. The mRNA expression of CCR2 and CXCR2 in the HTLV-1 infected group was elevated while eNOS expression reduced in homogenate aortic tissues. Also, in aorta tissue, the iNOS gene expression in both groups was not detectable.
Conclusion: The HTLV-1 infection can induce oxidative stress, increase of plasma triglyceride, CCR2, CXCR2 genes expression and decrease of eNOS expression in mice aortic tissue. These changes may promote atherosclerosis.
Keywords: HTLV-1, Oxidative stress, CCR2, CXCR2, eNOS, Aorta

S085119

Cardioprotective Effect of Ethanolic Leaf Extract of Melissa Officinalis L Against Regional Ischemia-Induced Arrhythmia and Heart Injury after Five Days of Reperfusion in Rats

Mehrnoosh Sedighi[1] , ,Hamed Seidi[2], Afshin Nazari[3*]

1. Cardiovascular Research Center, Shahid Rahimi Hospital, Lorestan University of Medical Sciences, Khoramabad, Iran.
2. Pharmacy Student Of Faculaty of pharmacy, Lorestan University of Medical Sciences,Khoramabad,Iran
3. Cardiovascular Research Center, Shahid Rahimi Hospital, Lorestan University of Medical Sciences, Khoramabad, Iran.

Background and Objective: We investigated the role of M. officinalis extract (MOE) against ischemia-induced arrhythmia and heart injury after five days of reperfusion in an in-vivo rat model of regional heart ischemia.
Materials and Methods: The leaf extract of MOE was standardized through HPLC analysis. Adult male rats (n = 32) were subjected to 30 min of ischemia by and 5 days of reperfusion. The rats (n=8) were randomized to receive vehicle or MOE as follows: group I served as saline control with ischemia, groups II, III and IV received MOE- (25, 50 and 100 mg/kg), by oral gavage daily for 14 days .
Results: Administration of MOE significantly improved ischemia/reperfusion induced myocardial dysfunction by reduction of infarct size, also, arrhythmias compared with that of the control group. Stabilized ST segment changes and QTc shortening increased the R and T wave amplitudes and the heart rate during ischemia. The extract also caused significant elevations in serum superoxide dismutase (SOD) activity as well as a significant decrease troponin I (CTnI), lactate dehydrogenase (LDH), and malondialdehyde (MDA) levels, 5 days after reperfusion. MOE-100mg/kg was the effective dose. Cinamic acid (21.81 ± 1.26 mg/gr) was the main phenolic compound of plant sample.
The results indicate that MOE has antioxidant and cardio-protective effects against ischemia-induced arrhythmias and ischemia-reperfusion induced injury as was reflected by reduction of infarct size and cardiac injury biomarkers.
Conclution: MOE in the treatment of heart ischemia- reperfusion disorders and even developing new anti-arrhythmias drugs after further investigations.
Keywords: Melissa officinalis; Ischemia; Reperfusion injury; Heart; Rat.

S085120

Exploration of saliva proteomics as a potent non-invasive and painless gateway to study neurological diseases

Arun Pratap Sikarwar[1], Krishna Gopal Pathak[2] and Pooja Chaudhary[3]

Assistant Professor, Department of Zoology, Faculty of Science, Dayalbagh Educational Institute (Deemed University), Agra, India

Since long ago, the blood has been a major choice for diagnosis and prognosis of most of human diseases in medical biology. The concept of salivary or oral diagnostics has come up in the last decade as a potent non-invasive method. The salivary constituents become detectably altered in response to certain disease states. The salivary biomarkers not only arise in correlation with oral-pathies but also those of distal tissues and especially to the ailments associated with the human brain. The proximity of the brain, the most important organ of our body, greatly reflects in the human salivary fluid. The family of neurological disorders affects brain health and includes neurodegenerative, neurodevelopmental and psychiatric problems. The advances in detection and quantification methods in genomics, proteomics, have led the saliva as a non-invasive biomarker. In today's busy world, stress and depression have become part and parcel of millions of people in the world leading to rampant increase in various neurological disorders. There is an urgent need for the development of an easily accessible, non-invasive and cost-effective diagnostic test that aims at early identification of neurological diseases. Human saliva contains a majority of brain associated proteins that can be informative for disease detection and brain health surveillance. Comprehensive analysis and identification of the proteomic content of saliva (salivaomics) is a potent first step towards the discovery of salivary protein biomarker for brain disease detection. Our lab is working towards studying quantitative saliva proteomics to develop biomarker signatures from human saliva for detection of schizophrenia disease.
Key words: Saliva, Proteomics, Brain, Neurological Disorders, Schizophrenia, Proteins

S085121

Pharmacological effects of targeted treatment of human metastatic breast cancer cells (SKBR3) through Docetaxel and cMET siRNA

Naime Majidi Zolbanin [1], Reza Jafari [2], Jafar Majidi [3], Fatemeh Atyabi [5,6], Alireza Mohajjel Nayebi* [7,8]

1. Department of Pharmacology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran
2. Department of Immunology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Department of Immunology, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.
4. Department of Pharmaceutics, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
5. Nanotechnology Research Centre, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
6. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
7. Pharmacology and Toxicology Department, School of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Targeted treatment of breast cancer via combination of chemotherapeutic drugs and siRNA has become attractive in recent researches. In this study we were aimed to evaluate mucin1 aptamer-conjugated chitosan nanoparticles containing docetaxel and cMET siRNA on SKBR3 cells.
Materials and Methods: Nano-drugs were characterized by transmission electron microscope and Zetasizer. siRNA entrapment onto nanoparticles and conjugation of mucin1 aptamer to nanoparticles were evaluated via separate electrophoresis. Cellular uptake of the targeted nanoparticles was evaluated through GFP-plasmid expression in mucin1+ SKBR3 vs. mucin1- CHO cells. Protein expression, cell viability and gene expression were assessed by Western Blotting, MTT assay, and Quantitative Real Time-PCR, respectively.
Results: Characterization of nano-drugs represented the ideal size and zeta potential. Different gel electrophoresis affirmed the conjugation of aptamers to nanoparticles and entrapment of siRNA onto nanoparticles. Cellular uptake of aptamer-conjugated nanoparticles vs. control was increased in GFP expression assay. Silencing of cMET gene was confirmed by Western Blotting. The impact of combination targeted therapy vs. control on cell viability was observed significantly. Significant decreased expression of the studied genes involving in tumorigenicity, metastasis, invasion, and angiogenesis (STAT3, IL8, MMP2, MMP9, and VEGF) was shown by targeted combination treatment vs. control.
Conclusion: The mucin1 aptamer-conjugated chitosan nanoparticles, containing docetaxel and cMET siRNA, is suggested for treatment of mucin1+ metastatic breast cancer cells. However, further studies should be conducted on animal models.
Keywords: Aptamer, Chitosan, cMET siRNA, Docetaxel, Metastatic breast cancer

S085122

Metformin enhances the sensitivity of multidrug resistant ovarian cancer cells to cisplatin

Vahid Shafiei-Irannejad[1], Arash Alizadeh[2], Bahman Yousefi[3], Nosratollah Zarghami[3], Nasser Samadi[3]

1. Cellular and Molecular Research Center, Cellular and Molecular Medicine Institute, Urmia University of Medical Sciences, Urmia, Iran.
2. Department of Pharmacology and Toxicology, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.
3. Department of Clinical Biochemistry and Laboratory Medicine, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Resistance to chemotherapy which is known as multidrug resistance (MDR) is the main obstacle against successful cancer chemotherapy. To overcome MDR, we investigated the activity and possible mechanism of the antidiabetic drug, metformin, in human cisplatin resistant ovarian cancer (A2780/R) cells.
Materials and Methods: The effect of metformin on the cytotoxicity of cisplatin was evaluated by MTT assay. Flow cytometeric analysis of apoptosis after staining with annexin V/PI was performed to evaluate the effects of metformin on cisplatin-induced apoptosis. MRP-2 mRNA/protein expression levels were determined using qRT-PCR and western blot analysis, respectively. Intracellular ATP content was determined using ATP assay kit. Data were analyzed using GraphPad Prism.
Results: Metformin considerably enhanced the cytotoxicity and apoptotic effect of cisplatin in A2780/R cells. There was no significant difference in MRP-2 mRNA/protein expression levels between sensitive and resistant ovarian cancer cells, indicating that MRP-2 is not involved in cisplatin resistance of A2780/R cells. Intracellular ATP content was also decreased after treatment with metformin in a dose dependent manner.
Conclusion: Our findings indicated that metformin could reverse MDR in cisplatin resistant ovarian cancer cells. Therefore, metformin can be suggested as a potent adjuvant for ovarian cancer chemotherapy.
Keywords: metformin, ovarian cancer, multidrug resistance, cisplatin

S085123

Gamma-Aminobutyric acid plus magnesium sulfate improves insulin sensitivity in type 2 diabetic rat model

Shahla Sohrabipour[1], Nepton Soltani[2], Mohammad Reza Sharifi [2], Mohammadreza Sharifi[3], Fateme Saljoughi[4], Ardeshir Talebi[5]

1. Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2. Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
3. Department of Genetics and Molecular Biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
4. Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
5. Department of Clinical Pathology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Background and Objective: combination of antidiabetic agents with complementary mechanisms arises in daily clinical practice. Gamma-aminobutyric acid (GABA) plus magnesium sulfate (Mg) have an important role in diabetic patients. Materials and Methods: Forty Wistar rats were divided into four groups: NDC was fed the normal diet, CD received a high-fat diet with streptozotocin, GABA + Mg animals received GABA and Mg, and Ins-CD group was treated with insulin. Body weight, abdominal fat, blood glucose, intraperitoneal glucose tolerance test (IPGTT), insulin tolerance test (ITT), the volume of urine and water drinking and also the food intake assessment were performed. The hyperinsulinemic euglycemic clamp was done for assessing insulin resistance. Glycated hemoglobin (HbA1c), plasma insulin and glucagon, glucagon receptor, Glucose 6 phosphatase, Phosphoenolpyruvate carboxykinase genes expression and Glucose transporter 4 (GLUT4) genes expression and protein translocation were evaluated. Results: GABA plus Mg or insulin therapy improved blood glucose, insulin level, IPGTT, ITT, gluconeogenesis pathway, glucagon receptor, body weight and body fat in diabetic rats. GLUT4 gene and protein expression increased. Glucose infusion rate in GABA plus Mg therapy was more than the insulin group. Conclusion: GABA + Mg could improve insulin resistance via rising GLUT4 and also decreasing the gluconeogenesis pathway and glucagon receptor gene expression.
Key words: Diabetes, GABA, Insulin resistance, Hyperinsulinemic euglycemic clamp, Gluconeogenesis, glucagon receptor

S086124

Evaluation of ischemia reperfusion-induced acute kidney injury by salivary assessment of renal function, apoptosis, oxidative stress and inflammation in male rats

Arash Abdi[1], Mehri Kadkhodaee[1], Behjat Seifi[1], Farzaneh Kianian[1], Sedigheh Shams[3], Enayatollah Bakshi[2], Gorbangol Ashabi[1], Keivan Lorian[1], Mina Ranjbaran[1]

1. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Biostatistics, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
3. Pediatrics Centre of Excellence, Department of Pathology, Children's Medical Centre, Tehran University of Medical Sciences, Tehran, Iran

Background: Renal ischemia reperfusion (IR) is the most important cause of acute kidney injury (AKI). Several studies have demonstrated the validity of saliva in the diagnosis of various diseases. Since blood collection causes stress and anxiety in many patients especially in children, the aim of this study was to evaluate the validity of salivary sample measurements comparing to plasma samples in AKI rats.
Method and materials: To establish a model of renal IR, both renal arteries were occluded for 55 min and then declamped to allow reperfusion for 3, 6 and 24 hours. Twenty-four rats were randomly assigned to four experimental groups:1) control 2) 3h IR 3) 6h IR and 4) 24h IR. Control group underwent laparotomy without cross clamping of renal pedicles. After reperfusion, rats received intraperitoneal injections of pilocarpine 1mg/kg to collect saliva. Blood samples were also collected. Renal functional parameters (creatinine, urea, uric acid), oxidant/antioxidant ratio, MDA levels, nitrite/nitrate ratio, Bax/Bcl2 ratio and corticosterone levels were measured in both plasma and salivary samples.
Results: Correlation was observed in renal functional parameters (creatinine, urea, uric acid), oxidant/antioxidant ratio, MDA levels, nitrite/nitrate ratio, Bax/Bcl2 ratio and corticosterone levels between saliva and plasma.
Conclusion: This study showed that correlation exist between plasma and saliva for different parameters in IR-induced acute kidney injury in male rats. Measurement of these parameters especially renal functional parameters in saliva may be reliable diagnostic tests for patients with AKI.
Key words: Saliva, Acute kidney injury, Ischemia-reperfusion

S086125

Crocin Ameliorates IL-18, p53 and Nox-4 Expression Levels and Prevent Diabetic Nephropathy

Habib Yaribeygi, MT. Mohammadi

The aim of this study was to evaluate possible effects of Crocin on improving main underlying mechanisms of diabetic nephropathy as oxidative damage, inflammation and apoptosis. Male Wistar rats were randomly divided into four separate groups as normal, normal treated, diabetic, and diabetic treated. Diabetes was induced by a single dose of streptozotocin (40mg/kg/iv). Treated groups received Crocin (40mg/kg, intraperitoneal) for 8 weeks. At the end of the8thweekof the study, all rats were sacrificed and urine, blood and tissue were collected. Levels of urea, uric acid, creatinine and glucose were determined collected sera, and proteinuria was measured in urine samples. Moreover, the contents of malondialdehyde, nitrate, and glutathione as well as catalase and superoxide dismutase enzymes activities were measured. The expression of NOX-4, IL-18, and p53 at both mRNA and protein levels were also assessed. Hyperglycemia significantly increased proteinuria in diabetic rats. Also, depressed antioxidant defense system potency, but increased NOX-4 expression and free radicals production resulting in oxidative stress, were observed. Moreover, expressions of IL-18 (as a marker of inflammation) and p53 (as a marker of apoptosis) were increased. These outcomes were accompanied by enhanced histological damages and renal failure but, treatment with Crocin improved these deteriorations, and ameliorated renal function. It potentiated renal cells antioxidant defense system and declined inflammation. Also, Crocin lowered apoptosis and improved histological damages in renal cells. Oxidative stress, inflammation and apoptosis are considered three main mechanisms underlying diabetic nephropathy. Treatment with Crocin prevented these deleterious effects and improved renal function under diabetic conditions.
Key words: Diabetic Nephropathy, Crocin, IL-18, NOX-4, p53

S086126

Remote limb ischemic preconditioning accelerates recovery of renal function following ischemia-reperfusion injury: the possible role of lactate as a mediator

Zahra Akbari[1], Hossein Fatemikia[1], Zeynab karimi[2], Kaveh Tanha[3], Mohammad Reza Farzaneh[4], Majid Asadi[3], Khalil Pourkhalili[1]

1. Department of Physiology, Faculty of Medicine, Bushehr University of Medical Sciences, Iran.
2. Nephro-Urology Research Center, Shiraz University of Medical Sciences, Iran.
3. Persian Gulf Nuclear Medicine Research Center, Bushehr University of Medical Sciences, Iran.
4. Department of Pathology, Faculty of Medicine, Bushehr University of Medical Sciences, Iran.

Background and Objective: Despite numerous studies showing protective effects of remote ischemic preconditioning (RIPC), the exact nature of the circulating mediators which carries the preconditioning signal from the remote site to the target organ have not been identified yet. Here we aimed to determine if RIPC alone increase lactate production in the circulation; and if exogenous administration of lactate could induce renal protection against ischemia reperfusion (IR) injury.
Materials and methods: Twenty-eight male Sprague Dawley rats were randomly divided into four groups: Sham (laparotomy without ischemia and reperfusion), IR group (Laparotomy with 45 min bilateral renal ischemia and 24 h reperfusion), RIPC+IR group (three cycles of RIPC cycles applied to the both hind limbs before laparotomy and then 45 min bilateral kidney ischemia and 24 h reperfusion) and Lactate+IR (750 mg/kg Sodium L-lactate before renal IR). Kidney function was assessed by quantitative evaluation of 99mTc-DMSA renal scan using a dual-head small-animal SPECT imaging system. Serum and urine sodium (Na+), potassium (K+), creatinine (Cr) and blood urea nitrogen (BUN) was measured and glomerular filtration rate (GFR) was estimated by creatinine clearance.
Results: Application of RIPC markedly increased lactate level in preconditioned limbs and significantly improved 99mTc-DMSA renal uptake, decreased serum K+, Cr and BUN levels and increased creatinine clearance as an index of glomerular filtration rate (GFR). Administration of lactate increased 99mTc-DMSA renal uptake and improved renal function parameters.
Conclusions: The results of this study indicate that lactate can be considered as a possible signal in the mediation of RIPC effects.
Keywords: Remote Ischemic Preconditioning, Renal Ischemia-reperfusion, Lactate

S086127

Mas receptor antagonist (A799) alters the renal hemodynamics responses to angiotensin II administration after renal moderate ischemia/reperfusion in rats: gender related differences

Maryam Maleki[1], Mehdi Nematbakhsh[2]

1. Department of Physiology, Ilam University of Medical Sciences, Ilam, I.R. Iran
2. Water and Electrolytes Research Center, Isfahan University of Medical Sciences, Isfahan, I.R. Iran

Background and Objective:Moderate renal ischemia/reperfusion (I/R) injury is one of the major causes of kidney failure. We examined the role of Mas receptor (MasR) antagonist (A779) alone and combined with angiotensin II (Ang II) type 2 receptor (AT2R) antagonist (PD123319) on renal hemodynamic responses to Ang II after moderate I/R in male and female rats. Materials and Methods: Anaesthetized Wistar rats underwent 30 min partial ischemia by reduction of renal perfusion pressure (RPP) and subjected to block vasodepressor receptors followed by Ang II (100 and 300 ng/kg/min) infusion. Mean arterial pressure (MAP), renal blood flow (RBF), and renal vascular resistance (RVR) responses were assessed during graded Ang II infusion at controlled RPP. Results: Thirty min post reperfusion, the Ang II infusion reduced RBF and increased RVR in a dose-related fashion ($P < 0.05$). However, A779 alone or A779 plus PD123319 infusion increased the RBF and RVR responses to Ang II infusion significantly ($P < 0.05$) in female but not in the male rats. MasR antagonist altered the RBF and RVR responses to Ang II infusion in female, and these responses were not altered statistically in dual blockade of MasR and AT2R. Conclusion:These findings suggest the important role of Mas receptor in renal vascular response to Ang II in female rats after moderate I/R.
Keywords: Angiotensin II, Ischemia/reperfusion, Mas receptor, Renal blood flow, Renal vascular resistance.

S086128

Evaluation of the protective effect of crocin on bleomycin-induced pulmonary fibrosis in rats

Alireza Malayeri[1], Masoud Mohammadi[1], Mehdi Goudarzi[1], Amir Siahpoosh[1], Hamidreza Khalili[2], Saeed Mehrzadi[3], Mehrnaz Mehrabani[4]

1. Medicinal Plant Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
2. Department of Pharmacology, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
3. Razi Drug Research Center, Iran University of Medical Sciences, Tehran, Iran.
4. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: Pulmonary fibrosis is one of common side effect of bleomycin (BLM), which is administered as a chemotherapeutic agent. The purpose of this study was to investigate the effect of crocin (CRO) on BLM-induced pulmonary fibrosis in rat.
Materials and Methods: Fourty male Wistar rats, weighting 200±20 g were randomly divided into four groups (n=10). Group 1 (control), received saline intratracheally (IT), group 2 received a single dose of bleomycin (7.5 UI/kg, IT) on7 day with no treatment, group 3 received CRO at the dose of 25 mg/kg orally one week before and three weeks after BLM administration and group 4 received CRO at the dose of 25 mg/kg orally gavage for four weeks. Malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), nitric oxide (NO), glutathione (GSH) content and tumor necrosis factor (TNF)-α in lung tissue were determined. Presence of fibrosis, inflammatory cells, connective tissue and collagen deposition in lung were evaluated microscopically by trichrome and hematoxylin-eosin (H&E) staining.
Results: The result showed that treatment with CRO significantly decreased BLM-induced elevation of lung MDA, NO and TNF-α level. CRO significantly increased CAT, GPx and GSH content. It remarkably ameliorated histological lung alterations which characterized by presence of inflammatory cells, connective tissue and collagen deposition in lung as well as increasing. CRO could prevent infiltration of fibroblast, inflammatory cells and alveolar thickening due to bleomycin.
Conclusion: The results revealed that CRO has probably a protective effect on bleomycin-induced pulmonary fibrosis.
Keywords: Bleomycin, Crocin, Pulmonary fibrosis, Rat

S086129

Expression level of endoplasmic reticulum stress genes in the lung tissue of obese male and female ovalbumin sensitized rats

Mohammad Reza Aslani[1*], Hassan Ghobadi[2], Hamdollah Panahpour[3], Mehdi Ahmadi[4], Rana Keyhanmanesh[4], Mohammad Reza Alipour[4], Majid Khaksar[5], Mansour Mehmannavaz[6].

1. Lung Inflammatory Diseases Research Center, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.
2. Internal Medicine Department (Pulmonary Division), Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
3. Department of Physiology, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.
4. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
5. Stem Cell Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
6. Medical student, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.

Background: Human and animal studies have shown a close relationship between obesity and the severity of asthma. In this study, we investigated the expression of endoplasmic reticulum stress (ER stress) genes in the lung tissue of obese male and female ovalbumin sensitized rats.

Methods: The rats were divided into eight groups (n=5 per group): female with the normal diet (F+ND), male with the normal diet (M+ND), female OVA-sensitized with the normal diet (F+SND), male OVA-sensitized with the normal diet (M+SND), female with high-fat diet (F+HFD), male with high-fat diet (M+HFD), female OVA-sensitized with high-fat diet (F+SHFD), and male OVA-sensitized with high-fat diet (M+SHFD). All rats were fed for 8 weeks with high-fat diet or standard pelts, and for another 4 weeks, they were sensitized with OVA or saline. At the end of the study, the tracheal responsiveness to methacholine, the ATF4, GRP78, XBP-1, and CHOP expression were determined by Real Time-PCR.

Results: OVA-sensitization and diet-induced obesity caused the curve of methacholine concentration response to shifting to the left. In addition, results indicated that the EC50 (the effective concentration of methacholine generating 50% of peak response) in F+SHFD rats was statistically lower than M+SHFD group ($p<0.05$). Moreover, the results showed that diet-induced obesity increased the expression of ATF4, GRP78, XBP-1 and CHOP in the experimental model of asthma, markedly in F+SHFD group.

Conclusion: These results suggest that ER stress may be involved in the pathogenesis of obesity associated with OVA-sensitized rat's condition, especially in female animals.

Key words: Asthma, Obesity, Endoplasmic reticulum Stress, ATF4, GRP78, XBP-1, CHOP

S086130

Inhibition of angiotensin II type I pathway ameliorate fibrosis and inflammation associated with colorectal cancer

Fereshteh Asgharzadeh[1,2], Seyed Mahdi Hassanian[3,4,*], Maryam Fakhraei[2], Amir Avan[1,3,5], Majid Khazaei[2,3]

1. Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Department of Medical Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Metabolic syndrome Research center, Mashhad University of Medical Sciences, Mashhad, Iran
4. Department of Medical Biochemistry, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
5. Department of Modern Sciences and Technologies, and Department of Medical Genetics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and Objective: A dysregulation of the angiotensin II type I receptor (AT1R) and its pathway is reported to be associated with poor prognosis in several malignancies, including colorectal cancer. We have explored the therapeutic-potential of targeting the AT1R using valsartan, and its pharmacological interaction with 5-FU, using in vivo models of colorectal cancer.
Materials and Methods: The role of antitumor activity of valsartan alone and mid with 5-FU was assessed in a CRC model in mouse, employing the following groups: (1) Control (untreated), (2) 5-FU (5mg/kg/every other day i.p), (3) Valsartan (40 mg/kg/day orally), and (4) a combination (valsartan + 5-FU) (n=6 in each group). We examined the anti-inflammatory and anti-fibrosis properties of agents as well as the oxidant and antioxidant markers: malondialdehyde (MDA) and total-thiols (T-SH) levels and superoxide-dismutase (SOD) and catalase (CAT) activity.
Results: Valsartan inhibited cell-growth and affected the anti-tumor properties of 5-FU by the induction of necrosis in the combination drug treated group. Furthermore, Valsartan inhibited tumor growth, which was more pronounced using the Valsartan/5-FU combination, and acted via induction of reactive oxygen species, MDA and down-regulation of SOD, catalase and thiol.
Conclusion: We have demonstrated that the AT1R blocker, valsartan that operates via the AT1R pathway, interferes with reduced-tumor size and ameliorate fibrosis and inflammation associated with colorectal cancer.
Keywords: Renin-angiotensin system, valsartan, colorectal cancer

S086131

Molecular Evaluation of Doxorubicin and Quercetin on Apoptosis and Drug Resistance of HT29 Cancer Stem and non- Stem Cells

Shekoufeh Atashpour[1], EbrahimAzizi[2], ShamilehFouladdel[2], Tahereh Komeili Movahhed[3], Mohammad H. Ghahremani[4], SeyedNaserOstad[4]

1. Department of Pharmacology, Jahrom University of Medical Sciences (JUMS), Jahrom, Iran. Email: Sh.atashpoor@gmail.com
2. Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA
3. Cellular and Molecular Research Center, Qom University of Medical Sciences, Qom, Iran
4. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Background and Objective: The colorectal cancer stem cells (CSCs) with the CD133+ phenotype are a rare fraction of cancer cells with the ability of self-renewal, infinite proliferation and chemoresistance. Quercetin has anticancer effects with the advantage of exhibiting low side effects. Therefore, we evaluated Doxorubicin, Quercetin and their combination effect on cell proliferation, apoptosis and dug resistance in HT29 cancer cells and isolated CD133+CSCs.
Materials and Methods: The HT29 CSCs were isolated using CD133 antibody conjugated to magnetic beads by MACS. Anticancer effects of Quercetin and Doxorubicin alone and in combination on HT29 cells and CSCs were evaluated using MTT cytotoxicity assay, flow cytometry analysis of cell cycle distribution and apoptosis induction and real-time PCR evaluation of Bcl2, Bax, BCRP and β-catenin gene expression.
Results: We showed that CD133+-cells accounted for almost 10% of HT29 cells. We found that CSCs chemoresistance is modulated by being quiescent, overexpression of Bcl2 protein, BCRP, excess activation of Wnt/β-catenin signaling pathway and downregulation of Bax protein. Quercetin and Dox alone and in combination inhibited cell proliferation and induced apoptosis in HT29 cells and to a lesser extent in CSCs. Quercetin enhanced cytotoxicity and apoptosis induction of Doxorubicin in both cell populations. Quercetin downregulated Bcl2, BCRP and β-catenin expression.
Conclusion: The CSCs were a minor population with significantly high level of drug-resistance within HT29 cancer cells. The combination of quercetin with doxorubicin chemotherapy may represent an effective strategy for inducing apoptosis, improving cytotoxicity effect of conventional chemotherapeutic agents and reducing chemoresistance in nonCSCs and CSCs.
Keywords: Cancer Stem Cells, colon cancer, Chemoresistance, Quercetin, Doxorubicin, Apoptosis, BCRP, Wnt/βcatenin signaling pathway

S086132

Exercise training mitigates the heart dysfunction and lung inflammatory response induced by exposing to waterpipe tobacco smoke

Siyavash Joukar[*1], Mohammad Reza Nakhaee[2], Mohammad Reza Zolfaghari[2], Nouzar Nakhaee[3] , Farzaneh Rostamzadeh[4], Yaser Masoumi-Ardakani[4], Maryam Iranpour[5], Mozhdeh Nazari[3]

1. Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences AND Department of Physiology and Pharmacology, Afzalipour School of Medicine, Kerman University of Medical Sciences, Kerman, Iran
2. Department of exercise physiology, School of Sport Sciences, Urmia University, Urmia, Iran
3. Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.
4. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
5. Pathology and Stem Cell Research Center, Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: Waterpipe tobacco smoking (WTS) in youth and even in athletes is increasing. Despite the lack of adequate information, some users believe that exercise can prevent the negative effects of WTS. We assessed the effects of WTS exposure with/without swimming exercise on lung inflammatory response, blood pressure (BP), and heart mechanical performance in male Wistar rats.
Materials and Methods: Animals were 4 groups as sedentary control (CTL), waterpipe tobacco smoking (S), mild endurance swimming exercise training (Ex) and waterpipe smoking plus exercise (S+Ex). Duration of WTS and exercise was 8 weeks.
Results: BP and heart rate did not show significant difference among groups. WTS increased the TNF-α level of heart and cardiac tissue lesions ($P<0.05$ versus CTL) and reduced +dP/dt max, -dp/dt max and heart contractility indices ($P<0.01$, $P<0.01$ and $P<0.05$ respectively vs. CTL and Ex groups) and increased the Tau index ($P<0.05$ vs.CTL and $P<0.01$ vs. Ex groups) of left ventricle. However, combination of exercise and WTS reduced the TNF-α level, improved the heart activity of superoxidase dismutase (SOD) and catalase enzymes and prevented the negative effects of smoking on heart function and its morphology. In addition, WTS increased lung damage, the pro-inflammatory cytokines and malondialdehyde levels of lung tissue and reduced the alveolar number/mm2. Combination of exercise with WTS significantly decreased these negative effects however, could not fully protect the lung from damage.
Conclusion: Mild exercise prevents WTS-induced cardiac dysfunction and to some extent lung damage partly via improvement of antioxidants and attenuation of pro-inflammatory cytokines.
Keywords: Waterpipe smoking; Exercise training; Left ventricular function; lung injury, Antioxidants; Cytokines

S086133

The effect of rat cardiac extract with different ages on differentiation neonatal rat bone marrow mesenchymal stem cells into cardiomyocyte

Fatemeh jamalzadeh, Fatemeh Halvaeipoor , Fatemeh safari , Fariba akhondzadeh, mansour Esmailidehaj*

Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Background and objective: Bone marrow-derived mesenchymal stem cells (BMSCs) are a promising stem cell source .These inactive cells differentiate into like-cardiomyocyte cells, when they are exposed to a stimulant such as 5-azacytidine (Aza). The heart tissue extract (HE), as a supplement, increases the effect of Aza. since cardiac stem cells and factors around heart, which affect differentiation, , are reduced, by aging, Hence the aim of this study was to evaluate the effect of HE with different ages(7,30,60day), on the differentiation of neonatal stem cells into cardiomyocytes.
Materials and Methods: BMMSCs for the cardiomyocyte differentiation were placed in medium containing HE , in different doses and ages, in presence and absence of Aza, for 24 h. Expression of specific cardiac genes in these groups was evaluated using Real Time RT-PCR technique on the days 18 and 27.
Result: Among the groups that were placed in the Aza + HE induction medium, only the 7-day-old rat`s HE plus Aza increased the expression of cardiac desmin and MHC marke the expression of these genes on day 27 increased from day 18, while the HE of the 30-day and 60-day-old rat significantly reduced the expression of these two cardiac genes.
Conclution: These result reveal that 7-day-old rat`s HE facilitates the differentiation process of BMSC into heart muscle precursor cells. While by increasing age, the HE has a negative effect on the expression of cardiac gene.
Keywords: Bone marrow mesenchymal stem cell, Heart extract, 5-azacytidine, Age, Differentiation, Desmin , β-MHC

S087134

Lack of weight loss and reduced food intake of tamoxifen or estrogen in aging animals compared with young mice: Leptin sensitivity

Mohammad Khaksari[1], Zeinab Farhadi[2], Shahriar Dabiri[3], Gholamreza AsadiKaram[4], Hossein Azizian[5]

1. Endocrinology and Metabolism Research Center ,Institute of Basic and Clinical Physiology Sciences ,Kerman University of Medical Sciences ,Kerman ,IR Iran
2. Department of Physiology ,Kerman University of Medical Sciences ,Kerman ,IR Iran
3. Department of Pathology , Kerman University of Medical Sciences ,Kerman ,IR Iran
4. Department of Biochemistry , Kerman University of Medical Sciences ,Kerman ,IR Iran
5. Department of Physiology ,Yazd University of Medical Sciences ,Yazd ,IR Iran

In this study will examine the effects of Tamoxifen(TAM) on obesity and response to leptin in aging and young animals intake of high-fat diet (HFD) and compare with estrogen (E2).Female mice c57 / 6J are intact (sham) ,ovariectomized (OVX) young mice and as well as aging animal consumed for three months with HFD, then divided into nine groups: Sham + Oil, Sham + E2, Sham + TAM, OVX + Oil, OVX + E2, OVX + TAM, Aged + Oil, Aged + E2, and Aged + TAM. TAM or E2 in both young animals prevented an increase in weight compared to the oil group, but E2 effect was higher than TAM. In addition, in aging animals, none of these drugs had an effect on body weight. Similar to the same body weight results, these results were repeated in food intake. On the other hand, E2 only significantly reduced subcutaneous fat compared to oil; both of the two drugs in Sham animals reduced visceral fat to subcutaneous fat ratio and did not have an effect on OVX and aging groups. After injection with leptin, it was found that TAM or E2 caused only leptin sensitivity (Reduce food intake and weight loss) in Sham and OVX young animals, not aging animals. TAM and E2 cause weight loss and food intake in young animals under the HFD diet, not in aging mice, and may lead to their beneficial effects through increased response to leptin.
Keywords: Tamoxifen, Estrogen, High fat diet, Leptin, Food intake, Body weight, Visceral fat, Subcutaneous fat

S087135

Effect of extraction of focus fig leaf on carbohydrate metabolism and insulin secretion from pancratic isolated islets in adult male diabetic rats

Hamid Farahani[1], Samira Khani[1], Zahra Farahani[2]

1. Department of Physiology and Pharmacology, School of Medicine, Qom University of Medical Sciences, Qom, Iran
2. Student research committee, School of medicine- Arak University of Medical sciences- Arak, Iran.

Background & objective: Recent studies have shown extraction of ficus carcia leaves have benefit effects on decreasing blood sugar of diabetic humans & animals, although its precise mechanism have not been detected yet. Aim of this research is study of the extraction of ficus carica leaves on insulin secretion of isolated pancreatic islets in diabetic animal.
Material & Methods: 36 adult male rats were divided to three control, diabetic & therapeutic groups. First of all, animals of diabetic & therapeutic groups were involved to diabetes type 2 by injecting streptozocin (STZ), & the therapeutic group received the extraction of ficus by gavage. Oral glucose tolerance test (OGTT) was performed in the 3 groups for one month. Then glucose stimulated insulin secretion (GSIS) was assessed.
Results: GSIS in the diabetic groups was significantly lower compared to the therapeutic & control groups. Plasma glucose level of the diabetic groups was significantly higher compared to the therapeutic & control groups. Plasma Insulin level of the diabetic groups was significantly lower compared to the therapeutic & control groups. Homeostasis model of insulin resistance assessment (HOMA) of three group was not significant.
Conclusions: The extraction of ficus carica leaves improves GSIS & glucose tolerance in the diabetic groups. Results of this study, approve more published studies about anti diabetic effects of the ficus carica leaves.
Key words: ficus carica leaves, diabetes, Rat

S087136

Beneficial effects of tamoxifen on leptin sensitivity in young mice fed a high fat diet: Role of brain's neuropeptides and estrogen receptor α

Zeinab Farhadi[1], Mohammad Khaksari[1], Hossein Azizian[2]

1. Department of Physiology & Pharmacology and Metabolism & Endocrinology Research Center, Kerman University of Medical Sciences, Kerman, Iran
2. Department of Physiology, Faculty of Medicine, Shahid Sadoughi Yazd University of Medical Sciences, Yazd, Iran

Purpose: Aging and menopause cause changes in body composition and energy balance. Tamoxifen (TAM) is a selective estrogen receptor modulator (SERM) that attaches to estrogen receptors (ERs). TAM plays an important role in the body's metabolism. The aim of this study was to determine whether TAM and estrogen (E2) have beneficial effects on leptin responsiveness in young and aged mice. Methods: Young (sham and ovariectomized (OVX) 4 months and aged (sham)19-21 female mice fed High Fat Diet (HFD) for 12 weeks and, then they were divided into nine groups included; Sham+Oil, Sham+TAM, Sham+ E2, OVX+Oil, OVX+TAM, OVX+E2, Aged+Oil, Aged+TAM, and Aged+E2. E2 and TAM were administered subcutaneously every four days for four weeks following received TAM and E2 for 4 weeks. Responsiveness to leptin was compared by measuring the brain's neuropeptides. Results: The results of this study show that E2 in both young and aged animals leads to decreased neuropeptide Y (NPY), Agouti-related protein (AgRP), and increased Alpha-melanocyte-stimulating hormone (α-MSH) secretion. Contrary to E2, TAM did not have any effect on the orexigenic peptides, in both young and aged animals. Also, TAM increased α-MSH only in aged. On the other hand, treatment with TAM increased the expression of ERα in the arcuate nucleus (ARC) in young animal. Our results indicated that TAM protects young HFD fed mice from obesity and improves leptin sensitivity and so, is a good candidate for E2 substitution.
Keywords: Tamoxifen, leptin sensitivity, Aging, brain's neuropeptides, ERα, High Fat Diet

S087137

High calorie diet induced insulin resistance and obesity upregulates the expression and secretion of Irisin peptide in adipose tissue of mice

Mohammad Reza Tabandeh, Shokooh salimi moghadam

Department of Basic Sciences, Division of Biochemistry and Molecular Biology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.

Background and Objective: Irisin is a novel hormone like polypeptide that is cleaved and secreted by an unknown protease from fibronectin type III domain-containing protein 5 (FNDC5). There is conflicting data about the regulation of Irisin gene in obesity and insulin resistance conditions in adipose tissue. The aim of this study was to evaluate the expression of Irisin gene in adipose tissue of high calorie diet obesity and insulin resistance experimental model in mice and its association with insulin resistance marker.
Materials and Methods: To induce insulin resistance and type 2 diabetes, male C57BL/6 mice were fed with high fat/ high carbohydrate (HF/HC) diet containing 10% saturated fat and 20% sucrose for 5 weeks and after that they were i.p. received 25 mg/kg of Streptozotocin. At day 1 and 14, and 28 days after induction of insulin resistance, the mRNA and protein levels of Irisin were analyzed in adipose tissue using qRT-PCR and ELISA methods. Serum Irisin, insulin and glucose concentration and HOMA-IR were measured.
Results: Our results demonstrate that serum Irisin concentration and its adipose tissue mRNA and protein levels were increased in obese, insulin resistance mice in concomitant with hyperglycemia and insulin resistance. Significant correlations were found between adipose and serum Irisin levels and insulin and HOMA-IR levels.
Conclusion: It was concluded that upregulation of Irisin expression in adipose tissue insulin resistant and obese animals may be a novel mechanism in pathophysiology of insulin resistance in obese patient.
Key words: obesity, insulin resistance, adipose tissue, Irisin

S087138

Clinical Pharmacology of Iranian Propolis on Type 2 Diabetes Mellitus: A Randomized Double-Blind Clinical Trial

Hemmati AA, Zakerkish M, Jenabi M, Zaeemzadeh N, Neisi N

Propolis is a natural product with many biological properties including hypoglycemic activity and modulating lipid profile. The present study was designed to evaluate the effect of Iranian propolis extract on glucose metabolism, Lipid profile, Insulin resistance, renal and liver function as well as inflammatory biomarkers in patients with type 2 diabetes mellitus (T2DM). A double-blind, placebo-controlled clinical trial was conducted. The duration of the study lasted 90 days. Patients with T2DM were recruited and randomly divided into an Iranian propolis group (1000 mg/day) (n = 50) and a placebo group (n = 44). There was a significant decrease in the serum levels of glycosylated hemoglobin (HbA1c), 2-hour post prandial (2hpp), insulin, homeostasis model assessment-insulin resistance (HOMA-IR), homeostasis model assessment of β-cell function (HOMA-β), High sensitive C-reactive protein (hs-CRP), tumor necrosis factor-α (TNF-α). However, there was a notable elevation in the serum HDL-C in the propolis group compared with the placebo group. In addition, a notable reduction in serum liver transaminase (ALT and AST) and blood urea nitrogen (BUN) concentrations in the propolis group was observed. Iranian propolis has beneficial effects on reducing post prandial blood glucose, serum insulin, insulin resistance, and inflammatory cytokines. It is also a useful treatment for preventing the liver and renal dysfunction, as well as, elevating HDL-C concentrations in patients with T2DM.

S087139

Exercise training improves angiogenesis through alterations in the expression levels of miR-503 and CDC25 in the heart tissue of diabetic rats

Gonja Javani[1], Arshad Ghaffari-nasab[1], Ali Aliaghdam[2]

1. Students' Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
2. Department of Physiology, Faculty of medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Background and Objective: Impaired myocardial angiogenesis is commonly observed in diabetic patients. Abnormal expression levels of miR-503 and one of the its target gene, CDC25, play important role in suppression of angiogenesis. The current study aimed to address the impact of exercise training on deficient angiogenesis and expression levels of miR-503 and CDC25 in the heart tissue of diabetic male rats.
Materials and Methods: Forty male wistar rats (250-300 g) were divided randomly in 4 groups: control, exercised, diabetic control, diabetic-exercised. Type1 diabetes was induced by intraperituneal injection of 60 mg/kg of streptozotocin in rats. After 8 weeks of treadmill exercise, heart tissue samples used for histological study and determination of miR-503 and CDC25 levels by Real-time quantitative PCR. Data were analyzed using SPSS.
Results: Our data confirmed the overexpression of miR-503 in response to diabetic condition and showed reduced expression levels of CDC25 and capillary density compared with control group. Exercise training leads to a decrease in expression levels of miR-503 and an increase expression levels of CDC25 and potentially improved angiogenesis in diabetic-exercised as compared to diabetic control rats.
Conclusion: This study suggests that exercise training improves myocardial angiogenesis in diabetic rats, which is possibly mediated through alterations in the expression levels of miR-503 and CDC25.
Keywords: Diabetes, Exercise, Angiogenesis, miR-503, CDC25

S087140

Progesterone Eliminates Estrogen-Mediated Cardioprotection Against Diabetic Cardiomyopathy in Ovariectomized Rats

Hossein Azizian[1,2], Mohammad Khaksari[3], Zeinab Farhadi[2], Gholamreza Asadikaram[4], Mansour Esmailidehaj[1]

1. Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Department of Physiology, Faculty of Medicine, Kerman University of Medical Sciences, Kerman, Iran.
3. Endocrinology and Metabolism Research, and Physiology Research Centers, Kerman University of Medical Sciences, Kerman, Iran.
4. Department of biochemistry, and Metabolism & Endocrinology Research Center, Kerman University of Medical Sciences, Kerman, Iran.

Purpose: Type 2 Diabetes (T2D) remains one of the most important causes of cardiovascular disease (CVD). Menopause leads to an increase in CVD and metabolic syndrome, which indicates the role of sex steroids as a protective factor. In the present study, we survey the effects of alone and in combination of 17β-estradiol (E2) and progesterone (P4) on cardiovascular dysfunction in T2D. Methods: Female ovariectomized (OVX) diabetic rats were divided into eight groups: Sham-Control, Diabetes (Dia), OVX+Dia, OVX+Dia+Vehicle, OVX+Dia+E2, OVX+Dia+P4, OVX+Dia+E2+P4 and OVX+Dia+E2+Vehicle. T2D was induced by high fat diet and streptozotocin. E2 and P4 were administrated every four days for four weeks. The heart cytokines and angiotensin II, lipid profile, insulin, water and food intake and cardiovascular indices were measured. Results: Results show that individual treatment with E2 decreased fasting blood glucose, water and food intake, atherogenic and cardiac risk indices, and blood pressure. Also, P4 led to a decrease in atherogenic and cardiac risk indices. TNFα and IL-6 levels were increased and IL-10 was decreased in Dia group, while E2 alone was able to inhibit these changes, the combination use of E2 and P4 eliminated the beneficial effects of E2 on these indices. Although, diabetes results in, an increment of cholesterol, LDL and triglyceride, hormone therapy with E2 was associated with improved dyslipidemia. Conclusion: The use of E2 alone (not P4 alone) and its combined use with P4 improved cardiovascular function in OVX diabetic animals, possibly by reducing the amount of inflammatory cytokines and improving metabolic parameters.
Keywords: Type 2 diabetes, 17β-estradiol, Progesterone, Cardiovascular, Cytokine, Lipid profile.

S087141

Oleopein protect myocardium in type 2 diabetic rats: role of inflammatory cytokines

Mohammad Shahbazian[1], Hossein Azizian[1], Mohammad Ebrahim Rezvani[1], Zeinab Farhadi[1], Mansour Esmailidehaj[1*], Azadeh shahrokhi Raeini[1]

Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Introduction: Type 2 diabetes mellitus (T2DM) is strongly associated with increased risk of myocardial dysfunction and cardiovascular disease (CVD). CVD is the leading cause of death in both men and women. Many studies have shown that Oleopein (Ole) has antioxidant and anti-diabetic effects. The aim of this study is to investigate the effects of Oleopein on infarct size, coronary flow and heart rate in type 2 diabetic rats.
Methods: Male Wistar rats were divided into five groups of eight each: group I, control, group II, diabetes (Dia), group III, Dia+Ole (25 mg/kg), group IV, Dia+Ole (50 mg/kg), group V, Dia+Ole (100 mg/kg). T2DM was induced by a high-fat diet and streptozotocin. T2DM rats received Ole through intraperitoneal once a day for one month. In the end, the heart rate was measured through the Langendorff apparatus and power lab. Infarct size was measured via coloration with TTC.
Results: Results showed that fasting blood glucose was alleviated by Ole. Infarct size in groups III and IV was significantly lower than the Dia group. Furthermore, Ole (25 mg/kg) and Ole (50 mg/kg) improved cardiac weight index, atherogenic index, and cardiac risk indices. Also, Ole (50 mg/kg) only decreased interleukin 6. Significant decrement in the level of interleukin 10 was observed in Dia group, whereas Ole (25 mg/kg) and Ole (50 mg/kg) increased the cardiac levels of interleukin 10. Conclusion: Our study suggested that the beneficial effects of Ole on diabetic cardiomyopathy is probably due to improved lipid profiles and inflammatory cytokines.
Keywords: Type 2 diabetes, myocardium, Oleopein, cytokines, lipid profiles.

S087142

The comparison of antioxidant effect of aspirin, metformin, atorvastatin and captopril co-administration in the heart and kidney tissues of diabetic rats

Maryam Paseban[1], Saeed Niazmand[1,2], Masumeh Mirzaee[1], Mahdiyeh Hedayati Moghadam[3]

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Neurogenic Inflammation Center, Mashhad University of Medical Sciences, Mashhad, Iran
3. Department of Physiology, School of Medicine, Jiroft University of Medical Sciences, Jiroft, Iran

The present study investigated the effects of co-administration of aspirin, metformin, atorvastatin and captopril, on serum lipid profile and oxidative stress in the heart and kidney of streptozotocin-induced diabetic rats. In this study rats were randomly divided into the following eleven groups: control (Cont), and diabetic (D), as well as 9 groups that were treated with metformin (M, 300 mg/kg) or aspirin (ASA, 120 mg/kg) alone or in different combinations with captopril (C, 50 mg/kg), or atorvastatin (AT, 40 mg/kg), as follows: (D+M), (D+ASA), (D+M+ASA), (D+M+C), (D+M+AT), (D+M+C+ASA), (D+M+C+AT), (D+M+AT+ASA), and (D+M+C+AT+ASA). The rats in treatment groups daily received drugs by gavage for six weeks. Finally, serum lipid profile and levels of oxidative markers in the heart and kidney tissues were evaluated. In diabetic rats, blood levels of glucose, cholesterol, TG, LDL, MDA and AIP significantly increased but those of HDL and total thiol as well as SOD and CAT activities significantly decreased. Treatment with different combinations of C, ASA, AT and M significantly ameliorated these parameters. This study showed Co-administration of ASA, M, C and AT, could improve glucose and lipid metabolism and oxidative stress markers in the kidneys and heart tissues of diabetic rats more marked than administration of these drugs alone.
Keyword: Diabetes, Metformin, Captopril, Atorvastatin, Aspirin, Heart, Kidney

S087143

Magnesium pathway on decreasing of blood glucose and insulin resistance in type 1 and two diabetes in different kinds of animal models and type 2 and non-insulin resistance patients

Nepton Soltani[1], Shahla Sohrabipour[2], Fatemah Kharazmi[1], Mitra Kamran[2] and Kyanoosh Malkzadeh[2]

1. Physiology Department School of Medicine Isfahan University of Medical Science, Isfahan, Iran
2. Molecular Research Center, Hormozgan Medical Science University, Bandar Abbas, Iran

The present study was designed to investigate the possible pathway of Mg2+ in suppression of gluconeogenesis pathway and insulin resistance in the insulin target cells. Our studies for more than 14 years showed that oral administration of MgSO4 in type one diabetic animals in compere to insulin therapy could improve IPGTT, lowered blood glucose levels via inhibition of gluconeogenesis pathway in the liver and increased GLUT4 gene expression and translocation on the cell membrane in the muscle. The part of this pathway was mediated by decreased in FOXO1 gene and proteins expression in muscle and liver, and increased in PPAR-γ, IRS1 and Akt2 genes and proteins expression and decreased in NFKB (p65) gene and protein expression in the muscle. While some of those results were not observed by insulin therapy. Mg2+ administration also improved hyperglycemia and insulin resistance by using hyperinsulinemic-euglycemic clamp technique in high fat diabetic animals via the same pathway as type 1 animal model. We also tried Mg 2+ therapy for non-diabetic insulin resistance and type 2 diabetic patients and our results showed that Mg2+ could improve plasma insulin level, lipid profile, and insulin resistance in both patients. These findings illustrated that MgSO4 improved hyperglycemia and insulin resistance in animal models of diabetes and diabetic patients.
Keywords: Magnesium, Diabetes, Insulin resistance.

S083144-1

Co-administration effects of nitrite and sodium hydrosulfide on oxidative stress in type 2 diabetic rats

Asghar Ghasemi[1], Sevda Gheibi[2], Sajad Jeddi[1], Mattias Carlström[3], Khosrow Kashfi[4]

1. Endocrine Physiology Research Center, Research institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Maternal and Childhood Obesity Research Center, Urmia University of Medical Sciences, Urmia, Iran
3. Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden
4. Department of Molecular, Cellular and Biomedical Sciences, Sophie Davis School of Biomedical Education, City University of New York School of Medicine, New York, USA

Background and Objective: Type 2 diabetes (T2D) is associated with increased oxidative stress as well as decreased nitric oxide (NO) bioavailability and deficiency in hydrogen sulfide (H2S). NO and H2S have been shown to exert protective effects against oxidative stress. In addition, there are important interactions between NO and H2S, and H2S increases NO bioavailability. The aim of this study was to determine the long-term effects of co-administration of nitrite and sodium hydrosulfide (NaSH) on oxidative stress in type 2 diabetic rats.
Materials and Methods: T2D was induced by a high fat-low dose streptozotocin regimen. Rats were divided into 5 groups: control, diabetic, diabetic+nitrite, diabetic+NaSH, and diabetic+NaSH+nitrite. Nitrite (50 mg/L in drinking water) and NaSH (0.28 mg/kg, daily IP injection) were administered for 9 weeks. At the end of the study, serum total antioxidant capacity (TAC), total oxidant status (TOS), glutathione (GSH), oxidized glutathione (GSSG), malondialdehyde (MDA), and activities of superoxide dismutases (SOD) and catalase (CAT) were measured.
Results: Compared to the non-treated diabetic rats, nitrite increased serum TAC levels and SOD and CAT activities. NaSH per se had no effect on serum oxidants and antioxidants levels. However, compared to the nitrite-treated diabetic rats, co-administration treatment resulted in further increases in serum TAC levels (155.9±9.5 vs. 132.8±8.1 μM, p=0.05) as well as SOD (45.0±2.3 vs. 36.8±4.5 U/mL, p=0.08) and CAT (7.1±0.6 vs. 5.8±0.5 U/L, p=0.04) activities.
Conclusion: Chronic nitrite administration decreased oxidative stress in type 2 diabetic rats. Co-administration of NaSH along with nitrite potentiated the anti-oxidant effects of nitrite.
Key words: Diabetes; NO, H2S; co-administration; oxidative stress; rat

S083144-2

Potential targets of nitric oxide system for therapeutic interventions in type 2 diabetes

Azhdar Heydari [1,2]

1. Department of Physiology, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran
2. Institute for Basic Sciences, Physiology Research Center, Kashan University of Medical Sciences, Kashan, Iran

Endothelial dysfunction and reduced nitric oxide (NO) NO generation and/or bioavailability have been reported in patients with type 2 diabetes mellitus (T2DM). There are increasing efforts to target the NO pathway pharmacologically. These therapeutic strategies include inorganic nitrite/nitrate supplementation, L-arginine-derived NO production, iNOS inhibition, arginase inhibition, phosphodiesterase-5 (PDE-5) inhibition, use of NO donors that directly or indirectly release NO, agents that increase NO bioactivity and NO-releasing hybrid drugs. A slow release of NO from hybrid NO-releasing antidiabetic drugs can sufficiently deliver NO in diabetic patients. Accumulating evidence indicates that a decline in the production of endogenous NO can be counterbalanced by the administration of exogenous NO through NO donors or NO-releasing drugs. Release of NO from antidiabetic drugs may help to restore NO bioavailability, and therefore has the potential to improve the clinical status of diabetic patients. However, long-term clinical studies with this type of drugs, including short- and long-term toxicity assessment, are still pending. It can be expected that future developments will include more new NO-donating drugs for lowering glucose levels and attenuating of insulin resistance in patients with type 2 diabetes. It must be keep in mind that NO donors and NO-releasing drugs unlikely to mimic the physiological fluctuations of NO, and that overproduction of NO may react with endogenous ROS to form other toxic free radicals, such as peroxynitrite.

S083144-3

Beneficial effects of nitrate and nitrite in type 2 diabetes: A nutritional perspective

Zahra Bahadoran & Parvin Mirmiran

Nutrition and Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Recent research punctuates that the nitrate (NO3)-nitrite (NO2)-nitric oxide (NO) pathway may be a potential therapeutic target in metabolic disorders and therefore NO3/NO2 can act as compensatory fuel for disrupted NO pathways in pathologic conditions like type 2 diabetes (T2DM). Nutritional aspects of the NO3-NO2-NO pathway has been highlighted by focusing on protective effects of some traditional high-NO3 diet such as Mediterranean and DASH (Dietary Approaches to Stop Hypertension) diet and their components including fruits and vegetables, especially green leafy vegetables, against development of T2DM and cardiovascular disease.

Several beneficial effects on glucose and insulin homeostasis have been reported following both acute and long-term administration of inorganic NO3 and NO2 in animal studies. Inorganic NO3 can decrease fasting blood glucose, glycosylated hemoglobin concentration, pro-insulin to insulin ratio, and improve glucose tolerance test. The underlying mechanisms by which NO3-NO2 can improve whole body glucose metabolism, are increased insulin secretion by increased pancreatic islet blood flow, improve peripheral glucose uptake by increasing GLUT4 translocation in the cell membrane of skeletal muscle and adipose tissue. Inorganic NO3 can also inhibit the production of reactive oxygen species (ROS) in adipocytes and dephosphorylation activity of protein-tyrosine phosphatase 1B, thereby facilitating phosphorylation of insulin receptor substrate and insulin signaling. There is however no sufficient data to confirm these findings in human.

The potential property of inorganic NO3 and NO2 to convert to NO, a key regulator of vascular homeostasis and a natural vasodilator, has also highlighted these anions as therapeutic options in short- and long-term vascular complications including vascular abnormalities, cardiovascular diseases, and hypertension in T2DM. In conclusion, providing inorganic NO3 and NO2 using natural food sources may be considered as a safe and effective nutritional strategy to manage T2DM and its complications.

S083144-4

Nitric oxide donors: New generation of anti-diabetic drugs

Hamid Reza Banafshe[1, 2]

1. Department of Pharmacology, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran
2. Institute for Basic Sciences, Physiology Research Center, Kashan University of Medical Sciences, Kashan, Iran

Diabetes mellitus is a metabolic disease that becomes a global health and social problem. High blood glucose levels, altered insulin signaling and reactive oxygen species lead to a decline in nitric oxide (NO) bioavailability. The reactive oxygen species oxidize the cofactors of the nitric oxide synthase, diminishing their active forms and consequently causing a decreased NO production. Diminish NO and enhanced oxidative stress play a central role in endothelial cell dysfunction and micro and macrovascular complication of diabetes mellitus. It has also been shown that, NO is implicated as a critical signaling molecule in glucose uptake and insulin signaling pathway. Finally, NO donors are suggested as a new potential therapeutic agent in insulin resistance and diabetes mellitus. This mini review explores some of the most promising recent advances in NO donor drugs (L-Arginine, DETA NONOate, SNAP, Spermine NONOate and etc) for treatment of diabetes and addresses the challenges associated with NO donors as a therapeutic agents.

S086145-1

Pathophysiology of myocardial ischemia-reperfusion injury

Mansour Esmailidehaj

Associate Professor, Department of Physiology, Faculty of Medicine. Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Myocardial ischemia-reperfusion injury is a major cause of death and disability among patients with cardiac diseases. Fifteen-twenty seconds following occlusion of coronary artery, anaerobic glycolysis became the main pathway of ATP production in myocardial cells. Inhibiting the glycolysis reduced the initiation time of contracture-rigor in cardiomyocytes from about 60 minutes to less than 5 min. On reperfusion, mitochondrial oxidative metabolism pathway returns to pre-ischemic levels within seconds, however contractile power gradually reaches pre-ischemic values. This, in turn, led to calcium overload and cell death through activation of $2Na^{+}/Ca^{2+}$ exchanger. Mitochondrial Permeability Transition Pore (mPTP), a nonselective channel of the inner mitochondrial membrane, also plays an important role in reperfusion injury. During reperfusion, the fate of the cell is determined by the extent of mitochondrial permeabilization. If minimal, the cell may recover; if moderate, the cell may undergoes programmed cell death; if severe, the cell may die from necrosis due to inadequate energy production. Accumulation of intracellular H^{+} and Ca^{2+} as well as disruption of mitochondrial membrane potential lead to generation of free radicals and subsequent activation of pro-inflammatory cytokines which play a critical role in ischemic-reperfusion injury through damage to cellular DNA, proteins and lipids as well as activating stress response pathways. This non-specific injury initiates the cytokine-mediated cascades, which result in the production of tumor necrosis factor alpha (TNFα). Excessive TNFα expression induces contractile dysfunction, hypertrophy, fibrosis and cell death. Additionally, increased intracellular Ca^{2+} concentration induces inflammation via generation of calcium pyrophosphate complexes. According to above information, ischemia and reperfusion-induced metabolic changes have a direct effect on tissue inflammation and integrity and therefore cell survival.

S086145-2

Cardioprotection: protective conditionings and interaction of cardiovascular co-morbidities and risk factors with conditioning interventions

Khalil Pourkhalili

Associate Professor, Department of Physiology, Faculty of Medicine, Bushehr University of Medical Sciences, Bushehr, Iran

Ischemic heart disease (IHD) is the major cause of mortality in the world. Most of the pathological consequences of IHD arise from acute ischemia-reperfusion (IR) injury, which also occur in cardiac interventions like angioplasty, coronary artery bypass grafting and heart transplantation. In recent years, novel therapeutic strategies have been introduced for reducing the clinical outcomes of IR injury and cardioprotection. One of these strategies, which have been extensively studied, is cardiac conditionings against IR injury. Among the various cardiac conditioning protocols, the most popular one is ischemic conditioning. Here, based on the time of implementation of the conditioning maneuver, we first introduce three methods of ischemic conditioning including ischemic pre-conditioning, ischemic per-conditioning and ischemic post-conditioning. Experimental evidences have revealed that these cardiac 'conditioning' are strongly protective and significantly decrease myocardial IR injury. In this accord, recent studies have focused on translating these cardioprotective paradigms from the laboratory to the clinic. However, most of the studies investigating ischemic conditioning-induced cardioprotection have been done in healthy animals and little is known whether mechanisms of conditioning strategies are operating in pathologically altered myocardium. Therefore secondly, we try to see how risk factors such as hypertension, diabetes, and hyperlipidemia may affect the severity of myocardial IR injury and render the heart resistant or even impair the efficacy of ischemic conditioning.
Keywords: Ischemia, Reperfusion, Ischemic Conditioning, Cardioprotection

S086145-3

Cardioprotection: new therapeutic targets and mediators

Hamid Soraya

Assistant Professor, Department of Pharmacology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran

Despite great advances in the understanding and treatment of coronary heart diseases and improved survival in patients with acute myocardial infarction (AMI), the related heart failure, which imposes a huge global burden on healthcare and economic resources, has increased over the past years. In the case of cardioprotection, several experimental and clinical studies with many endogenous and exogenous agents such as adenosine, atrial natriuretic peptide (ANP), exenatide, beta-blockers, and cyclosporine have been reported. The results were mixed, promising with some agents and neutral with others. Hence, there is a need to discover and investigate novel therapeutic targets. Our previous studies with metformin have demonstrated that activation of AMPK and inhibition of TLR-4 have cardioprotective effects in myocardial infarction. Most recently, we have reported that memantine, as an NMDA receptors antagonist, can be considered as a cardioprotective agent in heart failure. Prevention of mitochondrial ROS production, necrosis, necroptosis or pyroptosis at the time of reperfusion can be considered as a novel therapeutic targets for cardioprotection. In addition to targets mentioned above, novel therapeutic targets currently under investigation includes platelet-innate immune cells interaction, exosomes, microvesicles, Autophagy, G-protein coupled receptors (GPCRs), DPP-4 inhibitors, Toll-like receptors (TLRs), MMPs , calpains, the mitochondrial calcium uniporter, mitochondrial fission and fusion proteins, Connexin 43/20, mitochondrial metabolism and mitophagy. Other new targets are immune system cells particularly monocytes, macrophages, neutrophils, extracellular DNA and RNA and inflammasomes. Along with this target, our several publications with different agents showed cardioprotection through anti-inflammatory effects with focus on neutrophil's activity in the myocardium.

S086145-4

Cardioprotection against ischemia-reperfusion injury: translation from the experimental setting to the clinical arena

Reza Badalzadeh

Associate Professor, Department of Physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Ischemic heart disease and subsequent acute myocardial infarction (MI) and heart failure remain the main causes of death and disability worldwide. During the last three decades, many pharmacological treatments and various ischemic-conditioning strategies have been identified to confer robust cardioprotection in experimental animal models of myocardial ischemia-reperfusion (IR) injury. However, translation of these cardioprotective therapies into the clinical setting of MI for improving patient outcomes has been disappointing yet. In spite of recent therapeutic advances, the large number of patients undergoing interventions like angioplasty or coronary artery bypass graft surgery develop fatal arrhythmias and heart failure after reperfusion. Thus, novel therapies are required to protect the heart against the detrimental effects of IR injury. In addition, IR injury is a multifactorial phenomenon, causing cardiomyocyte death via multiple pathways and mechanisms. Also, patients with MI injuries simultaneously have other underlying risk factors and comorbidities, such as diabetes and hyperlipidemia, which can ultimately reduce the overall potency of cardioprotective strategies to activate end-effectors within cardiomyocytes. The preclinical studies have less focused on these important issues in designing their experimental models. In this regard, emerging data suggest that optimal cardioprotection may require the combination of additive or synergistic multitarget therapies. In this symposium, we will present the pathophysiology of myocardial IR injury, as well as the current state of cardioprotection and ischemic-conditionings in both the experimental and clinical settings, introduce the novel therapeutic targets and new combination therapy approaches for reducing myocardial IR, and then provide the practical recommendations for experimental modeling of cardioprotection to improve their translation into the clinical setting.

Keywords: Cardioprotection, ischemic conditioning, myocardial infarction, combination therapy

S081146-1

The Role of Inhibitors of the Renin-Angiotensin System in the Attenuation of Dexamethasone-induced Remodeling in the Trabecular Meshwork

Anna Krasilnikova[1*], Nurul Ainsya Bakry[1,2], Renu Agarwal[3], Siti Hamimah Sheikh Abdul Kadir[1,4], Igor Iezhitsa[1,2], Nafeeza Mohd Ismail[3]

1. Department of Pharmacology, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh Campus, 47000 Sungai Buloh, Selangor, Malaysia
2. Centre of Neuroscience, Faculty of Medicine, Universiti Teknologi MARA, Sungai BulohCampus, 47000 Sungai Buloh, Selangor, Malaysia
3. School of Medicine, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia.
4. Institute of Medical Molecular Biotechnology, Universiti Teknologi Mara, Sungai Buloh Campus, 47000 Sungai Buloh, Selangor, Malaysia

Introduction: Trabecular meshwork (TM) remodeling leads to aqueous humor outflow resistance while increasing intraocular pressure (IOP), one of the major risk factors for glaucoma.
Objective: To evaluate the effects of Renin-Angiotensin System (RAS) inhibitors on production and degradation of extracellular matrix (ECM) in dexamethasone co-treated human trabecular meshwork (HTM) cells as well as on changes in IOP and TM tissue in dexamethasone-treated rats.
Methods: In vitro study, HTM cells were divided into control group, group treated with dexamethasone 1E-7 M, and groups co-treated with dexamethasone 1E-7 M and enalaprilat dehydrate either losartan potassium. Both RAS inhibitors were used in several concentrations ranged from 1E-4 up to 1E-7 M. Cell viability as well as fibronectin (FN), a-smooth muscle actin (a-SMA), MMP-2, MMP-9, TIMP-1, and TIMP-2 were measured at 7 and 14 days. In vivo study steroid-induced ocular hypertensive (SIOH) Sprague Dawley rats were treated topically with enalaprilat or losartan for 21 days. SIOH rats and ocular normotensive rats were used as the control groups. IOP was detected twice a week. Aqueous humor was collected and MMP-2 and MMP-9 were detected. H&E staining of TM was done.
Results: Dexamethasone significantly increased production of FN, a-SMA and both TIMP-1 and 2 by day 14 of treatment, at the same time significantly reducing production of both types of MMPs. Co-treatment with either enalprilat or losartan significantly abolished the effects of dexamethasone on extracellular matrix deposition at all tested concentrations at both time points. Topical treatment with inhibitors of RAS caused significant IOP reduction up to 26.6% (enalaprilat) and 21.39% (losartan) compared to baseline. Both enalaprilat and losartan restored the thickness and cellularity of TM and increased concentrations of MMPs to nearly ocular normotensive group levels.
Conclusion: Inhibitors of RAS produce significant ocular hypotensive effect and attenuate TM remodeling in vivo and in vitro that likely contributed to increased production of MMP-2 and -9. Inhibitors of RAS, such as ACE inhibitors and angiotensin II type 1 receptor blockers are potentially attractive in the treatment of steroid-induced and open-angle glaucoma.
Keywords: Trabecular meshwork remodeling, dexamethasone, enalaprilat dehydrate, losartan potassium.

S081146-2

The discovery of a novel series of benzimidazoles as a new prospective class of ocular hypotensive agents

Igor Iezhitsa[1,2*], Adrian Julian Marcus[1], Renu Agarwal[1,3], Pavel Vassiliev[2*], Alexander Spasov[2], Olga Zhukovskaya[4], Vera Anisimova[4], Nafeeza Mohd Ismail[5]

1. Center for Neuroscience Research, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh Campus, Selangor, Malaysia;
2. Volgograd State Medical University, Research Institute of Pharmacology, Volgograd, Russia;
3. I-PPerForM, Faculty of Medicine, Universiti Teknologi MARA Sungai Buloh Campus, Selangor, Malaysia
4. Southern Federal University, Research Institute of Physical and Organic Chemistry, Rostov-on-Don, Russia;
5. International Medical University, IMU Clinical School, Seremban, Malaysia

Ocular hypertension is believed to be involved in the etiology of primary open-angle glaucoma. Although many pharmaceutical agents have been shown to be effective for the reduction of intraocular pressure (IOP), a significant opportunity to improve glaucoma treatments remains. In an effort to find new ocular hypotensive drug candidates, a total of 27 condensed benzimidazoles based compounds were screened. The first part of study (Study I) was done in normotensive rats and rebound tonometry was used to estimate IOP. All compounds were topically applied as a single drop, unilaterally, at 3 different concentrations (0.1%, 0.2% and 0.4%). The contralateral eye was instilled with vehicle and served as control. The IOP reduction was measured up to 6 h. It was observed that with a single topical instillation, compounds RU 551, RU 555, RU839 (pyrimido[1,2-a]benzimidazole derivatives), and RU 615 (imidazo[1,2-a]benzimidazole derivative) showed significant IOP lowering activities in ocular normotensive rats. All other compounds showed none, weak and inconsistent IOP lowering effect. The relationship between ability of IOP lowering and hypotensive activities was studied. According to the pharmacophore analysis, the class of pyrimido[1,2-a]benzimidazole is more promising than the class of imidazo[1,2-a]benzimidazole as a source of compounds with high IOP lowering activity. Pharmacophore analysis also showed that the critical features of high IOP lowering activity are methoxyphenyl and [phenyl]alkyl fragments, and non-conjugated six-membered heterocyclic ring. The next part of study (Study II) was aimed: (1) to evaluate the IOP-lowering effect of four compounds RU-551, RU-555, RU-839 (pyrimido[1,2-a]benzimidazole), and RU-615 (imidazo[1,2-a]benzimidazole) on steroid-induced ocular hypertension in rats after single drop and chronic applications; and (2) to test in silico and in vitro conventional rho-associated kinase (ROCK) inhibitory activity of the selected compound. This study demonstrated that RU-551, RU-555, RU-839, and RU-615 significantly reduced IOP in Sprague Dawley rats with dexamethasone (DEXA) induced ocular hypertension after single drop administration (0.1%), however RU-615 showed the best IOP lowering effect as indicated by maximum IOP reduction of 22.32%. Repeated dose topical application of RU615 caused sustained reduction of IOP from baseline throughout the 3 weeks of treatment with maximum IOP reduction of 30.31% on day 15. This study also showed that the steroid-induced increase in IOP is associated with increased retinal oxidative stress and significant retinal ganglion cells (RGCs) loss. Prolonged treatment with RU615 over 3 weeks results in normalization of IOP in DEXA-treated rats with partial restoration of retinal antioxidant status (catalase, glutathione and superoxide dismutase) and subsequent protective effect against RGC loss. Thus, IOP lowering activity of RU615 together with antioxidant properties might be the factors that contribute to prevention of further RGC loss. In vitro part of this study explored the ROCK inhibitory activity of RU-615 using dexamethasone-treated human trabecular meshwork cells as a possible mechanism of action of its IOP lowering activity. However, this study didn't show conventional ROCK inhibition by RU-615 which was later confirmed by in silico consensus prediction. Therefore, in the future studies it is important to identify the upstream target receptors for RU-615 and then delineate the involved intracellular signaling pathways which are likely to be other than ROCK inhibition.

Funding statement: We gratefully acknowledge financial support from by the MOH (Malaysia) under the project 600-RMI/RAGS 5/3 (46/2014).

S081146-3

Protective effect of palm oil tocotrienol-rich fraction against experimental model of diabetic retinopathy

Nurul Alimah Abdul Nasir[1], Muhammad Zulfiqah Sadikan[1], Renu Agarwal[2]

1. Centre for Neuroscience Research (NeuRon), Faculty of Medicine, Universiti Teknologi MARA (UiTM), Jalan Hospital 47000 Sungai Buloh, Selangor, Malaysia.
2. International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia.

Background and Objectives: With increasing prevalence of diabetes mellitus (DM) globally, the number of diabetic complications is expected to increase in near future. Diabetic retinopathy (DR) is one of the common ocular complications in DM. Current treatments for DR are suboptimal., therefore, the development of alternative therapy is important. Oxidative stress, chronic inflammation and angiogenesis are the key players in the pathogenesis of DR. In our study, we investigated the effects of tocotrienol-rich fraction (TRF), a potent antioxidant with multiple other beneficial biological properties, on neurodegenerative changes in a streptozotocin (STZ)-induced rat model of DR.
Materials and Methods: Sprague Dawley rats were induced by intraperitoneal injection (IP) of STZ to render them diabetic. The diabetic rats were divided into 2 groups: vehicle-treated (DV) and TRF-treated (DT). A third group consisted of normal rats (N). TRF was administered via oral gavage, and given daily for 12 weeks. Rats were then euthanized and retinas were processed for haematoxylin-eosin and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) staining. Retinal layer thickness (RLT) and TUNEL-positive retinal cells among groups were measured and analyzed.
Results: RLT in DV group was reduced compared to N ($p<0.001$), whereas, it was increased in DT which was greater compared to DV group ($p<0.05$). Number of TUNEL-positive retinal cells were higher in DV and DT groups compared to N group ($p<0.001$). However, DT showed lesser number of TUNEL-positive retinal cells compared to DV group ($p<0.05$).
Conclusion: Oral supplementation of TRF improves RLT and reduces number of TUNEL-positive retinal cells in STZ-induced rat model of DR.
Keywords: tocotrienol-rich fraction, diabetic retinopathy, neurodegenerative changes

S081146-4

Mechanisms of regulation of aqueous humour dynamics by trans-resveratrol in steroid-induced oculohypertensive rat model

Norhafiza Razali[1], Renu Agarwal[2], Puneet Agarwal[3], Minaketan Tripathy[4], Nafeeza Mohd Ismail[2]

1. Faculty of Medicine, Universiti Teknologi MARA, Sg Buloh Campus, Selangor, Malaysia.
2. Faculty of Medicine, International Medical University, Bukit Jalil, Selangor, Malaysia.
3. Faculty of Medicine, International Medical University, Clinical School Seremban, Negeri Sembilan, Malaysia
4. Faculty of Pharmacy, Adichunchanagiri University, Nagamangala Taluk, Mandya, Karnataka, India

Introduction: Glaucoma, a leading cause of irreversible blindness worldwide, is associated with raised intraocular pressure (IOP). Steroid-induced glaucoma is a common type of secondary glaucoma also associated with increased IOP and excessive extracellular matrix deposition in the trabecular meshwork. Currently available antiglaucoma treatments aim to reduce IOP. However they often have suboptimal efficacy and are associated with side effects which affect patients' compliance.
Objective: This study evaluated the oculohypotensive effects of topical trans-resveratrol in steroid-induced oculohypertensive (SIOH) rats, and whether this effect is mediated by adenosine receptors (AR).
Method: The involvement of AR was studied by observing the oculohypotensive effect of trans-resveratrol by pre-treating the animals with AR subtype-specific blockers. We also looked at the involvement of ERK1/2, PLC and increased MMP secretion in the aqueous humour as a downstream mechanism of AR involvement in trans-resveratrol-induced oculohypotension.
Results: Topical trans-resveratrol 0.2% produced maximum IOP reduction and twice-daily dose for 3 weeks significantly sustained the IOP reduction in SIOH rats. The oculohypotensive effect of trans-resveratrol was inhibited with adenosine A1AR antagonist pre-treatment. Trans-resveratrol-induced MMP-2 secretion was antagonised when SIOH rats were pre-treated with A1AR, PLC and ERK1/2 inhibitors.
Conclusion: IOP reduction induced by trans-resveratrol involves its agonistic action at the A1AR leading to PLC activation, ERK1/2 phosphorylation and elevated MMP-2 level. Although this study has demonstrated the significant IOP lowering effect of trans-resveratrol. via its action on A1AR, further investigations are necessary to fully understand the mechanisms of trans-resveratrol as a potential antiglaucoma drug.

S081146-5

Anna Peresypkina

S082147-1

Yaghoub Fathollahi

S082147-2

Alireza Asgary

S082147-3

The application of computational physiology to bedside

Abdol-Hossein Vahabie

School of Cognitive Sciences, Institute for Research in Fundamental Sciences (IPM), Tehran, Iran

Studies of computational physiology provide novel insights into the nature of physiological function in both health and disease. Physiological function arises from complex interactions both within (horizontal integration) and between (vertical integration) networks organized at different biological levels. Understanding how physiological function emerges from these network interactions may provide new insights to know pathophysiological basis of diseases and develop novel interventions and therapeutic strategies for management of patients.

S085148-1

The Association of Ambient Particulate Matter with Cardiovascular Dysfunction: A Focus on Natural Antioxidants

Mahin Dianat*, Maryam Radan, Mohammad Badavi

Department of Physiology, Physiology Research Center, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Background and objective: Air pollution is a main risk factor for cardiovascular disease such as cardiac arrhythmias, myocardial infarction, ischemic stroke, vascular dysfunction and atherosclerosis. The suggested molecular mechanisms for particulate matter induced cardiovascular disorders include increasing oxidative stress and activating inflammatory pathway. antioxidant therapy was suggested to beneficially interfere with development and progression of cardiovascular disorders. Here, we review our pervious experiments on ambient particulate matter exposure and the occurrence of different cardiovascular dysfunction and discussed the possible beneficial properties of some natural antioxidant for prevention of cardiovascular diseases caused by air pollution.
Materials and methods: Sprague-Dawley rats (male, 250–300 g) were divided into control, antioxidant (Gallic acid, Ellagic acid, Vanillic acid, Crocin, Berberine), PM10 in different concentrations and PM10+antioxidant groups. The following parameters were evaluated: electrocardiogram parameters (HR, QRS Complex, PR interval and QT interval) hemodynamic parameters (LVDP, LVSP, RPP, dp/dt) in ischemia-reperfusion isolated rat heart, ischemia-reperfusion induced arrhythmias, isoprenaline induced arrhythmias, and CaCl2 induced arrhythmias. Oxidative stress indexes such as MDA, SOD, CAT, GSH, and GPx were evaluation using specified kits.
Results: The obtained results showed that the exposure to PM10 caused to increase in oxidative stress biomarkers which associated with decrease in cardiac hemodynamic and electrocardiogram parameters. Also, Pre or co-treatment with antioxidant preserved the value of cardiac parameters and oxidative stress factors in rat hearts.
Conclusion: The obtained results suggest that natural antioxidant could be a potent therapeutic agent in prevention and management of health issues in the polluted areas of the world.
Keywords: PM10; Oxidative Stress; Antioxidant; Hemodynamic, Electrocardiogram

S085148-2

Spatial memory and brain hippocampus electrical activity impair following prolonged exposure to ambient dust storm in rats.

Sarkaki A.[1], Hajipour S.[2], Farbood Y.[2], Gharib Naseri MK.[2], Bakhtiari N.3, Dianat M.[2], Nesari A.[2], Goudarzi GR.[4], Rashno M.[5], Sarkaki B.[2]

1. Iran National Science Foundation, Science deputy of presidency, Ahvaz Physiology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz-Iran.
2. Physiology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz-Iran.
3. Pain Research Center, Imam Khomeiny Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz-Iran.
4. Department of Environmental Health, Health Faculty, Ahvaz Jundishapur University of Medical Sciences, Ahvaz-Iran.
5. Department of Immunology, Medicine Faculty, Cellular & Mollecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz-Iran.

Background and Objectives: Dust storm (DS) and ambient particulate matter (PM) is a serious environmental problem. The central nervous system (CNS) is emerging as an important target for adverse health effects of ambient PM. We aimed to evaluate the effects of long-term exposure to different concentrations of PM conveyed in a actual DS generator chamber on behaviors and brain electrical activity in rats.
Materials and Methods: Adult young male rats weighing 200±50 g were randomly assigned into different groups; 1) Sham ; in a clean environment with a standard concentration of PMs (50-150 µg/m3), 2) DS1 (mild); 200-500 µg/m3. 3) DS2 (moderate); 500-2000 µg/m3, and 4) DS3 (Sever); 2000-5000 µg/m3. Animals were exposed for 30 min, twice daily (morning and evening), at first 4 days of each week in a homemade dust generator chamber as an actual model of DS with ambient PMs. During last 3 days of exposure to PMs, spatial cognition in water maze and hippocampal long-term potentiation (LTP) performed in all animals.
Results: Exposure to DS with different concentrations of PM impaired significantly spatial learning and memory as dose dependently ($p<0.001$). On the other hand PM inhalation caused decay of hippocampal LTP significantly in rats exposed to DS3 ($p<0.01$).
Conclusion: Our results showed ambient PM contributes to neurodegenerative disorders with decreases brain LTP as a cellular mechanism of cognition in responses to increase of brain inflammation and oxidants. So we need to improve our understanding more about the mechanisms of PM effects on CNS through multidisciplinary research.
Keywords: Dust strom; Particulate Matter; cognition; Long-Term Potentiation; Rat

S085148-3

How Does Ambient Particulate Matter Air Pollution Affect The Respiratory System? In Vivo and In Vitro Evidence

M. Radan[1], M. Dianat[1], M. Badavi[1], SA. Mard[1], V. Bayati[2], GR. Goudarzi[3]

1. Department of Physiology, Faculty of Medicine, Persian Gulf Physiology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2. Cellular and Molecular Research Center, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran;
3. Department of Environmental Health Engineering, Health Faculty, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Particulate matter (PM) has been linked with several health problems. There is some evidence indicating that the major effect of PM on the pulmonary system is the influx of inflammatory cells, which is characterized by the increased cytokine production in the respiratory system. One of the mechanisms by which PM exerts its inflammatory effects is oxidative stress. Nuclear factor erythroid-2-related factor (Nrf2) is a key regulator to protect against the adverse effects of oxidative stress induced by ROS. It has been demonstrated that diminished Nrf2 activity contributes to oxidative stress which leads to many pathological conditions. The present experiment focused on the role of Nrf2 signaling pathway in lung and epithelial cells exposed to PM. This experiment was divided into the in vivo and in vitro part. Inflammatory parameters, oxidative stress indexes and Nrf2-pathway factors were assessed. PM groups in all concentration showed a considerable decrease in the expression of Nrf2 and its down-stream regulators genes both in lung and epithelial cells. Accordingly, the biosynthesis of glutathione and other antioxidant activities significantly decreased. The current study provided convincing evidence suggesting that PM induces pathologic changes in lung tissue and epithelial cells via inflammation, and oxidative stress due to the suppuration of Nrf2-antioxidant response element signaling pathway.

S085148-4

Effects of Gallic acid on behavioral and electrophysiological alterations induced by cerebral ischemia/reperfusion followed by exposure to ambient dust storm in rats

Bavarsad K.[1], Sarkaki A.[1], Farbood Y[2]., Khoshnam SE[2]., Mirshekar Jehangir H[2], Rashno M[3]., Dianat M[2]

1. National Institute For Medical Research Development, Physiology Research Center, Ahvaz jundishapur University of Medical Sciences, Ahvaz-Iran.
2. Department of Physiology, Physiology Research Center, Ahvaz jundishapur University of Medical Sciences, Ahvaz-Iran.
3. Department of Immunology, Cellular & Molecular Research Center, Ahvaz jundishapur University of Medical Sciences, Ahvaz-Iran.

Introduction: Ischemic stroke is one of the leading causes of death worldwide. A large body of literature reported the association of particulate matter (PM) of air with stroke. This study was carried out to investigate the protective effects of gallic acid (GA) on behavioral and electrophysiological alterations induced by 4VO cerebral ischemia/reperfusion (4Vo-I/R) in rats following exposure to ambient dust storm.

Methods: Adult male Wistar rats (200–250 g) were randomly divided into 8 groups and submitted to either sham surgery or 4VO-I/R after pretreatment with GA (100 mg/kg/2ml, gavage) or normal saline, for 10 consecutive days and continue 3 days after IR induction. Rats were exposed to ambient PM with <150 µg/m3 (clean air) or 2000 to ≥5000 µg/m3 (dusty air) in concentrations, 60 minute daily for 10 consecutive days before cerebral 4VO-I/R induction. Subsequently, spatial cognitive performance was evaluated in a Morris water maze (MWM), hippocampal LTP was recorded from hippocampal dentate gyrus region.

Results: The results showed that exposure to dusty air has exacerbated I/R-induced cognitive and hippocampal LTP impairments ($p<0.01$). Pretreatment with GA significantly improved I/R-induced cognitive and hippocampal LTP impairments following exposure to ambient dust storm ($p<0.01$).

Conclusion: Our data confirm that GA could prevent cognitive and LTP impairments due to cerebral ischemia following exposure to ambient dust storm. It has antioxidative and anti inflammatory actions that reverse the brain electrical activity as well as cognition.

Keywords: Ischemic stroke, Ambient dust storm, Long term potentiation, Gallic acid, Rats

S085148-5

Evaluation of the preventive effects of Gallic acid on blood brain barrier function and oxidative stress of brain caused by cerebral ischemia/reperfusion following exposure to ambient particulate matter in rats

Hamzeh Mirshekari jahangiri[1], Alireza Sarkaki[1], Yaghoob Farbod[2], Mahin Dianat[3], Gholamreza Goodarzi[4]

1. Physiology Research Center, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Golestan Blvd, Ahvaz, Iran
2. Physiology Research Center, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Golestan Blvd, Ahvaz, Iran
3. Physiology Research Center, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Golestan Blvd, Ahvaz, Iran
4. Department of Environmental Health Engineering, School of Public Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Dust storms are environmental natural events that transport high concentrations of particulate matter (PM) in living spaces, and mostly originate from arid and desert areas. Recent epidemiological studies have shown that air pollution is associated with stroke. Global cerebral ischemia/reperfusion (4VO- I/R) may occur after several clinical conditions such as cardiac arrest. In the present study we aimed to investigate the probable effects of gallic acid (GA) on blood brain barrier (BBB) disruption and oxidative stress induced by permanent arteria vertebralis heatblocked and temporary carotid arteries occlusion/reperfusion (4VO) following exposure to ambient particulate matter (PM) in rats. 4VO was induced on animals after 10 days of pretreatment by GA (100 mg/kg) and exposure to PM (2000-5000 µg/m3). 72 h later 4VO induction BBB permeability and oxidative stress of brain evaluation were done. Data showed that 4VO ischemia/reperfusion and PM have increased BBB permeability and oxidative stress. Pretreatment with GA reduced BBB permeability and oxidative stress significantly. disorders caused by 4VOI/R and PM are mainly caused injuries to brain cells due to the production of free radicals and inflammatory cytokines. GA is a protective factor against complications caused by both the 4VOI/R and the PM. The beneficial effects of GA may be due to its antioxidant and anti-inflammatory properties. GA can be considered as an agent to reduce the harmful defects caused by 4 VO-I/R and PM.

S084149-1

Role of " Pharmacological conditioning" in regenerative medicine

Ali Mohammad Sharifi

Department of Pharmacology, Medical School & Department of Tissue Engineering and Regenerative Medicine, School of Advance Sciences in Medical Sciences, Tehran, IRAN.

Degenerative diseases are substantially growing and serious health threat worldwide. Regenerative pharmacology as a branch of regenerative medicine is a novel therapeutic approach with goal of preventing, repairing and regenerating the progressive cell destruction which were mediated by various etiological factors causing such disorders. This approach works to identify the drug mediated molecular targets for regenerative and therapeutic purposes. By restoring the development and function of tissues and organs, regenerative pharmacology has the ability to improve therapies for many human diseases. Stem cell-based regenerative pharmacology supports the use of stem cells for derivation of novel therapeutics. Various regenerative pharmacological approaches such as pharmacological conditioning would be able to affect all aspect of stem cell and regenerative medicine as well as tissue engineering researches including; mobilization, expansion, differentiation, homing, functional improvement, reprogramming of stem cell, drug delivery, and many others. It has been shown that pharmacological conditioning strategy could significantly enhance efficacy of cell therapy and reduce the cost of treatment, potentiate homing, survival, viability of cells, reduction in apoptosis leading to efficacious therapy by tackling the obstacles in cell therapy.

Ultimately, stem cell-based regenerative pharmacology aims to establish stem and progenitor cells as effective treatments for preventing disease and for facilitating organ replacement or repair. This promising area of basic and clinicaly oriented research opens up numerous new opportunities for pharmacology.

S084149-2

The Amniotic Membrane Mesenchymal Stem Cell Derived Conditioned Medium Exerts Neuroprotection Against Cerebral Ischemia

Nahid Abootaleb

Objectives: It has been reported that conditioned medium obtained from mesenchymal stem cells (MSC-CM) possess many antioxidant and anti-inflammatory agents that can contribute to treatment of different diseases. We went on to investigate the protective effects of this medium against focal cerebral ischemia/reperfusion and clarify its potential mechanisms.
Methods: Middle cerebral artery occlusion (MCAO) was used as a procedure to create model in male Wistar rats. Stereotactic intracerebral infusion of MSC-CM was performed 30 min after reperfusion. Immunohistochemical assay was applied to evaluate the expression of Phospho-ERK1/ERK2, BDNF, VEGF, NGF, Bax, Bcl2 and caspase3. Nissl and TUNEL methods were used to examine neuronal loss and DNA fragmentation, respectively. 2,3,5-triphenyltetrazolium chloride (TTC) staining was used to evaluate infarction size.
Results: Results demonstrated that MSC-CM contributed to reduction of infarct volume and improvement of motor and sensory function ($P<0.05$). Likewise, MSC-CM attenuated neuronal loss and apoptotic cell death by targeting Phospho-ERK1/ERK2, BDNF, VEGF, and NGF ($P<0.05$).
Conclusion: Collectively, our findings confirm the validity of MSC-CM as a potential antioxidant and anti-apoptotic factor against ischemic stroke. Function of MSC-CM is based on stimulation of angiogenesis, neurogenesis and inhibition of apoptosis.
Keywords: Focal cerebral ischemia/reperfusion; Mesenchymal stem cells; conditioned medium; Phospho-ERK1/ERK2; BDNF; Apoptosis

S084149-3

Restoring the IL-1β/NF-κB-induced impaired chondrogenesis by using diallyl disulfide

Kobra Bahrampour Juybari[1] & Tunku Kamarul[2] & Mohammad Najafi3 & Davood Jafari[4] & Ali Mohammad Sharifi[4,5]

1. Department of Pharmacology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran
2. Tissue Engineering Group, (NOCERAL), Department of Orthopedic Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia,
3. Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
4. Department of Pharmacology and Razi Drug Research Center, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
5. Bone and Joint reconstruction research center and Department of Orthopedics Surgery, Shafa Orthopedic Hospital, Iran University of Medical Sciences, Tehran, Iran

Background and Objective: Due to the enhanced inflammation and oxidative stress in osteoarthritis (OA) microenvironment, differentiation of MSCs into chondrocytes would be impaired. This study aims to explore the effects of diallyl disulfide (DADS) on IL-1β-mediated inflammation and oxidative stress in human adipose derived mesenchymal stem cells (hADSCs) during chondrogenesis.
Materials and Methods: MTT assay was employed to examine the effects of various concentrations of DADS on the viability of hADSCs at different time scales to obtain non-cytotoxic concentration range of DADS. The effects of DADS on IL-1β-induced intracellular ROS generation and lipid peroxidation were evaluated in hADSCs. Western blotting was used to analyze the protein expression levels of IκBα (np & p), IκBα (p), NF-κB (np) and NF-κB (p). Furthermore, the gene expression levels of antioxidant enzymes in hADSCs and chondrogenic markers at days 7, 14 and 21 of differentiation were measured using qRT-PCR.
Results: The results showed that addition of DADS significantly enhanced the mRNA expression levels of antioxidant enzymes as well as reduced ROS elevation, lipid peroxidation, IκBα activation and NF-κB nuclear translocation in hADSCs treated with IL-1β. In addition, DADS could significantly increase the expression levels of IL-1β-induced impaired chondrogenic marker genes in differentiated hADSCs.
Conclusion: Treatment with DADS may provide an effective approach to prevent the pro-inflammatory cytokines and oxidative stress as catabolic causes of chondrocyte cell death and enhance the protective anabolic effects by promoting chondrogenesis associated gene expressions in hADSCs exposed to OA condition.
Keywords: Osteoarthritis, Diallyl disulfide, Inflammation, Oxidative stress, Chondrogenesis.

S084149-4

In vivo reprogramming as a new avenue to regenerative therapies in neurodegenerative diseases

Mohammad Javan

1. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University
2. Department of Brain Sciences and Cognition, Royan Institute for Stem Cell Research and Technology, Tehran, Iran

Recent studies demonstrate that astroglial cells can be directly converted into functional neurons and oligodendrocytes. We introduce a brief review on recent years achievements, then will foclus on two examples from our lab; the single transcription factor Sox10 as well as the chemicals which were able to reprogram astrocytes into oligodendrocyte-like cells, in vivo. For transdifferentiation, GFP expressing viral particles caring the coding sequence of TFs were injected into cuprizone-induced demyelinated mice brains after which we assessed for the presence of specific oligodendrocyte lineage cell markers in transduced cells by immunohistofluorescence (IHF). As control, another group of demyelinated mice received GFP expressing viral particles. For chemical conversion, astrocytes were exposed to the candidate compounds and then immediately transplanted to demyelinated mice brains. After weeks, the majority of transduced/treated (GFP+) cells in animals which received control vector were positive for oligodendrocyte lineage markers. We also used human astrocytes or extracted primary astrocytes from mouse pups and purified them. Human or primary astrocytes were used for confirming the results in vitro. This finding suggested a master regulatory role for Sox10 which enabled astrocytes to change their fate to OPC-like cells and establish an oligodendroglial phenotype. We also mentioned that chemicals could do in vivo conversion which promise for the safety of future approaches. We hope this approach lead to effective myelin repair in patients suffering from myelination deficit.
Keywords: In vivo reprogramming; Neurodegeneration; Demyelinating disease; Reactive astrocytes; Oligodendrocyte lineage cells; Transdifferentiation

S084149-5

Applications of microfluidics in regenerative pharmacology

Mohammad Adel Ghiass

Tissue Engineering Department, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Microfluidics provides the ability to precisely manipulate fluids in micron-scale structures. That in turn leads to many advantages such as low sample and reagent consumption, small physical and economic footprint, parallelisation, high-throughput capabilities and controlled mass transfer. Separation, sorting, detection, and screening with high resolution and sensitivity are some basic functions that can be implemented using microfluidics. Regenerative pharmacology is one of the most important fields that can utilise microfluidics to achieve outstanding results. Micro and nano structure carriers are generated using droplet microfluidics to encapsulate various types of drugs, small molecules, proteins, and nucleic acids. Also, micro packaged biosystems of mesenchymal stem cells, hepatocytes, and fibroblasts are fabricated to be used for cell-based therapies. Microfluidics makes it possible to handle single cells to facilitate high-throughput screening of thousands of cells in short periods of time. Moreover, local drug delivery is attainable using wearable and implantable microfluidic systems capable of real-time monitoring of biological factors. Lab-on-a-chip emerged with development of microfluidics to perform all steps of different biological assays like sample preparation, molecule extraction, amplification, purification, biochemical reactions, and detection on a self-contained, easy to use, cheap, and portable chip. The required components to perform an assay are integrated onto a single chip that takes the sample as the input and provides the results in suitable quantitative and qualitative manners. Besides, different organs are modelled biomimetically using microfluidics in another approach called organ-on-a-chip. As a result, a biological analysis is performed with low costs in conditions closer to real physiological conditions and considering the possible interactions. This is can be taken into account as a platform to develop whole body models. Usage of microfluidics paves the way for new applicable achievements in regenerative pharmacology.

S087150-1

فاقد چکیده

S087150-2

فاقد چکیده

S087150-3

فاقد چکیده

S087150-4

فاقد چکیده

S087150-5

فاقد چکیده

S087150-6

فاقد چکیده

S087150-7

فاقد چکیده

S087150-8

فاقد چکیده

S091151-1

Artificial intelligence and its impact on the physiology and pharmacology

Masoumeh Jorjani

Department of Pharmacology, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, IRAN

The pace of technology growth and developments of the Fourth Industrial Revolution have had a profound impact on health as well as other aspects of human life. In the age of intelligence, with the demarcation of the boundaries between scientific facts and human imagination, educational and research needs have also changed, so as to familiarize and empower the next generation in the face of this volume of transformation and the possibility of providing services to adapt to changes in practices. Their teaching and research is essential. Current educational tools, techniques, and curricula need to be revised to enhance the understanding of emerging technologies in learners and the ability to use artificial intelligence in individual teaching and learning and indeed learning. To increase permanence in individuals. Artificial intelligence, robotics, nanotechnology, 3D printers, virtual reality, micro-chips, bio-printers, big data, mobile internet and many new technologies in the physiology and pharmacology sciences have also undergone significant changes. Nowadays, by modeling, simulating, and visualizing biological trends in the computer, the effects of new drugs or proposed therapies in virtual settings can be assessed. Bioinformatics allows researchers to model metabolism, endocrine, nervous system, and blood circulation using large data sets. Human physiology has been simulated from whole organism to individual molecules using sophisticated mathematical models and numerical equations and variables. Computer-designed neural networks are able to predict the side effects of new therapies and thus reduce the potential risks for the patient and reduce His complaints are. Creating organs or functions similar to those of human organs and performing clinical trials in virtual bodies that fully mimic human physiology, in addition to reducing the cost of research and reducing costs, can pose risks to these studies in vitro. Or reduce human beings greatly. The development of new drugs with 3D printers enables rapid solubility of drugs and reduced number of prescription drugs. The presence of absorbable sensors using nanotechnology allows precise tracking of the pharmacokinetic pathway of drugs in the body and the transfer of information to smartphones. Pharmacogenomics also allows the patient to obtain their own proprietary and selective drug by individual genetic evaluation. This rapidly expanding set of developments has led to the development of digital health and its applications, providing individualized, cost-effective, and cost-effective therapies that require knowledge of technologies related to the physiology and pharmacology sciences.

S091151-2

Pharmacogenomics and personalized medicine

Ziai S.A.

Department of pharmacology, faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

The sequencing of the entire human genome and of the realization that medication errors constitute one of the leading causes of death has led many to believe that pharmacogenomics may be able to improve pharmacotherapy. As a result, a fairly uncritical series of hopes and predictions have led not only physicians and scientists to believe that genomics will lead to a new era of "personalized medicine".

Clinical genetic testing historically has been limited to germ line mutation detection for Mendelian diseases; however, the ongoing identification of deoxyribonucleic acid (DNA) sequence variants associated with common diseases prompted the availability of testing for personal disease risk estimation, and created commercial opportunities for direct-to-consumer genetic testing companies that assay these variants.

This germ line genetic risk, in conjunction with other clinical, family, and demographic variables, are the key components of the personalized medicine paradigm, which aims to apply personal genomic and other relevant data into a patient's clinical assessment to more precisely guide medical management.

S091151-3

Translational pharmacology: it is time to shift the paradigm

Hassan Niknejad

Department of Pharmacology, School of Medicine, Shahid Beheshti University of Medical Science, Tehran, Iran.

One of the important concerns in identifying future perspective of pharmacology is how to translate pharmacological findings into clinic. Translational Medicine (TM) is a field of medical research that aims to determine the link between human diseases and new discoveries of basic science to improve human health and lifespan. TM harmonizes the use of new scientific findings in therapeutic processes and feedback clinical observations and questions into scientific hypothesis in the laboratory. So, TM has a bidirectional concept: bench-to-bedside translation and bedside-to-bench transition. It seems stem cells are one of the building blocks of translation in the age of artificial intelligence. Stem cells as a potential therapeutic "tool" for a variety of degenerative diseases have attracted much attention in the basic and clinical medicine. Using of stem cells to establish tissue specific organoids, CAR-T cell therapy for cancer, differentiation of stem cells into specific lineage (such as neural cells, cardiomyocytes, hepatocytes and so on) by pharmacological small molecules, application of stem cells in microfluidic devices as lab on a chip and organ on a chip model (as a substitute for animal models), and pharmacological nanoparticle primed stem cells as new approach in drug delivery suggest that there will be a crossroad between stem cells and pharmacology in the near future. A crossroad which opens a new field entitled “regenerative pharmacology”. However, there are some drawbacks which must be circumvented; and as the first step, it is necessary to have a paradigm shift from conventional pharmacology to future perspectives of pharmacology.
Keywords: Translational Medicine, Basic Sciences, Clinical Research, Stem cells, Paradigm shift, Regenerative pharmacology

S091151-4

Virtual Neurophysiology

Mir-Shahram Safari

Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Understanding neurophysiology is for many students a particularly difficult task, especially the interpretation of different measures their physiological meaning and their interrelations. It could be of great help if the students could do the recordings themselves, according to the didactically advantageous strategy "learning by doing". When such experiments are not possible in regular students' courses, for whatever reasons (too difficult, no resources etc.), virtual laboratories can become valuable alternatives. To provide students a realistic neurophysiology research experience requiring only computers and no laboratory equipment, scientists have used several neural simulators. This programs simulates neural mechanisms underlying various physiological conditions and allows students to do realistic neurophysiological experiments to discover how neural circuitry works. Virtual lab also used for undergraduate students to gain a better understanding of the neurophysiology of action potentials and identification of different types of neuronal cells. This is accomplished by using a virtual dissection of a leech and subsequent probing of the leech's nervous system with a variety of tools. The oscilloscope readings of the action potential along with the morphology of the cells after contrast dye injection are used in comparison with an interactive atlas to help identify these cells. For example a Virtual Lab provides students the opportunity to explore the electrical activity of individual neurons by virtually stimulating the skin of a leech. A lab notebook, equipment list, atlas of cells and recordings is provided to simulate a lab activity. Some study have been shown isolated use of the virtual laboratory is not the best practice: the virtual laboratory serves as an effective preparation tool, and the blended laboratories may become the best laboratory teaching practice, provided that the software design for the virtual laboratory is further improved. In this talk I will review recent advances in virtual neurophysiology

S091151-5

Microfluidics & Microfabrication in Self-organization of Hepatocyte Morphogenesis

Mohammad Ajodanian

Recent advances in microfabrication technologies have enabled us to construct collagen gel microbeads, which can be cultured with hepatocytes. However, little is known about the hepatocyte–collagen gel microbead interactions. Here, we aimed to clarify the effects of the balance between cell–cell and cell–collagen gel microbead interactions on hepatocyte morphogenesis and functions. The magnitude of cell–microbead interactions was controlled by changing the size of the microbeads, which were smaller than, comparable to, and larger than hepatocytes. These small, medium, and large microbeads were cultured separately with primary hepatocytes. Phase-contrast and time-lapse imaging revealed that the medium microbeads significantly induced the construction of 3D structures composed of the microbeads and hepatocytes in a self-organizing manner, whereas hepatocytes formed 2D monolayers with the small or large microbeads. These results suggest that only the medium microbeads induced the 3D tissue formation of hepatocytes. Furthermore, liver-specific functions, such as albumin secretion and ammonia clearance, were significantly upregulated in the 3D structures. These findings are critical to understand how to control the construction of 3D hepatocyte tissues with hydrogel microbeads in the context of biofabrication.

S092152-1

Electrophysiological basis of neural epileptiform activity after traumatic brain injury

Mahyar Janahmadi[1, 2], Seyed Asaad Karimi[1-4], Narges Hosseinmardi[1,2], Mohammad Sayyah[5], Razieh Hajisoltani[1,2]

1. Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
4. Department of Neuroscience, School of Advanced Technologies in Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
5. Department of Physiology and Pharmacology, Pasteur Institute of Iran, Tehran, Iran

Recording the electrical activity of nerve cells is important for understanding the mechanisms of neuronal function under physiological and pathological conditions. Alteration in neuronal firing pattern activity may affect information processing underlying memory formation and cognition. In traumatic brain injury (TBI), which results in long-lasting cognitive and motor deficits, firing pattern changes from single spiking to burst firing. However, the underlying mechanisms have not been fully determined. Here, in order to understand what changes take place in intrinsic neuronal physiology in the hippocampus after blunt force trauma to the cortex, whole-cell patch-clamp recordings were made under current and voltage clamp conditions in the presence of fast synaptic blockers. Using a controlled cortical impact (CCI) as a model of TBI, the intrinsic firing properties of pyramidal neurons were examined one week after TBI induction in rats. Induction of TBI was associated with changes in the intrinsic firing pattern of pyramidal neurons from solitary spiking to burst firing. There was also a significant increase and decrease in firing frequency and in the rheobase current, respectively ($P < 0.05$). Since, hyperpolarization-activated cation current (Ih) currents may play a critical role in regulation of epileptiform discharges; therefore, its contribution to the TBI-induced hyperexcitability was assessed. In the TBI group, both the instantaneous and steady-state Ih current amplitudes were significantly smaller than those in the control group ($P < 0.05$) and the sag ratio was significantly less than control values ($P < 0.001$). The Ih current density was also significantly decreased ($P<0.001$). Findings indicated that TBI led to induction of epileptiform activity in CA1 pyramidal neurons and changes in Ih current could be, in part, one of the underlying mechanisms involved in this hyperexcitability.

Key words: Controlled Cortical Impact; CA1 pyramidal neurons; Firing Pattern; Ih channel current; Traumatic Brain Injury

S092152-2

Role of Glia in TBI-induced Electrophysiological and Behavioural Deficits

Narges Hosseinmardi1*, Amir Rezagholizadeh[1], Seyed Asaad Karimi[2], Mahyar Janahmadi[1], Mohammad Sayyah[3]

1. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
3. Department of Physiology and pharmacology, Pasteur Institute of Iran, Tehran, Iran

Traumatic brain injury (TBI) is a damage caused by an external mechanical force that can produce significant cognitive and memory impairment in humans. Evidence suggests that glial cells are influenced by TBI. Both protective and damaging roles have been attributed to active astrocytes, but their role after TBI has not been well understood. In this study, the role of glial cells in TBI-induced cognitive impairment and synaptic dysfunction was investigated. Glial cell-inhibitor, Fluorocitrate (FC), in a rat model of controlled cortical impact injury (CCI) was used. Male rats were randomly assigned to the following groups: Sham+PBS, sham+FC (1nmol/1µl), TBI+PBS, and TBI+FC (1nmol/1µl). Fluorocitrate was injected into the brain lateral ventricle 10 min after TBI induction and it was repeated every 24 hours until the seventh day. On days 8-13 post-injury, reference and reverse memory and on days 8-16 post-injury, working memory was assessed using the Morris water maze test (MWM). Injured animals showed a slower rate of acquisition with respect to the sham+PBS animals [(F (1, 84) = 7.398, P = 0.008), two-way ANOVA,]. FC administration could not attenuate the deteriorative effect of TBI on reference, reverse and working memory acquisition. There were no significant differences in escape latency and traveled distance between injured animals and TBI treated with FC ($p>0.05$, two-way ANOVA). Sham animals which received FC showed a considerable increase in escape latency ($P = 0.0183$, two-way ANOVA) and traveled distance ($P = 0.0043$, two-way ANOVA), compared to Sham+PBS animals. The results of field potential recording from the CA1 region of the hippocampus indicated that trauma reduced baseline responses, especially in high stimulation intensities ($F (36, 144) = 11.65$, $P < 0.0001$, Two way ANOVA). LTP induction in damaged animals (%112/7 ± 2/189, n=8) was decreased ($P<0.05$, Unpaired t-test). The inhibition of glial cells was further reduced the percent of potentiation (%99/10 ± 3/503, n=4, $P<0.05$, Unpaired t-test). Synaptic depression was increased due to trauma (%24/27 ± 3/984, n=8, $P<0.01$, Unpaired t-test) and the inhibition of glial cells prevented (%-0/2700 ± 1/805, n=4) this depression ($P<0.01$, Unpaired t-test). The present study demonstrates that memory deficit and metaplasticity induced by TBI cannot be improved by administration of FC. Our results suggest that inhibition of glial cells maybe resulted in the memory loss and synaptic dysfunction in uninjured animals.

Keywords: Traumatic brain injury; Cognitive and synaptic dysfunction; Glial cells; Fluorocitrate

S092152-3

The neuroprotective effects of erythropoietin on the neurological scores, brain edema and blood brain barrier permeability after severe traumatic brain injury in male rats: the role of AMPK

Ali Siahposht-Khachaki1*, Sayed Saeed Saed [2], Davood Farzin [3]

1. Department of Physiology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
2. Pharmacy Student, Mazandaran University of Medical Sciences, Ramsar International Branch, Sari, Iran
3. Department of Pharmacology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

Erythropoietin (Epo) is a cytokine that exists in all vertebrate groups. The main function of Epo in the nervous system is protection against apoptosis, reducing inflammatory responses and helping to migrate, and differentiating cells to replace dead or damaged cells. Therefore, in this study, we investigated the effects of neuroprotective erythropoietin and the role of AMPK after traumatic brain injury in male rats.The male Albino wistar rats received different doses of erythropoietin (2500, 5000, 10000 unit/kg, i.p.). All animals were intubated before surgery. In the TBI groups except sham and intact groups, diffuse TBI was induced by Marmarou method using a TBI induction device. The severe TBI was induced using a weight 450 gr. The neurologic scores (VCS) and brain water content, the beam-walk –balance task (WB) were recorded for 72 hours. After 72 h from Deep anaesthetized animals CSF was collected and then analysis AMPK with Elisa assay. Our results showed that traumatic brain injury led to significant brain edema and disrupt of blood brain- barrier and neurological defect and vestibulomotor dysfunction in the rat brain and decrease AMPK in CSF and vestibulomotor dysfunction in compare with TBI control group ($P<0.001$) but in 2500 dose results were better. These findings showed that Erythropoietin has a prominent role in TBI outcome's and perhaps protect neurons through modulating inflammatory and antioxidant pathways

Key word: Erythropoietin, TBI, neuroprotective, AMPK, rat

S092152-4

Investigating the effect of oral mucosa mesenchymal stem cells treatment on brain edema and behavioral and cognitive outcome caused by experimental traumatic brain injury

Zahra Soltani

Introduction: Traumatic brain injury (TBI) is one of the leading causes of morbidity and mortality throughout the world. It will probably become the third leading cause of death in the world by the year 2020. Despite extensive research, successful treatment for TBI has not been introduced yet. The use of stem cells is one of considered therapeutic approaches in medical research. The beneficial effects of mesenchymal stem cells (MSCs) in damage of the central nervous system (CNS), including some of TBI models, have been shown. The mesenchymal cells lining of the mouth (oral mucosal stem cells; OMSCs) as cells originating from the neural crest have considered because of their high reparative potency recently. Given the importance and recommendation the use of stem cells and on other hand, the failure of drug therapy in TBI, the effect of oral mucosal mesenchymal stem cells administration after TBI was evaluated on brain edema, neurological and histopathological outcomes, and cognitive, motor and like-anxiety behaviors in rats in current study.

Methods: In this experimental study, 56 male Wistar rats weighing 250-200 g randomly assigned to four groups sham, TBI, vehicle and stem cell. Brain edema (using brain water content) and histopathological outcome were assessed 24 and 48 h after TBI. Evaluating short- time neurological (using veterinary coma scale; VCS) and motor outcome (using standard beam tasks), and recording intracranial pressure (ICP) were performed before, 1, 4, 24 and 48 hours after TBI. Motor (using open field test, OFT) and neurological outcome (using standard neurologic severity score; NSS), and memory (using water maze Morris, MWM) and anxiety-like (using elevated plus maze, EPM) behaviors were evaluated 3, 7, 14 and 21 days after TBI. TBI was induced of moderate and diffuse type.

Results: An increase in brain edema occurred after TBI ($P<0.001$), at 24 and 48 hours agter injury, that reduced in SC group compared to the vehicle group ($P<0.001$). ICP increased at all times after the injury ($P<0.001$) and this increase at 1 hour ($P<0.05$), 4 hours (P,0.01), 24 and 48 hours after injury was inhibited in SC group compared to the vehicle group ($P<0.001$). NSS increased at all times after the damage ($P<0.001$) and reduced following administration of OMSC in the SC group compared to the vehicle group ($P<0.001$). Reduction in anxiety-like behavior post-injury was observed in the treatment group in comparison to TBI group. Reduction in this behavior was observed as increasing the time spent in the open arm ($P<0.001$), decreasing the time spent in closed arm ($P<0.001$) and increasing number of open arm entries ($P<0.001$) SC group in comparison to the vehicle group. Administration of OMSC also significantly improved short-term and long- term motor outcome ($P<0.001$) and balance SC group in comparison to the vehicle group ($P<0.001$). Increased inflammation, microglia and axonal degeneration after was attenuated following OMSCs administration compared to vehicle group ($P<0.05$).

Conclusion: This study showed that administration of OMSC reduced brain edema, inflammation, ICP, and microglia activity after TBI. Long-term neurologic and motor outcome deficits as well as anxiety-like behavior and memory impairment reduced following OMSC administration after injury. Improved motor, neurological, and cognitive-behavioral consequences after injury may be due to reducing inflammation and microglia proliferation after OMSC administration. The results suggest that using OMSC could be considered in TBI and perhaps other neurodegenerative disorders. However, further research is needed to finding the mechanisms involved as well as safety of this intervention.

Keywords: Traumatic brain injury, Stem cell, Brain edema, Intracranial pressure, Neurological outcome, Inflammation, Anxiety-like behavior, Histopathological outcome

S092152-5

Adjuvant therapy in prevention of post-traumatic epilepsy

Mohammad Sayyah

Department of Physiology and Pharmacology, Pasteur Institute of Iran, Tehran, Iran

Background and Objective: Five percent of all epilepsy cases are attributed to traumatic brain injury (TBI), which are known as post-traumatic epilepsy (PTE). Preventing the development of PTE is a major concern in epilepsy. However, no strategy is yet available to restrain the provocation of epileptogenesis by PTE. Remarkable feature of TBI is activation of microglia and subsequent neuroinflammation, which provokes epileptogenesis. The toll-like receptor agonist Monophosphoryl Lipid A (MPL) is safe, well-tolerated and effective adjuvant existing in prophylactic human vaccines. We examined the impact of MPL on the accelerated rate of epilepsy acquisition in the traumatic rats.
Materials and Methods: TBI was exerted to temporo-parietal cortex of anesthetized adult rats by Controlled Cortical Impact device through stereotaxic surgery. Rats received a single dose (1µg/rat) of MPL through intracerebroventricular injection either 5 days before or 30 min after induction of TBI. 24h after TBI, traumatic rats underwent electrical and/or chemical (Pentylenetetrazole) kindling.
Results: Traumatic rats showed less number of stimuli to become kindled ($p<0.01$, compared to non-traumatic sham-operated rats). MPL had no effect on the kindling rate in sham-operated rats. However, it inhibited the accelerated rate of kindling in the traumatic rats.
Conclusion: Considering that MPL is currently used clinically as well-tolerated vaccine with reliable safety, it has the potential to be used in prevention of PTE.
Keywords: Preconditioning; Postconditioning, Kindling, Rat

S093153-1

Deep Brain Stimulation in Movement Disorders

Mohammad Rohani

Division of Neurology – Hazrat Rasool Hospital, Iran University of Medical Sciences,Niyayesh St, Sattarkhan Ave, Tehran, Iran

More than 30 years has been passed since the introduction of deep brain stimulation for treatment of movement disorders. Now it is a popular worldwide therapeutic modality for treatment of many neurological and psychiatric disorders. Hundreds of thousands of patients received this treatment with good results. In neurology, deep brain stimulation (DBS) is a well-known and effective option for patients suffering from movement disorders. The most common one is Parkinson's disease. Other diseases with good results after receiving DBS are dystonia, tremor and tics.
Prospective, randomized controlled studies have confirmed that DBS results in improvement in quality of life, medication intake and the associated chronic care costs in movement disorders such as Parkinson's disease, essential tremor and dystonia. FDA approved the use of DBS for essential tremor in 1997, Parkinson's disease in 2002 and dystonia in 2003
There are various targets for implanting electrodes, the most commons are subthalamic nucleus, globus pallidus and ventral intermediate nucleus of thalamus. Many other targets are waiting for more studies to receive approval. The technology of electrodes and pulse generators have been progressed significantly in recent years. Herein the most recent findings and achievements in this field (DBS in neurological disorders) have been reviewed.

S093153-2

Deep Brain Stimulation as a promising intervention for treatment-refractory OCD

Mohammad Ghadirivasfi[1], Reza Arezoomandan[2], Mansour Parvaresh[3]

1. Research Center for Addiction and Risky Behavior (ReCARB), Iran University of Medical Sciences (IUMS), Tehran, Iran
2. Assistant Professor of Neuroscience, Addiction Department, School of Behavioral Sciences and Mental, Iran University of Medical Sciences, Tehran, Iran
3. Associate Professor of Neurosurgery, Iran University of Medical Sciences , Tehran, Iran

Obsessive-compulsive disorder (OCD) is one of the most debilitating of all psychiatric disorders. 10% of OCD patients remain resistant to all interventions and suffer from severe symptoms showing marked difficulties with fully functional areas. It has been shown that pathological hyperconnectivity between cortical and subcortical structures consider as potential causal factors for OCD symptoms.
Deep Brain Stimulation (DBS) is a neurosurgical treatment involving the implantation of electrodes in the specific brain area and send electrical impulses to this brain location. During the last decade DBS has become a routine method for the treatment a variety of neurological disorders including Parkinson's disease, essential tremor leading significant improvements in motor function and quality of life of these patients. In addition, DBS is currently used for treatment-resistant psychiatric disorders such as major depression, obsessive compulsive disorder (OCD) and Tourette syndrome.
Recently, in Iran University of Medical Sciences, we established "Psychosurgical Unit". For the first time in Iran, we used DBS as new approach for treatment of psychiatric disorders particularly OCD. Until now, in a small series, we used DBS for 4 patients with severe and treatment- refractory OCD. Based on preliminary data, the results yielded two major findings: a degree of changes with neuropsychological scores and clinical improvement.
Key words: Deep Brain Stimulation, Obsessive-compulsive disorder, neurosurgery

S093153-3

DBS-like stimulation of the orbitofrontal cortex prevents relapse to morphine seeking

Esmaeil Riahi

Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran

The orbitofrontal cortex (OFC) is involved in cue-, context-, and stress-induced reinstatement of drug seeking in animal models of addiction. Deep brain stimulation (DBS) was proposed to be an effective intervention for patients with treatment-refractory addiction. Therefore, we investigated the potential efficacy of DBS in the OFC for controlling addictive-like behaviors in rats.
Rats were bilaterally implanted with electrodes in the OFC and trained to the morphine conditioned place preference. DBS-like stimulation was applied during the conditioning or extinction trials. Following the extinction, morphine preference was reinstated by a priming dose of morphine.
When applied during the conditioning phase, DBS significantly decreased preference for the morphine-associated context. During the extinction phase it reduced the number of days to full extinction of morphine preference and prevented morphine priming-induced recurrence of morphine preference.
In conclusion, DBS of the OFC prevented morphine preference, facilitated extinction of morphine preference, and blocked drug priming-induced reinstatement of morphine-seeking. These findings may indicate a potential applicability of DBS in the treatment of relapse to drug use.
Keywords: Deep Brain Stimulation; Orbitofrontal Cortex; Morphine; Rats

S093153-4

Effect of deep brain stimulation on seizure and synaptic transmission

A Shojaeil, S. Ghafouri[1], A. Asgaril, K. Esmaeilnejad[2], J. Mirnajafi-Zadeh[1]

1. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran

Deep brain stimulation (DBS) is a potential therapeutic manner for drug-resistive epilepsy. However, the exact mechanisms of DBS on neuronal functions have not been completely determined. In a series of experiments, we checked the anticonvulsant effects of DBS on kindled seizures. Animals were kindled through electrical stimulation of hippocampal CA1 area. DBS was applied at the pattern of low-frequency stimulation (1 Hz) as 4 trains with 5 min intervals in fully kindled animals. Application of DBS significantly reduced the seizure severity and reduced the kindling-induced potentiation. To investigate the involved mechanisms of anticonvulsant effect of DBS, whole cell patch clamp recording was done in CA1 pyramidal neurons. Obtained results showed that DBS applying in kindled animals reduced the glutamatergic currents (EPSC) and increased the threshold intensity of these currents. Moreover, DBS increased the GABAergic currents (IPSC) and decreased the threshold intensities of inhibitory post-synaptic currents. Long-term potentiation (LTP) induction was also evaluated using whole cell recording of evoked excitatory and inhibitory post-synaptic potentials (EPSPs and IPSPs respectively) in CA1 neurons of the hippocampal slices. LTP induction was attenuated in excitatory and inhibitory synapses in the hippocampal slices of kindled rats. When DBS was applied in kindled animals, LTP was induced in both EPSPs and IPSPs. Obtained results showed that application of DBS in kindled animals reduced the excitatory- and increased the inhibitory-synaptic transmission. These changes may restore the brain excitability towards normal situation so that the ability of LTP induction in both EPSPs and IPSPs achieved in kindled animals.

S094154-1

Stress and addiction: biological mechanisms

Abdolrahman Sarihi[1], Zahra Taslimi[1], Alireza Komaki[1], Abbas Haghparast[2]

1. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
2. Neuroscience Research Center, Shaheed Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Stress increases drug-seeking behavior and the risk of addictive drug whose mechanisms are not clearly understood yet. Excessive activation of the neural reward system leads to its dysfunction and to hyperactivation of the brain's stress response, resulting in an increase in reward thresholds. We studied the effects of acute and chronic restraint stress and the role of glucocorticoid receptors (GRs) in basolateral amygdala (BLA) in the reinstatement of extinguished methamphetamine (METH) induced conditioning place preference (CPP) in rats.
Materials and Methods: After extinction of METH-induced CPP, animals were exposed to restraint stress (3-h period, as an acute stress) 60 min before subcutaneous administration of ineffective dose of METH (0.125 mg/kg) in order to reinstate the extinguished METH-induced CPP. For chronic stress induction during extinction phase, the animals were exposed to the restraint stress for one hour per day. In another set of experiments glucocorticoid receptors (GRs) in basolateral amygdala (BLA) were blocked by unilaterally microinjection of RU38486 as GRs antagonist (10, 30 and 90 ng/0.3 µl DMSO) prior to stress exposure during extinction phase or before reinstatement.
Results: Acute and chronic restraint stress can significantly induce reinstatement of METH-induced CPP by ineffective dose of METH. GR stimulation in the BLA is necessary for METH-seeking behavior and stress processing, while rate of GR activation is different in acute and chronic stress.
Conclusion: Biological mechanisms and related brain areas of interaction between stress and rewards systems and also involved neurotransmitters has been discussed in this paper.
Keywords: Stress, Addiction, Glucocorticoid Receptors, Basolateral Amygdala

S094154-2

A modulatory/regulatory role(s) for oxytocin in rewarding circuits; focus on dopaminergic activities in striatum and amygdala

Amir-Hossein Bayat*

*Department of Basic Medical Sciences, Saveh University of Medical Sciences

Oxytocin (OT), which has been highly preserved during mammalian evolution, regulates physiological functions related to reproduction and lactation, and in recent years, has been shown to modulate affiliative behavior. Intranasal oxytocin administration has been shown to reliably modulate neuropsychological functions in a series of studies in the absence of relevant side effects. Oxytocin is not transported across the blood–brain barrier. OT is a peptide with important actions in the NAc. OT is an endogenous neuropeptide that has been implicated in different processes related to addiction, including tolerance, reward, memory, and stress responses. Although there are no study so far has determined whether hypothalamic OTergic inputs to the NAc exist in male mice, injection of recombinant rabies virus into the NAc indicated that a direct axonal OTergic projection to the NAc. Thus, it demonstrated a significant synaptic source for OT in the NAc of male mice. Oxytocin release in the NAc promotes social reward by enhancing NAc 5-HT release, which activates 5-HT1b receptors that in turn reduce excitatory synaptic responses generated by unknown sets of inputs. Thus, OT could be a therapeutic target to modulate neural circuits that involve in reward and addiction processes in the brain.
Keywords: Oxytocin, Reward, Nucleus Accumbens, Addiction

S094154-3

Evaluation of the Effect of Sex reward and Sexual Deprivation on Morphine: Acquisition, Extinction, and Reinstatement

R. Arezoomandan[1], N. Sadegh Amal Nikraftar [2], E. Eilahi3, M. Nikbahktzadeh[3]

1. Addiction Department, School of Behavioral Sciences and Mental Health (Institute of Tehran Psychiatry) Iran University of Medical Sciences, Tehran, Iran
2. Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, Iran
3. Physiology Department, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

There is a high degree of overlap between brain regions implicated in processing natural rewards and drugs reward. Humans' functional neuroimaging studies have shown that natural rewards including playing video games, gambling, shopping, orgasm and the sight of appetizing food activate the brain areas that are implicated in drug reward and addiction (i.e. the mesocorticolimbic system and extended amygdala). Many reports showed that non-drug rewards can alter neural plasticity in regions of the brain that are affected by drugs of abuse. Also, pleasurable behaviors can reduce stress via brain reward pathways. In the current study, we investigate the effect of sex reward and sexual deprivation on morphine acquisition, extinction, and reinstatement. We used conditioned place preference (CPP) for evaluating rewarding effect of morphine in three groups of animals; control, sex rewarded and sex-deprived groups. Sex deprived group was exposed to females and during acquisition were isolated from them. In the sex reward group the male animals were isolated before acquisition but during acquisition were allowed to be exposed and having sexual behaviors with females. CPP was induced by subcutaneous injection of morphine (5mg/kg) for 3 days and the animals were tested for CPP score after 3 days intervention and co- morphine injection. In all three groups morphine injection induced significant CPP for morphine paired compartment. However, sex reward attenuated development of morphine CPP in comparison with sex-deprived groups. The first phase of our study showed that sex reward may attenuate the rewarding effect of morphine. In the next phase we will examine the effect of sex reward and sexual deprivation on morphine extinction and reinstatement. In this phase the male animals will expose or unexposed to opposite sex during extinction phase.
Keywords: Morphine, Conditioned place preference, Sex reward, Sexual deprivation

S094154-4

Measurement of the c-fos Protein Level and pCREB/CREB Ratio in the Ventral Tegmental Area in the Reinstatement Phase of Morphine-induced Conditioned Place Preference Confirmed the Modulatory Role of the Nucleus Accumbens CB1 Receptor

Hossein Khaleghzadeh-Ahangar[1&2], Fariba Khodagholi[3], Fatemeh Shaerzadeh[3&4], Abbas Haghparast[3]

1. Department of Physiology, School of Medicine, Babol University of Medical Sciences, Babol, Iran

2. Neuroscience Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

3. Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, P.O. Box 19615-1178, Tehran, Iran

4. Department of Neuroscience, University of Florida College of Medicine and McKnight Brain Institute, Gainesville, FL, 32610, USA

Background and Objective: Brain reward and motivation circuit begin from the ventral tegmental area (VTA) that its dopaminergic terminals project to various regions of the brain including the nucleus accumbens (NAc). This reward circuit is influenced by drugs of abuse such as morphine and cannabinoid.
Materials and Methods: The present study tried to investigate the role of the intraaccumbal CB1 receptor in the c-fos level and pCREB/CREB ratio in the VTA during reinstatement phase of morphine-induced conditioned place preference (CPP) by western blotting.
Results: The present data revealed that intra-accumbal administration of CB1 agonist, WIN55,212-2 (0.5, 1 and 2 mM/0.5 µl DMSO) before/during extinction period of morphine-induced CPP, significantly decreased the VTA c-fos protein level in the reinstatement phase; whereas the pre-reinstatement administration of the CB1 agonist, increased the c-fos protein level. The present data show that intra-accumbal administration of CB1 antagonist, AM251 (15, 45 and 90 µM/0.5 µl DMSO) during/after extinction period of morphine-induced CPP affects the VTA c-fos protein level in the reinstatement phase. Also, intra-NAc microinjection of AM251 during the extinction period reduced pCREB/CREB ratio in this region.
Conclusion: The results presented here provide compelling evidence of the modulation and involvement of the cfos and the CREB molecules in the cannabinoid-opioid interaction of the brain reward system in the CPP paradigm.
Keywords: CB1 receptor, Morphine, Nucleus accumbens, Ventral tegmental area, c-fos, CREB

S094154-5

Limbic Structures and Fear Memory Extinction: A decade of study

Abbas Ali Vafaei[1, 2], Ali Rashidy-Pour[1, 2], Samira Omoumi[1,2], Masoumeh Dadkhah[1,2], Shahla Nourizad[1, 2]

1. Research Center of Physiology, Semnan University of Medical Sciences, Iran

2. Department of Physiology, Faculty of Medicine, Semnan University of Medical Sciences, Iran

In the last years there has been a growing interest on conditioned fear memory extinction, one specific phase of memorization process, induced by memory retrieval. Understanding the mechanisms underlying this mnemonic process may allow to work out therapeutic interventions for treatment of human fear and anxiety disorders, such as phobias and post-traumatic stress disorder. Fear extinction is induced when the conditioned stimulus is repeatedly presented without the aversive outcome unconditioned stimulus, resulting in a decline of conditioned fear response. In rodents, fear responses are typically assessed via freezing behavior or the fear-potentiated startle reflex.
In this review, we discuss the role of the most important brain sites involved in fear memory extinction. Also we review some behavioral, pharmacological and neurochemical studies from our laboratory on rodents, contributing to our understanding of the complex processes of memory extinction. More importantly, we discuss the effects of temporary inactivation and pharmacological manipulations of amygdala, hippocampus and pre or infra-limbic regions of medial prefrontal cortex (mPFC) on fear memory extinction. Our findings indicate that mPFC, amygdala and hippocampus play a critical role in the regulation of fear extinction memory in rodents.
Keywords: Fear memory extinction, Amygdala, Hippocampus, Medial prefrontal cortex

S095155-1

The role of pharmacoepigenetics in personalized therapy: promises and opportunities

Zahra Fazeli Attar

Department of Medical Genetics, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Numerous pharmacoepigenetic studies have been revealed that the epigenome variation influenced on the inter-individual differences observed in the drug response. The epigenetic changes have been demonstrated to play a role in the expression and efficiency of the proteins involving in the transport and metabolism of the drugs. Furthermore, the novel drugs have been established to manage the diseases through the intervention in the epigenetic regulation of gene expression. The administration of these epidrugs in the clinical trials accelerated the control of the disease progression, especially cancers. Although the complexity of the human genome established the obstacle in the prosperity of individualized drug therapy, the identification of the epigenetic variations provided the suitable opportunity for the effective management of the diseases and improvement of the health care system.
Key words: DNA methylation; miRNA; Personalized medicine; Epidrug; Drug response

S095155-2

Treatment response prediction in obsessive-compulsive disorder: The application of data mining methods

S Asadi[1], A Ahmadiani[2], J Shams[3], H Hasanpour[4]

1. Neurobiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3. Behavioral Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

4. Faculty of Computer Science and Engineering, Shahid Beheshti University, Tehran, Iran

Obsessive-compulsive disorder (OCD) is a debilitating psychiatric disorder causing intrusive thoughts or repetitive behaviors. Clinicians use serotonin reuptake inhibitors (SRIs) for OCD treatment, but 40-60 percent of patients don't respond to them adequately. Currently, no effective tool exists for early prediction of treatment response in OCD. Converging lines of evidence indicate that serotonin transporter has a role in response to selective serotonin reuptake inhibitors (SSRIs) pharmacotherapy in a variety of neuropsychiatric disorders. Here, the association of four functional loci of the serotonin transporter gene (SLC6A4) with fluvoxamine treatment outcome in Iranian patients with OCD has been investigated. Besides, we describe an association rule data mining approach for treatment response prediction using Iranian OCD dataset. A total of 352 Iranian OCD patients who had fulfilled the criteria for DSM-IV-TR with Y-BOCS scores higher than 9 were screened for the treatment outcome. Pharmacotherapy was defined as 12 weeks of treatment with fluvoxamine (150mg-300mg), and patients were categorized to three groups (responders, non-responders, and refractory). Results detected significant associations of two SLC6A4 haplotypes with treatment response. Moreover, low obsession and compulsion severities, family history of mental illness, poor insight, and illness duration less than five years, being married and female are the most associated variables with responsiveness to fluvoxamine pharmacotherapy. Application of data mining methods in personalized medicine may help clinicians in taking a right therapeutic decision.

S095155-3

Role of pharmacogenetics on drug metabolism

Cheraghi Z , Ziai A

Department of pharmacology, faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Pharmacogenetics is a branch of pharmacology which aims to optimize drug therapy with respect to the patient's genotype and maximum efficacy with minimal adverse effects. Pharmacogenetics affects dosing, efficacy and toxicity of drugs. Liver metabolism is a main way to study effects of Pharmacogenetics on drug's pharmacokinetic profile. CYP family is the leading "Drug metabolizing enzymes group" and are found in the liver, small intestine, kidneys and lungs and metabolizes drugs. The most common CYP involved in drug metabolism is CYP3A4, which belongs to a superfamily of hem-containing mono-oxygenases protein that is responsible for metabolizing 30% of drugs. CYP2C, CYP2D and CYP2E subfamilies have also had a significant role here. Liver metabolism is divided into 4 groups in the human population: poor, intermediate, extensive and ultrarapid metabolizers. Pharmacogenetic has become one of the most important frontiers of cancer therapeutic strategies, tailored for individualized patients. It has been developed into a general modular for detecting genetic polymorphisms for optimal therapeutic interventions in cancer patients but have not been perfected yet. Detection of multidrug resistance's gene polymorphism helps to predict drug resistance and therapeutic failure in individual cancer patients.

S095155-4

Implementation of nextgeneration sequencing testing in a clinical pharmacogenomic

Sayyed Mohammad Hossein Ghaderian

Department of Medical Genetics, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Pharmacogenomics is the study of how genes can influence responses of individual to pharmacological treatments. Next-generation sequencing (NGS) analysis has become generally accepted as a critical role in personalized medicine, providing a comprehensive profile of DNA variation. Recently, this multiple genes data can be used to evaluate data use to identify individual-specific genetic variants (genotyping). It is envisioned that the implication of NGS into clinical investigation and discovery of pharmacogenomic markers improve power in precision-medicine-guided drug development.
Unfortunately, there is still a lack of knowledge in the genomic literacy among medical doctors and other health care professionals according to drug treatment and drug response.
Here, we propose some strategy to apply NGS as a technique in a clinical pharmacogenomics.

S096156

Cassia fistula emulsion comparing with mineral oil on pediatric functional constipation

Seyyed Ali Mozaffarpur[1], Mohsen Naseri[2], Mohammad Reza Esmaeilidooki[3], Mohammad Kamalinejad[4], and Ali Bijani[5], Hoda Shirafkan[6]

1. Traditional Medicine and History of Medical Sciences Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
2. Iranian Traditional Medicine Clinical trial Research Center, Shahed University, Tehran, Iran.
3. Non Communicable Pediatric Diseases Research Center, Babol University of Medical Sciences, Babol, Iran.
4. Department of Pharmacognosy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5. Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran.
6. Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Background and objective: Cassia fistula is used as laxative in Persian Medicine. The prevalence of Pediatric Functional Constipation (FC) is between 0.7% to 29.6%. This study compare the laxative effect of cassia fistula emulsion (CFE) with mineral oil (MO) on FC.
Materials and methods: A randomized clinical trial (registered in IRCT:IRCT201303196932N2) in Amirkola Children's Hospital, Babol, Iran was carried on 81 children (age range: 4–13 years) with FC based on RomeIII criteria. They received CFE emulsion or MO randomly for three weeks. Children were counted as improved when they exited from RomeIII criteria of FC.
Results: After medication, 84% of children in CFE (n=41) and 50% in MO (n=40) exited from the criteria of FC ($p = 0.002$). All measurable criteria improved in both groups. The frequency of defecation in CFE improved from 1.7 per week to 10.6 while from 2 to 6.1 in MO ($p < 0.001$). The severity of pain during defecation and consistency of stool improved significantly in CFE than MO ($p < 0.05$), but there were not any significant differences between groups in fecal incontinence and retentive posturing. Anal leakage of oily material occurred as an important complication in MO while the children in CFE did not complaint it. Drug's compliances were not significantly different in the two groups. CFE and MO did not cause clinically significant side effects.
Conclusion: CFE was most effective than MO in the 3-week treatment of children with FC.
Keywords: Functional constipation, Children, Cassia fistula, Mineral oil, Traditional Iranian Medicine, Randomized Clinical Trial (RCT)

S096157

Effect of neck dry cupping on thyroid factors in patients with hypothyroidism

Sheida Kolahi Jahromi [1], Gholamali Jelodar[2], Yousha Mahmoudi [3]

1. Master of Physiology, Shiraz University, Shiraz, Iran
2. Department of physiology, College of Veterinary Medicine, Shiraz University, Shiraz, Iran
3. Doctor of Medicine, Kerman, Iran

Background and Objective: Cupping is one of the oldest and most traditional methods of traditional medicine in Iran, which, despite its influence on the prevention and treatment of diseases, its effects and its side effects are not well known. The aim of this study was to determine the effect of neck dry cupping on thyroid factors in patients with hypothyroidism.
Materials and Methods: In this study, Medical records of 10 patients (men) who were referred to the cupping center due to hypothyroidism for dry cupping of their neck were examined. Then all blood samples were taken before and 30 days after the intervention, and factors T3, T4 and TSH were measured.
Results: The results showed a significant decrease in the rate of TSH of the patients, but no significant changes were observed in the level of T3 and T4. (P-Value < 0.05)
Conclusion: According to the results of this study, the effect of the dry cupping on the neck caused reduction of TSH and subsequently decreased levothyroxine dosage in patients with hypothyroidism.
Keywords: Dry cupping, Hypothyroidism, Traditional medicine

S096158

The effect of Allium jesdianum hydroalcoholic extract on sleeping time and the level of anxiety in mice

Fatemeh Mahan[1], Mehrdad faizi[2,*], Mona Khoramjou[2], Mahdi Moridi Farimani[1], Parvin Ramak[3]

1. Department of Phytochemistry, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, G. C., Evin, Tehran, Iran
2. Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Sciences Pharmaceutical Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Lorestan Agricultural Research and Natural Resources Center, Khorramabad, Iran

Background and Objective: Insomnia is one of the problems that chronically affects many people for various reasons. Regarding the many side effects of sedatives drugs, using medicinal plants have been considered. Allium jesdianum is an endemic species in Iran and aerial parts of this plant is useful for abdominal pain, rheumatic pain and urinary stones [1]. The aim of this study was to investigate the effect of hydroalcoholic extract of the aerial parts of the plant on sleeping time and the level of anxiety in mice.
Materials and Methods: In this experimental study, 64 mice (20-25g) were randomly divided into 8 equal groups. Animals were divided into four experimental groups and one control group. The locomotor activity of the animals was examined by open field test. In order to measure the sleeping time, sleep induced by Pentobarbital method were applied. Different doses of the hydroalcoholic extract of A.jesdianum (25, 50, 100, 200 mg/kg, IP) were intraperitoneally injected into the treated groups. After 30 minutes of injection, all the groups received pentobarbital sodium (40 mg/kg i.p.) and hypnotic behaviors were recorded using Righting reflex. But, the controls received normal saline intraperitoneally in both of the methods. Diazepam (2 mg/kg) was used as a positive control in all experiments.
Results: A.jesdianum extract increase sleeping time in all doses compared to the control group and decrease total distance movement in open field test ($p<0.01$).
Conclusion: Our results showed that the extract of A.jesdianum incerases the sleep period and decreases locomotor activity in mice.
Keywords: Allium jesdianum, sleeping time, locomotor activity, sedation effect

S096159

Analysis of Biochemical Parameters in Animals under Radiation Emitted from Wi-Fi and Jammer

Shojaeifard M.B[1, 2], Farahani S.[2], Kadivar F.[2], Jarideh S[2]

1. Physiology Department, Fasa University of Medical Sciences, Fasa, Iran; and
2. Ionizing and Non-Ionizing Radiation Protection Research Center (INIRPRC), Shiraz University of Medical Sciences, Shiraz, Iran.

Background: The massive exposure to electromagnetic radiation (EMR) of WLAN has raised concerns for human health. Although various studies have investigated the effects of EMRs, there have been reports of conflicting experimental evidence. Accordingly, this study has been designed to quantify the effects of Wi-Fi and Jammer, a signal blocking device, on biochemical parameters of kidney and Liver functions.
Materials and Methods: Twenty one adult male Sprague-Dawley rats in the weight range of 200 to 250g were divided into sham, Wi-Fi and Jammer exposed groups (n=7 in each group). Rats were in a cage set in a circular pattern with a radius of 100 cm from the Wi-Fi modem or Mobile jammer device and exposed for fourteen days, two hours per day. The experimental conditions similar to treated groups were applied to the sham group, except that the device was turned off during the treatment period.
Results: The liver and kidney parameters of exposed animals compared with sham-exposed samples were examined. EMF exposure caused significant decreased in the total protein, globulin, LDL, AST and ALT levels. In contrast, no significant differences were observed in the other investigated parameters (creatinine, albumin, glucose, blood urea nitrogen, cholesterol, HDL, ALP, triglyceride, and total and direct bilirubin).
Conclusion: The results show that probably Jammer's ray has been able to improve the performance of organs such as the liver and kidneys by blocking the harmful signals emitted from the Wi-Fi around the animal's environment.
Keywords: Non-Ionizing Radiation ,Wi-Fi, Jammer, kidney, Liver

S096160

Flaxseed Oil Supplementation Improve Gene Expression Levels of PPAR-γ, LP(a), IL-1 and TNF-α in Type 2 Diabetic Patients with Coronary Heart Disease

Elmira Akbari, Zatollah Asemi

Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, Islamic Republic of Iran

Background and Objective: This study was carried out to determine the effects of flaxseed oil administration on gene expression levels related to insulin, lipid and inflammation in overweight diabetic patients with coronary heart disease (CHD).
Materials and Methods: This randomized double-blind, placebo-controlled trial was conducted among 60 diabetic patients with CHD. Subjects were randomly allocated into two groups to intake either 1000 mg n-3 fatty acid from flaxseed oil containing 400 mg α-Linolenic acid [ALA (18:3n-3)] (n = 30) or placebo (n = 30) twice a day for 12 weeks. Gene expression related to insulin, lipid and inflammation were quantified in peripheral blood mononuclear cells (PBMC) of diabetic patients with CHD with RT-PCR method.
Results: RTPCR demonstrated that after the 12-week intervention, compared with the placebo, flaxseed oil supplementation could up-regulate gene expression of peroxisome proliferatoractivated receptor gamma (PPAR-γ) (P = 0.02), in addition, taking flaxseed oil supplements down-regulated gene expression levels of lipoprotein(a) [LP(a)] (P = 0.001), interleukin-1 (IL-1) (P = 0.001) and tumor necrosis factor alpha (TNF-α) (P = 0.02) in PBMC of diabetic patients with CHD. We did not observe any significant effect of flaxseed oil supplementation on gene expression levels of low-density lipoprotein receptor (LDLR), IL-8 and transforming growth factor beta (TGF-β) in PBMC of diabetic patients with CHD.
Conclusion: Overall, flaxseed oil supplementation for 12 weeks in diabetic patients with CHD significantly improved gene expression levels of PPAR-γ, LP(a), IL-1 and TNF-α, but did not influence LDLR, IL-8 and TGF-β.
Keywords Flaxseed oil · Gene expression · Insulin · Lipid · Inflammation · Type 2 diabetes mellitus

S096161

Metformin via activation of AMPK inhibits inorganic polyphosphate-induced inflammation in local, systemic short- and long-term mice models

Maryam Fakhraei[1], Fereshteh Asgharzadeh[1], Seyed Mahdi Hassanian[2, 3], Majid Khazaei[1,3]

1. Department of Physiology, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Department of Clinical Biochemistry, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Metabolic syndrome Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and Objective: polyphosphate (PolyP) is a linear anionic polymer that regulates inflammation through up-regulation of the mammalian target of rapamycin complexes (mTORC) 1 and 2 signaling pathways in vascular system. mTOR signaling is repressed via the activation of AMP-activated protein kinase (AMPK). In this study we investigated protective effects of an AMPK activator, metformin, on polyP-induced hyper-permeability in skin, liver, kidney, brain, heart, and lung in different models including local, systemic short- and long-term approaches in mice.
Materials and Methods: PolyP-induced hyper-permeability was performed according to three different models including local (50-200 µg polyP/Mouse), systemic short-term (4-400 µg polyP/Mouse), and systemic long-term (4 and 40 µg polyP/Mouse/day for 10 days). In each model, mice were divided into four groups: control, mice received normal saline, PolyP group, Metformin/polyp group, and Dorsomorphin /Metformin/polyP group. To visualize vascular permeability, the Evans Blue (EB) dye (20mg/ml) was injected into the tail vein of anesthetized mice intravenously (iv), tissues were isolated and maintained in formamide solution. Histological changes were assayed and oxidative stress markers were measured using specified kits.
Results: PolyP at concentration of 50 µg/Mouse elevated permeability in skin. We also observed that increase in polyP dosage could increase in vascular permeability in liver, lung, brain and heart organs. In addition Long-term administrations lower doses of polyP (4 and 40 µg/Mouse) were tolerated.
Conclusion: In this study, we showed for the first time that metformin potentially impaired polyP-mediated inflammatory response in cellular and animal models by activation of AMPK signaling pathway.
Keywords: Inorganic polyphosphate, Vascular permeability, AMPK signaling Metformin

S096162

Metformin via activation of AMPK inhibits inorganic polyphosphate-induced inflammation in local, systemic short- and long-term mice models

Maryam Fakhraei[1], Fereshteh Asgharzadeh[1], Seyed Mahdi Hassanian[2, 3], Majid Khazaei[1, 3]

1. Department of Physiology, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Department of Clinical Biochemistry, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Metabolic syndrome Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and Objective: polyphosphate (PolyP) is a linear anionic polymer that regulates inflammation through up-regulation of the mammalian target of rapamycin complexes (mTORC) 1 and 2 signaling pathways in vascular system. mTOR signaling is repressed via the activation of AMP-activated protein kinase (AMPK). In this study we investigated protective effects of an AMPK activator, metformin, on polyP-induced hyper-permeability in skin, liver, kidney, brain, heart, and lung in different models including local, systemic short- and long-term approaches in mice.
Materials and Methods: PolyP-induced hyper-permeability was performed according to three different models including local (50-200 µg polyP/Mouse), systemic short-term (4-400 µg polyP/Mouse), and systemic long-term (4 and 40 µg polyP/Mouse/day for 10 days). In each model, mice were divided into four groups: control, mice received normal saline, PolyP group, Metformin/polyp group, and Dorsomorphin /Metformin/polyP group. To visualize vascular permeability, the Evans Blue (EB) dye (20mg/ml) was injected into the tail vein of anesthetized mice intravenously (iv), tissues were isolated and maintained in formamide solution. Histological changes were assayed and oxidative stress markers were measured using specified kits.
esults: PolyP at concentration of 50 µg/Mouse elevated permeability in skin. We also observed that increase in polyP dosage could increase in vascular permeability in liver, lung, brain and heart organs. In addition Long-term administrations lower doses of polyP (4 and 40 µg/Mouse) were tolerated.
Conclusion: In this study, we showed for the first time that metformin potentially impaired polyP-mediated inflammatory response in cellular and animal models by activation of AMPK signaling pathway.
Keywords: Inorganic polyphosphate, Vascular permeability, AMPK signaling Metformin

S096163

The effect of acute Taxus Baccata on electrocardiogram activity in the rat

Yousef Panahi, Dara Azizi, Mohammadreza Abaschian

Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.

Background and Objective: The Common Yew (Taxus baccata) contains poisonous taxine alkaloids that are contained in yew berries, needles or bark. Cardio toxic effects of the yew plant have been known for more than 2000 years. In this study, it was used to evaluate its acute effect on electrocardiogram (EEG) disorders caused by Taxus Baccta.
Materials and Methods: Twenty rats randomly allocated to 4 groups: control (n=5), Taxus Baccata groups (n=15) that treatment with Taxus Baccata (2, 4 and 6 mg/kg). Combination of ketamine-xylazine (80+8 mk/kg) was used to induce anesthesia. The EEG recorded by elab setup and analyzed by eTrace software.
Results: The results of this study showed that single acute Taxus Baccata intraperitoneal doses of 2, 4 and 6 mg/kg had no significant effect on the EEG of anesthetized rats.
Conclusion: Our results showed that acute Taxtus Baccata had no inhibitory or stimulatory effect on EEG activity and did not cause cardiac arrhythmias.
Keywords: Taxtus Baccata, EEG, Rat

S096164

Cytotoxicity evaluation of novel acetophenonic isoxazolin derivatives on MCF7 and HT29 cancerous cell lines

Hoda Abolhasani[1], Ahmad Abolhasani[2], Fatemeh Heidari [3], Mohammad Amin Habibi[4]

1. Cellular and Molecular Research Center & Departement of Pharmacology, School of Medicine, Qom University of Medical Sciences, Qom, Iran.
2. Department of Biotechnology, Faculty of Advanced Sciences and Technologies, Isfahan University, Isfahan, Iran.
3. Department of Anatomy, School of Medicine, Qom University of Medical Sciences, Qom, Iran.
4. Student Research Committee, Qom University of Medical Sciences, Qom, Iran.

Background and Objective: Nowadays cancer is one of the leading causes of death worldwide, so it is one of the most serious threats to human health in the world. Although great advancements have been made in the treatment and control of cancer progression, but cancer incidence is still increasing rapidly and significant deficiencies for improvement remain. Recently isoxazoline and spiroisoxazoline scaffold attracted as drug candidates due to demonstrating different effects, such as anti-cancer activities. So cytotoxicity evaluation of new synthesized compounds with isoxazoline scaffold is very valuable for investigation about anticancer drugs.
Materials and Methods: In this study, cytotoxic activity of novel acetophenonic isoxazolin derivatives were evaluated as an anticancer agent and was compared with cisplatin as a well-known anti-cancer drug. The cytotoxic effects of novel acetophenonic isoxazolin derivatives and cisplatin on MCF7 (breast) and HT29 (colon) cell lines were evaluated by MTT assay at 48 hours at five concentrations. ELISA reader was used at 570 nm wavelengths to determine the survival of cells. IC50 values were calculated by fitting the data in a sigmoidal dose-response curve by non-linear regression analysis using graphpad prism software (version 6.01) for each cell line.
Results: Based on the results of biological evaluations of this study, novel acetophenonic isoxazolin derivatives have growth inhibitory effects comparable to cisplatin on the 2 cancerous cell lines MCF7 and HT29.
Conclusion: The results of this study propose that acetophenonic isoxazolin derivatives are suitable scaffolds for designing new anti-cancer agents with anti-proliferative activities.
Keywords: Acetophenonic isoxazolin, MTT assay, HT29, MCF7, Anticancer drugs.

S096165

Xanthomicrol retards tumor growth and progression in a mouse melanoma (B16F10) allograft model

Foad Ghazizadeh, Masoumeh Shafiei, Parvaneh Rahimi-Moghaddam

Department of Pharmacology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

Background and Objective: To evaluate the in vivo anti-cancer efficacy of xanthomicrol and its molecular mechanism in an in vivo tumor model.
Materials and Methods: Effect of xanthomicrol on B16F10 melanoma cell viability was determined using MTT assay. For in vivo experiments, C57BL/6 animals were implanted subcutaneously with B16F10 cells. Five days after tumor implantation, mice were divided randomly into three 10-animal groups: vehicle control (CMC 0.5%), thalidomide (200 mg/kg), and xanthomicrol (50 mg/kg). Drugs were administered intraperitoneally once a day for 21 consecutive days. Animals were observed for appearance of initial tumor growth. Tumor diameters were measured every other day. On the 26th day, blood samples were analyzed for serum VEGF. Tumor tissues were weighted and applied for angiogenesis assessment, phosphorylation levels of Akt and Erk and mRNA expression of HIF-1α and VEGF.
Results: Xanthomicrol showed much nearly 50 fold cytotoxic effects on B16F10 melanoma cells than thalidomide. The initial tumor growth ($P < 0.05$), tumor volume ($P < 0.05$), weights ($P < 0.05$) and angiogenesis ($P < 0.05$) were significantly decreased in xanthomicrol-treated animals compared with those in vehicle group. Protein expression of phosphorylated Akt ($P < 0.05$), mRNA expression of HIF-1α ($P < 0.01$) and VEGF ($P < 0.01$) in tumor tissues, as well as serum VEGF ($P < 0.05$) were significantly decreased in xanthomicrol-treated animals compared with those of vehicle group.
Conclusion: Xanthomicrol may exert its anti-tumor and anti-angiogenic effects in melanoma via interfering with PI3K/Akt signaling pathway and inhibition of VEGF secretion in malignant cells.
Keywords: Xanthomicrol, Mouse melanoma, Akt, VEGF, HIF-1α

S097166

Fahanik babaei javad

فاقد چکیده

S097166

Raheleh Gholamzadeh

فاقد چکیده

S097166

Fatemeh zarei

فاقد چکیده

S097166

Abdollah Abdollahpour

فاقد چکیده

S097166

Negin saeedi

فاقد چکیده

S097166

Raheleh Gholamzadeh

فاقد چکیده

S097166

Donya nazari nia

فاقد چکیده

S091167-1

Bayesian brain (updating of past experiences)

Mohammad-Reza Vaez-Mahdavi[1], Leila Nasiri[2], Hamid Bohloli[3]

1. Physiology dept. Medical Sciences Faculty, Shahed Medical University
2. Department of Biology, Faculty of Science, Shahed University, Tehran, Iran.
3. Faculty of Law and Political Science, University of Tehran

People, when faced with feelings about changes in the internal environment or the social environment, often ask themselves what strategy to take against these changes, which ensures maintaining greater health in their physical, psychological and social dimensions. If the answer to this question is doubtful, it means that the brain is not able to apply the preferences to choose possible options and thus the concept of social stress could be formed, consequently. Also, when the selective options include concurrent benefits and risks, the context of the stressful processes in the brain will be created. To cope with such conditions, the body aims to preserve the internal stability and, by activating the hypothalamic-pituitary-adrenal axis (HPA), begins to strive to manage stress. In turn, glucocorticoids, by reducing the threshold of brain cell stimulation, facilitate the acquisition of information for the central nervous system, and the brain reaches a new level of preferences in strategy selection scenarios by spending more energy and acquisition of more information. But if new preferences are not enough to allow scenario selection for the brain, stressful conditions continue to work, and the HPA axis will lead to changes in immune regulation.
Our brain, despite being able to access small parts of the world, is capable of predicting future results by statistical methods, even under conditions of uncertainty. According to Bayesian law, our brains by updating our initial beliefs with new evidence acquire a novel and improved belief. In other words, this law allows us to inferring from an effect to its probable cause. All past experiences over the life course have ultimately formed the prior beliefs, which form the basis for how the Bayesian Brain makes predictions or decisions. Humans are capable of computing unstable situations, and that their beliefs about uncertainty mediate the strength of their stress responses. Moreover, the better people tune their beliefs about social challenges and instability, the better they were able to cope with challenges and design the future. Therefore, our life experiences, provide the context of decisions making, and the ability to cope with different situations. Our strong positive or negative experience in life supposing “brain finger points” influence how the brain can manage stressful situations, and improve quality of chooses a for future health. It is supposed that the prefrontal cortex (PFC), pre-supplementary motor area (pre-SMA) and ventromedial prefrontal cortex/orbitofrontal cortex (vmPFC/OFC) areas in human brain involve in providing brain predictions during unpredictable situations.
Keywords: Stress, Bayesian Brain, Uncertainty, Past Beliefs, Updating, Strategy Selection

S091167-2

Early life stress effects on addictive behavior is related to changes in Opioid receptors in rat brain

Nayere Askari[1,2*], Ali Mousavi[2], Mohammad Reza Vaez-Mahdavi[1], tooba ghazanfari[1]

1. Immunoregulation Research Center, Shahed University, Tehran, I.R. Iran
2. Department of Biology, Faculty of Sciences, Shahid Bahonar University of Kerman, Kerman, I.R. Iran

Background and Objective: Early-life environmental conditions significantly affect the offspring's development. Maternal deprivation (MD) can induce persistent changes in the brain that give rise to neuropsychiatric diseases including substance abuse disorders. However, long-lasting mechanisms that determine vulnerability to drug addiction remain unknown. We assume that changes induced by MD in Opioid system, HPA (hypothalamic-pituitary-adrenal) axis activity, and BDNF (brain-derived neurotrophic factor) may be involved in the drug abuse in later life.
Material and Methods: Male offspring of Wistar rats (n=8 per group) were subjected to 3h of daily MD during postnatal days 1–14. In adulthood, morphine-induced CPP (conditioned place preference) was investigated using two doses of morphine (3 and 5 mg/kg). Serum corticosterone level was measured by ELISA method. The expression level of genes was determined by qPCR (quantitative PCR).
Results: A greater morphine-induced CPP was observed in deprived rats with 3 and 5 mg/kg morphine compared to nondeprived animals. MD group had a higher corticosterone level. A significant decrease in the expression of BDNF and GR (glucocorticoid receptor) genes and a significant increase in μ and κ Opioid receptors gene expression was observed in the brain of maternally deprived rats.
Conclusion: Our results suggest that MD induces alterations in the HPA axis function, BDNF level, and Opioid receptors system that enhance vulnerability to morphine at adulthood.
Key words: Maternal deprivation, Morphine-induced CPP, Corticosterone, GR, BDNF, Opioid receptors

S091167-3

Evaluation and Comparison of Effects of Different Types of Social Stress on Immune Response Regulation

Tooba Ghazanfari[1], Mohammad-Reza Vaez-Mahdavi[2], Leila Nasiri[3]

1. Immunology Research Center, Shahed University, Tehran, Iran.
2. Physiology dept. Medical Sciences Faculty, Shahed Medical University
3. Department of Biology, Faculty of Science, Shahed University, Tehran, Iran.

Health inequity and its multiple aspects are important signs of social injustice. Several studies have shown that mental and physical health during adulthood is not independent of childhood. As a result, those at a lower socioeconomic level have a higher mortality rate and lower life expectancy. The utilitarian individualism in social relationships has led to the formation of extensive social instability, poverty, deprivation, and inequality. In addition to its social effects, it has harmful effects on the critical systems and organs through interference with multiple biological systems. Today, people live in very stressful societies. Studies have established a link between the increased prevalence of diseases and social and physiological stresses. Studies into both normal and induced stresses have shown significant effects on the immune response. Animal studies have found that increased incidence of aggressive behaviors result from increased cytokine production and immune cellular activity. Based on the type of stimulus and duration of contact, chronic stress influences both innate and acquired immune factors. Stress affects the immune system by activating the hypothalamus-pituitary-adrenal axis. It also affects the innate immune agents, such as monocyte, macrophage, and pro-inflammatory cytokines by increasing stress hormones (glucocorticoid-catecholamines). Chronic stress influences the acquired immune components by changing the immune cell population and disturbing the balance between immune cells and secreted cytokine levels.
Keywords: Social Stress, Inequality, Poverty, Lipofuscin, Safety, Inflammatory Cytokines, Pain

S091167-4

Social Inequality May Affect on Animal Health; an Experimental Study

Mohammad Reza Vaez-Mahdavi[1], Fatemeh Heidari[2], Farshad Momeni[3], Bagher Minaei[4], Mehrdad Roghani[1], Nader Fallah[5], Reza Gharabaghi[6]

1. Physiology Department, Shahed University, Medical School, Tehran, Iran
2. Physiology Department, Shahed University, Medical School, Tehran, Iran
3. Economy Department, Allameh Tabatabaei University, Tehran, Iran
4. Histology Division, Anatomy Department, Medical School, Tehran University of Medical Sciences, Tehran, Iran
5. Statistical Analysis Division, Social Medicine Department, Shahed University, Tehran, Iran
6. Middle East Cancer Institute, Tehran, Iran

Background and Aim: Extensive research has been conducted on the effects of psychological factors on cardiovascular diseases. In countries with low socioeconomic status as well as in areas with social inequalities, the risk of cardiovascular disease increases. Animal studies have shown that manipulating the social level of the samples can cause cardiovascular disease. This study was performed to investigate the effect of food inequality on lipofuscin pigmentation in white rabbits.
Materials and Methods: Thirty-two New Zealand male white rabbits were randomly divided into four groups. The first group had food deprivation for eight weeks duration with one-third of normal food but without exposure to the other groups. The second group suffered from food deprivation for 8 weeks and was exposed to the third and fourth groups. The third group was deprived for two weeks and then had access to adequate food and the fourth group had access to adequate water and food throughout the study period. At the end of the study, the hearts of the animals were studied histopathologically and evaluated for the presence of lipofuscin pigments. Statistical analysis was performed by Mann Whitney and Kruskal Wallis.
Results and Conclusion: The results showed that there was a significant difference in the incidence of lipid pigment with $p < 0.05$ between the first and second groups. In other words, inequality in food intake has caused these tissue changes in animals. Given that lipid pigment is one of the aging factors, it can be said that the feeling of inequality accelerates the aging process in the rabbit heart. The findings are published in the well-established journal of PLOS ONE.
Key words: Social Inequality, Cardiovascular Diseases, Lipofusion, Food Deprivation, Socioeconomic Status, Rabbit

S091167-5

Effect of melatonin treatment on epididymal sperm parameters, testis structure, apoptosis and oxidative stress after inequality in rats

Shiva Nasiraei Moghadam[1], Kazem Parivar[2], Abolhasan Ahmadiani[3], Mansoure Movahedin[4] and Mohamad-Reza Vaez-Mahdavi[5]

1. Biology dept. Tehran North branch of Islamic Azad university
2. Biology dept. Bioscience Faculty, Sciences &Researches Branch of Islamic Azad University
3. Neuroscience research center of Shahid behesti medical university
4. Anatomy dept. Medical Sciences Faculty, Tarbiat Modares University
5. Physiology dept. Medical Sciences Faculty, Shahed Medical University

Background and objective: Evaluation of the effect of food deprivation as a social stress on testis structure, sperm parameters and effects of melatonin treatment as an antioxidant component and inequality on the effect of food deprivation are our goals. Methods: 42 male rats divided in 7 groups: control, sham, melatonin received (M), food deprivation (1/3 of control daily food) (FD), FD + melatonin(FDM), isolated FD (FDi), and FDi + melatonin (FDMi). After 14 days, rats' testes structure were studied using immunohistochemistry, TUNEL and hematoxylin-eosin to determine the number of apoptotic cells and testes structure. Biochemical evaluation was taken on Malondialdehyde (MDA) and glutathione (GSH) and epididymal sperm analysis. ANOVA and Tukey's tests were done to analysis the data. $P<0.05$ was considered significance. Results: Sham was declined. In FD group, MDA and apoptotic cells was increased, GSH was decreased. In FDi group, was not effect on the ratio of oxidative stress. Melatonin could decrease apoptotic cells and MDA concentration in the FD group. Privation in FD led to demolition of testes structure and decrease of epididymal sperm parameters and melatonin can improved them. Conclusion: Food deprivation leads to increase of apoptosis, demolition of testes structure and oxidative stress but Food deprivation with isolation (FDi) hadn't these effects. Melatonin as an antioxidant has positive effect on inequality and apoptosis. These changes confirmed mechanism of oxidative stress and inequality.
Keywords: Food deprivation, Inequality, Apoptosis, Melatonin, oxidative stress

S091167-6

Food Intake Inequality, Deprivation, and Intermittent Fasting Effect on Oxidative Balance of the Brain and Liver, and Anxiety Behavior

Mohammad Reza Vaez-Mahdavi [1,2*], Saeedeh Rezaei[1,2], Ahmad Ali Noorbala[3], Mehrdad Roghani[2], Frouzandeh Jalilvand[4]

1. Equity and health research group, Shahed University, Tehran, Iran
2. Department of physiology, faculty of medicine, Shahed University, Tehran
3. Department of Psychiatry, Imam Khomeini Hospital, Psychosomatic Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran
4. Institute of Biochemistry and Biophysics, University of Tehran, Iran

Background: It is shown that dietary restriction (DR) may improve health and longevity. The current study aimed at studying the weight changes, anxiety behavior, and oxidative stress parameters in the brain and liver tissue of adult male rats during three weeks of an intermittent fasting (IF) diet.
Methods: Sixteen rats were randomly assigned into the control and the IF groups. Rats in the control group had free access to regular food freely, but the animals in the IF group had restricted access to regular chow during a limited interval — from 09:00 AM to 11:00 AM — and then, the excess food was cumulated. The study investigated the effects of IF on weight variation, anxiety behavior, serum concentration of corticosterone and cholesterol, and oxidative stress parameters including lipid peroxidation, paraoxonase (PON) enzyme activity, glutathione (GSH), lipofuscin, total peroxide and total cholesterol concentrations.
Results: The obtained results demonstrated that IF induced weight-loss with no significant change in anxiety. In addition, compared to the ad libitum fed rats some examined biochemical parameters significantly changed in the IF group. IF decreased the final weight of the rats by 8% from the initial weight. The weight-loss process was not constant and most of the weight-loss occurred in the first nine days with a steep gradient and, then, became virtually stable.
Conclusion: The current investigation showed that IF sometimes promoted tissue-specific changes in tissue redox state in a manner distinct from those of the other restrictive dietary interventions. Besides, IF induced reduction in age pigment accumulation in brain.
Key words: Inequality, Deprivation, Intermittent Fasting, Anxiety, Oxidative Stress, Age Pigment

S093168-1

"Heart Failure and more; from the bed to the benchtop"

Yoshihiro Ishikawa

Professor and Chair Cardiovascular Research Institute Yokohama City University School of Medicine

It is well known that the cardiac function is regulated by the neuro-hormonal, i.e., sympathetic nervous system, and the hemodynamic, i.e., Frank Starling mechanism. The sympathetic nervous system is a major mechanism of increasing cardiac function. The synaptic terminal releases noradrenaline, which binds to the adrenergic receptor on the cardiac myocyte. This initiates the cascade of reactions starting from the stimulatory G proteins, adenylyl cyclase, leading to the production of cAMP, and thus activation of protein kinase A. Protein kinase A phosphorylates multiple molecules, such as L-type calcium channel or phospholamban, which are involved in enhancing cardiac ino-tropism and chrono-tropism. In the past decades, molecular diversity within this cascade has been elucidated, and the role of each molecule in pathophysiology has been explored. Our laboratory first started the study in the 90's to identify the role of G proteins under both physiological and pathophysiological conditions. In order to address this issue, we developed a mouse model with cardiac overexpression of G protein by the use of a myosin heavy chain promoter. This was the first demonstration that cardiac function can be altered by cardiac specific overexpression of a functional molecule. This animal model demonstrated that sympathetic activation is beneficial in enhancing cardiac function in the early stage while prolonged activation leads to the development of heart failure. This was the first identification why beta-blockade therapy is necessary in the treatment of heart failure. We also identified adenylyl cyclase subtypes that are dominantly expressed in the heart. We have also demonstrated that the unique character of cardiac autonomic regulation is largely dependent upon this enzyme subtype. Thus, the diversity of molecules involved in cardiac sympathetic regulation in the past 30 years widened our understanding of the role of sympathetic nervous system from the bench to the bed and also from the bed to the bench.

S093168-2

Congenital cardiac disease: factors underlying exercise limitation and dyspnea

Ashima Anand

The reversal of clinical symptoms such as exercise limitation and dyspnea in patients with congenital cardiac diseases such as mitral stenosis or MS (by valvulotomy) and in Eisenmenger syndrome or ES (by sildenafil treatment) that are characterised by increased pulmonary interstitial pressure and pulmonary hypertension respectively, were investigated for the mechanism of their origin.
The mechanism was found to be related to attenuation of the neural activity of sensory receptors known as juxta-pulmonary capillary (J) receptors lying in the lung parenchyma that are sensitive to mechanical changes in the interstitial environment and which reflexely give rise to accelerated breathing and dyspneic sensations.
The evidence is based on the observation that the amelioration of patients' clinical symptoms appears before any changes in skeletal muscle peak exercise oxygen consumption or muscle structure or biochemistry changes or improvement in lung function (MS patients) or resting arterial oxygen consumption (ES patients) but by the surgical intervention or medications aimed at pulmonary vasodilatation that lead to a fall in J receptor stimulation that is thence accompanied by an improvement in the patient's dyspnea-free physical activity

S093168-3

Lavender oil and probiotics protect heart against injury in myocardial infarction induced by Isoprenaline in rats: a hemodynamic, biochemical, and histopathological evaluation

Vakili abedin[1,2], Sadeghzadeh Jafar[1], Hamid Reza Sameni[3]

1. Research Center of Physiology, Semnan University of Medical Sciences, Semnan, Iran.
2. Department of Physiology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran
3. Nervous System Stems Cells Research Center, Department of Anatomical Sciences, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran

Introduction: Lavender and probiotics are used in traditional and complementary medicine for different therapeutic purposes. Despite, its potential therapeutic effects in ischemic heart disease and its possible mechanisms remains to be investigated.
Material and methods: Lavender oil (200, 400, and 800 mg/kg) and probiotics (at 106 and 2 × 106 CFU/ml) were administered to the rats daily for 14 days before the induction of infarct-like myocardial injury (MI) using Isoprenaline. After 14 days and 24 h after MI, the right carotid artery and left ventricle (LV) were catheterized for recording blood pressure and LV systolic pressure (LVSP), LV end-diastolic pressure (LVEDP), the maximum rate of LV pressure increase (LV dp/dt max; contraction velocity), and the maximum rate of LV pressure decline (LV dp/dt min; relaxation velocity). At the end of the experiment, the heart was removed for the evaluation of histopathological and biochemical parameters.
Results: The induction of acute MI resulted in significant ($P \leq 0.01$) LV dysfunction, as shown by increase in LVEDP, decrease in LVSP and, LV dp/dt max, LV dp/dt min, and blood pressure ($P < 0.001$). Pretreatment with lavender oil (200 and 400 mg/kg) and probiotics significantly reduced myocardial injury, troponin I and TNF-α and improved LV function parameters and antioxidant enzyme activity ($P < 0.01$).
Conclusions: This study shows that lavender oil and probiotics has cardioprotective effect against infarct-like MI through suppressing TNF-α and stress oxidative pathways in a rat model. We suggest that lavender oil and probiotic supplements may be helpful in prevention or attenuation of heart injury in patients with high risk of myocardial infarction and/or ischemic heart disease.
Key words: Myocardial infarction, Lavender, Probiotics, TNF-α, Troponin I, Isoprenaline,
Antioxidant enzymes, Rat

S093168-4

Oxytocin and cardioprotection

Ali Mohammad Alizadeh

Development of cardioprotective agents to improve myocardial function, decrease the incidence of arrhythmias, delay the onset of necrosis, and limit the total extent of infarction during ischemic heart disease is of great clinical importance, and oxytocin (OT) may indeed be one of the candidates. OT is the first peptide hormone structurally assessed and chemically synthesized in biologically active form. This hormone acts as an essential factor in a human reproductive system, particularly during pregnancy and lactation in women. So far, different therapeutic roles for OT have been identified as a spectrum from central and peripheral actions on male and female reproductive systems, cardiovascular system, musculoskeletal system, etc. Some in vitro and in vivo studies also revealed that OT is responsible for bivariate biological functions involved in cardioprotection as following. There is increasing experimental evidence indicating that OT may have cardioprotective effects either by decreasing the extent of injuries or by pharmacologic preconditioning activity. We would show that in the presence of oxytocin, the cardioprotective effects may be increased to some extent. The presented board of evidence focuses on the valuable results of oxytocin on cardiovascular function and candidates it for future clinical studies in the realm of cardiovascular diseases.

S093168-5

The effect of high intensity interval training on cardioprotection against ischemia-reperfusion injury

Khoshbaten A

The aims of the present study were to determine whether short term high intensity interval training (HIIT) could protect the heart against ischemia reperfusion (IR) injury; and if so, to evaluate how long the exercise-associated protection can be lasted. Sixty-three rats were randomly assigned into sedentary (n = 15), sham (n = 7), and exercise groups (n = 41). Rats in the exercise groups performed 5 consecutive days of HIIT on treadmill: 5 min warm up with 50 % VO2max, 6×2 min with 95-105 % VO2max (about 40 to 45 m/min), 5×2 min recovery with 65-75 % VO2max (about 28 to 32 m/min), and 3 min cool down with 50 % VO2max, all at 0 % grade. Animals exposed to an in vivo cardiac IR surgery, performed at days 1, 7, and 14 following the final exercise session. Ischemia-induced arrhythmias, myocardial infarct size (IS), plasma lactate dehydrogenase (LDH) and creatine kinase (CK) activities were measured in all animals. Compared to sedentary rats, exercised animals sustained less IR injury as evidenced by a lower size of infarction and lower levels of LDH and CK at day one and day 7 post exercise. In comparison of sedentary group, IS significantly decreased in EX-IR1 and EX-IR7 groups (50 and 35 %, respectively), but not in EX-IR14 group (19 %). The exercise-induced cardioprotection disappeared 14 days following exercise cessation. There were no significant changes in ischemia-induced arrhythmia between exercised and sedentary rats. The results clearly demonstrate that HIIT protects the heart against myocardial IR injury. This protective effect can be sustained for at least one week following the cessation of the training.
KEYWORDS: cardioprotection; exercise training; ischemia; reperfusion

S094169-1

From traditional medicine manuscript to the prevention of relapse in opioid-dependent patients

Mohsen Naseri[1*]; Abdolali Moosavyzadeh[1]; Farzaneh Ghaffari[2]; Razieh Jafari Hajati[1]; Azarakhsh Mokri[3]; Seyed Mohammad Nazari[1]

1. Traditional Medicine Clinical Trial Research Center, Shahed University, Tehran, Iran.
2. School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3. Psychiatry Department and National Center for Addiction Studies, Tehran University of Medical Sciences, Tehran, Iran.

The school of Persian Medicine (PM) has a comprehensive approach to physical and psychological aspects and considers health as a priority. Along with the spread of drug addiction in Iran during the Safavid era, Iranian scientists have also come up with scientific and precise methods to prevent and cure this problem. For example, the first scientific book on the treatment of opiate addiction has been written by Iranian scholars. Currently, extensive research on PM in the field of addiction and psychological and spiritual aspects of human health with scientific methodology is ongoing. The efficacy of different herbal drugs has been proven by animal and clinical studies.
Hab-o Shefa is an herbal product from PM manuscript idea for treatment of opiate addiction. Animal studies of this product did not show a significant difference in the total score between the methadone group and Hab-o Shefa group. Clinical studies of Hab-o Shefa was showed that this product as a maintenance treatment in people with opioid abuse reduced craving, anxiety, and depression over time. Score of craving, anxiety, and depression showed a decreasing trend after drug discontinuation and 6 month fallow up.
Key Words: Adiction, Hab-o Shefa, Persian Medicine

S094169-2

Report on activity and researches were performed in the department of Traditional Medicine, Shahed University based on breastfeeding as personalized medicine in Iranian Traditional Medicine

Maryam Jahangir[1] ,Hasan Namdar[2], Elham Emaratkar[2], Shahrbanou Nakhaie[3], Mahnaz Sadeghian[3], Soghrat Faghihzadeh[4] Children,s

1. Ph.D. candidate, Department of Iranian Traditional Medicine, School of Medicine, Shahed University, Tehran, Iran
2. Assistant Professor, Department of Iranian Traditional Medicine, School of Medicine, Shahed University, Tehran, Iran
3. Associate Professor and Pediatric Gasteroentrologist, Department of Pediatrics, Ali-Asghar Children,s Hospital, School of Medicine, Iran University of Medical Sciences Tehran, Iran
4. Professor of Bioestatistics, Department of Biological Statistics and Epidemiology, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran

Background and Objective: Today breastfeeding is not only receiving a meal, rather is a smart dynamic biophysical process. In this bilateral relationship between mother and her infant physical, psychological and spiritual exchanges happen in all time of breastfeeding period. Iranian Traditional Medicine (ITM) scholars believed that the best milk for infant is her/his own mother's milk, which leads to her/his growth and development. The aim of this study is explanation of ITM points of view about breastfeeding function as personalized medicine.
Materials and Methods: In this review article the breastfeeding effects on infantile health were searched and analyzed from ITM references such as Qanon, Mofarah-Alqolub and Zakhire-Kharazmshahi.
Results: From ITM perspective breast milk is the most similar feeding to intrauterine nutrition for every neonates and infants, so the best milk for each infant is her/his own mother's milk. Breast sucking also relieves a lot of discomforts and illnesses from infant even no milk in breast. Upon Persian Medicine point of view the first step in treating infantile diseases is to pay attention to and improve her mother's health and prescribe medication to her if needed. So cause of this specific function of breastfeeding on personalized health of infants, the importance of exclusive breastfeeding is more demonstrated.
Keywords: Breastfeeding, Personalized medicine, Iranian Traditional Medicine, Health

S094169-3

Report on activity and researches were conducted in school of Traditional Medicine, Iran University of Medical Sciences based on recommended foods and remedies in Iranian traditional medicine for the treatment of different diseases

Amir Hossein Jamshidi[1,2], Bahareh Sadat Yousefsani[1,2]

1. Research Institute for Islamic and Complementary Medicine, Iran University of Medical Sciences, Tehran, Iran.
2. School of Persian Medicine, Iran University of Medical Sciences, Tehran, Iran.

Both physiology and pharmacology are considered in Iranian traditional medicine (ITM). In ITM physiological functions of the human body are considered to be based on main factor, known as Temperament [Mizaj] and humor. Normally there are four senses of humor in the human body: Phlegm or Balgham, Blood or Dam, Yellow bile or Safra, and Black bile or Sauda. Their imbalances in the body cause some disorders. In ITM many herbs and foods were used as medications for the treatment of different diseases. In the faculty of traditional medicine, Iran University of Medical Sciences, various studies and clinical trials evaluated the efficacy of these herbs as a promising candidate for the therapy of different disorders. For example, the effect of turmeric on glycemic status, lipid profile, hs-CRP, and total antioxidant capacity in hyperlipidemic type 2 diabetes mellitus patients was evaluated. Furthermore, the effect of a kind of whey protein (Ma'oljobon) on insomnia was established as well as the effect of thyme (*Zataria multiflora*) on fatty liver disease. Also, the efficacy and safety of Amla (*Phyllanthus emblica* L.) in non-erosive reflux disease, the effect of Lemon balm (*Melissa officinalis*) on sexual dysfunction in women, anticonvulsant activity of Dorema (*Dorema ammoniacum*) gum, the effect of cotton thistle (*Onopordon acanthium* L.) in antihypertensive patients, anti-inflammatory effects of eugenol, the effect of Bindii (*Tribulus terrestris*), ginger, saffron, and cinnamomum on menopausal symptoms and many others. The results of these researches were published in authentic journals.
The purpose of this study is the evaluation of the herbs and remedies used in the treatment of various diseases at the school of Persian medicine, Iran University of Medical Sciences which had successful results.
Key words: Iran University of Medical Sciences, Iranian traditional medicine, foods, herbs, remedies

S094169-4

Report on activity and researches were performed in a school of Traditional Medicine, Shahid Beheshti University of Medical Sciences based on pulmonary phlegm and its association with

mucus from the perspective of Iranian traditional medicine and its laboratory evidence

Rsool Choopani, Sohrab Dehghan

Traditional Medicine and Materia Medica Research Center, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Asthma is a chronic inflammatory airway disease with increasing prevalence which can decrease the quality of life those affected. Despite the efforts, there is not any decisive treatment for those suffering from asthma; therefore the tendency for using complementary medicine for management of asthma has increased recently. In Iranian Traditional Medicine references, the symptoms of an ailment called "Rabv Balghami" to a large extent conforms with the symptoms of asthma. One of the recommendations remedies for Rabv Balghami in Iranian Traditional Medicine is the use of Compound Honey Syrup. The aim of this study is to evaluate the effect of Compound Honey Syrup in reducing the inflammatory response and peribronchiolar smooth muscle contraction in asthmatic mice due to Ovalbumin induction to show association between pulmonary phlegm with mucus.
Materials and Methods: Sixty mice were allocated to five groups: sensitized and challenged with Ovalbumin (OVA) group, oral Compound Honey Syrup- treated group, inhalational Compound Honey- treated group and budesonide-treated group and negative control group. Airway hyperresponsiveness (AHR), blood and bronchoalveolar lavage (BAL) eosinophilia, lung histology and cytokines levels of BAL were evaluated.
Results: Compound Honey Syrup significantly decreased the inflammatory response and peribronchiolar smooth muscle contraction in asthmatic mice.
Conclusion: The present data shows that Compound Honey Syrup as a phlegm repulsive drug can help to treat asthma patients and patients with abnormal mucus secretion in the lung.
Keywords: Allergy, Iranian Traditional Medicine, Compound Honey Syrup

S094169-5

Clinical trials for controlling cancer complications based on principles of Persian medicine

Ghazaleh Heydarirad, Sajjad Sadeghi

Traditional Medicine and Materia Medica Research Center, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Cancer rates are increasing worldwide. According to the World Health Organization (WHO) statistics, there were about 12.7 million cancer patients in 2008, and this number is expected to rise to 21 million by 2030. Studies have shown that cancer patients are increasingly inclined to use complementary and traditional medicine (CTM). Persian medicine as an ancient medicine which has several-thousand-year old history, was based on the theory of four humors comprising phlegm, blood, yellow bile, and black bile. The aim of this study was investigating clinical trials for controlling cancer complications based on principles of Persian medicine.
Materials and Methods: In this study, the keywords "cancer", "cancer complication", "traditional medicine" and "Persian medicine" were searched in the Iranian Registration Center of Clinical Trials (IRCT). Also, current investigations on related subjects were considered through a search of the Pub Med and Google Scholar databases.
Results: We could find that most clinical trials were conducted to evaluate the effects of psycho-educational interventions, aromatherapy, Iranian herbal medicine, massage, reflexology, and acupuncture on cancer complications. Most of the cancers which were evaluated were breast, prostate, and gastrointestinal cancers, especially colorectal cancer. Most of the complications that were assessments include nausea and vomiting, anxiety, depression, sleep disorders, fatigue, hot flashes, pain and neuropathy.
Conclusion: The clinical trials which conducted based on principles of Persian medicine indicate that traditional interventions might have beneficial effects on improving cancer complications, but the found evidences were few. Future large and randomized controlled studies are necessary to confirm the benefits of CTM on cancer complications.
Key words: Persian medicine, clinical trial, Iranian, traditional

S094169-6

Evaluation of Effects of Food Products Based on Traditional Persian Medicine on Hemorheology in Polycythemia

Mahdi Yousefi[1*], Hamideh Naghedi Baghdar[2]

1. Assistant Professor, Department of Persian Medicine, school of Persian and Complementary Medicine, Mashhad University of Medical Sciences
2. Department of Persian Medicine, school of Persian and Complementary Medicine, Mashhad University of Medical Sciences

Background and Objective: Blood viscosity as a basal parameter in hemorheology is mainly determined by hematocrit levels, plasma viscosity, deformability and aggregation of red blood cells. Disturbance of any of these factors leads to decrease of blood fluidity, increased vascular resistance, and decreased tissue oxygenation. In this study the effectiveness of nutrition in patients with increased blood viscosity was assessed.
Materials and Methods: In the single-blind study, 40 male patients age range of 35 to 60 years, with polycythemia were randomly assigned to equal groups of control and intervention. Outcomes were blood viscosity, hematocrit, fibrinogen, lipid profile, and blood glucose and blood osmolarity. A diet regimen for 6 weeks and phlebotomy at baseline considered for the intervention group. The control group has been received the only phlebotomy at the beginning of the study. Both candidates were instructed to maintain their usual diet but a food avoidance instruction during the study period (6 weeks).
Results: Whole blood viscosity, hematocrit, plasma fibrinogen, and triglyceride decreased significantly in both groups. The difference of the mean changes of before and after the study between groups showed a significant improvement in whole blood viscosity, hematocrit, and plasma fibrinogen in the intervention group ($p< 0.05$), whereas there was no significant difference of the mean changes in TG between groups ($p< 0.05$). Total cholesterol, LDL-cholesterol, VLDL-cholesterol, HDL-cholesterol, osmolarity, and FBS significantly reduced in intervention group only.
Conclusion: food products based on Traditional Persian Medicine could improve blood rheology and decreased blood viscosity in patients with polycythemia.
Key words: Hemorheology, Food product, Persian medicine

S094169-7

The Effect of Citrullus on Neuronal Conduction Velocity, Memory and Thyroid Function in Rats

Mousa-Al-Reza Hadjzadeh[1, 2, 3*], Mahdi Yousefi4, Mahmoud Hosseini[1, 2, 3], Ali Taghipour[5], Shiba Yousefvand[1], Majid Jafari Nejad Bajestani[4]

1. Department of Physiology, School of Medicine Mashhad University of Medical Sciences, Mashhad, Iran
2. Division of Neurocognitive Sciences, Psychiatry and Behavioral Sciences Research center, Mashhad University of Medical Sciences, Mashhad, Iran
3. Neurogenic inflammation research center, Mashhad University of Medical Sciences, Mashhad, Iran
4. Department of Persian Medicine, School of Persian and Complementary Medicine, Mashhad University of Medical Science, Mashhad, Iran
5. Department of Epidemiology & Biostatistics, School of Health Social Determinants of Health Research Center,

Background and Objective: To perform normal activities, body temperature should be in a normal range. Hypothermia changes normal activity. To investigate the effect of coldness on body activity, watermelon (CT) with a cold nature was used. In present study, the effect of consumption of watermelon extract (in drinking water) on thyroid hormone level (T4), animals' weight, water and food consumption, nerve conduction velocity, and memory in Wistr rats were investigated.
Materials and Methods: 24 male rats were used, and divided in three groups: control, CT 1500 mg/kg, and CT 3000 mg/kg.
Results: watermelon increased the level of T4, and animals presented hyperthyroid symptoms (weight loss, increase in food and water consumption). The results showed that, animals weight in both treatment groups decreased VS control ($p<0.05$, $p<0.01$ respectively). Water and food consumption and the level of T4 increased VS control group in both treatment groups ($p<0.001$). Nerve conduction velocity in both treatment groups decreased VS control group ($p<0.001$). Spatial memory and Passive avoidance memory in both treatment groups significantly decreased VS control group ($p<0.05$, and $p<0.01$ respectively).
Conclusion: Based on this study and accordance with traditional medicine documents watermelon with a cold nature cusses coldness, and the animals rendered hyperthyroid; so lost weight, increased in food and water consumption. Impairment in memory, and decrease in nerve conduction velocity were also occurred in animals treated with watermelon extract.
Keywords: Coldness, Citrullus, Hyperthyroidism, Memory impairment, Nerve conduction velocity

S094169-8

Report on activity and researches were performed in the school of Traditional Medicine, Babol University of Medical Sciences based on standardizing personalized viewpoint of Persian Medicine (Mizaj) and some RCTs on Herbal drugs

Seyyed Ali Mozaffarpur[1], Mortaza Mojahedi[2], Roshanak Saghebi[3], Reyhaneh Moeini[3], Narges Gorji[1], Zahra Memariani[3], Hoda Shirafkan[4]

1.Traditional Medicine and History of Medical Sciences Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

2. Department of History of Medical Sciences, School of Persian Medicine, Babol University of Medical Sciences, Tehran, Iran

2. Department of Persian Medicine, School of Persian Medicine, Babol University of Medical Sciences, Tehran, Iran

4. Health Research Institute, Babol University of Medical Sciences, Babol, Iran

Background and objective: Traditional medicine in Iran has a history of more than 3,000 years. In traditional Persian medicine (PM), more than 14,000 non-recurrent references have been identified, of which about 12,000 are now available. There are now TPM schools in 8 medical universities, and there are PM departments in Medical schools in 10 other medical universities. Researches in PM can categorized in to fundamental and applied studies. One of the most important principles of the PM is Mizaj that focus on a personalized viewpoint. Standardizing questionnaires of Mizaj is one of the focal points of research in PM.

Materials and methods:

The reports of researches in School of Persian Medicine of Babol University of Medical Sciences is reported

Results: Developing questionnaire of whole body Mizaj as a mega project has been programming since 6 years ago. Weighing the items of Mizaj assessment and defining the items have been 2 axis of this kind of studies. Two self-report questionnaire have been published yet. The reliability of an expert-based questionnaire has been completed and its validity is measuring. Some clinical trials have been completed including investigating the effect of Eryngium Syrup on dysmenorrhea, KAASER (Zingiber officinale, Carum copticum, Piper nigrum) capsul on Patients with functional bloating, Alpinia officinarum on Spermogram factors, Nardostachys jatamansi extract on Clinical symptoms of functional dyspepcia, Quince syrup on Pediatric gastroesophageal reflux compare with ranitidine syrup, Topical products of sambucus ebulus on Clinical severity of patients with hand, Achillea millefolium on Candidial volvovaginitis, Silybum marianum on Hot flashes in postmenopausal women, Medicago sativa on Spermogram Parameters in Idiopathic infertility, and Pomegranate juice on hyperbilirubinemia in neonate

Conclusion: Besides the Clinical studies using medicinal herbs, studying on principles of PM (mostly Mizaj) should be considered to improve it.

Keywords: Persian Medicine, Medicinal herbs, Questionnaire

S094169-9

Cassia fistula emulsion comparing with mineral oil on pediatric functional constipation

Mohammad Reza Esmaeilidooki[1], Seyyed Ali Mozaffarpur[2], Mohsen Naseri[3], Mohammad Kamalinejad[4], and Ali Bijani[5], Hoda Shirafkan[6]

1. Non Communicable Pediatric Diseases Research Center, Babol University of Medical Sciences, Babol, Iran.

2. Traditional Medicine and History of Medical Sciences Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

3. Iranian Traditional Medicine Clinical trial Research Center, Shahed University, Tehran, Iran.

4. Department of Pharmacognosy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

5. Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran.

6. Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Background and objective: Cassia fistula is used as laxative in Persian Medicine. The prevalence of Pediatric Functional Constipation (FC) is between 0.7% to 29.6%. This study compare the laxative effect of cassia fistula emulsion (CFE) with mineral oil (MO) on FC.

Materials and methods: A randomized clinical trial (registered in IRCT:IRCT201303196932N2) in Amirkola Children's Hospital, Babol, Iran was carried on 81 children (age range: 4–13 years) with FC based on RomeIII criteria. They received CFE emulsion or MO randomly for three weeks. Children were counted as improved when they exited from RomeIII criteria of FC.

Results: After medication, 84% of children in CFE (n=41) and 50% in MO (n=40) exited from the criteria of FC ($p= 0.002$). All measurable criteria improved in both groups. The frequency of defecation in CFE improved from 1.7 per week to 10.6 while from 2 to 6.1 in MO ($p < 0.001$). The severity of pain during defecation and consistency of stool improved significantly in CFE than MO ($p < 0.05$), but there were not any significant differences between groups in fecal incontinence and retentive posturing. Anal leakage of oily material occurred as an important complication in MO while the children in CFE did not complaint it. Drug's compliances were not significantly different in the two groups. CFE and MO did not cause clinically significant side effects.

Conclusion: CFE was most effective than MO in the 3-week treatment of children with FC.

Keywords: Functional constipation, Children, Cassia fistula, Mineral oil, Traditional Iranian Medicine, Randomized Clinical Trial (RCT)

S095170-1

Seyed Mahdi Rezayat

S095170-2

Structures of science convergence in Medical Sciences Universities

S Fazli Tabaei

Department of Physiology, Faculty of Medicine, Tehran Medical Sciences Islamic Azad University

Member of Basic Sciences Department of Academy of Medical Sciences & Member of the Department of Convergence Sciences of the Academy of Medical Sciences

Basic medical sciences are the basis of medical knowledge. Therefore, it is considered as one of the most important subjects of the higher education system in the country. Nowadays, basic medical education in the world is the new attitude and converging sciences that have led to the emergence of emerging technologies in this field. Thus, the basic medical sciences need special attention. The basic medical science is considered as one of the most important subjects of the higher education system in the country. Universities have major role in the development of new sciences and technologies. For the production of knowledge, both disciplines and interdisciplinary sciences are needed, and the convergence of sciences will bring about a coherent academic environment. The convergence approach seeks to provide learners with the opportunity to become familiar with a variety of principles, methods, and topics in a variety of scientific fields by organizing a particular type of training. This does not mean, to negate the benefits of a disciplinary system, since it is defined because of its awareness, organization, and patterns, and this is an important concession that should be considered in the convergence approach. The convergence approach of new technologies has led to a remarkable evolution in human life and civilization in order to enhance human capabilities and improve the quality of individual and social life. One of the main areas of convergence is the modern science and technology in basic medical sciences. There are many potentials for human development in the field of medicine and health with the help of converging technologies.

S095170-3

Alireza Hamzehei

S095170-4

The Role of Converging Technologies in Promoting Health and Human Empowerment

Ashkan Zolriasatein

Assistant Professor of Materials Engineering-Nanomaterials, Center of Nanotechnology Development, Niroo Research Institute (NRI).

Investigation of the recent scientific breakthroughs and advances and review of recent technological developments show the important role of four fields of nanotechnology, biotechnology, information technology and cognitive science. Effective results of these four rapidly advancing technologies or briefly NBIC, have helped to solve many human problems. Meanwhile, the role of nanotechnology is very significant due to its interdisciplinary nature and the uniqueness of the universe at the atomic scale. Future research in these technologies shows that further advances will not be made by each of these technologies alone, but in order to reach the highest peaks in the development of modern human society, we must have a convergence or a synergy between these technologies. The convergence approach of new technologies has led to a remarkable evolution in human life and civilization in order to enhance human abilities and improve the quality of individual and social life. This approach will have important social, cultural, economic and even political implications. One of the main areas of convergence is the modern science and technology in basic medical sciences. Many potentials in the field of human development in the field of medicine and health can be created with the help of converging technologies, such as enhancing physical and mental capabilities, physical capabilities, control capabilities, memory, processing speed, rapid performance, resistance to diseases, communication with other people and objects and systems, new ways of learning and training, and technologies include on-chip lab technologies for rapid screening and early detection of diseases; intelligent prostheses interacting with patients' brain signals; Nanotechnology-based alternatives to human organs or monitoring of physiological health; Nano-robots; Brain-to-brain and brain-machine interfaces.

S096171-1

Fiber optic probe and nanomaterial mediated Optogenetics: Current and Future opportunities

M.I.Zibaii1, A. Ghorbani[1], S.M.Nazari[1], E.Sadeghi[1], H.Sarafraz[2], M. Khoee[2], S.J Ashtiani[2], A.Haghparast[3], L.Dargahi[3], H.Latifi[1]

1. Laser and Plasma Research Institute, Shahid Beheshti University, Tehran, Iran
2. School of Electrical and Computer Engineering, College of Engineering University of Tehran,Tehran,Iran
3. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Light-assisted manipulation of cells to control membrane activity or intracellular signaling has become a major avenue in life sciences. Optogenetics is a biological technique that uses light to turn specific neuron groups in the brain on or off. There is a wide-range of potential uses for optogenetics that have not yet been exploited because the technology is still being developed.

One of the major issues with optogenetics research, particularly in vivo, is the delivery of sufficient light to the area of interest. Optical fiber is used for light delivery which is invasive and can cause tissue damage and alter behavior. We have developed different ways based on advanced optrodes to less-invasively, and even non-invasively, deliver light to specific neurons in the brain. The optrodes are now capable of simultaneously performing electrophysiology studies and stimulation based on light pulses. We present emergent neurotechnologies for developing neural recording electrodes with high spatial integration, long-term stability, and multiple functionalities which providing unprecedented opportunities for neuroscience research in the future.

Due to the problems related to the limitations of genetic modifications required by optogenetics, direct light stimulation of unmodified neurons remained a potential alternative. Applications of nanotechnology in basic and clinical neuroscience are only in the early stages of development, partly because of the complexities associated with

interacting with neural cells and the mammalian nervous system. We present an emerging treatment approach in neuroscience based on neuro-nano-technology and optic to cell regeneration and differentiation, cell protection, and optical stimulation of neural cells.
Therefore, in the future scientific progress across many fields may be facilitated by the continued development of more efficient opsins, targeting one or more opsins to specific cells, better ways of focusing light onto a single cell or multiple cells in a specific temporal pattern, and miniaturized device as wireless and battery-free for freely-behaving animals. Optogenetics could also be more fully integrated with other technologies that are used to study circuits in the brain, including electrophysiology and optical imaging which could help pave the way for clinical applications.

S096171-2

Use of Neuroimaging Techniques in Neuroscience

Reza Khosrowabadi

Institute for Cognitive and Brain Sciences, Shahid Beheshti University

Neuroimaging as a part of brain mapping uses medical imaging technology to study the structure and function of the brain for medicine and in particular for neuroscience and psychology. Specifically imaging technology allows us to study: a) Anatomy of the central nervous system with different contrasts sensitive to different components of tissues using Computed axial tomography(CT) and magnetic resonance imaging (MRI) ; b) Brain functional activations in terms of electrical activities using Magnetoencephalography (MEG) and Electroencephalography (EEG), and changes in blood de/oxygenation and blood flow using functional MRI and functional near infrared spectroscopy (fNIRS); c) Physiology in particular blood flow; d) Metabolism and biochemistry using magnetic resonance spectroscopy. Despite the relatively low temporal or spatial resolution of many of these techniques, scientists have used them to study the nervous system in various levels from single unit to the whole systematic view. Both modular and connectionist approaches have been implied that are briefly reviewed with some of their application in this talk. Subsequently, some of their applications in neurodevelopmental disorders are discussed.

S096171-3

Multi-electrode array systems; costs and benefits for Iranian researchers

Amir-Mohammad Alizadeh

Neuroscience Research Center, Shahid Beheshti University of Medical Sciences.

Since its re-introduction and refinement in 50s, Extra-cellular single unit recording has produced a sizable part of our knowledge about functions of the central nervous system. Despite invention of modern functional imaging techniques such as fMRI or Calcium imaging, versatility, mobility, flexibility, compatibility with variety of other techniques and simplicity of extra cellular recording remains unmatched. Developments in electronics have brought powerful computer and data acquisition systems about and this has enabled us to acquire data from multiple arrays of tens of electrodes simultaneously. While collecting more data with less expense, less animal suffering and much faster compared to old-school methods is generally very desirable, challenges of sorting, analyzing and interpreting such large datasets are big as well. In this short presentation, I will try to review costs and benefits of Multi-electrode array systems, discuss the challenges in data collection and analyses and finally address the potentials and obstacles Iranian researchers are facing in this regard. Indeed, Iranian neuroscientists who wish to upgrade to MEA recording systems, face many more obstacles which makes this move very difficult and costly. However, advantages are also not negligible and it seems that these are necessary steps for the Iranian scientific community to keep up with the evolving world.

S096171-4

Applications of in vivo whole cell patch-clamp in neurophysiology

Mir-Shahram Safari

Neuroscience Research Center, Shahid Behreshti University of Medical Sciences

Membrane potential of neuron is changing moment by moment by synaptic inputs from excitatory or inhibitory neural circuits and is fundamental for understanding of mechanisms of brain functions. In this lecture I will review

recent progress in whole-cell patch-clamp recordings for low-noise measurement of neuronal membrane potential in anesthetized and awake behaving and freely moving animals. With this technique directly measure neuronal activity, such as spiking responses or membrane potential dynamics and quantify synaptic inputs from excitatory and inhibitory circuits in living animals. This approach enables us to directly unravel different synaptic components and to understand their roles in particular brain functions. Combining in vivo patch-clamp recording with other techniques, such as two-photon imaging or optogenetics, can provide even clearer functional dissection of the synaptic contributions of different neurons or nuclei. Dual whole-cell recordings reveal behavioral modulation of membrane potential synchrony and properties of synaptic transmission in vivo. Dendritic whole-cell recordings and imaging, single-cell delivery of drugs and DNA, RNA expression profiling and study on cell-type-specific membrane potential dynamics of retrogradely or genetically labeled neurons are another applications that I will discuss.

S096171-5

Virtual Reality in Neuroscience: Applications and Future

Mohammad-Reza A. Dehaqani

Simulated experience using virtual reality (VR) have been rapidly progress in the last decade. Recently, the VR setups for neuroscience applications have been developed and utilized to investigate the underlying mechanism of neural circuits and behavior. Such systems became very popular since they applied the state-of-the-art technologies to measure neural responses in behaving human and animals. The VR systems allow measuring behavior that cannot be easily used with classical behavior setup. In this lecture, I will present an overview of VR application in neuroscience, specifically the recent results from related research in rodent VR technologies. Furthermore, I will discuss the merits and issues of different approaches and exploit the potential of VR in neurosciences. Finally, I will present our custom-made rodent VR and comment on possible use cases in brain sciences .

S097172-1

Physical activity and brain plasticity and functions

Ali Rashidy-Pour

Research Center of Physiology, Semnan University of Medical Sciences, Semnan, Iran

Recent studies indicated that exercise can improve brain plasticity and functions in experimental animals and humans. Exercise is also able to improve cognitive deficits that induced by aging, chronic use of morphine, ischemia, etc. Although the biological mechanisms that underlie such beneficial effects are still to be completely elucidated, but there are several possible mechanisms mediating these beneficial effects including the enhancement of neurogenesis, synaptic plasticity and brain-derived neurotrophic factor levels in the hippocampus, activation of noradrenergic and serotonergic systems and increased neuronal uptake of circulating insulin like growth factor-I. In this talk, we focus on our recent findings in the effects of exercise on cognitive functions, brain behaviors and plasticity in physiological and pathophysiological conditions.
Keywords: Exercise, Brain plasticity, Brain disorders, cognitive functions

S097172-2

Environmental enrichment and Addiction-related behavior disorders

Hossein Miladi-Gorji

Laboratory of Learning and Memory, Research Center and Department of Physiology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran;

Environmental enrichment (EE) has been proposed for the treatment of the drug-related behavioral disorders. However, the effect of EE on susceptibility to drug abuse and sensitization is unknown. In our previously studies, we found that access to EE could lead to a decrease of withdrawal signs, depressive and anxiety-like behaviors and drug craving in morphine and METH-dependent and withdrawn rats and also in morphine withdrawn rats receiving methadone maintenance treatment. Also, exposure of rats to an EE during morphine abstinence in morphine dependent both parents before mating attenuated the anxiety/depressive-like behavior, and voluntary morphine consumption in the pubertal male and female rat offspring. Thus, EE may be a potential therapeutic strategy for ameliorating some of the behavioral consequences of physical and psychological dependence on morphine and METH.

Keywords: Environmental enrichment, Addiction-related disorders, Morphine

S097172-3

Role of Endocannabinoid system in the antidepressant and anxiolytic effects of exercise

Ali Ahmadalipour, Ali Fakhari, Leila Hosseinzadeh Anvar, Ghazal Koohkan Saadi, Fatemeh Sheykhkanlu Milan, Mahdi Dolatyari, Siamak Razavi, Ahmad Mobed

Research Center of Psychiatry and Behavioral Sciences, Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran

The mechanisms underlying the antidepressant effects of exercise remain unclear. Several credible mechanisms have been proposed, and one of the most famous suggested mechanisms is the endorphin hypothesis. The endorphin hypothesis explains that exercise has a positive effect on depression because of increased secretion of β-endorphins following exercise. Endorphins use opiate receptors and are related to a positive mood and an overall enhanced sense of well-being. However, because β-endorphin cannot cross the blood-brain barrier, it remains unclear if rise in plasma endorphins are directly linked to a reduction in depression. Recently, it has been shown that the phenomenon of "runner's high" or "euphoria",i.e. reduction in anxiety, which is often attributed to endorphin release, is not blocked by naloxone injection, an opiate antagonist. New studies suggest that other factors may be involved in the anxiolytic and antidepressant effects of exercise. One of the recently recognized systems is the endocannabinoid system (EC) which is a prominent promoter of the emotional homeostasis, mediating the effects of different environmental signals including rewarding stimuli. Recent evidence suggests that changes in EC system could be involved in some actions of antidepressants. The pharmacological enhancement of EC activity appears to exert an antidepressant-like effect and a reduced activity of the EC system seems to be associated with the animal model of depression. Moreover, many studies have reported an interaction between antidepressants and the EC system. New findings suggest that exercise anxiolytic and antidepressant effects might depend on EC system. The enhanced anxiolytic and analgesic effects of exercise are shown to be absent in the EC receptor-deficient mice, lacking CB1 receptors in γ-aminobutyric acid neurons (GABA-CB1–/–). Therefore, recent findings suggest that EC system mediates some of the positive effects associated with exercise.

S097172-4

Neurodegenerative diseases and oxidative stress: Physical exercise as a preventive or disease-modifying treatment

Iraj Salehi[1,2], Seyed Asaad Karimi[1, 2], Reza Ghahremani[1]

1. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran.
2. Department of Neuroscience, School of Science and Advanced Technologies in Medicine, Hamadan University of Medical Sciences, Hamadan, Iran.

Neurodegenerative diseases are characterized by progressive damage in neural cells and neuronal loss, which lead to compromised motor or cognitive function. Common neurodegenerative diseases include Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), and spinocerebellar ataxia (SCA). Despite growing evidence suggesting, that oxidative stress is critical to neuronal death, its precise role in disease etiology and progression has not yet been fully understood. Physical exercise (PE) activates the release of neurotrophic factors and promotes angiogenesis, thereby facilitating neurogenesis and synaptogenesis, which in turn improve memory and cognitive functions. Research has shown that the neuroprotective mechanisms induced by PE are linked to an increased production of superoxide dismutase, endothelial nitric oxide synthase, brain-derived neurotrophic factor, nerve growth factor, insulin-like growth factor, and vascular endothelial growth factor, and a reduction in the production of free radicals and oxidative stress in brain areas such as the hippocampus, which is particularly involved in memory. The aim of this study is to provide an overview on the role of oxidative stress and physical exercise in neurodegenerative disorders, with emphasis on AD and PD.

Keywords: Alzheimer's disease; Parkinson's disease;Oxidative stress;Exercise; Prevention

S097172-5

Talk 5: Therapeutic Effects of Exercise against PTSD

Skineh Shafia

Department of Physiology, School of Medicine, Mazandran University of Medical Sciences, Sari, Iran

Post-traumatic stress disorder (PTSD) is a condition that develops after an individual has experienced a major trauma. The traumatic event is often re-experienced following trauma reminders and recurrent nightmares. Moreover, persistent highly aversive memories related to the trauma and inabilities to extinguish these fear memories are major characteristics of this disorder. Exercise is currently advocated as a behavioral intervention to alleviate neurological deficits by impending neurological loss following several neurodegenerative diseases. Physical exercise can increase the levels of BDNF, neurogenesis, synaptic plasticity and improve learning and memory. In a series of experiments, we found that treadmill exercise can alleviate behavioral deficits, hypothalamic-pituitary adrenal axis dysfunction, alternations in hippocampal BDNF and apoptosis in single prolonged stress, a valid rat model of PTSD, in both male and female rats. Moreover, female rats had more resilience than male rats and this may be related to the effects of gonadal hormones. Our findings suggest that exercise is an appropriate non-pharmacological treatment for PTSD.

S092173-1

Art-Health Relation Methodology

Reza Dehqani

Musician and Architecture and Urban Design Phenomenology Researcher

It is tried to methodologically, discuss the relation between art (music and architecture specifically) with health. If this relation was to be assessed, what are the dimension of this assessment and how can it be demonstrated? The first question is directed at art. What concept of art is to be discussed? Can considering art in its broader sense (meaning anything that is categorized as art in terms of form and is necessarily recognized as such) help resolve the issues? Or should a specific philosophical concept of art be considered for this relation? The second question is directed at health. Should health be discussed as is represented in the medical sciences (covering the hygiene of body and mind)? Or does art place another way for this discussion? Two other basic concepts that play key roles are cognition and impression. For art to leave an impression (here the impact on creating health is meant), it must first be recognized. Are all forms of art recognizable and understandable by all audiences to generate an expectation of leaving an impression in the audiences' health? Attention to the concepts of cognition and impression paves our way to other disciplines of thought. Cognition requires a familiarity with the world and is a platform in whose correlations, an artistic form finds meaning. Recognizing an artistic form requires a certain kind of living. Therefore, in the realm of art correlations, artistic appreciation is related to life style.

S092173-2

Cinema and Movie Therapy

Shadmehr Rastin

Architectural Engineer & Screen Writer

Movie therapy , also known as cinema therapy, involves the therapist -directed viewing of movies for therapeutic purposes. The combination of thematic elements—music, dialogue, lighting, and images—can often evoke deep feelings in viewers, both allowing for personal reflection and providing new perspective on external events.
Metaphor, symbolism, and imagery might often be used by therapists as they help those in treatment explore thoughts and feelings and address areas of concern. Some therapists work with people in treatment to explore and analyze dreams , for example, and others may use guided imagery as a therapeutic technique. Thus, many may find the integration of movies and other forms of media, in which these and other literary elements are often widespread, to be logical. Not only do movies contain symbols, they also might generate empathy , increase communication skills, and allow those in therapy to become more aware of their own feelings and desires. Movie watching allows viewers to engage in a number of ways —linguistically, visuospatially, interpersonally, and intrapsychically. Proponents of movie therapy believe this may be helpful because learning has been shown to occur more quickly when information is processed in more than one way.
Film can lead people to experience a wide range of emotion. Who has not walked out of a movie theater feeling sad , scared, inspired, or otherwise moved? Movies can potentially open a person's eyes to new solutions to any number of difficulties and may provide many therapeutic benefits in addition to entertainment. They might offer hope , provide role models, and reframe problems. Film characters may also serve to exemplify different issues people face. A person addressing alcohol abuse in therapy might, for example, find viewing a movie in which a character achieves recovery from the same concern to be both inspirational and helpful.
additionally, movies can provide a safe way for people to discuss their thoughts and feelings. Direct questions from a therapist may be intimidating to some people, especially those who have difficulty openly sharing their feelings. The use of film in therapy can provide a less overwhelming way to talk about feelings, as it allows people to explore concerns indirectly by relating them to those of characters in the film. Some individuals might also be more likely to realize the presence of certain issues in their relationships and personal life when they first experience them in a movie. A person in an emotionally abusive relationship might not realize the relationship is abusive, but a fictional depiction of a relationship understood to be abusive may give the person a greater understanding of what constitutes abuse.
Film can help enhance the connection between people. It can be a great way to enhance rapport between the therap

S092173-3

The Impact of Teaching Acting on Amateur Actors and its Relation with Behavioral Therapy

Amir Sharifi

Actor, Director and Writer

In an acting course, the student is usually introduced to the concepts of body, breathing techniques, nurturing emotions, etc. The Stanislavski method is one of the main acting methods and stresses on realistic acting. Stanislavski believes that to affect audiences, one must be like a human, which in turn requires having emotions and feelings. In fact, in this method, the student, using different tools, begins to recognize his/her emotions and discovers the physical act that is related to the feeling. In another acting method, Jacques Lecoq stresses on beginning from the bodily physique in order to transcend feelings.
I would like to analyze the impact of these trainings on the personal behavior of an amateur theater actor. My efforts are directed towards stating the positive and negative impacts of this type of training on the person, using several examples.
To do this, we first must start with the characteristics of an amateur actor:
1. Looking for a good feeling
2. Having dreams and not knowing the goals
3. Fear and judgment
4. Lack of self-confidence

Then we will discuss the difference in the goals and the similarities in the behaviors of the instructor and the therapist. After that, we analyze the mental and physical changes during the acting course on the student.
Here, the focus is on not giving an answer as to the positive or negative nature of the result in teaching acting to students. Because this conclusion requires a more expansive data from a more accurate target group. Furthermore, because of the involvement of complicated human feelings, acting training has different impacts on different people, which in turn, calls for more accurate tests.

S092173-4

Revealing the Hidden World of the Brain; Note and Music

Abdolrahman Najl Rahim

Neurologist and Neuroscientist

Music is important as it is an art as it uses brain functions to establish relations with other. music therapy is 'an interpersonal process in which the therapist uses music and all of its facets to help patients to improve, restore or maintain health, a systematic process of intervention wherein the therapist helps the client to promote health, using musical experiences and the relationships that develop through them as dynamic forces of change' it is claimed that five factors contribute to the effects of music therapy

1.Modulation of Attention: The first aspect is the modulation of attention.Music grabs our attention and distracts us from stimuli that may lead to negative experiences (such as worry, pain, anxiety and so on) .This may also explain the anxiety and pain-reducing effects of listening to music during medical procedures

2. Modulation of Emotion: The second way music therapy work is through modulation of emotion .Studies have shown that music can regulate the activity of brain regions that are involved in the initiation, generation, maintenance, termination, and modulation of emotions

3. Modulation of Cognition: Music also modulates cognition .Music is related to memory processes including the encoding, storage, and decoding of musical information and events related to musical experiences. It is also involved in the analysis of musical syntax and musical meaning

4. Modulation of Behavior: Music therapy also works through modulating behavior .Music evokes and conditions behaviors such as the movement patterns involved in walking, speaking and grasping

5. Modulation of Communication: Music also affects communication .In fact, music is a means of communication. Therefore, music can play a significant role in relationships, as alluded to in the definition of music therapy.

The fact that music is diversified in different social conditions can create a good platform for researchers to discover. Music as culture and a historical background works towards a certain result and a unique position during time and culture and social conditions have a special impact on this cultural phenomenon. Art is a cultural mechanism that prepares and trains people for the realities of life.

Keywords: Brain, music therapy, modulation of attention, emotion, cognition, behavior, communication

S102174-1

Orexin-mediated modulation of opioid dependence

Saeed Semnanian, Hossein Azizi

Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Orexin neuropeptides, synthesized in hypothalamic neurons, have been implicated to play critical roles in the expression of various behavioral manifestations. Orexin ligands activate orexin type-1 and orexin type-2 receptors each displaying a distinct selectivity and distribution profile. Orexinergic neurons innervate various brain structures among which the locus coeruleus (LC) and the lateral paragigantocellularis (LPGi) nuclei are well established as the two key mediators of opiate dependence and tolerance. Both nuclei express orexin receptors and the LC receives excitatory and inhibitory inputs from LPGi. Interestingly, the expression of opiate withdrawal signs is temporally associated with hyperactivity of LC neurons. Numerous studies support the involvement of orexin system in mediating opiate effects via affecting the neural circuitries within the LC and LPGi. Extensive research has long been focused on the role of ventral tegmental area as a critical center in mediating orexin effects as well as reward processing and addiction. However, accumulating evidence supports the involvement of some other brain nuclei in these phenomena. The mutual contribution of these structures has not been previously addressed in the literature. The present talk aims to discuss and piece together the recent findings on the role of orexin in modulating opiate withdrawal and tolerance with an emphasis on the involvement of the paragiganto-coerulear pathway.

Keywords: Orexin, Locus coeruleus, Lateral paragigantocellularis, Dependence, Opioid

S102174-2

Brain Orexinergic System and Reward-related Behaviors

Abbas Haghparast

Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

The orexin peptides are neuropeptides synthesized by a cluster of neurons in the lateral hypothalamus (LH) and perifornical area. Orexin neurons receive a variety of signals related to environmental, physiological and emotional stimuli. Orexin neurons are "multi-tasking" neurons regulating a set of vital body functions, including sleep/wake states, feeding behavior, energy homeostasis, reward systems, cognition and mood. Orexinergic neurons project from the LH to many areas of the mesolimbic 'reward pathway' including the ventral tegmental area (VTA) and nucleus accumbens (NAc). These neurons are primarily implicated in reward seeking behavior. Studies of the neurobiology of reward are important to advance affective neuroscience, and provide insights into the several psychopathologies including drug addiction, eating disorders, obsession and depression.
Our studies over past decade in the field of orexin related reward and addictive behaviors indicate that chemical stimulation of LH and activation of its orexinergic neurons solely could induce conditioned place preference and application of orexin directly into a target site of interest or chemical stimulation of orexinergic neurons in the LH produces significant place preference, which is an indication of the fact that orexin exerts part of its rewarding effects through structures including VTA and NAc. Furthermore, we showed specific roles of orexin receptors in the different subregions of hippocampus on acquisition, expression and reinstatement of drug seeking behaviors.
So, our current knowledge indicates that orexinergic system may represent a useful target for developing novel therapeutics for substance use disorder which is a worldwide health problem requiring new and effective interventions

S102174-3

Brain Orexinergic system and stress pathophysiology

Mahmoud Elahdadi Salmani

Department of Animal Biology, School of Biology, Damghan University, Damghan, Iran

Orexin, secreted from lateral hypothalamic (LH) neurons, is involved in different behavioral paradigms. The peptide is produced following activation of corticotopin releasing hormone receptor type 1(CRHr1) and glutamate receptors reside on the neuron membranes, both of which are targeted by stress induced activated regions, paraventricular nucleus and amygdala, respectively. In turn, orexinergic axons are projected to different stress affected regions which indicate a type of stress projection and activate the two orexin type-1 and orexin type-2 receptors, simulating the stress effects. Hippocampus is among the target regions involved in learning and memory as well as being vulnerable to stress injuries. This structure receives orexinergic afferents directly from LH area and noradrenergic fibers indirectly from locus coeruleus, a brain stem nucleus. Bidirectional connection of hippocampus and LH area affects the stress inhibiting function of hippocampus which may exacerbate the stress condition through hypothalamic pituitary adrenal (HPA) over-activation which terminates in higher corticosterone production. This presentation will be focused on the role of orexin on stress damages in LH area and hippocampus from histology, molecular and behavioral perspectives with an emphasis on HPA functionality.
Keywords: Orexin, Lateral Hypothalamic Area, Hippocampus, Learning and memory

S102174-4

The Orexinergic (Hypocretin) System and Nociception: An Update to Supraspinal Mechanisms

Azhdari-Zarmehri H

Neuroscience Research center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

Chronic pain is a multifaceted and complex condition that is divided into somatic, visceral, and neuropathic pain. Although opioids and nonsteroidal anti-inflammatory drugs cause analgesia and are effective in the treatment of chronic pain, their utility is hampered by side effects, abuse potential, and development of tolerance to their pain-relieving effects. So, finding alternative analgesics with good efficacy and low side effects is of great interest and the orexinergic system is a potential candidate. Orexin-A and -B are exclusively expressed in the lateral hypothalamus and are involved in the feeding, sleep/wake cycle, cardiovascular function, hormone secretion, seizure, and pain modulation. Orexin peptides and their receptors have been proposed as opportunities for developing analgesic drugs. In experimental studies, orexin peptides induce analgesia that is comparable to morphine. Furthermore, there is evidence that orexin receptors 1 and 2 participate in responsiveness to both stressful stimuli and pain. Thus, direct and indirect activation of the orexinergic system is a new therapeutic approach to pain control. This article will review the most recent and important studies describing the role of orexins in pain modulation. This published in Bentham Science Publishers; For any queries, please email at epub@benthamscience.org.
Key words: Neuropeptides; hypocretin; neuropathic pain; orexin; orexin receptors; pain.

S105175-1

Comparison of ischemic acute kidney injury induced by clamping renal arteries, veins, or pedicles

M. Karami[1], E. Nikeghbal[1], S.M. Owji[2], S.M. Shid Moosavi[1]

1. Department of Physiology, The Medical School, Shiraz University of Medical Sciences, Shiraz, Iran
2. Department of Pathology, The Medical School, Shiraz University of Medical Sciences, Shiraz, Iran

Animal models of ischemic acute kidney injury (AKI) are valuable tools, but their therapeutic outcomes are not usually translated to humans. Ischemic AKI in murines is mostly induced via renal pedicle-clamping, which is different from patients with AKI that is due to renal artery hypoperfusion or vein thrombosis. It was designed to compare the traditional pedicle-clamping with artery or vein occlusion alone in rat models of ischemic AKI. Anaesthetized male Sprague-Dawley rats were subjected to 30-min clamping of renal arteries, veins or pedicles followed by either 0, 30-min or 2-h reperfusion period in different groups. It was found that either 0, 30-min or 2-h reperfusion following 30-min ischemia induced AKI with the effects of clamping of renal vein >> pedicle ≥ artery. The transmission of high arterial pressure into renal microvessels during venous-clamping caused rupture of capillary walls and occurrence of haemorrhagic congestion that along with more vascular congestion created extensive no-reflow areas in the kidney during reperfusion. Consequently, the interstitial congestion and the lower renal blood flow led to severer vascular and tubular injuries and oedema, which resulted in more disturbed Na+ reabsorption, K+ and urea excretion, and urine concentrating ability. The probable back-flow of blood from veins into kidney during renal artery-clamping resulted in lower levels of kidney tissue damage along with less intensive renal functional disorders compared to pedicle-clamping. In conclusion, the differences in renal disturbances induced by artery, vein and pedicle clamping strongly suggest use of appropriate experimental model for each type of human ischemic AKI.

S105175-2

Angiotensin 1-7 and Renal Circulation

Mehdi Nematbakhsh

Water & Electolytes Research Center, Isfahan University of Medical Sciences, Isfahan Iran

The two important arms of renin angiotensin system (RAS) are angiotensin II (Ang II) and angiotensin 1-7 (Ang1-7). Both of these peptides are present locally in the renal system; however the renal hemodynamic responses to these peptides act differently in kidney circulation. Ang1-7 has been known as an inactive agent in the renal system in normal physiological condition; however some of the experimental and clinical studies indicated the protective role of Ang1-7 in renal hemodynamics and functions under different circumstances. In addition, the renal vascular and functions responses to Ang1-7 were reported to be gender and hormone related. There are also some controversial reports against protective role of Ang1-7 in renal circulation.
In general, it seems that the protective role of Ang1-7 in renal system mostly related to the improvement of endothelial function or struggle with serious hazard and damage induced by AngII in the kidney. However, the paradoxical protective role of Ang1-7 is related to various parameters. Still, the certain protective conclusion for Ang1-7 in the renal system is a bit crude and need to be studied and discussed more, but in general hopes for future are visible.

S105175-3

Regenerative medicine and stem cell in kidney: A novel approach

Khajavi-Rad[1,2], S. Shahraki[1], M. M.Matin[3], SH. Havakhah[1] , A. Ebrahimzad-Bideskan[4], M. Aslzare[5], AR Bahrami[3]

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
3. Novel Diagnostics and Therapeutics Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran
4. Department of Anatomy and Cell Biology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
5. Urology and Nephrology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Renal failure is one of the serious and expensive health problems. The lack of required number of kidney donors is a limitation of organ transplantation to patients that suffer from end-stage renal failure. Regenerative medicine is a promising field in the context of kidney disease, and stem cell therapy is the most advanced regenerative therapy strategy. The beneficial effects of stem cell transplantation have been demonstrated in various models of acute and chronic kidney injury. Unlike many other tissues, the kidneys are organized from more than 20 types of cells, and the functional heterogeneity and complex cellular architecture present many challenges to cellular therapies. Most studies over kidney repair and regeneration include effects of mesenchymal stromal/stem cells and their paracrine mechanisms of action. In our lab, we were able to demonstrate the beneficial action of employing BM-derived mesenchymal stem cell (MSC) in improving renal function in an ischemia reperfusion kidney injury model. It was demonstrated that the MSC can improve kidney function and tissue structure after 3 days.
Tissue engineering is a newly emerging biomedical technology, which aids to successful replacement or repair of diseased organs. One of the new strategies is the use of the decellularized tissue which is becoming more common. The great advantage of tissue bioengineering is the possibility of ex vivo generating of complex organ, such as kidney, and transplanting functional organ to the patient that suffering from CKD. In this regard, we showed that using human renal tissue as a natural scaffold can be a helpful and effective method for the aim of renal regenerative medicine. In this investigation using natural human renal scaffold was an effective framework for supporting proliferation and differentiation of MSCs into the kidney cells. Although bioengineering and regenerative medicine are distinct, new developments in science and gaining new insights, can help them to complete each other. In the future, new techniques not only may contribute to the repairment and regeneration of the kidney, but probably also to the construction of an entire organ.

S105175-4

Interrelationship between multiple gasotransmitter systems in acute and chronic renal injuries

B. Seifi[1,2], M. kadkhodaee[1], H. Askari[1], A. Sener[2], P. Luke[2]

Department of Physiology, Faculty of Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Matthew Mailing Centre for Translational Transplant Studies, London Health Sciences Centre, Ontario, Canada
Chronic kidney disease (CKD) is a serious public health issue and renal transplantation is the preferred treatment option for patients suffering from end-stage renal disease. Ischemia reperfusion injury (IRI) is an unavoidable consequence of organ procurement. The question is whether endogenous gasotransmitters, NO, CO and/or H2S play constitutive roles in the maintenance of renal function. The protective effects of NaHS on chronic kidney disease-induced by 5/6 nephrectomy and the role of nitric oxide in these effects were investigated in male rats. The cytoprotective effects of combining H2S and carbon monoxide (CO) is of interest to determine if synergistic effects may arise in renal IRI. Sodium hydrosulfide as a donor of H2S, L-NAME (a non-specific NOS inhibitor) and aminoguanidine (a selective inhibitor of iNOS) were used in 5/6 nephrectomy. Twelve weeks after 5/6 Nx, creatinine clearance (CCr), urine neutrophil gelatinase associated lipocalin (uNGAL) as a marker of kidney damage, proteinuria, oxidative/antioxidant status indices, urinary nitrite and nitrate concentrations, iNOS and eNOS gene expression, caspase-3 and NFκB were measured in all groups. Intraperitoneal injections of NaHS 10 min before the onset of ischemia and immediately after the onset of reperfusion were administrated in a model of renal IRI. In addition an in vitro model of renal IRI was used to examine H2S and CO effects. NaHS treatment attenuated renal dysfunction, oxidant/antioxidant imbalance, the protein expressions of NF-κB and caspase-3, increased eNOS and reduced iNOS and histopathological injuries in the kidney compared to 5/6 Nx group. Eight weeks L-NAME treatment attenuated the beneficial effects of hydrogen sulfide. In contrast aminoguanidine augmented some beneficial effects of hydrogen sulfide as indicated by improved apoptosis and histopathological changes in the kidney. H2S protected renal IRI through reducing oxidative stress. Combining an optimal dose of CO donor and H2S donor does not increase cell viability compared to treatment with each one alone. These findings suggest that long term NaHS treatment is useful in preventing the progression of CKD through promoting oxidant/antioxidant balance and reducing inflammation and apoptosis in the kidney. Some interactions between NO and H2S in these effects might be considered.

S105175-5

Therapeutic Effect of Adipose-derived Mesenchymal Stem Cells on Renal Function and Histopathology in Ischemia-Reperfusion Acute Kidney Injury

S Changizi-Ashtiyani[1], L Hafazeh[1], F Ghasemi[2]

1. Department of Physiology, Arak University of Medical Sciences, Arak, Iran
2. Department of Medical Biotechnology, Iranian Blood Transfusion Research Center, Tehran, Iran

Both preclinical reports and clinical trials of stem cells used for treatment kidney disease are increasing rapidly. Kidney disease, including acute kidney injury (AKI) and chronic kidney disease (CKD), is a significant global public health problem, with incidence and mortality rates increasing in recent Decades. Despite advances in management of AKI with medications and renal replacement therapy, AKI remains a significant health issue. Mesenchymal stem cells (MSCs) are isolated from diverse tissues, including bone marrow and adipose tissue. Among all cell populations applied for therapeutic purposes in AKI, MSCs have been evaluated in the largest number of experimental and even clinical investigations so far. They may be isolated and expanded from bone marrow, adipose tissue, umbilical cord and other sources. They have the characteristics of multipotent cells, with multi-lineage differentiation, self-renewal, and proliferative potential. There is some evidence indicating that MSCs originate from renal pericytes, which form a network around the microvasculature. In addition, MSCs can secrete many different cytokines and growth factors, which regulate immune activity and enhance the potential of expansion and differentiation of host cells, thus promoting the recovery of damaged tissues. They also play critical roles in the modulation of renal blood flow, capillary permeability, endothelial cell survival, and immunological responses. Therefore, MSCs with potential angiogenic and immunomodulatory properties, are also a promising source of cells for the recovery of damaged sites and the treatment of various pathological conditions, such as renal injury and renal failure, making them an ideal therapeutic strategy for regenerative kidney therapy. Experimental evidence and clinical trials have demonstrated the feasibility, safety, and efficacy of using MSCs for kidney disease therapy. However, there is still some doubt about the real effects of MSCs on kidney disease.

S104176-1

Vascular oxidative stress: the link between diabetes and cardiovascular diseases

Mohammad Badavi

Dept. of Physiology, Persian Gulf Physiology Research Center, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

An imbalance between the formation of ROS and ROS-degrading antioxidant systems leads to the accumulation of superoxide, hydrogen peroxide, and other products and a deviation from the steady state. The Endothelial dysfunction is an early correlate for coronary artery disease in humans and occurs in type 2 diabetes and other diseases, including rheumatoid arthritis, and thereby accelerates atherosclerosis and causes cardiovascular mortality. A recent estimation by the World Health Organization from October 2018 states that "the number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014," with a more rapid increase in middle- and low-income countries. This figure is only expected to rise dramatically within the next decades. In addition to being a leading cause of mortality, diabetes is the most common cause of blindness, nontraumatic amputations, and end-stage renal disease in adults. The mechanism by which diabetes causes cardiovascular complications is complex, but damage to the vascular endothelium is a clear contributor. Proteins in the plasma and cell membrane are altered by chronic exposure to hyperglycemia through the process of nonenzymatic glycosylation, leading to the attachment of glucose molecules. Advanced glycation end-products (AGEs) are formed which then proceed to inactivate nitric oxide (NO), leading to impairment of endothelium-dependent vasodilation. Studies in diabetic rats have found increased AGE/RAGE signaling, impairment of NO/cGMP signaling, and also an association with NADPH oxidase-induced oxidative stress and vascular complications. Some of the vascular dysfunction is attributable to a vital crosstalk between oxidative stress and AGE/RAGE components.

S104176-2

Apelin and blood pressure, role of oxidative stress

Yaser Azizi

Physiology research center and department of physiology, faculty of medicine, Iran University of Medical Sciences, Tehran, Iran

Hypertension is a complex risk factor for cardiovascular diseases and heart failure. One of the most important risk factor for hypertension is obesity. Cardiovascular diseases such as hypertension induce low grade inflammation. Oxidative conditions increase pro-inflammatory factors such as angiotensin II that may be responsible for vascular inflammation, in turn generates inflammatory mediators that cause endothelial dysfunction. Adipokines increase in the inflammatory conditions and may provide insight mechanistic differences in hypertension. Apelin peptide is expressed in several organs, demonstrates blood-pressure-lowering, inotropic, chronotropic, anti-apoptotic, angiogenic and anti-oxidative stress properties. Concentration of apelin is related to decreasing blood pressure and adiposity. Apelin and its G-protein-coupled receptor (APLNR) are expressed in many tissues, and all apelin forms exert their effects through APLNR signaling. Apelin is a potent vasodilator in cardiovascular system and its expression reduces in the spontaneously hypertensive rats. Free radicals and reactive oxygen species (ROS) are the major inducers of cardiovascular diseases and antioxidants protect against ROS induced damages, inflammation and hypertension. However, changes of apelin and biomarkers related to oxidative conditions are not well understood, especially during chronic hypertension. It has been reported that hypertension increases oxidative stress and apelin exerts anti-oxidant properties. On the other hand, antioxidant supplementation and aerobic exercise up-regulates apelin expression in the cardiovascular system, which decrease oxidative stress and inflammatory process. Several studies demonstrated that apelin and APLNR are expressed in cytotrophoblasts, syncytiotrophoblasts, and also endothelial cells of fetal capillaries in the placenta of normal and preeclamptic subjects, indicating paracrine effects of apelin system. Apelin treatment in preeclamptic rats decreases preeclampsia symptoms, improves signaling via nitric oxide (NO) and attenuates oxidative stress. Apelin and APLNR are also expressed in pulmonary vessels and involved in the pulmonary arterial hypertension (PAH) and remodeling of the pulmonary arteries. In patients with PAH apelin expression in the pulmonary endothelial cells decreases and also they have lower plasma levels of apelin. In the systemic circulation, apelin regulates endothelial nitric oxide synthase (eNOS) expression, induces eNOS-dependent vasodilatation and reverses vasoconstriction induced by angiotensin-II. Apelin attenuates vasoconstriction in isolated rat pulmonary arteries, and chronic treatment with apelin attenuates the development of pulmonary hypertension (PH) in animal studies. Apelin increases vasodilation via endothelium dependent mechanism, while it causes vasoconstriction by acting directly on smooth muscle cells. On the other hand apelin induces temporary hypotension in animal models. Injection of apelin or overexpression of apelin in the rostral ventrolateral medulla increases blood pressure. Thus apelin and APLNR can be suggested as a potential new therapeutic target for Preeclampsia, PH, and may be systemic hypertension.

S104176-3

Aging and hypertension: role of oxidative stress

Nasser Ahmadiasl

Hypertension is a extremely predominant condition with abundant health risks especially among older adults. Recent advances in hypertension research have unraveled novel oxidative and inflammatory mechanisms of vascular dysfunction that motivate augmented vascular aging in hypertension and accompanying cardiovascular diseases.

The role of superoxide anion (O2 −), produced by the nicotinamide adenine dinucleotide phosphate (NADPH) oxidases, in vascular disease is generally well known. Some effective factors such as adipokines, through Nax activation and redox-sensitive mitogen-activated protein kinase signaling, exerts proapoptotic, proinflammatory, and proliferative effects in human vascular cells.
The present paper provides evidence that ROS in the central nervous system (CNS), the kidney, and the vasculature contribute to hypertension, and recent data will be reviewed showing how adaptive immunity is activated by oxidative events and can contribute to hypertension by interacting with these organs.

S104176-4

Pulmonary arterial hypertension and role of oxidative stress

Hamid Najafipour[1], Ahmad Beik[2], Soodeh Rajabi[3], Saeedeh Jafarinejad[2]

1. Department of Physiology and Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of medical science, Kerman Iran
2. Department of Physiology and Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of medical science, Kerman, Iran
3. Endocrinology and Metabolism Research Center, Kerman university of medical science, Kerman Iran

Background and Objective: Pulmonary arterial hypertension (PAH) is a lung vascular disease characterized by elevated pulmonary arterial pressure (PAP) due to small arteriole remodeling and vasoconstriction.
Compelling data from molecular and cellular experiments, together with animal studies, implicate a role for oxidative stress in systemic hypertension. However, the evidences for role of oxidative stress in PAH is still controversial. This review provides current insights on the mechanisms of the oxidative stress in experimental and clinical PAH and presents our results about the role of oxidative stress in experimental PAH in rats.
Methods: Forty two male NMRI rats, randomly divided into six groups of control, monocrotaline (MCT), vehicle and the plant antioxidant derivatives: perillyl alcohol (PER), berberine (BER) and quercetin (QUE) groups. MCT (60 mg/kg) or vehicle injected subcutaneously once in day 0. Treatment was performed daily from day 7-28. Total antioxidant capacity (TAC), glutathione peroxidase (GPX), superoxide dismutase (SOD), and catalase (CAT) were measured in the lung homogenized supernatant at end of week four.
Results: Right ventricular hypertrophy and systolic pressure, along with lung histopathology confirmed the induction of PAH by MCT. PAH significantly reduced TAC (8.304 to 6.977nmol/mg protein), GPX (0.024 to 0/016 U/mg protein), SOD (2.161 to 1/552 U/mg protein) and CAT (3.120 to 2/220 U/mg protein). PER, BER and QUE recovered antioxidants to almost normal level ($p<0.05$).
Conclusion: PAH is associated with increase in lung oxidant and decrease in antioxidant indices. All three plant derivatives ameliorated oxidative stress and recovered reduction in antioxidant production.
Key words: Pulmonary arterial hypertension, oxidative stress, MDA, GPX, SOD, CAT, Rat

S104176-5

Effect of acute hypertension induced by aortic constriction on the brain and heart infarction: role of oxidative stress

Mohammad Taghi Mohammadi

Department of Physiology and Biophysics, School of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran

Background and Objective: Hypertension is a major risk factor to the development of stroke and coronary artery disease. Different types of hypertension could develop reactive oxygen species (ROS) in body tissues. Accordingly, we examined the effects of oxidative stress induced by acute model of hypertension on the injuries of ischemia-reperfusion (IR) in the brain and heart of rats.
Methods: Two groups of rats; normal and hypertensive, were randomly divided into sham and IR subgroups. Acute hypertension was induced by aortic constriction above renal arteries. After 7 days IR was induced in the brain and heart at separate animals. Oxidative stress parameters of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX) and malondialdehyde (MDA) were measured in the brain and heart tissues.
Results: Aortic constriction significantly enhanced arterial pressure by 35% compared to normal rats. SOD and CAT activity and GPX content significantly decreased and MDA significantly increased in the brain and heart of the hypertensive rats. IR-induced infarction volume enhanced in the brain but decreased in the heart of the hypertensive rats cocmpared to infarction volume in the normotensive group.
Conclusion: Aortic constriction-induced acute hypertension decreases the antioxidant capacity of the brain and heart that leaded to tissue oxidative stress. It is suggested that ROS induced by acute hypertension might change the injuries induced by IR differently in the brain and heart.
Keywords: Acute hypertension, Oxidative stress, Ischemia-reperfusion, Heart, Brain, Aortic constriction

S106177-1

Effect of hydrogen sulfide on the induction and treatment of diabetic enteropathy

Seyed Ali Mard

Baground: H2S as the third known gas-transmitter plays many physiological roles in mammalian body. This endogenous gas in GI system has different well-known activities. The inhibitory effects of H2S on spontaneous contractions of smooth muscles of small and large intestines well-documented but its role in the pathophysiology of diarrhea has not been identified. Therefore, this study evaluated the role of exogenous H2S (NaHS) on diabetic-induced diarrhea and determined mRNA expression of cystathionine β-lyase (CBS) and cystathionine γ-synthase (CSE) in diabetic rats.
Methods: In order to evaluate antidiarrheal effect of H2S, normal and diabetic rats received NaHS and L-Cysteine and the total number of fecal pellets (FP) determined. The effect of NaHS on intestinal transit ratio (ITR) was also evaluated in diabetic rats. The level of mRNA expressions of CBS and CSE determined in smooth muscles of jejunum, ileum, and colon in normal, and diabetic rats. The effect of NaHS on frequency and tension of spontaneous contractions of smooth muscle strips of colon, ileum, and jejunum were investigated.
Results: diarrhea successfully occured in rats two weeks after receiving alloxan monohydrate. NaHS decreased ITR, total number of FP, frequency and tension of spontaneous contractions of colon, ileum, and jejunum muscle strips in diabetic rats. The level of mRNA expression of CSE and CBS in diabetic rats were lower than in normal rats. NaHS, and L-Cysteine decreased the number of FP in normal rats.
Conclusion: the outcomes of this study revealed that hydrogrn sulfide has a modulatory effect on the intestinal motility at physiologic dose while can inhibit GI motility at pharmacological dose. As the current results showed at low concentration of this gas, hypermotility and diarrhea occured in rats.These findings also showed NaHS effectively controlled diarrhea in diabetic rats through decreasing the frequency, and tension of spontaneous contraction of smooth muscles of large, and small intestines. The increased frequency and tension of spontaneous contractions of smooth muscles in diabetic rats may be due to down-regulation of H2 S biosynthesis enzymes.
Key words: H2S, Diabetic diarrhea, Rats, Hypermotility

S106177-2

Protective effects of isoflavones against non-alcoholic fatty liver disease: mechanisms of action

Mohammad Reza Alipour[1,2]

1. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

2. Department of Physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Non-alcoholic fatty liver disease (NAFLD), the most common cause of liver disease, includes a wide spectrum of liver complications ranging from simple steatosis to non-alcoholic steatohepatitis (NASH) and liver fibrosis, which in a small percentage can result in cirrhosis and hepatocellular carcinoma. Phytoestrogens are plant-derived compounds with a similar structure to 17-beta-estradiol. Isoflavones, the most well-known class of phytoestrogens, exert a significant protective role against NAFLD through several molecular mechanisms. Here, the mechanisms of action of isoflavones (genistein, daidzein, formononetin, biochanin A, and puerarin) in NAFLD were summarized.
Isoflavones exert anti-obesity, anti-diabetic, hypolipidemic, antioxidant, and hepatoprotective effects. These compounds inhibit hepatic lipid accumulation through decreasing de novo lipogenesis (down-regulating expression of lipogenic genes) and increasing fatty acid β-oxidation (up-regulating expression of genes which are related to fatty acid oxidation) in the liver. On the other hand, isoflavones exert protective role against NAFLD/NASH and liver fibrosis through the modulation of adipocyte metabolism, suppression of c-Jun N-terminal kinase (JNK) and nuclear factor-kappa B (NF-κB)-mediated inflammatory cascade, inhibition of transforming growth factor β/Smad-2/3 signaling-mediated fibrosis, improvement of hepatic insulin signaling, reduction of serum endotoxin levels, and improvement of leptin mediated signaling via the Janus kinase 2/signal transducers and activators of transcription 3 (JAK2/STAT3) signaling pathways.
Conclusion: Isoflavones exert protective effects against NAFLD development and progression through several molecular mechanisms. Preclinical evidence places the use of isoflavones as an attractive and potential therapeutic strategy for delaying the progression of NAFLD.
Keywords: Non-alcoholic fatty liver disease, Isoflavones, Inflammation, Fibrosis

S106177-3

Influence of Sleep Deprivation on the 24-Hour Ghrelin Secretion Pattern

Parvin Zareian

Background: Blood concentration of many hormones fluctuates during a 24-hour period and sleep deprivation affects this circadian rhythm. The ghrelin hormone is secreted from gastric cells and stimulates hunger. There are a few studies regarding the 24-hour ghrelin secretion pattern in normal subjects, but no studies have addressed the effects of sleep deprivation on this pattern.
Objectives: To assess the 24-hour ghrelin secretion pattern and the effect of sleep deprivation on this pattern.
Methods: This work was conducted on 16 young soldiers (age: 19 - 23 years old) who served in AJA University of Medical Sciences. The participants were divided into two groups. The first group had regular sleep-wake cycle (n = 8). The second group did not have normal arousal cycle (n = 8). Six blood samples were taken from each subject within 24 hours. The samples were centrifuged and serum was frozen to -20°C until the various assays were performed. Serum cortisol and ghrelin levels were measured by the enzymelinked immunosorbent assay (ELISA).
Results: Cortisol showed a diurnal rhythm with a peak at 06.00 A.M. in the normal and disrupted sleep subjects. However, ghrelin did not show a significant diurnal rhythm in neither group. Sleep deprivation did not have a significant effect on the time pattern of the cortisol and ghrelin secretion.
Conclusions: It seems that in real life, ghrelin does not show a circadian rhythm and sleep deprivation does not impact this rhythm.
Keywords: Sleep Deprivation, Ghrelin, Circadian Rhythm

S106177-4

Targeted drug delivery of capecitabine to mice xenograft gastric cancer by PAMAM dendrimer nanocarrier

Fatemeh Nabavizadeh

Aims: In this study, we used an animal xenograft model of gastric cancer induction to investigate the therapeutic effects of capecitabine polyamidoamine (PAMAM) dendrimer complex against cancer, and its potential side effects.
Methods and Materials: Human gastric cancer tissue was obtained from patients with gastric carcinoma and transplanted into mice. Anticancer drug capecitabine was loaded into PAMAM dendrimer nano-carrier and injected

into the animals. All animals received cyclosporine before the surgery.
Results: Capecitabine-dendrimer complex reduced the size of the axillary implanted tumor, the levels of AST and ALP and the drug-induced adverse effects on other body organs. Furthermore, it increased apoptotic and necrotic responses in the grafted tumor, RBC, WBC and platelet counts in comparison to free capecitabine.
Conclusions: In gastric cancer setting, PAMAM dendrimer drug delivery method effectively improved therapeutic index and outcomes, and reduced undesirable side-effects of the capecitabine.
Keywords: Gastric cancer, Xenograft, Capecitabine, Cyclosporine, Poly amidoamine dendrimer (PAMAM), Mice.

S107178-1

Lipids and lipoprotein metabolism -recent progress

Behshid Ghadrdoost

Rajaie cardiovascular medical and research center, Iran University of medical sciences, Tehran, Iran

Research into lipid and lipoprotein metabolism has developed because understanding lipid and lipoprotein metabolism has important clinical indications. Recent advances include the identification of factors in the synthesis and secretion of triglyceride rich lipoproteins, chylomicrons (CM) and very low density lipoproteins (VLDL). These included the identification of microsomal transfer protein, the cotranslational targeting of apoprotein B (apoB) for degradation regulated by the availability of lipids, and the characterization of transport vesicles transporting primordial apoB containing particles to the Golgi. The lipase maturation factor 1, glycosylphosphatidylinositol-anchored high density lipoprotein binding protein 1 and an angiopoietin-like protein play a role in lipoprotein lipase (LPL)-mediated hydrolysis of secreted CMs and VLDL so that the right amount of fatty acid is delivered to the right tissue at the right time. Expression of the low density lipoprotein (LDL) receptor is regulated at both transcriptional and post-transcriptional level. Proprotein convertase subtilisin/kexin type 9 (PCSK9) has a pivotal role in the degradation of LDL receptor. Plasma remnant lipoproteins bind to specific receptors in the liver, the LDL receptor, VLDL receptor and LDL receptor-like proteins prior to removal from the plasma. Reverse cholesterol transport occurs when lipid free apoAI recruits cholesterol and phospholipid to assemble high density lipoprotein (HDL) particles. The discovery of ABC transporters (ABCA1 and ABCG1) and scavenger receptor class B type I (SR-BI) provided further information on the biogenesis of HDL. Cholesterol content in cells is regulated by several transcription factors, including the liver X receptor and sterol regulatory element binding protein. Multiple genes and complex pathways are involved in lipoprotein metabolism and cholesterol and lipid homeostasis. These include pathways of intestinal chylomicron secretion and liver VLDL secretion and cholesterol homeostasis with HDL providing a driving force for reverse cholesterol transport. Hormonal and nutritional factors further regulate lipoprotein metabolism.

S107178-2

Cholesterol efflux and reverse cholesterol Transport

Yaser Azizi

Department of physiology, Iran University of medical sciences, Tehran, Iran

Reverse cholesterol transport (RCT) is a pathway by which accumulated cholesterol is transported from the vessel wall to the liver for excretion, thus preventing atherosclerosis. Major constituents of RCT include acceptors such as high-density lipoprotein (HDL) and apolipoprotein A-I (apoA-I), and enzymes such as lecithin:cholesterol

acyltransferase (LCAT), phospholipid transfer protein (PLTP), hepatic lipase (HL) and cholesterol ester transfer protein (CETP). A critical part of RCT is cholesterol efflux, in which accumulated cholesterol is removed from macrophages in the subintima of the vessel wall by ATP-binding membrane cassette transporter A1 (ABCA1) or by other mechanisms, including passive diffusion, scavenger receptor B1 (SR-B1), caveolins and sterol 27-hydroxylase, and collected by HDL and apoA-I. Esterified cholesterol in the HDL is then delivered to the liver for excretion. In patients with mutated ABCA1 genes, RCT and cholesterol efflux are impaired and atherosclerosis is increased. In studies with transgenic mice, disruption of ABCA1 genes can induce atherosclerosis. Levels of HDL are inversely correlated with incidences of cardiovascular disease. Supplementation with HDL or apoA-I can reverse atherosclerosis by accelerating RCT and cholesterol efflux. On the other hand, pro-inflammatory factors such as interferon-gamma (IFN-γ), endotoxin, tumour necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β), can be atherogenic by impairing RCT and cholesterol efflux, according to in vitro studies. RCT and cholesterol efflux play a major role in anti-atherogenesis, and modification of these processes may provide new therapeutic approaches to cardiovascular disease.

S107178-3

Dynamic Macrophages: Mechanisms of Activation in Atherosclerotic Vascular Disease

Kamran Rakhshan

Department of physiology, Iran University of medical sciences, Tehran, Iran

Evidence suggests that metabolic reprogramming of macrophages triggers either a pro-inflammatory, anti-inflammatory or pro-resolving behavior. Dynamic changes in bioenergetics, metabolome or influence from bioactive lipids may promote resolution or aggravation of inflammation. Direct cell-to-cell interactions with other immune cells can also influence macrophage activation. Both paracrine signaling and intercellular molecular interactions either co-stimulate or co-inhibit activation of macrophages as well as their paired immune cell collaborator. More pathways of activation can even be uncovered by inspecting macrophages in the single cell level, since differential expression in key gene regulators can be screened in higher resolution compared to conventional averaged gene expression readouts. Reduction of inflammation, specifically targeting the interleukin-1β (IL-1β) pathway activation, independent of LDL cholesterol lowering, can significantly lower coronary artery disease (CAD) morbidity and mortality. Antagonizing the IL-1β signaling resulted in marked reduction of plasma high-sensitivity C-reactive protein (hs-CRP) levels among patients with elevated hs-CRP levels and history of myocardial infarction, which eventually led to decreased major adverse cardiac/CV events (MACE and MACE+) (4) hs-CRP is a predictive marker of the severity of atherosclerosis and extent of future cardiovascular events.

S107178-4

Novel risk markers - what do they tell us?

Sedigheh Saedi

Rajaie cardiovascular medical and research center, Iran University of medical sciences, Tehran, Iran

Numerous lipid and nonlipid biomarkers have been proposed as potential risk markers for cardiovascular disease. Apolipoprotein B: Apolipoprotein B (apo B) is the major protein moiety of all lipoproteins except for HDL. The most abundant form of apo B, large B or B100, constitutes the apo B found in LDL and very-low-density

lipoproteins (VLDL). Because both LDL and VLDL each contain 1 molecule of apo B, measurement of apo B reflects the total number of these atherogenic particles, 90% of which are LDL.
Apolipoprotein AI: HDL contains 2 associated apolipoproteins, (ie, AI and AII). HDL particles can also be classified by whether they contain apolipoprotein AI (apo AI) only or whether they contain both apo AI and apolipoprotein AII (apo AII).
Apolipoprotein E: Apolipoprotein E (apo E) is the primary apolipoprotein found in VLDLs and chylomicrons. The apolipoprotein E (APOE) gene is polymorphic, consisting of 3 epsilon alleles (e2, e3, e4). It has been proposed that various APOE genotypes are more atherogenic than others and that APOE measurement may provide information on risk of CAD above traditional risk factor measurement.
HDL Subclass: HDL particles exhibit considerable heterogeneity, and it has been proposed that various subclasses of HDL may have a greater role in protection from atherosclerosis. Particles of HDL can be characterized based on size or density and/or on apolipoprotein composition.
LDL Subclass: Two main subclass patterns of LDL, called A and B. Subclass pattern B is a commonly inherited disorder associated with a more atherogenic lipoprotein profile, also termed "atherogenic dyslipidemia."
Lipoprotein (a): Lipoprotein (a) (Lp[a]) is a lipid-rich particle similar to LDL. Apo B is the major apolipoprotein associated with LDL; in Lp(a), however, there is an additional apo A covalently linked to the apo B. It has been proposed that levels of Lp(a) may be an independent risk factor for CAD.
Non–Lipid Markers: B-Type or Brain Natriuretic Peptide
Cystatin C
Fibrinogen

S103179

Effects of Melatonin on Calcium Action Potential of Helix aspersa Neurons in a Pentylenetetrazol Induced Epileptic Model: Experimental and Theoretical Studies

Mahin Ganjkhani[1], Maryam PasdarNavvab[2], Alireza Valizadeh[2]

1. School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran.
2. Department of Physics, Institute for Advanced Studies in Basic Sciences (IASBS), Zanjan , Iran

Background and Objective: There is considerable evidence that shows the effect of light and dark periods on epileptogenesis and there is probability that melatonin fluctuations have a role in this regard. In the present study, the effects of melatonin on pentylenetetrazole (PTZ) induced epileptiform activity and calcium action potential (AP) was assessed and also a minimal conductance-based neuronal model used to test the validity of hypotheses.
Materials and Methods: Intracellular recordings were made under the current clamp condition neurons of Helix aspersa. For studying on calcium currents, NaCl was replaced by 4-AP (5mM) and TEA (80mM). The Effects of extracellular application of melatonin (100 µM) before and after PTZ (25mM) were investigated on the firing pattern and calcium action potentials. Recoding data were simulated based on an important neuronal model, the Morris-Lecar (ML) equation with potassium and calcium currents.
Results: Our results showed a decrease in action potential amplitude, frequency and after hyperpolarization (AHP) amplitude but the duration of spikes, time to peak of action potential and membrane resting potential increased. The simulation results confirmed that the observed results of the application of melatonin on the spiking activity of the real neurons can be a result of the change in the conductivity of potassium and calcium channels.
Conclusion: The simulation results confirmed that the observed results of the application of melatonin on the spiking activity of the real neurons can be a result of the change in the conductivity of potassium and calcium channels.
Keywords: Epilepsy, Melatonin, Morris-Lecar model.

S103180

Role of vitamin D3 in memory improvement and nitric oxide level in demyelinated hippocampus of rat

Zahra Ataie[1], Samira Choopani[2], Forogh Foolad[3], Fariba Khodagholi[4], Mahdi Goudarzvand[5*]

1. Assistant Professor of Pharmaceutics, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran.
2. Master of Sciences in Medical Physiology, Physiology and Pharmacology department, Pasteur Institute, Tehran, Iran.
3. Philosophy of Sciences in Physiology, Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

4. Associate Professor of Biochemistry, Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

5. Associate Professor Physiology, Medical School, Alborz University of Medical Sciences, Karaj, Iran.

Studies have revealed the beneficial role of vitamin D3 in neuro-cognitive functions. Additionally, there is supporting evidence on the involvement of nitric oxide (NO) in the neuro-protective action. However, reports on its role have been contradictory. In this study, demyelination was induced by injection of ethidium bromide (EB) into the right side of the hippocampus area of male Wistar rats. Vitamin D3 was administered to rats for 7 and 28 days prior to behavioral experiments using Morris Water Maze (MWM). Travelled distance, time spent to reach the platform, and time spent in target zone, were considered for learning and memory evaluation. Nitrite oxide (NO2-) concentration was measured as an indicator for nitric oxide production. Demyelination was successfully induced in rats by EB. Vitamin D3 decreased the time spent to reach the platform and also the travelled distance on day 28 significantly compared to 7 days. Time spent in target quadrant was significantly altered by administered vitamin on day 28. Therefore, considering a number of studies that have shown the effect of vitamin D3 on cognition, these findings could support their potential effect. Besides, nitric oxide concentration significantly differed in 28 days of vitamin D3 treated group compared with the groups treated with EB or 7 days of vitamin D3.
Keywords: Vitamin D3, nitric oxide concentration, spatial memory, ethidium bromide, Morris Water Maze, demyelination

S103181

The Role of Glial Cells in Spatial Working Memory Deficits in a Rat Model of Traumatic Brain Injury (TBI)

Amir Rezagholizadeh[1,2], Seyed Asaad Karimi[1-3], Narges Hosseinmardi[1,2*], Mahyar Janahmadi[1,2], Mohammad Sayyah[4]

1. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2. Neurophysiology Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

4. Department of Physiology and pharmacology, Pasteur Institute of Iran, Tehran, Iran

Traumatic brain injury (TBI) is damage caused by an external mechanical force that can produce significant cognitive and memory impairment in humans. Evidence suggests that glial cells are influenced by TBI. Both protective and damaging roles have been attributed to active astrocytes, but their role after TBI has not been well understood. In this study, the role of glial cells in TBI-induced cognitive impairment was investigated. Glial cell-inhibitor, Fluorocitrate (FC), in a rat model of controlled cortical impact (CCI) injury was used. Male rats were randomly assigned to the following groups: Sham+PBS, sham+FC (1nmol/1µl), TBI+PBS, and TBI+FC (1nmol/1µl). Fluorocitrate was injected into the brain lateral ventricle 10 min after TBI induction and it was repeated every 24 hours until the seventh day. On days 8-16 post-injury, working memory was assessed using the Morris water maze test (MWM). Injured animals showed a slower rate of acquisition with respect to the sham+PBS animals [(F (1, 84) = 7.398, P = 0.008), two-way ANOVA]. FC administration could not attenuate the deteriorative effect of TBI on working memory acquisition. There were no significant differences in escape latency and traveled distance between injured animals and TBI treated with FC ($p>0.05$, two-way ANOVA). Sham animals which received FC showed a considerable increase in escape latency (P = 0.0183, two-way ANOVA) and traveled distance (P = 0.0043, two-way ANOVA), compared to Sham+PBS animals. The present study demonstrates that memory deficit induced by TBI cannot be improved by administration of FC. Also, Our results indicated that inhibition of glial cells may result in the memory loss in uninjured animals. These observations suggest a crucial role for glial cells in normal cognitive functions.
Keywords: Traumatic brain injury; Cognitive dysfunction; Learning and memory; Glial cells; Fluorocitrate.

S103182

The role of hippocampal glial glutamate transporter (GLT-1) on synaptic dysfunction in morphine dependent rats

Negin Saeedi, Amir Rezagholizadeh, Narges Hosseinmardi, Mahyar Janahmadi

Department of Physiology and Neuroscience research center, Medical School, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Background and Objective: Drug addiction is considered to be a chronic and recursive neurological disorder. Chronic consumption of addictive drugs including opioids creates false memories in nervous system by inducing maladaptive plasticity. Morphine could change the capacity of synaptic plasticity by dysregulation of GABA and

glutamate balance in CA1 region of the hippocampus. Astrocytes play an important role in regulation of neurotransmitters concentration in synaptic space by releasing gliotransmitter and uptaking neurotransmitter.Glial glutamate transporter (GLT-1) makes up more than 80% of hippocampal glutamate transporters and removes 90% of extracellular glutamate. Since opioids alter the expression of GLT-1, we investigated the role of this transporter in morphine induced-metaplasticity.
Materials and Methods: Morphine sulfate (10 mg/kg) was injected to male rats subcutaneously at an interval of 12 h for 9 days. To activate glial glutamate transporter (GLT-1), rats received ceftriaxone (0.5 mmol/0.5 µl) in the CA1 region thirty minutes before each morphine administration. Field excitatory postsynaptic potentials (fEPSP) were recorded from the stratum radiatum of the CA1 area following Schaffer collateral stimulation.
Results: Morphine dependence caused augmented LTP in CA1 area. fEPSP slope potentiation in this group (146.04±9%) was statistically (unpaired t-test, $p<0.01$) more than control animals (125.83±9.98%). Animals receiving intra-hippocampal microinjection of ceftriaxone before morphine demonstrated a significant reduction (unpaired t-test, $p<0.001$) in potentiation (132.01±11.2%) compared to those which received vehicle.
Conclusion: These data suggest that hippocampal glial glutamate transporter may mediate some effects of morphine on CA1 metaplasticity.
Keywords: Morphine dependence; Synaptic plasticity; GLT-1; CA1 area of the hippocampus; Field potential recording

S103183

Intra-BLA administration of L-arginine and L-NAME dose not reduce the acquisition of nicotine-induced place preference in the rats

Hedayat Sahraei[1], Cyrus Jalili[2], Yousef Sadeghi[3]

1. Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, IRAN.
2. Department of Anatomy, Faculty of Medicine, Kermanshah University of Medical Sciences
3. Department of Anatomy, Faculty of Medicine, Shahid Beheshti University of Medical Sciences

Background and Objective: Studies have shown that nitric oxide (NO) play a pivotal role in nicotine-induced place preference and basolateral amygdala (BLA) function as well. In the present study, the effects of intra-BLA administrations of the NO precursor, L-arginine, and nitric oxide synthase inhibitor, L-NAME on the expression and acquisition of nicotine-induce place preference were studied.
Materials and Methods: Male Wistar rats (220-250 g) received different doses of nicotine (0.4, 1, and 1.5 mg/kg) for place conditioning. L-Arginine and L-NAME were administered intra-BLA before each nicotine injection (acquisition) or after the session completed (expression).
Results: Our results showed that nicotine can induced place conditioning in dose of 1.5 mg/kg. Moreover, L-arginine (1, 5 and 10 µg/rat) administration into the BLA area augmented the acquisition but reduced the expression of nicotine-induce place preference, whereas L-NAME (1, 5 and 10 µg/rat) into the BLA area reduced the acquisition of nicotine-induced CPP.
Conclusion: These results indicated that intra-BLA L-arginine and L-NAME administration leads to a change in place conditioning induced by nicotine in the rats which may be indicated a role for nitric oxide in this brain area on nicotine-induced positive reinforcement.
Key Words: Basolateral Amygdala; Nicotine; Nitric oxide; Conditioned Place Preference; Rat.

S103184

The effect of ghrelin on the MK801- induced memory impairment

Hamideh Zahiria[1], Mohammad Rostampour[2,3,4], Behrouz Khakpour[2,3,4], Kambiz Rohampour[2,4]

Student Research Committee, Guilan University of Medical Sciences, Rasht, Iran

Department of Physiology, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
Cellular and Molecular Research Center, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
Neuroscience Research Center, Guilan University of Medical Sciences, Rasht, Iran
Background and objective: Learning and memory are the essential phenomena of the CNS. N-Methyl-D-Aspartate (NMDA) receptors are critically involved in the learning and memory formation and dizocilpine (MK-801) is an

antagonist of NMDA receptor. Ghrelin plays a crucial role in learning and memory processes. The present study was conducted to the evaluation of ghrelin effect on passive avoidance memory impairment induced by MK-801.
Materials and Methods: In this experimental study, 24 male wistar rats were randomly distributed into 3 groups of 8 each. Passive avoidance tests of animals were evaluated using Shuttle Box apparatus. One week after the surgery, ghrelin (3nmol) was injected intra- hippocampally, 15 min before the test session. MK-801 (0.15 mg/kg) was injected intraperitoneally (i.p.), 10 min before the test session.
Results: Pre-test injection of MK-801 significantly decreased STL (step through latency) and increased TDC (time spent in dark compartment) at 24 h, 48 h and 10 days after training as compared to control group. Pre-test injection of ghrelin + MK-801 received group significantly increased STL and decreased TDC at 24 h, 48 h and 10 days after training as compared to MK-801 received group.
Conclusion: it seems that pre-test injection of MK-801 impaired passive avoidance memory and administration of ghrelin before MK-801 ameliorated memory impairment induced by MK-801. It is possible that ghrelin modulate memory through interaction with NMDA receptor.
Keywords: passive avoidance memory, ghrelin, MK-801

S103185

The role of 5-HT1A receptors and neuronal nitric oxide synthase on the neuronogenesis of dentate gyrus in seizure- induced kindling model in rat

Zinat Heidarnia[1], Omid Gholami[2,3], Bahareh Amin[2,3], Akbar Pejhan[2,3], Sajad Sahab-Negah[4], Mohammad Mohammad-Zadeh[5,*]

1. MSc of Physiology, Department of Physiology and Pharmacology, Sabzevar University of Medical Sciences, Sabzevar, IRAN
2. Cellular and Molecular Research Center, Sabzevar University of Medical Sciences, Sabzevar, IRAN
3. Department of Physiology and Pharmacology, Sabzevar University of Medical Sciences, Sabzevar, IRAN
4. Neuroscience Research Center, Mashhad University of Medical Sciences, Mashhad, IRAN
5. Department of Physiology, Mashhad University of Medical Sciences, Mashhad, IRAN

Aim: Dentate gyrus (DG) has a high density of 5-HT1A receptors, that play an important role in neurogenesis. The purpose of this study was to investigate the role of 5-HT1A receptors in the neurogenesis of dentate gyrus in seizure induced by kindling.
Methods: Thirty rats (280 ± 20 gr) were divided into five groups: (1) Sham, (2) kindled+vehicle, (3) kindled+WAY100635 (5-HT1A antagonist, 0.1mg per rat. icv), (4) kindled+ 7-NI (a nNOS inhibitor, 15 mg/kg), (5) kindled+WAY100635+7-NI (n = 6). Daily, for 20 minutes, field potentials from the DG were recorded. Immediately after that, kindling stimulations were applied within 10 days (12 stimulations per day for 1 hour) and during this time, the seizures and electrophysiological parameters were recorded. At the end, GFAP (Glial fibrillary acidic protein) expression rate in the DG was measured as an index of neurogenesis.
Results: Kindling acquisition was significantly faster in the kindled+WAY100635 and kindled+7-NI+ WAY100635 groups than the kindled+vehicle group ($P < 0.001$). The slope fEPSP at the end of 10 days in the kindled+7-NI+WAY100635 group was significantly lower than the kindled+vehicle group ($p < 0.001$). Immunohistochemistry showed that cell proliferation in the kindled+7-NI+WAY100635 group was significantly higher than in the kindled+vehicle group ($p < 0.001$).
Conclusion: According to the obtained results, it can be concluded that inhibition of neuronogenesis in the DG (maybe by inhibition of nNOS), by enhancing the release of inhibitory neurotransmitters, increases the inhibitory activity of the hippocampal circuits and prevents the spread of seizures.
Keywords: Seizure, Serotonin, Kindling, Neurogenesis, Dentate gyrus, Neuronal nitric oxide synthase

S103186

The interplay between angiotensin II and vasopressin receptors in parvocellular portion of the paraventricular nucleus of hypothalamus on the cardiovascular response: effects on hypovolemia hypotension

Fatemeh Haddad, Nafiseh Mirzaei Damabi, Bahar Rostami, Fahimeh Yeganeh and Masoumeh Hatam

Dept. of Physiology, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: It has already shown AngII influences PVN neurons to release vasopressin (VP) by AT1 receptor (AT1R), the presence of AT2 receptors in VP containing neuron has been approved. The present study to

determine the probable role of AngII of parvocellular divisions of PVN (PVNP) in the control of VP secretion and vasopressin of the PVNP in the control of AngII on cardiovascular responses. we also explored whether central vasopressin of the PVN plays a regulatory role during hypovolemic-hypotension induce by hemorrhage and role of V1a vasopressin receptor.
Materials and methods: AngII, argenine VP (AVP), losartan an AT1 receptor antagonists and PD123319, an AT2 antagonist and V1a receptor antagonists were microinjected into PVNP , arterial pressure (AP) and heart rate (HR), recorded in urethane anesthetized rats. Hypovolemic-hypotension induced by bleeding from the venous catheter
Results: AngII and AVP microinjected into the PVNP produced pressor and tachycardic responses. The cardiovascular responses to AngII were blocked by V1a receptor antagonists , and AVP were blocked by AT2 antagonist . We also found that AVP regulates arterial pressure toward normal during hypotension and after-hemorrhage injection of V1a antagonist, into PVN caused reduction in MAP.
Conclusion: these data provide the first evidence that
AngII and vasopressin microinjected into the PVN produced a pressor and tachycardia .The AngII pressor response mediate by V1a receptor and the AVP by AT2 receptors. During the hemorrhage sensitivity of PVN by V1a receptor to vasopressin increased.
Keywords: Paraventricular nucleus PVN, Arterial pressure , Angiotensin II, Vasopressin, Hemorrhage

S103187

Molecular, histological and behavioral evidences for neuroprotective effects of minocycline against nicotine-induced neurodegeneration and cognition impairment: possible role of CREB-BDNF signaling pathway

Majid Motaghinejad[1], Manijeh Motevalian[2,3] and Sepideh Safari[3]

1. Research Center for Addiction and Risky Behaviors (ReCARB), Iran Psychiatric Center, Iran University of Medical Sciences, Tehran, Iran.
2. Department of Pharmacology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
3. Razi Drug Research Center, Iran University of Medical Sciences, Tehran, Iran.

Background and Objective: Neurodegeneration is one of the serious adverse effects of psychostimulants. The role of CREB-BDNF signaling pathway in mediating the neuroprotective effects of minocycline against nicotine-induced neurodegeneration in rats was evaluated in current study.
Materials and Methods: Seventy adult male rats were divided randomly into seven groups. Morris water maze (MWM) was used to evaluate learning and spatial memory in rats treated in different groups. Hippocampal neurodegenerative parameters and also CREB/BDNF expression levels were evaluated in isolated hippocampus. Also hippocampal cell density and tissue changes were evaluated by H & E staining.
Results: Nicotine attenuated the learning and memory. Simultaneous treatment with various doses of minocycline reduced the nicotine-induced cognition disturbances. In addition, nicotine treatment increased lipid peroxidation and the levels of oxidized form of glutathione (GSSG), IL-1β, TNF-α and Bax, while decreasing reduced form of glutathione (GSH), Bcl-2, P-CREB and BDNF levels in the hippocampus. Nicotine also reduced the activity of SOD, GPx and G in the hippocampus. Minocycline attenuated nicotine-induced neurodegeneration and elevating CREB (both forms) and BDNF levels, and decreases oxidative stress, inflammation and apoptotic biomarkers. Minocycline at high doses caused inhibition of nicotine induced cell density and changes in both areas of dentate gyrus (DG) and CA1 in hippocampus.
Conclusion: It can be concluded that minocycline, probably through activation of P-CREB/BDNF signaling pathway, confers neuroprotection against nicotine-induced neurodegeneration in hippocampus.
Keyword: Nicotine, Minocycline, Neurodegeneration, CREB, BDNF.

S103188

Is there any relevance between serum heavy metals concentration and BBB leakage in Multiple sclerosis patients?

Babak Paknejad[1], Hamid Shirkhanloo[2], Mehdi Aliomrani[3]

1. Department of Pharmacology and Toxicology, School of Medicine, AJA University of Medical Sciences, Tehran, Iran.
2. Iranian Petroleum Industry Health Research Institute (IPIHRI), Tehran, Iran.
3. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran.

Background and Objectives: Sharp increase in multiple sclerosis (MS) incidence rate has been observed in Iranian people. In addition, it has been suggested that increased S100B level may be useful as an indicative factor of Blood Brain Barrier disruption. The propose of this study was to measuring blood arsenic, lead and cadmium concentration and serum S100B concentration in a group of healthy and multiple sclerosis patients in Tehran as the most polluted city in Iran.
Methods and Materials: All subjects were interviewed regarding age, medical history, possible chemical exposure, acute or chronic diseases, smoking and dietary habits. Blood heavy metals level were measured by an atomic absorption spectrometer conjugated with a graphite furnace atomizer. Also, a serum S100B protein concentration was determined using a commercial ELISA kit.
Results: It was observed that all male subjects had higher blood metals level in comparison with healthy controls. Also, MS patients had higher arsenic and cadmium blood concentration in comparison with healthy individuals. Regarding the S100B concentration, it was observed that it had a significant relationship with smoking habit (P value= 0.0001). In addition, arsenic had a greater correlation (63%) with increased serum S100B biomarker level among other elements.
Conclusion: BBB leakage was higher in multiple sclerosis than in healthy subjects due to increased S100B release. In addition with regards to the heavy metals exposure especially arsenic and cadmium, these are associated with an increased BBB disruption and it is possible to play a crucial role as a developing agent of multiple sclerosis.
Keywords: Multiple sclerosis; Lead; Heavy metal; Cadmium; Arsenic; BBB; S100B.

Poster Presentation

P-101

The role of dopamine D2-like receptors on the inhibitory effects of low frequency electrical stimulation in perforant path kindling in rat

Mahmoud Rezaei

Introduction: Low frequency stimulation (LFS) has been considered as a new treatment for drug resistant epileptic patients. It has been suggested that the LFS antiepileptogenic mechanisms maybe similar to mechanisms involved in long term depression (LTD) and /or depotentiation. Dopamine is a neurotransmitter in the central nervous system

which exerts anticonvulsant effects and mediates depotentiation through its D2-like receptors. In this study, the role of dopamine D2-like receptors as a mechanism of the inhibitory effect of LFS on kindling progression and kindling-induced potentiation was investigated.Material and methods: Male wistar rats weighing 270-290 g underwent stereotaxic implantation a bipolar stimulating electrode in perforant path and a monopolar recording electrode in dentate gyrus. Animals were assigned to 6 groups. In kindled group animals received daily kindling stimulation until they showed stage 5 seizure. In Kindled+LFS (KLFS) group LFS were applied daily at 5 minutes after the last kindling stimulation. Animals of Kindled+LFS+Sulpiride (KLFS+Sulpiride) group received the same experimental procedure except that sulpiride (dopamine D2-like receptors antagonist, 10µg/1µl i.c.v.) was applied prior to daily LFS application. In all groups, field potentials were recorded in freely moving animals for 20 minutes before applying kindling stimulations. Result: Daily kindling stimulation increased cumulative daily behavioral seizure stages, daily afterdischarge duration (dADD) and population spike amplitude (PS) in kindled group, while LFS application prevented the kindling-induced increase in these parameters in KLFS group. In addition, kindling potentiated the early (10-50 ms) and late (150-1000 ms) paired-pulse inhibition and decreased the paired pulse facilitation (70-100 ms). Sulpiride inhibited the preventive effect of LFS on kindling development and kindling-induced increment of PS amplitude and prevented the increasing paired-pulse inhibition (early and late) and decreasing paired-pulse facilitation in animals of KLFS+Sulpiride group significantly. Conclusion: Results of this study suggest that LFS exerts its preventive effect on kindling development, at least partly, through the activation of dopamine D2-like receptors.

Keywords: Dopamine D2-like receptors; Sulpiride; Low frequency stimulation; Kindling; Dentate gyrus

P-102

Sanguinarine reverses cisplatin resistance in multidrug resistant ovarian cancer cells

Vahid Shafiei-Irannejad, Morteza molaparast, Roya sarkhosh, Adel Mohammadzadeh

Cellular and Molecular Research Center, Cellular and Molecular Medicine Institute, Urmia University of Medical Sciences, Urmia, Iran.

Background and Objective: Ovarian Cancer is one of the most life threatening cancers of women and cisplatin-based treatment is considered as the first line chemotherapy option. However, resistance to cisplatin is the main obstacle against successful cancer chemotherapy. Intracellular gluthatione content is the major mechanism for resistance to cisplatine. In this study, we investigated the effects and possible mechanism of sanguinarine, a plant-derived alkaloid, on sensitivity to cisplatin in human cisplatine resistant ovarian cancer (A2780/R) cells.
Materials and Methods: The effect of sanguinarine on cytotoxicity of cisplatin was evaluated by MTT assay. Flow cytometeric analysis of apoptosis was performed to examine the effects of sanguinarine on cisplatin-induced apoptosis. Intracellular gluthatione content was determined using GSH assay kit after treatment with different concentrations of sanguinarine in different time intervals.
Results: Our results indicated that combination therapy with sanguinarine, enhances the sensitivity of A2780/R cells to cisplatine. Sanguinarine also increased the apoptosis-inducing effects of cisplatin. Moreover, intracellular gluthatione content was decreased after treatment with sanguinarine in a dose-dependent manner, while, time had no significant effect on gluthatione content.
Conclusion: These findings indicate that sanguinarine enhanced the sensitivity to cisplatin and reversed the multidrug resistance in cisplatin resistant ovarian cancer cells. Therefore, sanguinarine can be considered as a potential adjuvant for combination therapy in ovarian cancer.

Keywords: ovarian cancer, multidrug resistance, cisplatin, sanguinarine, gluthatione

P-103

Effect of oxytocin on brain edema and aquaporin-4 in an experimental model of stroke

Shahein Momenabadi[1,2], Mahdi Zahedi khorasani[1,2], Azam Abareshi[1,2], Abedin Vakili[1,2]

1. Research Center of Physiology, Semnan University of Medical Sciences, Semnan, Iran.
2. Department of Physiology, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran.

Background and Objective: Oxytocin (OXT) has important role in the regulation of several social processing such as emotion recognition, reward-based learning, pair bonding, maternal behavior and reducing social anxiety/stress. In addition, there is evidence that OXT may have potential therapeutic target for cerebral stroke. Present study was designed to determine the effect of intranasal application of OXT on brain edema and expression of aquaporin-4 (AQP4) in acute phase of stroke in mice.
Material and methods: Focal cerebral ischemia produced by middle cerebral artery occlusion (MCAO) for 60 min and 24h reperfusion in mice. OXT at dose of 8 IU/ per mouse was given intranasally at initial phase of ischemia. Brain edema and AQP4 proteins were evaluated at 24h after cerebral ischemia by dry/wet method and western blotting technique.
Results: OXT at dose 8 IU/per mouse significantly reduced brain edema and up-regulated expression of AQP4 in the brain ($P < 0.001$).
Conclusion: Finding of current study indicated intranasal application OXT limited brain edema formation may be through increase of AQP4 expression in acute phase cerebral ischemia in mice model of stroke. It seems that AQP4 reduced edema through accelerating the transfer of water from parenchymal brain to CSF space and intraventricular compartment.
Key words: Focal cerebral ischemia, Oxytocin, brain edema, aquaporin-4, Mice

P-104

The role of mGluR4 receptors within the nucleus accumbens in the expression of morphine-induced conditioned place preference in male rat

Zahra Ebrahimi Farzad, Nazanin Kahvandi-, Abdolrahman Sarihi-, Alireza Komaki-, Asad karimi

Neurophysiology Research Center, Hamadan University of Medical Science, Hamedan, Iran

Background and Objective: Several studies have shown that glutamate in the nucleus accumbens (NAc) is required for the development of morphine-induced conditional place preference (CPP). Metabotropic glutamate receptors (mGluRs) in the nucleus accumbens also play an important and key role in the reward pathway. However, the role of different subtypes of these mGluR in different steps of the morphine-induced conditioning place preference is less well known. In the present study we investigated the effect of bilateral intra-accumbal infusion of VU0155041, a specific mGluR4 agonist on the expression of morphine induced CPP in male rats.
Materials and methods: Male Wistar rats weighing 200-250 g were bilaterally implanted with cannulae above the NAc. VU0155041, at the doses 10,30 and 50 µg / µl was injected bilaterally into the nucleus accumbens during the day of conditioning (expression). Conditioning scores and locomotor activity were recorded by maze router software.
Results: The results showed injection of mGluR4 agonist in to the NAc before expression had no effect on morphine-induced CPP expression.
Conclusion: There is specificity in the role of different mGluR subtypes in reward pathways which has been discussed in this paper.
Keywords: Metabotropic glutamate receptor type 4, morphine, nucleus accumbens, conditioning place preference.

P-105

Betulinic acid attenuated motor, cognitive and globus pallidus electrical power deficits in animal model of Parkinson's disease.

Abrishamdar M.1, Sarkaki A.2, Farbood Y.2 , Khoshnam S.E1

1. Physiology Research Center, Ahvaz Jundishpur University of Medical Sciences, Ahvaz-Iran.
2. Department of Physiology and Physiology Research Center, Medicine Faculty, Ahvaz Jundishpur University of Medical Sciences, Ahvaz-Iran.

Background: Parkinson's disease (PD), is a slowly progressive neurodegenerative disorder which is strongly associated with motor, brain electrical activity and cognitive impairments. Betulinic acid (BA) is a nutural active

compound with potent antioxidant activity. The aim of this study was to investigate whether BA affects motor dysfunctions, memory impairments and pallidum local Electroencephalography (EEG) power in the rat model of PD induced by 6-hydroxydopamine (6-OHDA).
Materials & Methods: Male Wistar rats (300-350g) were used and divided randomly into 6 groups with 7 in each. Sham, PD, 3 treated groups with BA (0.5, 5, and 10 mg/kg, ip) and a positive control received L-DOPA (20mg/kg, P.O) for 7 days. Right medial forebrain bundle (MFB) was lesioned by injection of 6-OHDA (20 µg/kg) under streotaxic surgery in anesthetized rats. PD was established by (0.5 mg/kg, ip) apomorphine for induction contralateral rotation 14 days after 6-OHDA lesion. Treatment of rats begun just after the approved rotation test. Different motor behavioral tests such as bar test, foot print, Morporgo's (catalepsy) and passive avoidance memory in shuttle box and also ultimately Pallidal local EEG recording were done.
Results: Treatment the PD rats with BA significantly reversed the 6-OHDA-induced motor complication ($P<0.001$, $P<0.01$respectively), as well as cognitive impairment and globus polidus frequency bands' powers ($P<0.05$).
Conclusion: Our results showed that BA could affect as a potent natural free radical scavenger which removes brain tissue oxidants in PD. It can account as a possible promise as a good therapeutic agent for motor and non-motor complications in PD.
Keywords: Parkinson; Betulinic acid; Motor activity; Passive evoidance memory; local EEG.

P-106

Effect of Cerebrolysin on the structural change of the bladder wall and spinal cord in the animal model of spinal cord injury

Nasrin Abolhasanpour[1,2*], Sakineh Hajebrahimi[3], Akram Eidi[2], Siamak Reyhani rad[4], Hanieh Salehi pourmehr[5], leila Hosseini[6]

1. Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran.
2. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran
3. Research Center for Evidence-Based Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
4. Department of Medical Laboratory Sciences, Islamic Azad University, Marand, Iran.
5. Neurosciences Research Center (NSRC), Tabriz University of Medical Sciences, Tabriz
6. Department of physiology, Tabriz University of medical sciences, Tabriz, Iran.

Background and objective: Spinal cord injury (SCI) is one of the most common phenomena among the central nervous system. Neurogenic detrusor overactivity is an important clinical problem following the SCI. cerebrolysin (CL) as a drug containing various neurotrophic factors and essential amino acids is one of the therapeutic strategies in neurodegenerative disease. The aim of this study was the evaluation of CL effects on tissue structure of the spinal cord and bladder after spinal cord injury.
Material and methods: After induction of complete transection at T9-T10 spinal vertebrate, CL (1, 2.5 ,5ml/kg/i.p.) was injected daily both of the acute (7 days) and chronic (28 days) phase. Histological and statistical evaluation of spinal cord and bladder tissue was done after tissue preparation.
Results: Histological examinations in the spinal cord showed that in acute phase 5 ml/kg dose and in the chronic phase, 2.5, and 5 ml/kg dosages of CL regenerative changes in the structure of tissue was observed in different parts of white and gray matter. Histological examinations in the bladder revealed that in the groups received CL 2.5, and 5 ml/kg in short and long-term, tissue integrity was observed in the epithelium and bladder tissue. Image J software analyzing showed that collagen deposition increased in the SCI group. These changes decreased in the chronic phase and in two 2.5 and 5 dosages of the drug.
Conclusion: The results showed that CL as a mixed growth factor can induce neuroprotective effects in the spinal cord and bladder tissue after SCI.
Keywords: Cerebrolysin, Spinal cord injury, neurogenic bladder, Rat

P-107

Blockade of Glutamate Receptors within the Prelimbic Cortex Attenuate Concentration of Excitatory Amino Acids in the Morphine Self-administration in Rats

Fateme Aboutalebi[1], Hojjatallah Alaei[2], Shahrbanoo Oryan[1], Ziba Rajaei[2]

1. Department of Animal Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran.
2. Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

Background and Objective: The attitude of research on addiction has been done on the key role of glutamate. As a regard, the prelimbic cortex (PrL) has an important role in addiction, learning, and memory. We tried to investigate the level of glutamate and aspartate concentration after glutamate receptors blockade in this region in the morphine-addicted rats.
Materials and Methods: In this study, we examined the effects of local infusion of the N-methyl-D-aspartate receptor and α-amino-3-hydrox y-5-methylisoxazole-4-propionic acid receptor antagonists, 2-amino-5-phosphonovaleric acid (AP5), and 6-cyano-7-nitroquinoxaline-2, 3-dione (CNQX), into the PrL cortex on the level of excitatory amino acids (EAAs) and glycine. After 11 days of self-administration, the prelimbic area of the brain was taken out, and the EAAs and glycine concentration was measured by high-performance liquid chromatography.
Results: Morphine resulted in the significant increase in the EAAs concentration within this area ($P \leq 0.001$). Microinjection of AP5 into this region before using of morphine significantly decreased the morphine-induced glutamate and aspartate concentration ($P \leq 0.001$). CNQX had the same effect and significantly reduced the EAAs concentration compared to the morphine group ($P \leq 0.001$).
In addition, microinjection of AP5 and CNQX simultaneously increased glycine concentration ($P \leq 0.001$).
Conclusions: These results show that morphine stimulates the EAAs release in the prelimbic area.
It seems that microinjection of AP5 or CNQX in this region is effective in reducing morphine-induced EAA. It is suggested that EAA transmission in the PrL cortex may be a possible target for treatment of morphine addiction.
Keywords: Glutamate, high-performance liquid chromatography, morphine, prelimbic area

P-108

Possible interaction of the Nucleus accumbens shell endocannabinoid system and GABA (A) system on locomotor activity in Male rats.

Hatam Ahmadi[1], Mohammad Reza Zarrindast [2], Mohammad Nasehi [3]

1. Department of Basic Sciences, Farhangian University, Tehran, Iran
2. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
3. Department of Biology, Faculty of Basic Sciences, Azad University, Garmsar Branch, Semnan, Iran

Background and Objective: It has been recently reported that the inhibition of γ-aminobutyric acid (GABA) synthesis in the brain increases locomotor activity. In addition, one of the main roles of the endocannabinoid system is the regulation of GABA release. This study has investigated the interaction of Nucleus accumbens (NAc) shell cannabinoid and GABA systems in regulating locomotor activity.
Materials and Methods: This study was performed on 9 groups of 8 male rats. The open field apparatus that automatically recorded locomotor activity, was employed. Bilateral intra-NAc shell injection of drugs was done.
Results: Bilateral intra-NAc shell injection of GABA(A) receptor antagonist (Bicuculline; 0.9 μg/μl) but not -Muscimole (GABA (A) receptor agonist; 0.1, 0.2 and 0.4 μg/μl) increased locomotor activity ($P<0.05$). Moreover, bilateral injection of ACPA (CB1-selective agonists; 0.00625, 0.0125 and 0.025 μg/μl) into this region did not alter locomotor activity. In addition, intra-NAc shell administration of the subthreshold dose of ACPA (0.0125 μg/μl) stopped the effect of higher dose of Bicuculline on locomotor activity.
Conclusion: The results showed that the activation of the cannabinoid system in the NAc shell attenuated the inactivation of GABA (A) system in the NAc shell on locomotor activity.
Keywords: ACPA, GABA(A) system, Nucleus accumbens, locomotor activity

P-109

Effects of vanillic acid on learning and memory in male rats with Alzheimer's disease induced by β-amyloid

Nesa Ahmadi[1], Naser Mirazi[1], Alireza komaki[2],Samaneh Safari[1]

1. Department of Biology, faculty of basic science, Bu-Ali Sina University, Hamedan, Iran.
2. Neurophysiology Research Center, Hamadan University of Medical Science, Hamadan, Iran.

Background and Objective: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a progressive decline in cognitive function, due to the accumulation of beta-amyloid peptide (Aβ) in the extracellular space. Aβ stimulates the production of active oxygen species and thus leads to oxidative stress and cell death. In this study, due to Vanilic Acid (VA) properties, the effect of this compound on memory and learning in Alzheimer's rats was studied.
Materials and Methods: Our experiments were conducted on 50 male Wistar rats randomly assigned to 5 groups (n = 10): control, sham (intraventricular saline injections), AD (Aβ; intraventricular Aβ injections), VA treatment (50 mg/kg) and AD with VA treatment. Standard passive avoidance test and morrise water maze Test were used to evaluate retention and recall evaluation of memory and learning. After behavioral evaluation, data were analyzed by SPSS. Statistical significance was set at $p \leq 0.05$.
Results: Step-through latency in passive avoidance test in AD group significantly was lesser than other groups. Measuring of spatial memory by water maze test showed that in AD group, time of locating submerged escape platform was greater than other groups.
Conclusion: Our results showed that VA treatment could prevent memory dementia and suggest improve AD in rats.
Keywords: Vanilic acid, Alzheimer disease, Rat, Learning and memory

P-110

Increases in the expression of MIAT1 and BC1 lncRNAs in rat hypothalamus are related to the gene expression of inflammatory cytokines and their receptors in morphine-tolerant rats

Shamseddin Ahmadi, Kaivan Masoudi, Mohammad Zobeiri, Shiva Mohammadi Talvar, Shima Fotouhi, Amir Khanizad

Department of Biological Science, Faculty of Science, University of Kurdistan, Sanandaj, Iran

Background and Objective: Recent reports have implicated inflammation in morphine tolerance. However, its mechanisms and site of action in the brain remain to be understood. We aim to examine changes in the expression of some long non-coding RNAs (lncRNAs), inflammatory cytokines and their receptors in the hypothalamus in morphine-tolerant rats.
Materials and Methods: Two groups of male Wistar rats received saline (1 ml/kg) or morphine (10 mg/kg) twice daily for 8 consecutive days. A hotplate test of analgesia was used to assess the induction of morphine analgesic tolerance on day 8 of the schedule. On day 8 of the treatments, each rat was anesthetized, decapitated and the hypothalamus was dissected on an ice-chilled surface. The gene expression of TNF, IL1, IL6 and their receptors, as well as MIAT1 and BC1 long-non-coding ANAs were examined using a real-time quantitative polymerase chain reaction (qPCR) method.
Results: The hotplate test revealed that the 8 days morphine treatments induced anti-nociceptive tolerance to the opioid. The qPCR results indicated that the MIAT1 and BC1 lncRNAs expression and also the gene expression of TNF, IL1 and their receptors were increased but IL6 remained with no significant changes in the hypothalamus of morphine-tolerant group compared to the saline-treated group.
Conclusion: It can be concluded that the increases in the lncRNAs expression affects the expression inflammatory cytokines and their receptors in the hypothalamus, which may underlie, at least partly, the neuroinflammation and the decreases in morphine-induced analgesia after repeated use of the opioid.
Keywords: Morphine tolerance, Hypothalamus, Inflammatory cytokines, Long Non-coding RNAs, Gene Expression

P-111

Low-frequency electrical stimulation reduces the impairment in synaptic plasticity following epileptiform activity in rat hippocampal slices through α1, but not α2, adrenergic receptors

Nooshin Ahmadirad[1], Yaghoub Fathollahi[1,2], Mahyar Janahmadi[3], Amir Shojaei[1,4], Zahra Ghasemi[1], Victoria Barkley[5], Javad Mirnajafi-Zadeh[1,2*]

1. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Institute for Brain Sciences and Cognition, Tarbiat Modares University, Tehran, Iran 3- Department of Physiology, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Brain and Cognitive Sciences, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran
4. Krembil Research Institute, University Health Network, Toronto, Canada

Low frequency stimulation (LFS) has anticonvulsant effect and may restore the ability of long-term potentiation (LTP) to the epileptic brain. The mechanisms of LFS have not been completely determined. Here, we showed that LTP induction was impaired following in vitro epileptiform activity (EA) in hippocampal slices, but application of LFS prevented this impairment. Then, we investigated the involvement of α-adrenergic receptors in this effect of LFS. EA was induced by increasing the extracellular K+ concentration to 12 mM and EPSPs were recorded from CA1 neurons in whole cell configuration. EA increased EPSP amplitude from 6.9±0.7 mV to 9.6±0.6 mV. For LTP induction, the Schaffer collaterals were stimulated by high frequency stimulation (HFS; two trains of 100 pulses, 100 Hz at the interval of 20 s). The application of HFS resulted in 40.9±2.3% increase in the amplitude of EPSPs. However, following EA, HFS could not produce any significant changes in EPSP amplitude. Administration of LFS (1 Hz, 900 pulses) to Schaffer collaterals at the beginning of EA restored LTP induction to the hippocampal slices and HFS increased the EPSPs amplitude up to 41.7±3.1% of baseline. When slices were perfused by prazosin (α1-adrenergic receptor antagonist; 10 µM) before and during LFS application, LFS improvement on LTP induction was reduced significantly. Perfusion of slices by yohimbine (α2-adrenergic receptor antagonist; 5 µM) had no effect on LFS action. Therefore, it may be concluded that following epileptiform activity, LFS can improve the impairment of LTP generation through α1, but not α2, adrenergic receptor activity.

Key words: Brain stimulation; Epileptiform activity; α-adrenergic receptor; Long term potentiation

P-112

Possible Involvement of Opioidergic Mechanisms and L-arginine/NO/cGMP/KATP channel pathway in Antinociceptive Effects of Cnicus benedictus L. and cnicin in Male Rat

Davoud Ahmadimoghaddam[1,2], Reihaneh Sadeghian[3,4], Akram Ranjbar[1,2], Zohreh Izadidastenaei[4], and Saeed Mohammadi[5]

1. Department of Pharmacology and Toxicology, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran.
2. Medicinal Plants and Natural Products Research Center, Hamadan University of Medical Sciences, Hamadan, Iran.
3. Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran
4. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran.
5. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran.

Background and Objective: The medicinal herb, Cnicus benedictus, traditionally has been used for treatment of arthritis and stomach pains. In this study, possible efficacy of Cnicus benedictus leaf methanolic extract (CBME) and also cnicin, one of its major constituent, were measured on pain.
Materials and Methods: In this study, pain assessment tests include writhing, tail-flick (TF), formalin-induced paw licking test (FIPLT), and glutamate-induced paw licking (GIPL) were used. To evaluate the possible mediated anti-nociceptive mechanism of CBME, opioid mechanism(s) and involvement of the L-arginine/NO/cGMP/ATP-sensitive potassium channel pathway (LNCaP) was scrutinized.
Results: In GIPL, TF, and writhing tests, using the CBME (300 mg/kg, i.p) were remarkably exhibited anti-nociceptive effect in comparison to control. Furthermore, CBME in comparison to control showed noteworthy anti-nociceptive effect ($p<0.01$) in the tonic phase of FIPLT. In the writhing test, administration of selective opioid antagonist (naltrindole, nor-binaltorphimine, and naloxonazine) attenuated the anti-nociceptive effect of CBME in comparison with control. Moreover, pre-treatment with Nω-nitro-L-arginine methyl ester hydrochloride, L-argininehydrochloride and glibenclamide significantly blocked the CBME antinociception ($p<0.05$) while administration of sodium nitroprusside remarkably potentiated ($p<0.05$) the antinociception induced by CBME in tonic phase of the FIPLT. Besides, cnicin (30 mg/kg) showed noteworthy anti-nociceptive effects in writhing, GIPL, TF, and FIPLT paradigms. CBME also did not alter the locomotion of animals in the rota-rod test.
Conclusion: We elucidate that both CBME and cnicin have anti-nociceptive effects in behavioral tests. The possible mechanisms of CBME antinociception may involve in various neural signaling and modulatory pathways including LNCAP and opioidergic mechanisms.
Keywords: Cnicus benedictus, Cnicin, Opioid Receptor, l-arginine/NO/cGMP/K(ATP), Peripheral antinociception

P-113

Investigating the activity of the pyramidal neurons of the CA1 area following the administration of lovastatin in male intact rat

Azade Eskandary

Department of Biology, Faculty of Science, Shahid Chamran Univerity, Ahvaz, Iran

Background and Objective: In the past decade data has emerged for the neuroprotective effect of statins. Experimental studies have shown their beneficial effects on cognitive function in animal models of vascular dementia, amnesia and after traumatic brain injury. The aim of the present study was investigated the effect of lovastatin treatment in neuronal responses of CA1 pyramidal cell of hippocampus using in vivo single unit recording technique in rat without brain injury. Material and Methods: In this experimental study, rats were randomly divided into two groups. Group 1: after baseline recording (15 minutes), lovastatin (20 mg/kg, IP) was injected and the recording was continued for 105 minutes afterward. Group 2: after baseline recording DMSO 5%, as lovastatin vehicle, was injected and the recording was continued for 105 minutes afterward. Neuronal response to injection of lovastatin and its vehicle were investigated in pyramidal neurons of CA1 region of hippocampus. Results: The findings of this research showed that acute administration of lovastatin 20 mg/kg resulted in increased spontaneous spiking frequency of CA1 pyramidal cell ($P<0.05$). Conclusion: This research recommends that acute use of lovastatin increases the neuronal response in the pyramidal neurons of the hippocampus CA1 region.
Keywords: Single unit recording, Pyramidal neuron, Lovastatin, Rat

P-114

The effect of Lipopolysaccharide (LPS) pretreatment on hippocampal apoptosis in traumatic rats

Mansoureh Eslami[1], Leila Alizadeh[2], Parastoo Morteza-zadeh [2,3], Mohammad Sayyah

1. Department of Basic Sciences, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Shefa Neuroscience Research Center, Khatam Alanbia Hospital, Tehran, Iran
3. Department of Biology, Faculty of Basic Sciences, Kharazmi University, Tehran, Iran
4. Department of Physiology and Pharmacology, Pasteur Institute of Iran, Tehran, Iran.

Background and ObjectiveBackground and Objective: Traumatic brain injury (TBI) is a serious medical problem that affects the quality of life. Apoptosis is a form of programmed cell death happen after trauma. Effector caspases are responsible for initiating the apoptosis.

Materials and Methods : In the present study, we examined the effect of LPS preconditioning (0.1 and 0.5 mg/kg, ip; 5 days prior controlled cortical injury) on apoptosis, 4 and 12 hours after trauma. We investigated possible mechanisms on the expression of caspase3 and caspase7 in hippocampal CA1 and CA3 areas by using immunohistochemistry and Western blotting techniques and also TUNEL-positive cells.

Results: Higher expression of caspase3 and caspase7 were accompanied by higher number of dead neurons in traumatic rats 4 and 12 hours after trauma($P<0.05$). LPS preconditioning significantly decreased caspase3 and caspase7over-expression and the number of death neurons in the hippocampus($P<0.05$).

Conclusion: Our data indicate that LPS preconditioning inhibits neural damage and apoptosis induced by trauma in the hippocampus.

Keywords: Controlled cortical injury; LPS preconditioning; Apoptosis; Caspase 3; Caspase7

P-115

Diabetic encephalopathy affects mitochondria and axonal transport proteins

Maryam Eslami Gharaati[1], Arezo Nahavandi[1,2,3], Torandokht Baluchnejad Mojarad[1], Mehrdad Roghani[4]

1. Department of Physiology, Faculty of Medicine, Iran University of Medical Science, Tehran, Iran
2. Neuroscience Research Center, Iran University of Medical Science, Tehran, Iran
3. Department of Advanced Technologies in Medicine, Iran University of Medical Science, Tehran,Iran
4. Departmentof Physiology, Neurophysiology Research Center, Shahed University, Tehran, Iran

Background and Objective: Diabetic encephalopathy is described as any cognitive and memory impairments and associated with hippocampal degenerative changes, include neurodegenerative process and decreased number of living cell. Mitochondrial Diabetes (MD) appears fallowing activation of mutant mitochondrial DNA and is combination of diabetes and cognitive deficit. In this research we showed the correlation of diabetic encephalopathy, dysfunctional mitochondria and change in expression of axonal transport proteins (KIF5b, Dynein).

Materials and Methods: Twenty four male Wistar rats were divided into three groups: (n=8):1_Control+saline 2_Diabetic, 3_Diabetic+Insulin. Before starting the experiments, animals with blood sugar lower than150mg/dl entered the study. Diabetes induction was carried out by STZ, IP administration. FBS and body weight was checked after 1week and at the end of the 8week. Then behavioral studies (elevated plus maze, Y-maze and passive avoidance learning) were performed. After behavioral studies, blood samples were taken to measure serum insulin level and HgbA1c. Then fresh hippocampal tissue was collected. Gene expression of motor proteins was assessed by R-T PCR and mitochondrial membrane potential was assessed by Rhodamine123.

Results: Our results showed impairment of HgbA1c, serum insulin, FBS and weight in diabetic group ($p<0.05$).Behavioral tests, revealed different degrees of impairment in diabetic rats ($p<0.05$).KIF5b mRNA expression was increased in hippocampus ($p<0.05$) with no change in dynein gene expression. These changes were associated with abnormal mitochondrial membrane potential ($p<0.05$).

Conclusion: KIF5b mRNA up-regulation in hippocampal neurons of STZ-diabetic rats is a factor which can be involved in abnormal axonal transport and decreased MMP, leading to impairment of mitochondrial function. These manifestations showed mitochondrial dysfunction on diabetes and resulted in abnormal behavioral tests and diabetic encephalopathy.

Twenty four male Wistar rats were divided into three groups: (n=8):1_Control+saline 2_Diabetic, 3_Diabetic+Insulin. Before starting the experiments, animals with blood sugar lower than150mg/dl entered the study. Diabetes induction was carried out by STZ, IP administration. FBS and body weight was checked after 1week and at the end of the 8week. Then behavioral studies (elevated plus maze, Y-maze and passive avoidance learning) were performed. After behavioral studies, blood samples were taken to measure serum insulin level and HgbA1c. Then fresh hippocampal tissue was collected. Gene expression of motor proteins was assessed by R-T PCR and mitochondrial membrane potential was assessed by Rhodamine123.

Results: Our results showed impairment of HgbA1c, serum insulin, FBS and weight in diabetic group ($p<0.05$).Behavioral tests, revealed different degrees of impairment in diabetic rats ($p<0.05$).KIF5b mRNA expression was increased in hippocampus ($p<0.05$) with no change in dynein gene expression. These changes were associated with abnormal mitochondrial membrane potential ($p<0.05$).

Conclusion: KIF5b mRNA up-regulation in hippocampal neurons of STZ-diabetic rats is a factor which can be involved in abnormal axonal transport and decreased MMP, leading to impairment of mitochondrial function. These manifestations showed mitochondrial dysfunction on diabetes and resulted in abnormal behavioral tests and diabetic encephalopathy.

Key words: Diabetes mellitus type 1; Mitochondrial Encephalopathy; Axonal transport; mitochondria; KIF5b protein; Dyneins

P-116

The effect of nanocurcumin on the threshold of clonic seizures induced by intravenous penthylenetetrazol

Zahra Esmaili[1], Leila Moezi[2], Roksana SoukhakLari[1,3], Fatema Pirsalami[2], Maryam Moosavi[4]

1. Shiraz Neuroscience Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
2. Department of Pharmacology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.
3. Student Research Committee, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.
4. Nanobiology and Nanomedicine Research Centre, Shiraz University of Medical Sciences, Shiraz, Iran.

Background and Objective: Epilepsy, as one of the most common neurologic diseases invoked by the abnormal discharge of brain neurons. Previous reports have shown that curcumin supplementation at high doses reduces the seizures signs in some models of epilepsy. However, oral curcumin treatment had no effect on seizures in some animal models of epilepsy, possibly because of its low biavailability. Using nanotechnology to break down curcumin increases its bioavailability and improves its effect on the brain. BSA, as a non-toxic protein with high binding capacity, was used to break curcumin to nanosize and to explore the effect of nanocurcumin on the threshold of clonic seizures induced by intravenous injection of PTZ in male mice.
Materials and Methods: In this study nanocurcumin (25, 50, 100, 200, 400 and 800 mg/kg/oral gavage) was administered to male NMRI mice weighing 20–25 g. Animals received acute nanocurcumin 60 min before administration of PTZ. The threshold of clonic seizure was assessed by intravenous injection of PTZ.
Results: The results showed that BSA-based nanocurcumin administered in doses 400 and 800 mg/kg significantly increased clonic seizure threshold compared to control group.
Conclusion: This study indicates that breaking curcumin to nanosize improves its anticonvulsant effect in intravenous PTZ-induced seizure.
Keywords: Nanocurcumin. Curcumin, seizure, pentylenetetrazole, mice

P-117

Study of the effect of intracerebroventricular injection of kaempferol and its intraction with type B GABA recrptor on pain in male rat

Maryam esmaeili salem, Mohammad Zarei, Siamak shahidi, safoora raufi

Neurophysiology research center, Hamadan university of Medical sciences, Hamadan, Iran.

Background and Objective: kaempferol is one of the most important herbal active constituent with antinociceptive and anti inflammatory effects. The aim of this study was to evaluate the effect of intracerebroventricular injection of kaempferol and its interaction with Gaba type B receptors on pain in male rats.
Materials and Methods:In this experimental study, male rats (200-250 g) were divided to the following groups: sham(DMSO),naloxan, morphine, kaempferol at dosages of 0.5,1, and 1.5 mg/rat, baclofen, CGP35348, baclofen plus kaempferol (1 mg/rat) and CGP 35348 plus kaempferol (1 mg/rat). After cannula implantation in cerebroventricular area, the rats received target components and then evaluated by pain assessment test (tail flick test). data were analyzed by one-way anova followed by Tukey,s post-test.
Results:The result showed that administration of both kaempferol doses (0.5 and 1 mg/rat) had significant effect in comparisonto the control group on the tail flick test ($p < 0.05$)
Conclusion:The kaempferol probably has acute antinociceptive effects and exert this activity at least in part by activating GABA B receptors.
Keywords:kaempferol, GABA type B receptors, pain, central nervous system

P-118

Protective Role Of Luteolin Against Memory Impairment Induced By Traumatic Brain Injury(TBI) In The Male Rats

Zeinab Ashaari, Gholamreza Hassanzadeh

Department of Anatomy, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Background and Objective: Traumatic brain injury (TBI) is generally recognized as a major risk factor for memory impairments and Alzheimer's disease (AD). In this experimental study, our aim was to investigate the ameliorating effects of luteolin (LUT) on the memory impairments and oxidative stress (OS) induced by TBI in rats.
Materials and Methods: The adult male Wistar rats were randomly divided into 5 groups including: Control (Co), sham, TBI, TBI+LUT (10mg/kg), TBI +LUT (30mg/kg). Rats of treatment group received luteolin was injected intraperitoneally at 48 hour after the surgery for 1 week..The TBI was moderate and from diffuse kind by Marmarou method. To evaluate the protective effects of LUT on memory of the rats, passive avoidance test (PA) using shuttle box was performed. Finally, the animals were anesthetized and the brain tissues were removed and analyzed for oxidative stress parameters.
Results: There was a significant decrease in the latency time to enter the dark compartment in PA test in TBI animals. This latency time was significantly increased in TBI+LUT(30mg/kg) group along with significant increases in superoxide dismutase and catalase activity in the hippocampal zone and a decrease in malondialdehyde (MDA).
Conclusion: In the present study, LUT showed neuroprotective effect , improvement in learning and reduction in memory impairment induced by TBI in rats. Further work is necessary to investigate luteolin is potentially a suitable therapeutic candidate for neural disorders such as Alezimer.
Keywords: Luteolin, Traumatic Brain Injury, Oxidative stress, Learning and memory, Rat

P-119

Ischemic post-conditioning improved neuronal cytoskeletal markers against ischemic brain injury in the hippocampus of young adult but not aged rats

Ghorbangol Ashabi, Hedayat Samandari

Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Objectives: Brain ischemia/reperfusion (I/R) injury leads to failure of the microtubules function and ultimately initiates neuronal death. Ischemic post-conditioning is defined as a series of rapid alternating interruptions of blood flow in the first seconds of reperfusion. We evaluated caspase-3, Microtubule associated protein-2 (MAP-2), Protein kinase C (PKC), c-fos and synaptophysin in the hippocampus of focal I/R and/or post-conditioning I/R models in a time dependent study in aged and young rats. Method and materials: Adult and aged rats were subjected to right MCAO for 30 minutes and post-conditioned for 10 minutes. Sensory-motor tests, locomotion and anxiety-like behavior were evaluated. Molecular tests were done by detection kit, RT-PCR and Western blotting techniques. Results: Neurological signs, locomotion and anxiety-like behavior were improved in I/R post-conditioned young rats in 96 hours after I/R post-conditioning compared with 6 hours after I/R post-conditioning ($P<0.001$). Post-conditioning decreased ischemic area in young rats following 96 hours I/R compared with 6 hours after I/R. Caspase-3 activity was declined in the hippocampus of I/R post-conditioned young rats in 96 hours after I/R compared with 6 hours after I/R ($P<0.001$). Also, MAP-2 mRNA and protein expression, PKC, c-fos and synaptophysin protein levels were enhanced during post-conditioning in young rats in 96 hours after I/R. Conclusions: The results suggested early post-conditioning might candidate as a therapeutic method against I/R in the adult animals. Inhibition of cell death in post-conditioned ischemic rats was regulated by some neuroprotective molecules as well as MAP-2 and c-fos in young not old rats.
Keywords: Focal cerebral ischemia; post-conditioning; young; aged; MAP-2; synaptophysin

P-120

The effect of isoflavones on epilepsy disorder in ovariectomized rats

Nastaran Afsordeh

Background and Aim : Epilepsy is the third neurological disorders commonly in the world. It has been shown that sex hormones are one of the most effective parameters in this disease. The isoflavones have estrogenic effects. The purpose of the present study was to evaluate the effect of soy and genistein on the threshold of pentylenetrazole induced seizure in the ovariectomized rats.
Materials and Methods:In this study, 60 female Wistar rats were divided into 6 groups, four groups were ovariectomized. In the pre-treatment groups after ovariectomy and recovery, soybean hydrochloric extract (20 mg / kg) and genistein (5 mg / kg and 15 mg / kg for 28 days) were administered . At last, colonic seizure with injection of 90 mg/kg PTZ was evaluated and the animals' behavior was observed for 30 minutes.
Results: The onset of seizure in the ovariectomy group was significantly lower than the vehicle group. $P<0.01$, while the onset of clonic seizure in the low dose of genistein was significantly increased. ($P<0.05$) compared to the vehicle group.
Conclusion: Chronic administration of genistein increases the threshold of clonic seizure in ovariectomized rats
Key words: Epilepsy, ovariectomy , genistein , soy.

P-121

Preventive effects of Brassica nigra against the memory deterioration in the: kindled male wistar rats

Fatemeh Aghaie

Background and Objective: Previous study on the medicinal plants reported the beneficial effect of Brassica nigra against the experimental pentylenetetrazol (PTZ)-kindled animals. In addition, there are numerous studies reported that epilepsy causes memory deficit. Here, in this present report, the effect of B. nigra extract (BNE) against the memory loss on the PTZ-kindled animal model of epilepsy was studied.
Materials and Methods: In this experimental study, twenty-four male Wistar rats were randomly choosen and divided into experimental and control groups. The experimental groups were treated by intraperitoneal (i.p.) injection of 75, and 150 mg/kg of BNE, the control negative group received saline and the control positive group received phenobarbital (30 mg/kg, i.p.) treatment. All groups were kindled by sub-threshold dose (35 mg/kg, i.p.) of PTZ for 12 times. When the kindling procedure was done, the seizure behaviors and the memory function evaluated by passive avoidance test (PAT). At the end of the experiment, rats were killed and the brain was removed for measurement of catalase and superoxide dismutase (SOD). Data were analyzed using SPSS.
Results: Statistical analysis was showed that the administration of the BNE significantly prevented memory dysfunction in epileptic rats. In addition, the BNE increased the SOD and catalase levels in the brain tissues.
Conclusion: As shown by this study BNE has a beneficial effect for prevention of memory impairment against PTZ-kindling epilepsy in rats. By the way of explanation, this effect might cause by its antioxidant properties and acts via the enzyme activity mechanism.
Keywords: Epilepsy, Memory, Brassica nigra, PTZ, Kindling

P-122

Investigation of the Antioxidant Activity of Curcumin against b-amyloid Induced Cell Damage in SH-SY5Y Cells

Leila Elyasia[1*], Hamed Ghazvinib[2]

1. Neurosciences Research Center, Department of Anatomy, Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Iran
2. Immunogenetic Research Center, Mazandaran University of Medical Sciences, Sari, Iran

Introduction: Alzheimer's disease (AD) is regarded as a neurological condition in which continuous degeneration of dopaminergic neurons occurs selectively. Currently, most treatments for neurodegenerative diseases are palliative. According to in vitro and in vivo models of AD in recent studies, Curcumin showed protective properties during neuron damage. Moreover, recent reports demonstrated the induction of Curcumin. We aimed at analyzing the protective effect of Curcumin, as a major flavanone constituent by determining its effect on b-amyloid-mediated oxidative stress.
Methods: The study employed 150 µM of b-amyloid to induce cellular damage. Also, 3-(4, 5-dimethylthiazol-2-Yl)-2,5-diphenyltetrazolium bromide (MTT) test was performed to analyze cellular viability. Fluorescence spectrophotometry was performed to measure the level of intracellular reactive oxygen species (ROS), and intracellular calcium. Based on the findings, b-amyloid could reduce cell viability. We analyzed the impact of Curcumin on neurotoxicity, mediated by b-amyloid, in SH-SY5Y cells by an in vitro model of AD.
Results: Moreover, intracellular ROS, intracellular calcium, and DNA fragmentation vastly improved in cells exposed to b-amyloid. SH-SY5Y cell incubation with Curcumin (1 and 10 µg/mL) induced protective effects and decreased the biochemical markers of cell apoptosis. According to the findings, Curcumin showed protective features against neurotoxicity, caused by b-amyloid. These protective properties were accompanied by anti-apoptotic features.
Conclusion: It was revealed that Curcumin affected the management of AD. Given the preserved mitochondrial function of Curcumin, and its antioxidant and anti-apoptotic properties in neuroblastoma cell lines, this compound has neuroprotective effects on b-amyloid.
Keywords: Curcumin; Parkinson's disease; b-amyloid ; Apoptosis ; Curcumin

P-123

Effect of ceftriaxone on synaptic plasticity of hippocampal dentate gyrus neurons in OKA-induced model of Alzheimer disease in rats

Mohammad Amani[1,2], Nasrin Hamidi [1], Abdollah Nozad[1], Hamid Sheikhkanloui Milan[1]

1. Department of Physiology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran
2. Department of Pathology & Cell Biology and the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University, New York, NY 10032, USA

Background and Objective: Glutamate-mediated excitotoxicity contributes to cognitive dysfunction and cell death in AD. Ceftriaxone (CFT), a well-known upregulator of GLT-1, selectively induces the expression of glutamate transporter-1 (GLT-1) in different brain regions and therefore can be posed as a potential candidate for elimination of glutamate-induced excitotoxicity which is an early prominent event in AD brains. This study was designed to investigate the electrophysiological and behavioral effects of the β-lactam antibiotic ceftriaxone in okadaic acid (OKA)-induced model of AD.
Materials and Methods: Male Wistar rats divided into four control, ceftriaxone (CFT), OKA, and OKA plus ceftriaxone (OKA+CFT) groups. OKA was injected intracerebroventricularly (i.c.v., 200 ng/5 µl) into lateral ventricles and after two weeks the evoked field potential recorded from hippocampal perforant path-DG synapses in order to evaluate the effect of ceftriaxone treatment (200mg/kg/day, i.p.) on long-term potentiation (LTP) and paired-pulse responses.
Results: Results of this study revealed that ceftriaxone treatment significantly ameliorates the OKA-induced attenuation of field excitatory post-synaptic potential (fEPSP) slope and population spike (PS) amplitude following high-frequency stimulation and paired-pulse paradigm indicating its beneficial effects on both short-term and long-term plasticity in these neurons. Ceftriaxone also has an improving effect on OKA-induced impairment in short- and long-term memories evaluated by alternation behavior and passive avoidance tasks in rats.
Conclusion: Therefore, this study suggests that GLT-1 might be a promising therapeutic target for treatment of neurodegenerative disorders such as AD in the future.
Keywords: Ceftriaxone, Okadaic acid, Synaptic plasticity, Dentate gyrus, Alzheimer's disease

P-124

Hepatoprotective effect of estrogen receptors against liver injury induced by traumatic brain injury in male rats: oxidative stress role

Sedigheh Amiresmaili[1], Nader Shahrokhi[2], Mohammad Khaksari[3]

1. Physiology Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.
2. Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.
3. Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences. Kerman, Iran.

Background and Objective: It has been shown that estradiol has neuroprotective effects after traumatic brain injury (TBI) in rats. The present study evaluated the impact of 17β-estradiol(E2) on the hepatic function alteration after TBI. Also investigated the role of estrogen different receptors (ER-α, ER-β, GPER) and oxidative stress on liver injury induced by TBI.
Materials and Methods: The animals were divided into10 groups: Sham, TBI, TBI + OIL, TBI + E2, TBI + Vehicle + E2, TBI + ICI + E2, TBI+ G15+ E2, TBI + ICI + G15 + E2, TBI+ MPP + E2, TBI+PHTPP + E2 group. After 24 h from TBI, the levels of serum aminotransferase, and hepatic oxidative stress biomarkers were determined by commercial kits.
Results: The results showed that TBI could induce significant elevations in liver enzymes (ALP, ALT, AST), γ-GGT and oxidative stress biomarkers (MDA, NO) and decreased antioxidant system (SOD, GSH) in the hepatic tissue, while estrogen reverses these effects. It was also found simultaneous administration of the ICI182780 and G15 eliminates the inhibitory effect of estrogen on ALP and ALT enzymes but not AST. Whereas administration MPP, PHTPP, G15, and ICI182780 can reverse the effects of estrogen on oxidative stress biomarkers, but the level of this biomarkers was lower in PHTPP group than in other groups.
Conclusion: Current findings demonstrated that both classical (ERα, ERβ) and nonclassic (GPER) receptors probably are involved in the mediation of estrogen hepatoprotective function after TBI, although the role ERα is more dominant than other receptors.
Keywords: Traumatic brain injury, Liver injury, Estradiol, Classic estrogen receptors, Non-classic estrogen receptor.

P-125

Formulation and characterization of Rosa damascena extract nanoniosome as an herbal neutral adjuvant for topical ophthalmic drugs

Zeinab amiri, Majid Hassanpour-ezatti

Dept of Biology, Basic Sciences School, Shahed University, Tehran, Iran

This study presents the nano-niosome approach for increasing of the aqueous solubility and thereby bioactivity of Rosa damascena petal extracts which has high penetration and low side effects in order to use as an analgesic adjuvant. Nano-niosome of the petal extract of this plant was prepared by thin film method using cholesterol. Prepared nano-niosome was characterised by transmission electron microscope. Activity and toxicity of the nano-niosomes formulation was assessed by corneal pain model in rats and corneal and retinal histopathology after topical intraocular application in rats. Nano-niosome size was observed to fall in range of 300.1 ± 12.6 nm, most of the particles were having spherical shape and smooth topology. This synthesized nano-niosome was no analgesic effective on corneal pain than their crude extracts. The nano-niosome showed no toxic histological effect on cornea and retinal tissue in rats. It was concluded that the nano-niosome can be used as an ideal neutral adjuvant which contains plant extract with antioxidant herbal content.
Keywords: Rosa, nanostructures, plant extracts, transmission electron microscopy, cornea, retina.

P-126

Overexpression of Protein Kinase Mζ in the Hippocampus Improves Cognitive Performance in a Rat Model of Alzheimer's Disease

Niloufar Amini[1], Hamid Gholami Pourbadie[2*], Reza Roosta Azad[1]

1. Biotechnology Group of Chemical Engineering Department, Sharif University of Technology, Tehran, Iran
2. Physiology and Pharmacology Department, Pasteur Institute of Iran, Tehran, Iran

Background and Objective: Accumulation of amyloid beta (Aβ) in the cerebral parenchyma is the mainstream concept underlying Alzheimer's disease (AD) in which one suffers from a defect in forming and maintenance of new memories. Protein Kinase Mζ (PKMζ) has been shown to be necessary and sufficient for LTP maintenance. However, the role of this brain-specific enzyme in AD pathogenesis has not yet been established. In this study, we examined the effect of PKMζ overexpression in the CA1 region on behavioral performance.
Materials and Methods: The oligomeric form of Aβ was prepared, and the CA1 region of male Wistar rats was microinjected with Aβ by vehicle under stereotaxic surgery. After one week, 2µl of a lentiviral vector injected into the CA1, and one week later, the brains were cross-sectioned and green cells were detected by fluorescent microscopy in order to confirm the gene expression. The passive avoidance test, reference and reverse spatial memory test (Morris water maze) were used to evaluate behavioral performance. The level of AMPA subunits, GluR1 and GluR2, were investigated by immunohistochemistry.
Results: Histological observation confirmed that PKMζ was expressed in the CA1 region. Overexpression of PKMζ in the CA1 region improves behavioral performance in Aβ treated group. Also, the level of GluR2 increased in the CA1 following PKMζ overexpression. The improved effect was blocked by microinjection of ZIP, PKMζ inhibitor, into the hippocampus.
Conclusion: Our data indicate that overexpression of PKMζ in the CA1 probably boosted memory performance in a signaling pathway dependent on AMPA trafficking.
Keywords: Alzheimer's Disease, Amyloid Beta, PKMζ, Memory, Hippocampus

P-127

N-acetyl cysteine treatment protects brain mitochondria in hyperammonemic mice

Ahmadreza Aminian[2], Hossein Niknahad[1,2], Reza Heidari[2*]

1. Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Department of Pharmacology and Toxicology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Liver failure and hyperammonemia is associated with oxidative stress, impaired locomotor activity, and cognitive deficit, which could lead to permanent brain injury, coma, and death if not appropriately managed. A role for brain mitochondrial damage and energy crisis has been considered in hyperammonemia. It has been found that ammonia induces mitochondrial impairment as a result of a multifaceted interaction of different signaling molecules. Hence, ammonia-induced mitochondrial injury and compromised brain energy metabolism might play a vital role in the pathogenesis of ammonia neurotoxicity. N-acetylcysteine (NAC) acts as an antioxidant and is a good source of thiol groups. The positive effects of NAC on mitochondrial function have been repeatedly investigated. This study aimed to evaluate the effect of NAC supplementation on liver failure-associated locomotor activity impairment and oxidative stress in the brain. Mice received acetaminophen (APAP; 800 mg/kg,i.p) and plasma biochemical parameters, plasma and brain ammonia level, and animals' locomotor activity were monitored. Moreover, brain tissue markers of oxidative stress were measured. It was found that plasma and brain ammonia was increased, and markers of liver injury were significantly elevated in the APAP-treated group. Impaired locomotor activity was also detected in the APAP group. Moreover, an increase in markers of oxidative stress was evident in the brain of APAP-treated mice. It was found that NAC supplementation (100, 200, and 400 mg/kg, i.p) improved brain mitochondria indices of functionality and alleviated biomarkers of oxidative stress. These data suggest NAC as a potential protective agent with therapeutic capability against liver hyperammonemia-associated brain injury.
Keywords: Bioenergetics; Hepatic encephalopathy; Hyperammonemia; Neuroprotective; Neurotoxin; Oxidative stress

P-128

The Effect of 40-Hz Light Therapy on spatial memory impairment in STZ-induced dementia rats

Mozhdeh Anjomani [1, 2], Rasoul Ghasemi [2], Javad Fahanik-Babaei [2], Afsaneh Eliassi [1, 2]

1. Department of Physiology, Medical School, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Alzheimer's disease is the most frequent neurodegenerative disorder and the most common cause of dementia in the elderly. A short-duration intervention with 40 Hz light flicker has been shown to reduce brain Aβ load in transgenic mice. We aimed to test the effect of 40 Hz light flicker in STZ-induced learning and memory impairment in male rats.
Methods: Rats were randomly divided into the following groups (n=10): 1Control (intact rats), 2Sham (normal saline injected), 3Sham+Light, 4STZ (that received single bilateral icv-STZ (3 mg/kg) and ۵STZ + Light group (STZ-injected rat exposed to 40 Hz light flicker). Rats are exposed to 40 Hz light stimuli for 7 continuously day from 7th day of injection. Spatial learning and memory were assayed from 14th by MWM test for 4 days.
Results: There were no statistical differences in swim speed, suggesting that the velocity is similar in all groups. During the training phase, all rats learned the platform location, as revealed by a decrease in the latency and the distance traveled. However, the training was delayed for the icv-STZ rats as they needed more time and traveled a longer distance to find the platform than the control rat. Learning and memory significantly improved by 40 Hz light induced in STZ+light compared to STZ group ($P<0.05$).
Conclusion: Therefore, these results demonstrate 40 Hz light could improve the learning impairment, following the STZ treatment, and it may lead to an improvement of AD-induced cognitive dysfunction.
Keywords: Alzheimer, 40 Hz light, gamma oscillations, STZ

P-129

Protective effect of crocin, an active constituent of saffron, against 6- hydroxydopamine neurotoxicity in SH-SY5Y cells as a model of Parkinson's disease

Fariba Ansari[1], Maliheh Aminzadeh[1], Mehrdad Roghani[2]

1. School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective: Studies indicate that crocin as the main constituent of Crocus sativus L. has an antioxidant effect. In this study, the protective effect of crocin was investigated in the cell model of Parkinson's disease (PD) induced by the neurotoxin 6-hydroxydopamine (6-OHDA) in SH-SY5Y cells.
Materials and Methods: SH-SY5Y cells were cultured in 9 groups including control, 4 pretreatment groups with crocin at concentrations of 5, 10, 25 and 50 µM, and
4 treatment groups with crocin at concentrations of 5, 10, 25 and 50 µM and 6-OHDA (400 µM). Cell viability in SH-SY5Y cells was measured using MTT assay. Expression of cathepsin D, mitochondrial membrane potential (MMP), and oxidative stress parameters including reactive oxygen species (ROS), nitrite oxide (NO), malondialdehyde (MDA), and catalase activity were finally assessed.
Results: Cell survival was maintained by different concentrations of crocin. In addition, crocin (25 and 50 µM) reduced expression of cathepsin D after 6-OHDA exposure. Meanwhile, crocin pretreatment of 6-OHDA-challenged groups partially and in a concentration-dependent pattern was capable to restore MMP and catalase activity and to attenuate oxidative stress parameters.
Conclusion: The neuroprotective effect of crocin in 6-OHDA-cell model of PD may be due to lower expression of cathepsin D and maintenance of MMP in addition to mitigation of oxidative stress.
Keywords: Crocin, 6-hydroxydopamine, SH-SY5Y cell, Cathepsin D, Oxidative stress, Parkinson's disease

P-130

Monitoring of molecular factors of STIM1, STIM2 and cell death in the striatum of male rats in neurotoxic model of Huntington disease

Nazila Iranipour[1], Farrin Babaei-Baderlou[1], Mehdi Moslemi[2], Fariba Khodagholi[2]

1. Department of Biology, Faculty of Sciences, Urmia University, Urmia, Iran
2. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Huntington disease (HD) is a neurodegenerative disorder characterized by unwanted choreatic movements, behavioral disturbances and dementia. Evidences indicate that dysregulation of intracellular neuronal calcium signaling plays important role in HD. On the other hand, studies implicated that Stromal interaction molecule 1(STIM1) and Stromal interaction molecule 2 (STIM2) protein function as link between plasma membrane and endoplasmic reticulum to regulation of intracellular calcium concentrations.
Materials and Methods: We assay STIM1/STIM2 level and progression of cell death in striatum of rats injected by 3-nitropropionic acid (3-NP) to induce Huntington neurotoxic model. Adult male rats (250-300 g) were divided into six groups: control group and five groups that they received 3-NP (20 mg/kg) in 1,2,3,4 or 5 days (one time a day). Brains removed and striatum of them were kept for western blotting to assay STIM expression. For detection of cell death coronal sections stained with crystal violet. Data were analyzed using GraphPad Prism.
Results: On the first and second days, the expression of STIM1 and STIM2 proteins decreased, while expression of these proteins start to increase from third day and on the fifth day showed the highest expression level. Furthermore, during these days striatum neurons moved gradually toward cell death.
Conclusion: Our results showed that Huntington neurotoxic model affected calcium homeostasis by modulating expression of STIM proteins. Although STIM1/STIM2 proteins expression increase compensationally, this increase cannot resist calcium homeostasis disruptions, as striatum cells move toward neuronal death.
Keywords: Huntington disease, STIM1, STIM2, Cell death, 3-NP

P-131

Study the interaction effect of the intracerebroventricular injection of the Apelin and the agonist and antagonist of Vanilloid type 1 receptor on pain in male Wistar rat.

Zohre Izadidastenaei, Mohammad Zarei*, Abdolrahman Sarihi, Alireza Komaki

Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran.

Apelin is an endogenous peptide that is present in areas of the brain that are effective in pain. The aim of this study was to investigat the analgesic effect of apelin through the vanilloid pathway and the possible interaction of apelin with agonist and antagonist of transient receptor potential vanilloid type 1 (TRPV1) in the rat. The experimental groups were: control group, saline group, DMSO group, morphine group, capsaicin group, capsazepine group, Apelin group, capsaicin + Apelin group, capsazapine + Apelin group. Rats have been surgically treated and the cannula was implanted into the right brain ventricle. The rats were subjected to nociception test including tail flick tests, writhing tests, and formalin test. In this study, the capsaicin (as the TRPV1 agonist) and capsazepine (as an antagonist of TRPV1) were used. The results of this study showed that both apelin and capsaicin had significant analgesic effects compared to control groups ($P < 0.001$). Co-administration of capsazepine and apelin caused a significant decrease in apelin antinociceptive effect which had a significant difference compare to the apelin group alone ($P < 0.001$). In conclusion, apelin reduced pain in a time-dependent manner. This study also showed that at least part of the apelin analgesic effect in tail-flick, writhing and formalin tests is due to interaction with TRPV1 pathway.
Keyword: Apelin, Capsaicin, Capsazepine, Nociception, Rat, Intracerebroventricular

P-132

Crocin as an active ingredient of saffron attenuates cognitive deficits due to intracerebroventricular injection of colchicine in the rat

Ensie Azadi Ahmadabadi[1], Farzane Fereidoni[1], Shahram Jalalzadeh[1], Zahra Kiasalari[2], Mehrdad Roghani[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective: Cognitive dysfunction is a typical phenotype of Alzheimer's disease (AD). Crocin has shown beneficial effect in different models of cognitive decline. In this study, we evaluated whether crocin could prevent cognitive dysfunction due to intracerebroventricular injection of colchicine in the rat.
Materials and Methods: Male rats (n = 32) were assigned to four experimental groups as follows: Sham, lesion (receiving intracerebroventricular colchicine bilaterally at a dose of 15 microg), and two lesion groups receiving crocin p.o. at doses of 10 or 50 mg/kg in addition to colchicine. Finally, passive avoidance and Y-maze tests were used to assess cognition.
Results: Our data demonstrated that intracerebroventricular colchicine could significantly lower alternation in Y-maze and step-through latency in passive avoidance and administration of crocin to lesion group at a dose of 50 mg/kg could significantly improves performance of animals in these tasks.
Conclusion: Crocin at a dose of 50 mg/kg could effectively ameliorate learning and memory decline due to intracerebroventricular injection of colchicine in the rat.
Keywords: Colchicine, Cognitive decline, Crocin, Saffron

P-133

Orexin is involved in naloxone induced hyperactivity of locus coeruleus in morphine dependent rats

Niloofar Aghajani, Hossein Azizi, Saeed Semnanian

Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Background and Objective: Repetitive administration of opioid agonists is associated with the induction of dependency to the effects of these substances and thus limits their application. The locus coeruleus (LC) is a key brain structure implicated in opiate dependency and tolerance. Orexin is involved in morphine tolerance and dependence and its type 1 receptor (OXR1) has been detected in LC nucleus. We studied the effect of OXR1 blockade on naloxone induced hyperactivity of LC neurons in morphine dependent rats.
Method: Male Wistar rats weighing 250-300 g were used in this study. To incite dependency, morphine was injected (10 mg/kg, i.p.) twice a day for 10 days. The LC neural activity was investigated using in vivo extracellular single unit recording. A selective OXR1 antagonist (SB-334867) was microinjected into the right cerebral ventricle (10 µg/10 µl. i.c.v.) while recording, immediately before naloxone injection. In the molecular level we used RT-PCR in order to measure the expression of orexin 1 receptor in LC neurons.
Results: Morphine injection during 10 days led to the induction of morphine dependency in LC neurons which was observed as a significant increase in responsiveness of LC neurons to naloxone injection. Administration of SB-334867 before naloxone injection attenuated naloxone induced hyperactivity of LC neurons. Furthermore, chronic administration of morphine caused an increase in OXR1 expression in LC.
Conclusion: The results indicate that orexin receptors are involved in naloxone induced hyperactivity of LC neurons and morphine withdrawal signs
Keywords: Morphine, Locus coeruleus nucleus, Orexin, Single unit recording, RT-P

P-134

Effect of sodium nitroprusside on lipopolysaccharide-caused spatial memory and synaptic plasticity impairment in rats

Akbar Anaeigoudari[1], Mahmoud Hosseini[2]

1. Department of Physiology, School of Medicine, Jiroft University of Medical Sciences, Jiroft , Iran
2. Division of Neurocognitive Sciences, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: lipopolysaccharide (LPS) impairs cognitive behaviors. NO donors such as sodium nitroprusside (SNP) have been suggested to have neuro-protective. The purpose of present study was to evaluate the effect of SNP on lipopolysaccharide-caused spatial memory and synaptic plasticity impairment in rats.
Materials and methods: The animals were divided into 4 groups: 1- Control (Saline), 2 - LPS, 3 - SNP-LPS and 4 - SNP. LPS (1mg/kg) and SNP (2 mg/kg) were dissolved in saline and administered intraperitoneally. LPS was injected 2 h before the behavioral and electrophysiological experiments and SNP was administered 30 minutes before LPS. Morris Water Maze (MWM) test and Electrophysiological studies were done.
Results: In MWM test, the latency time and traveled distance to reach the platform in LPS group were longer than control whereas, in SNP-LPS group they were shorter than LPS group. The amplitude and slope of field excitatory post synaptic potential (fEPSP) decreased in LPS group compared to control group whereas, there was not any significant difference in these parameters between LPS and SNP-LPS groups.
Conclusion: Although SNP improved deleterious effects of LPS on learning and memory in MWM test, it could not restore LPS-caused synaptic plasticity impairment in rats.
Keywords: Lipopolysaccharide, Sodium nitroprusside, Morris Water Maze, synaptic plasticity

P-135

Evaluating the role of astrocytes on progesterone control of seizures in a pilocarpine epileptic model

Effat Baran, Mahmoud Elahdadi Salmani, Iran Goudarzi, Taghi Lashkarbolouki

School of Biology, Damghan University, Damghan, Iran

Introduction: Epilepsy is a brain disease with periodic and unpredictable occurrence of seizures with higher severity in females. Epileptic women, experience seizures with different severity during the periods, and even more severe in the periods of progesterone deficiency. On the other hand, astrocytes functions to reduce hyperexcitability. Accordingly, the protective effects of high, medium and low doses of progestrone in epilepsy and the involvement of the astrocytes were investigated.
Material and Method: In this study, six groups of female Wistar rats weighing (180-240 gr) were studied. The pilocarpine model was used to induce seizure. Daily progestrone (0.2, 2, 20 mg/kg) was administered, subcutaneously, from 2 days before to 2 days after pilocarpine injection. Pilocarpine administered (30 mg/kg), intraperitoneally, and then the behavior of rats was monitored. Then amount of total hippocampal glutamate, GABA and the activity of glutamine synthetase (GS) enzyme were measured.
Result: The latency for generalized tonic-clonic convulsions was reduced in group receiving high doses of progesterone. However, seizure duration of tonic-clonic convulsions meaningfully reduced in groups treated with progesterone. Hippocampus GABA content was increased in pilocarpine group relative to OVX group and it was reduced in progestrone treated groups significantly in respect to pilocarpine group and no significant change was seen in hippocampal glutamate and GS activity.
Conclusion: The results showed that administration of progestrone have anticonvulsant properties probably, independent of astrocyte by a more prominent effect in high doses of progestrone.
Keywords: Epilepsy, Progestrone, Hippocampus, Glutamate synthase, Glutamate, GABA

P-136

Neuroprotection of Iranian brown propolis on ischemic neuronal damage in mice: a potential antioxidant property

Gholamreza Bazmandegan[1], Zahra kamiab[2], Mohammad Ali Zakeri[3], Mitra Abbasifard[4], Hussein esmaeili noroozi[5]

1. Physiology-Pharmacology Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
2. Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, & Department of Social Medicine, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
3. Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
4. Department of Internal Medicine, Ali-Ibn Abi-Talib Hospital , Rafsanjan University of Medical
5. Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Background and Objective: Oxidative stress plays a key role in ischemic neuronal damage. Superoxide dismutase (SOD), glutathione peroxidase (GPx) and malondialdehyde (MDA) are considered as oxidative stress biomarkers. Propolis is a resinous hive product consisting phenol compounds with a set of biological activities. In the this study, the effect of Iranian Brown Propolis (IBP) was evaluated on oxidative stress responses in a mouse model of permanent middle cerebral artery occlusion (MCAO).
Materials and methods: The water extracts of propolis (WEPs) were obtained from two regions of Iran. The chemical description and total phenol content were determined by GC-MS and Folin–Ciocalteu assays respectively. Experimental groups included surgical sham group, control group and six groups of WEPs-treated animals. The WEPs were injected at the doses of 30, 100 and 200 (mg/kg, IP), during four different time points. Oxidative stress biomarkers (MDA content, SOD and GPx activity) and infarct volume were measured 48 h post stroke. Behavioral tests were evaluated 4 and 48 h after stroke.
Results: Samples were not considerably different in concentration of the total polyphenol substances. In doses of 100 and 200 mg/kg of both samples, WEPs treatment resulted in significant recovery of SOD and GPx activity as well as MDA level. Infarct volume, in treated groups, was significantly lower versus control group. Sensory-motor impairment and neurological deficits were improved significantly as well.
Conclusion: IBP prevent the ischemic brain injury and this seems to be mediated by its antioxidant properties.
Keywords: Cerebral ischemia, Iranian Brown propolis, Neuroprotection, Oxidative stress

P-137

Effects of Lavandula officinalis hydroalchoholic extract on mouse reserpine induced depression

Banafsheh Bagheri[1], Batool Rahmati[2], Faezeh Ghozatloo[1] , Mohsen Khalili[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran
2. Neurophysiology Research Center, Shahed University, Tehran, Iran

Background and Objective: Lavandula officinalis commonly is known as Ustokhoddus in Iran, recommended for depression disease in Iranian traditional medicine. This study was designed to determine the effects of L. officinalis extract on mouse model of reserpine induced depression.
Materials and Methods: Seventy-two mice were randomly divided into 9 groups: Normal saline, control extract (200 mg/kg), reserpine, fluoxetine (10 mg/kg or 20 mg/kg) + reserpine, fluoxetine (10 mg/kg) + extract (200 mg/kg) + reserpine, Three extract pretreated groups (100-200 and 400 mg/kg) + reserpine. Extract and fluoxetine were administrated by gavages daily, for 10 days, 30 min before reserpine (0.5 mg/kg) injection in peritonealy. Behavioral evaluations were done by forced swimming, tail suspension and open field tests.
Results: Immobility time was enhanced by reserpine (210.37 ± 2.43 in compared with normal saline 109.75 ± 3.13) and the extract decreased it, dose dependently (140.75± 5.84 and 110.125 ± 6.46 200 and 400 mg/kg respectively) as the same as fluoxetine, in forced swimming test. Combination of extract and fluoxetine caused reduction of immobility time more effective than each one alone. The results obtained from tail suspension are similar to forced swimming test. On the other hand, while swimming time was decreased by reserpine, extract elevated it, dose dependently as the same as fluoxetine. Total crossed numbers that is equal to total motility in open field test, were not influenced by each one of agents.
Conclusion: L. officinalis hydroalcoholic extract improved the depression like behavior caused by reserpine.
Keywords: Lavandula officinalis, Reserpine, forced swimming test, tail suspension test, open field test.

P-138

Respiratory-related evoked potential in emotional contexts by automated stimulation inspiratory apparatus

Sobhan Bamdad[1], Mohammad Mikaeili [1], Mohammad Reza Raoufy[2]

1. Biomedical Engineering Department, Shahed University, Tehran, Iran.
2. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.

Background and Objective: Respiratory-related evoked potential (RREP) is a non_invasive technique recorded from electroencephalogram by applying short occlusion during respiration to study neural processing of respiratory signals. We set up and programmed an automated apparatus to apply occlusion automatically on inspiratory phase or expiratory phase. In this study, RREP was elicited by paired inspiratory occlusions (S1 and S2) in pleasant, unpleasant and neutral emotional contexts and N1 peak was assessed. Respiratory sensory gating was calculated as the relation such as ratio or difference in averaged RREP peak N1 amplitude between the second (S2) and the first occlusion (S1) in emotional contexts.
Materials and Methods: Sixteen healthy volunteers participated and pulmonary function test was performed. EEG electrode cap was positioned, EEG was recorded, subjects were watched 3 collections of emotional pictures and when subjects were breathing, paired inspiratory occlusions were applied by automatic respiratory apparatus. Data were analyzed using Matlab and GraphPad-Prism.
Results: The result of automated stimulation respiratory apparatus support previous findings those were manual. N1_RREP amplitude from S2 was smaller than N1_RREP amplitude from S1. The latency of N1 RREP from S2 was significantly earlier than the latency of S1 ones. The amplitude of N1_S1 pleasant was bigger than N1_S1 neutral which was bigger than N1_S1 unpleasant.
Conclusion: We made an automated device to apply respiratory stimuli. And different emotional contexts have effects on RREP and respiratory sensory gating.
Keywords: Respiratory-related evoked potential, RREP, sensory gating, N1, Automatic respiratory stimulation

P-139

Evaluation effects of Toxoplasma gondii infection on motor dysfunction and striatal histological alterations in experimental rat model of Parkinson

Zahedeh Bavandi, Mahnaz Taherianfard, Moslem Riahi

Background and Objective: Parkinson disease is a neurodegenerative disorder associated with progressive destruction of dopaminergic neurons. Toxoplasma gondii (TG) is an obligate intracellular parasite that able to increases the level of dopamine in the brain. The purpose of this study was to investigate the effect of TG infection on motor disorders and histological alterations of the striatum in Parkinson's model of the male rat.
Material and Method: 60 Sprague Dawley male rats were randomly divided into 5 groups: sham group (intrastriatal injection of ACSF), Parkinson group, Infected with toxoplasma group, Experimental group 1 (induction of TG infection before inducing Parkinson), Experimental group 2 (induction of TG infection after inducing Parkinson). Induction of Parkinson's was performed by intrastriatal injection of 6-hydroxydopamine. The elevated body swing test was used to confirm Parkinson induction and evaluation of TG infection on motor disorders of PD rats. TG infection was induced by IP injection of tachyzoites. The histological alterations were determined by counting of Nissl-stained neurons of the striatum by cresyl violet staining.
Result: TG significantly decreased the body swing bias in both experimental groups (fig 1) compared to the Parkinson group ($p<0.001$). As well as protected neurons against 6-OHDA(fig 2) and nissle-stained striatal neurons in both experimental groups were significantly more than the Parkinson group ($p<0.001$).
Conclusion: The results of this study show that TG infection via a neuroprotective effect on the striatal neurons improved the motor dysfunction of PD rat's model.
Keywords: Parkinson disease, Toxoplasma Gondii , motor disorders, histological alterations

P-140

The effect of hippocampal cis-p tau injection in learning and memory and synaptic plasticity

Fatemeh Bakhtiarzadeh[1], Koorosh Shahpasand[2], Javad Mirnajafi-Zadeh[1]

1. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Department of Brain and Cognitive Sciences, Cell Science Research Center, Royan institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Introduction: Experimental models of Alzheimer's disease (AD) are critical to gaining a better understanding of pathogenesis and to assess the potential of novel therapeutic approaches. The aim of this study is to introduce a new model for AD.
Materials and methods: Male C57BL/6 (3-6 months) were divided into three groups: control, sham and cis-p tau groups. We injected 2 µg/µl cis-p tau or its vehicle bilaterally into the hippocampal CA1 region. Short term memory assessed (by Y-maze test) and spatial learning and memory (by Barnes maze test were evaluated. In vitro field potential recordings were done in all three groups. Primed-burst stimulation (PBS) protocol was applied to induce long-term potentiation.
Results: Hippocampal injection of cis-p tau significantly decreased spontaneous alternation 17 and 31 days ($p<0.01$) after injection although had no effect at 4 months after injection. One month after cis-p tau injection, primary and scape latency and also primary and total error increased in Barnes maze test ($p<0.05$) but not at 17 days and 4 months after injection. Field potential recording showed that hippocampal injection of cis-p tau significantly ($p<0.01$) disrupted maintenance of LTP in dorsal hippocampal region but had no effect on ventral region.
Conclusion: Cis-p tau injection as a new model of Alzheimer's-like disease decreased short term memory, learning and spatial memory. Bilaterally injection of cis-p tau impaired long term potentiation and synaptic plasticity in dorsal region of CA1 hippocampal area

P-141

Study the effect of Ultra-low dose naloxone on KCC2 cotransporter expression in morphine tolerant and hyperalgesic rats

Mozhgan baratzadeh

Background and Objective: Long-term adminstration of morphine downregulates the KCC2 expression within neurons through the activity of microglia. It has been shown that ultra-low dose naloxone could reduce the activity of microglia.There is no evidence about the effect of ultra-low dose of naloxone on KCC2 expression in situations that KCC2 downregulation decreases morphine analgesia. So the aim of this study is to investigate the effect of simultaneous injection of Ultra-low dose of naloxone and morphine on the spinal KCC2 expression during chronic morphine administration.
Materials and Methods: 4 groups were included in the study(n=6). Morphine sulfate (10 mg/kg), saline, ultra-low dose of naloxone (15ng/kg) with saline and with morphine were injected intraperitoneally for 8 consecutive days and then stop for 48 hours. Development of morphine tolerance examined from day 1 to 8 by tail flick and thermal hyperalgesia by paw withdrawal test on day 10. After behavioral tests, spinal cords were removed on day 8 and 10 and KCC2 expression was investigated by immunohistochemical technique.
Results: Behavioral experiments indicated development of morphine tolerance from day 5 to 8 and thermal hyperalgesia developed on day 10. Injection of morphine along with ultra-low dose of naloxone decreased morphine tolerance and thermal hyperalgesia. Immunohistochemical analysis showed increasing in KCC2 expression in spinal cord.
Conclusion: Our finding suggests that KCC2 could have a impotrant role in developing of morphine tolerance and hyperalgesia.
Keywords: Morphine tolerance, Hyperalgesia, Ultra-low dose naloxone, KCC2.

P-142

Isoniazid prevents the acquisition of morphine dependence: a study using naloxone-induced withdrawal behaviors in morphine-dependent mice

Amir Abbas Barzegari, Kamran Shahabi

Department of Biology, Faculty of Basic Science, University of Maragheh, Maragheh, East Azerbaijan Province, IR Iran

Background and Objective: Repeated use of morphine may lead to dependence on the drug. Abrupt cessation of morphine administration in morphine-dependent persons can induce withdrawal signs that are an obstacle for morphine addiction treatment. Finding new drugs that can prevent or alleviate the withdrawal signs of morphine may be helpful for prevention of relapse to morphine abuse. Previous research has shown that GABAergic brain systems might alter morphine-withdrawal signs; therefore, the present investigation was conducted to evaluate the effects of modulation of GABAergic systems of brain by isoniazid on naloxone-induced withdrawal signs in morphine-dependent male mice.
Materials and Methods: Mice rendered dependent on morphine by the administration of 10 high doses of morphine on four days: nine doses of morphine (50, 50 and 75 mg/kg, s.c.)× 3 days and a single morphine dose (50 mg/kg, s.c.) on the fourth day. For evaluation of isoniazid effects on the acquisition of morphine dependence, four groups of animals received saline or isoniazid (25, 50 and 75 mg/kg, i.p.) before administration of the high doses of morphine for dependence induction. On the test day, two hours after the last morphine dose, all the animals received naloxone (5mg/kg, i.p.).
Results: Isoniazid administration before morphine could reduce the naloxone-precipitated withdrawal signs (Jumping, rearing, and diarrhea) in morphine-dependent mice, significantly.
Conclusion: Isoniazid may be a good candidate for the prevention of morphine withdrawal syndrome.
Keywords: Morphine, Isoniazid, Naloxone, Withdrawal, Mice

P-143

Morphine consumption during pregnancy exacerbates neonatal Hypoxia-Ischemia injury in rat through enhancing inflammation, oxidative stress and reducing BDNF

Morad bornavard

Objective: Hypoxia-Ischemia is the most common causes of death and disability in human infants and is associated with chronic cognitive, motor, and sensory disorders. About 80-90% of women who use opiate are at reproductive age. The use of opiates in women has a particular problem and is the effect of these substances on their children.
Materials and methods: In this study, a total of 24 female wistar rats were used in range of 200-220g. Rats were randomly assigned into 2 (12 in each group): 1- Rats during pregnancy and lactation did not receive treatment. 2- Rats during pregnancy and lactation received morphine. After delivery, offspring were divided into 4 groups (20 in each group) including: 1-SHAM 2- SHAM/Morphine 3- Hypoxia-Ischemic 4- Hypoxia-Ischemic/Morphine. Seven days after HI induction, neurobehavioral tests were done and then brain tissue was taken from the skull to measure cerebral edema, infarct volume, inflammatory factors and oxidative stress.
Result: Total antioxidant capacity and Brain-derived neurotropic factor level in HI/MO significantly lower than HI and SHAM groups. Tumor necrosis factor, C-reactive protein and total oxidant capacity level in HI/MO significantly higher than HI and SHAM groups. Cerebral edema and infarct volume in HI/MO group were significantly more than HI group. Conclusion: Based on our results, morphine consumption during pregnancy and lactation enhanced deleterious effect of HI injury in puppies. Likely, this effect of morphine consumption mediated through increase in inflammatory and oxidative stress and reduction in BDNF levels.

P-144

Administration of levothyroxine on behavior and cognitive decline in rat model of multiple sclerosis: a biochemical study

Elham Basiratnia[1], Mohammad Ali Mirshekar[1,2], Hamed Fanaei[2*]

1. Department of Physiology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
2. Clinical Immunology Research Zahedan University of Medical Sciences Center, , Zahedan, Iran

Background and Objective: MS is a CNS autoimmune disease. since levothyroxine play a crucial role in the development and physiological functioning of the CNS and reduces memory impairment, the effect of levothyroxine on the improvement of cognitive deficits of MS induced by LPC was studied in rats.
Materials and Methods:40 Wistar rats randomly divided into five groups, sham group, levothyroxine group, MS group, MS group receiving levothyroxine and positive control group. levothyroxine with dose 100µg/kg injected to each rat. The Shuttle Box and Morris water maze were used to investigate passive avoidance and spatial memory. Also, the hippocampal level TAC, MDA, TNF alpha, CRP were measured by a special kit.
Results: MDA, TNF-α and CRP in the levothyroxine treated group showed a significant reduction compared to the MS group. The hippocampus level TAC was significantly lower. Behavioral evaluation also showed that levothyroxine significantly improved the ability to store information and remind them in the passive avoidance and to improve spatial memory in the Morris water maze.
Discussion: It seems that treatment with levothyroxine is able to prevent conitive deficits. Positive effects of levothyroxine may be due to a decrease in TNF-α concentrations as a pro-inflammatory factor, MDA as lipid peroxidation index and increase TAC. Therefore, these results suggest that levothyroxine can be used as an effective ingredient in the treatment of MS

P-145

Bilateral intra-hippocampal infusion of Modafinil prevented chronic sleep deprivation– induced spatial memory retention deficits: in Morris Water Maze in male rats

Maryam Belaran

Background and Objective: Sleep deprivation, also known as insufficient sleep or sleeplessness, is the condition of not having enough sleep. It can be either chronic or acute and may vary widely in severity. It adversely affects the brain and cognitive functions.
Materials and Methods: In the present study, the effects of four-day bilateral intra-hippocampal infusion of modafinil (100 µM/side) on spatial memory retention in chronic sleep deprivated (CSD; 18 hours in each day for 7 consequtive days) male rats in Morris water maze (MWM) were investigated. DMSO was used as a control for modafinil –treated animals. Rats were trained for 4 days (days 4th-7th of chronic sleep deprivation protocol) ; each day included one block of four trials. Post-training probe trial retention tests were performed 72 h after last training trial in MWM.
Results: Bilateral intra-hippocampal infusion of modafinil (100µM/side) decreased escape latency and traveled distance parameters and increased time spent in target qudrant in probe test. Also, modafinil decreased oxidative stress parameters and increased CREB, pCREB and BDNF protein markers expression by western blot method.
Conclusion: Taken together, modafinil (100µM/side) prevented CSD –induced spatial memory retntion impairment in MWM.
Key words: Modafinil, Chronic sleep deprivation, Morris water maze, Spatial memory retention, Hippocampus

P-146

Ferulic acid through attenuation of oxidative stress and neuro-immune response exerts antinociceptive effect in mouse model of formalin test

Shima Balali-Dehkordi[1], Rahil Mohajerian[1], Saeed Habibian Dehkordi[2], Hossein Amini-Khoei[3]

1. Department of Basic Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
2. Department of Basic Sciences, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran
3. Medical plants Research Center, Basic Health Sciences institute, Shahrekord university of Medical Sciences, Shahrekord, Iran

Background and Objective: Ample indication suggests that neuroinflammation and oxidative stress states increased the neural sensitivity indicating that neuro-immune response is involved in the pathophysiology of pain. Ferulic acid (FA), a natural antioxidant exist in some fruits, has possessed some pharmacological effects. We aimed to evaluate the antinociceptive effect of FA in mouse model of formalin test focusing its anti-neuroinflammatory and antioxidative stress effects.
Material and Methods: FA at dose of 40 mg/kg, piroxicam at dose of 2 mg/kg and normal saline were injected via intraperitoneal route. One hour late formalin injected at the plantar surface of hind paw of mice and pain behavior was recorded for 60 min. Then mice were sacrificed, MDA level and antioxidant capacity measured in the blood samples. In addition, prefrontal cortex samples were taken and expression of inflammatory cytokines including TNF-α as well as IL-1β evaluated.
Results: Findings showed that FA significantly decreased the pain behavior following injection of formalin (Fig 1). Furthermore, administration of FA significantly decreased the MDA level (Fig 2) and increased the antioxidant capacity (Fig 3) in the blood samples. We found that FA decreased the expression of TNF-α and IL-1β in the prefrontal cortex samples (Fig 4).
Conclusion: We conclude that FA partially, at least, through attenuation of oxidative stress and neuro-immune response exerts antinociceptive effect in mouse model of formalin test.
Keywords: Feruli acid, pain, formalin, oxidative stress, neuroinflammation

P-147

Spinal cell death fluctuations are potentially responsible for variation in hyperalgesia during persistent peripheral inflammation

Mansoureh Baniasadi[1], Jalal Zaringhalam[1]

Department of Physiology, neurophysiology research center, Shahid Beheshti University of Medical Sciences

Aim: Microglia have an effect on the initiation and maintenance of inflammatory pain, however, adequate information has not been provided about exact mechanisms of its operation. We investigated the relation between hyperalgesia variation with spinal neuronal apoptosis variation which is mediated by microglial activity during acute and chronic phases of CFA-induced inflammation.
Methodology: CFA induced inflammation was induced on day 0 by single injection of Complete Freund's adjuvant (CFA) into the rats' hindpaw. Evaluation of spinal microglial activity, spinal neuronal apoptosis and hyperalgesia was performed by Immunohistochemistry, Western blotting and plantar test respectively on 0, 7 and 21 of the study. Minocycline (microglial inhibitor) was administered daily from days 1-21 after CFA injection (i. p.).
Results: In the CFA group, hyperalgesia significantly increased on day 7 compared to day 0 and decreased on day 21. In addition, our data revealed that CFA- induced hyperalgesia on the 7th day was correlated with increase in microglial activity and spinal neuronal apoptosis and decreasing hyperalgesia on day 21 was correlated with decrease in microglial activity and spinal neuronal apoptosis. Moreover minocycline caused a significant reduction in hyperalgesia which is aligned with decreased apoptotic cell death.
Conclusion: Our findings indicated that, by affecting cell death, fluctuations of microglial activity during different phases of persistent peripheral inflammation can play an important role in hyperalgesia variations.

P-148

Hippocampal orexin infusion develops anxiety behaviors

Saeedeh Bahramzadeh Zoeram, Mahmoud Elahdadi Salmani, Iran Goudarzi, Taghi Lashkarbolouki

Faculty of biology, Damghan University

Background and Objective: Orexin plays a crucial role in the regulation of arousal, wakefulness, anxiety and the stress response. The hippocampus, a structure involved mainly in memory processes, is highly susceptible to stress effects and has a high expression level of orexin receptors. This study aimed to compare the effect of once or repeated infusion of orexin-A in the hippocampus on the anxiety like behaviors and corticosterone (CORT) level.
Materials and Methods: Animals underwent cannula implantation in the hippocampal region. After the ending of infusions (single or ten days of single daily injections), anxiety behaviors; immobility or open and closed arm times, were examined using open field (OF) and elevated plus maze (EPM), respectively. Then, plasma was sampled for CORT measurement.
Results: Results showed that, orexin infusion (single and repeated) raised plasma CORT level. Single and repeated infusion of orexin-A lead to increased immobility and closed arm time in the OF and EPM, respectively.
Conclusions: Our results indicate that, orexin, either single or repeated, infusions may promote the anxiety like behaviors, partially through CORT build up.
Key words: Orexin-A, Hippocampus, Anxiety like behavior.

P-149

The effect of stress on sleep alterations after learning and the role of Cinnamaldehyde on this interaction in rat

Farideh Bahrami[1,2], Fatemeh Erfani Sharifian[1], Zahra Bahari[1,2]

1. Department of Physiology and Medical Physics, Faculty of Medicine, Baqiyatallah University of Medical Science, Tehran,Iran.
2. Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

Background and Objective: Over more than a century of research has established the fact that sleep benefits the learning and retention of memory. On the other hands stress can develop sleep disorders and inadequate sleep induces emotional disorders. In this study we investigate the effect of immobilization stress on alteration of sleep stages after learning process. Cinnamon as an herbal medicine and potent antioxidant can modulate the sleep, stress and learning interaction.
Materials and Methods: Thirty five male Wistar rats were subjected to 2 hours of immobilization per day in a narrow, uneven and stony place for 3 consecutive days. The electroencephalogram (EEG) and the electromyogram (EMG) were recorded for sleep analysis. The sleep stages were recorded before and after stress, and after learning procedures for 3 consecutive days. The Barnes maze, were used for learning assay. For treatment the rats received Cinnamaldehyde (20 mg/kg/day) via gavage method during the examination.
Results: Our results indicated that immobilization stress significantly decreased the REM
sleep but the learning protocol induced an increase in REM sleep. However the stress could not prevent the REM sleep increment after training. Furthermore Cinnamaldehyde treatment could repair REM reduction induced by immobilization stress and it could induce increase in both REM and NREM sleep after learning procedure.
Conclusion: The immobilization stress could not disturb learning effect on sleep and the Cinnamaldehyde treatment improve the REM and NREM sleep stages after performance of learning protocol.
Key word: sleep, stress, learning and memory, Cinnamaldehyde

P-150

The effect of platelet-rich plasma on neuropathic pain induced by spinal cord injury in male rats

Zahra Behroozi[1], Atousa Janzadenh[2], Farinaz Nasirinezhad[3]

1. Department of Physiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Radiation Biology Research Center,Iran University of Medical Sciences, Tehran, Iran
3. Research Center and Department of Physiology, Iran University of Medical Sciences, Tehran, Iran.

Background and Objective: Neuropathic pain which happens following the injury or dysfunction of the peripheral or CNS is one of the important medical challenging to treat. Humane platelet-rich plasma (HPRP) is a rich source of growth factors. In this study, the effect of HPRP was investigated on neuropathic pain caused by spinal cord injury (SCI).
Materials and Methods: 60 rats were randomly divided to 6 groups: control, sham, SCI, vehicle (SCI+platelet-poor plasma), SCI+ PRP1 (PRP was injected 48 after SCI) and SCI+PRP2 (PRP was injected 14 days after SCI).
SCI was induced on the T12-T13 level of the spinal cord. PRP was injected intraspinally 2 or 14 days after injury. Behavioural tests were conducted weekly after injury for six weeks. Allodynia and hyperalgesia were assessed by acetone drop and plantar test. Also, the motor performance was determined by the BBB test. Data were analyzed using PRISM software.
Results: The injection of PRP significantly ($P<0.001$) improved motor function. Also the allodynia and hyperalgesia scores of rats with spinal cord injury was significantly different ($P<0.05$) from animals injected with PRP. Also, injection of PRP on 48 hours after SCI showed better improvement than injection of PRP 14 days after injury.
Conclusion: The results showed that PRP significantly improves motor function and reduces SCI-induced allodynia and hyperalgesia. Therefore, using HPRP could open a new window in treating the pain caused by injuries to the nervous system.
Keywords: Spinal cord injury, Pain, PRP, Allodynia, Hyperalgesia

P-151

Protective effects against brain tissues oxidative damage as a possible mechanism for learning and memory improving effects of captopril in scopolamine treated rats

Farimah Beheshti[1,2], Hamid Reza Akbari[3], Hamid Reza Sadeghnia[4], Soleyman Bafadam[3], Yousef Baghcheghi[5], Mahmoud Hosseini[6]

1. Neuroscience Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran
2. Department of Physiology, School of Paramedical Sciences, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran
3. Neurogenic Inflammation Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
4. Pharmacological Research Center of Medicinal Plants, Mashhad University of Medical Sciences, Mashhad, Iran
5. Student Research Committee, Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
6. Division of Neurocognitive Sciences, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: Angiotensin converting enzyme (ACE) inhibitors are suggested to have some beneficial effects on the brain. In the present study the protective effects against brain tissues oxidative damage as possible mechanism for learning and memory improving effects of captopril was investigated in scopolamine treated rats.
Materials and Methods: Fifty male Wistar rats were divided into seven groups and treated: saline as a control group, Sco (scopolamine) and Sco-Capto10, 50 and 100 (captopril 10, 50 and 100 mg/ kg before scopolamine). Treatment was passive avoidance test and then the cortical tissues were collected to measure malondialdehyde (MDA), nitric oxide (NO) metabolites , thiol, super oxide dismutase (SOD) and catalase (CAT). Data were analyzed using SPSS version 11.5.
Results: Scopolamine decreased the latency to enter the dark in passive avoidance test compared to control group ($P<0.01$- $P<0.001$). It also increased MDA and NO metabolites ($P<0.001$) while decreased thiol, SOD and CAT in comparison with control group ($P<0.001$). Captopril increased the latency to enter the dark ($P<0.05$- $P<0.001$). It also decreased MDA and NO metabolites ($P<0.01$ $P<0.001$) while, increased thiol, SOD and CAT ($P<0.05$- $P<0.001$).
Conclusion: Captopril protected from the brain tissues oxidative damage to improve learning and memory impairment induced by scopolamine.
Keywords: Scopolamine, Captopril, Oxidative stress, Nitric oxide, Learning, Memory

P-152

The effects of Nigella sativa extract on Cell survival rate of Dorsal Root Ganglion (DRG) sensory neurons after axotomy

Belal pashaie[1], Rahim Hobbenaghi[1], Milad Bahrami[2]

1. Department of Pathobiology, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.
2. Department of Basic Sciences, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.

Background and Objective: The aim of this study was designed to evaluate the possible protective effects of Nigella sativa (NS) on primary afferent neurons (dorsal root ganglion [DRG] cells) after sciatic nerve transection (Axotomy) in (newborn, 3days old) wistar rats .
Materials and Methods: Rats divided into control and four treated groups with seven rats in each group. On the first day of the process the left side sciatic nerves of treated group (A, B and C) and sham groups were transected at mid thigh region. The treatment procedure for group A was 1mg/kg, 50mg/kg for group B and 100mg/kg for group C. All groups after 28 days were euthanized and tissue samples were obtained for histopathological investigation. After Serial sections and Tissue staining, healthy neurons of dorsal root ganglion were counted and results were analyzed.
Results: Results showed that in the sham group (only transected), the DRG neurons in transected side extensively degenerated with picnotic nuclei and cell number is less than of healthy side. Treatment of NS in low dose (1mg/kg) markedly reduced spontaneously decreased and degenerated number of neurons. However, higher doses increase cell number reduction.
Conclusion: We conclude that NS in limited extent protects adult sensory neurons from axotomy-induced death. Nigella sativa, its oil, and the active principle thymoquinone (TQ) have been shown to have potent antioxidant and antiapoptotic effects.
Keywords: Nigella sativa, axotomy, thymoquinone, apoptosis.

P-153

Antidepressant effects of ethanolic extract of Propolis using mice model of depression induced by reserpine

Rahmatollah Parandin

Department of Biology, Faculty of Sciences, Payame Noor University, Iran.

Background and Objective: Recent studies have shown that propolis contains a broad spectrum of compounds such as polyphenols, terpenoids, steroids, and amino acids that have many biological activities. The objective of this study was to assess the antidepressant effects of ethanolic extract of Propolis in forced swim test (FST) and tail suspension test (TST) in mice.
Materials and Methods: In this experimental study, 42 male mice were randomly divided into 6 groups of 7 mice: including control (normal saline), reserpine (negative control), fluoxetine (positive control), and three reserpine groups treated respectively with 50, 100 and 200 mg/kg of ethanolic extract of propolis via the intraperitoneal injection. Depression was evaluated using FST and TST. Brain total antioxidant capacity (TAC) and malondialdehyde (MDA) levels were also determined. The data were analyzed by SPSS statistical software and OneWay ANOVA test. The significant was shown with ($p<0.05$).
Results: Reserpine treatment significantly ($p<0.001$) increased the time of immobility in FST and TST tests. Extract at 100 ($p<0.05$) and 200 ($p<0.001$) mg/kg significantly ($p<0.001$) reduced the immobility time in FST. Extract at 100 ($p<0.01$) and 200 ($p<0.001$) mg/kg significantly ($p<0.001$) reduced the immobility time in TST. Reserpine treatment significantly ($p<0.001$) decreased brain TAC and increased MDA level in the brain. Extract at 100 ($p<0.05$) and 200 ($p<0.01$) mg/kg significantly increased brain TAC and reduced the MDA level.
Conclusion: The present data suggest that propolis has antidepressant activity which may be mediated by its antioxidant components.
Keywords: Propolis, Forced swimming test, Antidepressant, reserpine, mice

P-154

Improvement of autistic-like behaviors in adult rats prenatally exposed to valproic acid through early suppression of NMDA receptor function

Somayeh Mohammadi[1], Majid Asadi-Shekaari[2*], Mohsen Basiri[2], Mahdieh Parvan[3], Mohammad Shabani[2], Masoumeh Nozari[3*]

1. Department of Anatomical Sciences, Afzalipour School of Medicine, Kerman University of Medical Sciences, Kerman, Iran
2. Neuroscience Research Center, Neuropharmacology Institute, Kerman University of Medical Sciences, Kerman, Iran
3. Neuroscience Research Center, Institute of Neuropharmacology, Department of Physiology and Pharmacology, Afzalipour School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

Rationale: Autism spectrum disorder (ASD), the fastest growing neurodevelopmental disorder, is characterized by social deficits, repetitive/stereotypic activity, and impaired verbal and nonverbal communication and is commonly diagnosed at early stages of life. Based on the excitatory-inhibitory imbalance theory of autism, some recent animal experiments have reported amelioration in autistic-like phenotypes in adult animals following acute treatment of NMDA antagonists. However, we suggested the neonatal period as a critical period for NMDA antagonist intervention.
Objectives: This experiment was designed to determine the role of postnatal MK-801, an NMDA receptor blocker, in the prenatal valproic acid (VPA) rat model of ASD.
Methods: The model of autism was induced by subcutaneous administration of valproic acid (600mg/kg) to pregnant rats at the gestational day 12.5. The effects of MK-801(0.03mg/kg, from postnatal day 6-10) in correcting ASD-associated behaviors in male offsprings were assessed by open filed, three-chambered social interaction tests. Moreover, the nociceptive threshold was measured by tail flick and hot plate. Behavioral tests were performed on PND 55–60. Nissl staining was performed to confirm the safety of 0.03 mg/kg MK-801 for the brain.
Results: We reported that MK-801 rescued social deficits, repetitive behaviors (self-grooming), anxiety-related behavior, and the low nociceptive threshold in the VPA-treated rats. Further, histological examination showed that there were no significant differences among all the groups in terms of the neuronal survival rate.
Conclusions: Our results showed that postnatal low-dose MK-801 improved ASD-associated behaviors in the VPA-treated rats and that early exposure to NMDA antagonist resulted in permanent changes in adult behavior.
Keywords: Autism; Valproic acid; MK-801; NMDA antagonist; Postnatal period

P-155

Neuroprotective and antioxidant effects of Carvacrol in the ketamine- induced model of mania in the rat

Marzieh Pashmforosh[1], Hosein Rajabi Vardanjani[2], Mohammad Sabaghan[1], Ali Veisi[1]

1. Behbahan Faculty of Medical Sciences, Behbahan, Iran
2. Medical Plants Research Center, Basic Health Sciences Institue, Shahrekord University of Medical Sciences, Shahrekord, Iran

Background and Objective: Bipolar disorder (BD) is a chronic illness characterized by recurrent manic and depressive episodes. Increasing evidence suggests that oxidative stress is involved in the etiology of BD. The present work investigated the protective effect of carvacrol, one of the main active ingredients of Zataria multiflora, in a model of mania induced by ketamine administration in rat.
Materials and Methods: Female Wistar rats were pretreated with carvacrol (20, 40, and 80 mg/kg, PO, once a day) or vehicle (saline, PO, once a day) or lithium chloride (45 mg/kg, positive control) for 14 days. Between days 8 and 14, the rats were treated with vehicle (saline, i.p.) or ketamine (25 mg/kg, i.p.) once a day. On the 15th day of treatment, the animals received a single injection of ketamine or saline, and the locomotor activity was assessed in the open-field apparatus. Then malondialdehyde level, and superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR) activities were determined in the hippocampus.
Results: Our results indicated that ketamin increased locomotor activity in the open-field test and pretreatment with carvacrol (40 and 80 mg/kg) significantly ($p<0.05$) blocked this effect. In addition, ketamin increased lipid peroxidation and reduced the activity of the antioxidant enzymes, which were reversrd by carvacrol treatment.
Conclusion: This study indicated that carvacrol could prevent locomotor hyperactivity and oxidative stress elicited by ketamine in rats.
Keywords: Carvacrol, Mania, Ketamine, Oxidative stress, Rat

P-156

A conditioned place preference study of isoniazid influence on the expression of morphine rewarding properties

Ali Pourahmadi, Amir Abbas Barzegari, Kamran Shahabi

Department of Biology, Faculty of Basic Science, University of Maragheh, Maragheh, East Azerbaijan Province, IR Iran

Background and Objective: Isoniazid is a drug for the treatment of latent and active tuberculosis. This agent can easily enter the brain and affects the brain GABAergic systems. Because GABAergic agents have modulatory effects on morphine reward, the purpose of the present study was to evaluate the effects of isoniazid on the expression of conditioned place preference of morphine.
Materials and Methods: For assessing the rewarding effects of morphine conditioned place preference (CPP) conducted on female mice. Standard maintenance conditions were provided for all the laboratory animals. Different groups of animals conditioned with saline, morphine (0.5, 1, 2.5, 5 and 10 mg/kg, s.c.) or isoniazid (25, 50 and 75 mg/kg, i.p.). For evaluation of isoniazid effects on the expression of morphine CPP, four groups of mice, in the conditioning phase of CPP received the effective dose of morphine (5 mg/kg, s.c); then on the test day, 40 minutes before the test session, four groups of animals received saline or isoniazid (25, 50 and 75 mg/kg, i.p.).
Results: Morphine but not isoniazid induced a significant place preference compared to the saline. The most effective dose of morphine (5 mg/kg, s.c) was used for CPP induction in the next phase. Isoniazid administration on the test day reduced the CPP induced by the effective dose of morphine, significantly.
Conclusion: Isoniazid may interfere in morphine rewarding effects.
Keywords: Morphine, Isoniazid, Conditioned place preference, Expression, Mice

P-157

Arbutin Improves Functional Recovery in LPC-induced demyelition model in rat optic chiasm through Regulation of Inflammatory and Oxidative processes

Fereshteh Pourabdolhossein[*1,2], Frough Ebrahim tabar[3], Atena Nazari[2], Samaneh Dehghan[4], Mahdi Pouramir[5], Manuchehr Ashrafpour [1,2]

1. Neuroscience Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
2. Physiology Departments, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran
3. Student Research Committee, Babol University of Medical Sciences, Babol, Iran
4. Physiology Departments, Faculty of Medicine, Tarbiat Modares University, Tehran, Iran
5. Biochemistry Departments, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran

Background and Objective: Multiple sclerosis (MS) is an inflammatory demyelinating disease in the central nervous system. Demyelination, neuroinflammation, astrocytes activation and oxidative stress are pathological features of MS. Arbutin, a natural polyphenol; possess anti-oxidant, anti-inflammatory properties which its therapeutic potential was not reported in MS. The main objective of the current study was to assess the effectiveness and mechanisms of Arbutin on lysolecthin (LPC)-Induced local demyelination model in rat optic chiasm.
Materials and Methods: Local demyelination was induced by micro-injection of LPC (1%) into the rat optic chiasm and the treated group was received daily injection of arbutin (50mg/kg, i.p) at the same time. Visual-evoked potentials (VEPs) recordings were used to functionally assess visual pathway. The expression level of inflammatory and stress oxidative related mediators were evaluated by qPCR. The Myelin and astrocyte specific immune-staining were performed to evaluate demyelination extension and glia activation.
Results: We found that Arbutin significantly reduced P1-latency of VEPs waves and demyelination extention at 7 and 14 days post demyeliation. Also, Arbutin decreased inflammatory cytokines (IL1, Il17, TNF-α) and iNOS mRNA expression level. Furthermore, the expression level of anti-inflammatory cytokine (IL10) and antioxidant mediators (Nrf2 and HO1) were enhanced by Arbutin treatment. Arbutin increased MBP and Olig2 levels and attenuates GFAP as an astrocye activation marker.
Conclusion: Arbutin enhances functional recovery and myelin repair in the demyelinated optic chiasm through hampering of inflammation, astrocyte activation and oxidative stress. These findings might open new potential promising avenues for treating demyelinating disorders such as Multiple Sclerosis.
Keywords: Arbutin, Demyelination, Inflammation, Astrocyte activation, Oxidative stress

P-158

Effects of Intracerebroventricular and Intra-Arcuate Nucleus Injection of Ghrelin on Pain Behavioral Responses and Met-Enkephalin and β-Endorphin Concentrations in the Periaqueductal Gray Area in Rats

Samaneh Pirzadeh, Javad Sajedianfard

Department of Basic Sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

Background and Objectives: Ghrelin is an endogenous ligand for orphan growth hormone secretagogue receptors. Ghrelin receptors have been found in CNS areas responsible for pain modulation and transmission. This study investigated the effects of intracerebroventricular (ICV) and intra-arcuate nucleus (ARC) injection of ghrelin on pain behavioral responses and levels of β-endorphin (β-EP) and met-enkephalin (MENK) in the periaqueductal gray area (PAG) during the formalin test in rats. Materials and Methods: Thirty-five male rats were studied in five groups. Ghrelin was injected into the left lateral ventricle (ICV, 5 µL) or into the ARC (1 µL). After 15 minutes, formalin (2.5%) was subcutaneously injected into the left hind paw. Behavioral nociceptive scores were recorded for 60 minutes. MENK and β-EP were collected by microdialysis in the PAG and determined by HPLC. Results: ICV and ARC injection of ghrelin significantly reduced pain in all phases of the formalin test ($p<0.001$). Dialysate concentrations of MENK and β-EP in the PAG increased in all the phases ($p<0.01$). Conclusion: In conclusion, the present study shows that the ARC nucleus and the endogenous opioid system are involved in ghrelin-induced pain modulation.

Keywords: ghrelin; formalin test; met-enkephalin; beta-endorphin;

P-159

Bilateral intra-hippocampal infusion of Modafinil prevented chronic sleep deprivation – induced spatial learning impairments in Morris Water Maze in male rats

Maryam Belaran[1], Marjan Aghajani[2], Susan Azadi[3] and Kaveh Tabrizian[3]

1. Department of Physiology, Faculty of Medicine, Zabol University of Medical Sciences, Zabol, Iran
2. Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
3. Department of Pharmacology and Toxicology, Faculty of Pharmacy,
4. Zabol University of Medical Sciences, Zabol, Iran

Background and Objective: Sleep deprivation, also known as insufficient sleep or sleeplessness, is the condition of not having enough sleep. It can be either chronic or acute and may vary widely in severity. It adversely affects the brain and cognitive functions.

Materials and Methods: In the present study, the effects of four-day bilateral intra-hippocampal infusion of modafinil (100 µM/side) on spatial learning (acquisition phase) in chronic sleep deprivated (CSD; 18 hours in each day for 7 consequtive days) male rats in Morris water maze (MWM) were investigated. DMSO was used as a control for modafinil –treated animals. Rats were trained for 4 days (days 4th-7th of chronic sleep deprivation protocol) ; each day included one block of four trials. Post-training probe trial test were performed 24 h after last training trial in MWM.

Results: Bilateral intra-hippocampal infusion of modafinil (100µM/side) decreased escape latency and traveled distance parameters and increased time spent in target qudrant in probe test. Also, modafinil decreased oxidative stress parameters and increased CREB, pCREB and BDNF protein markers expression by western blot method.

Conclusion: Taken together, modafinil (100µM/side) prevented CSD –induced spatial learning impairment in MWM.

Key words: Modafinil, Chronic sleep deprivation, Morris water maze, Spatial learning, Acquisition, Hippocampus

P-160

Intranasal insulin effects on brain insulin level and peripheral glucose and insulin concentrations in type 2 diabetes

Nihad Torabi

Background and Objective: Information from previous studies about insulin concentrations in the brain of diabetic animals is controversial. Insulin action in the brain has been shown to affect the metabolism of the periphery. These observations have led to intranasal insulin (INI) being investigated as a possible therapeutic method.
Materials and Methods: Diabetes was induced by a single intraperitoneal injection (45 mg/kg) of streptozotocin (STZ) on day 1. Insulin and saline were given intranasally from day 4 to 14. We measured the brain insulin concentration on day 15, and the serum insulin and glucose concentrations on days 0, 7 and 14.
Results: In the current study, brain and serum insulin concentrations were ~12 ± 0.38 ng/ml and 1.2 ± 0.06 ng/ml, respectively. In our experimental type 2 diabetes mellitus model (T2DM), we observed that brain and serum insulin levels were ~31± 2.7 ng/ml and ~3.01± 0.38 ng/ml, respectively. Our results demonstrate that INI delivery raises the brain insulin roughly ~12.5 and 6.54 times higher in control and diabetic groups compared to intranasal saline groups. In the current study, as in control rats, repeated INI delivery (11 days) increased serum insulin under diabetic condition (~1.5 folds). INI delivery also decreases the serum glucose in diabetic rats.
Conclusion: The results of this study showed that INI delivery increased the levels of insulin in the brain and in the serum. INI delivery also reduced the serum glucose, probably through central mechanisms, in diabetic animals.
Keywords: Intranasal insulin, type 2 diabetes, Brain, Insulin level, Rats

P-161

The effect of safranal in prevention of cognitive decline in intracerebroventricular streptozotocin model of Alzheimer's disease in the rat

Shahram Jalalzadeh[1],Ensie Azadi [1], Farzane Fereidoni[1], Zahra Kiasalari[2], Mehrdad Roghani[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective: Cognitive decline is associated with Alzheimer's disease (AD) that is a chronic and progressive syndrome with a neurodegenerative nature that finally leads to irreversible deterioration of neurons. In this study, we evaluated whether safranal could prevent cognitive decline in intracerebroventricular streptozotocin (STZ)-induced model of AD in the rat.
Materials and Methods: Male rats (n=32) were assigned to four groups, i.e., Sham, lesion (receiving intracerebroventricular STZ bilaterally at a dose of 3 mg), and two lesion groups receiving safranal p.o. at doses of 10 or 50 mg/kg in addition to intracerebroventricular STZ. Finally, performance of rats in passive avoidance and Y-maze tests was assessed to explore cognition.
Results: Our obtained data indicated that intracerebroventricular STZ is associated with significant dysfunction in Y-maze and passive avoidance tasks and administration of safranal to intracerebroventricular STZ group at a dose of 50 mg/kg significantly improves performance of animals in these tests.
Conclusion: Collectively, safranal at a dose of 50 mg/kg could significantly attenuate cognitive dysfunction induced by intracerebroventricular injection of STZ in the rat.
Keywords: Streptozotocin, Safranal, Cognition

P-162

Therapeutic effects of Levodopa/Carbidopa on olfactory function, depression-like and anxiety like behaviors in 6-OHDA- induced Parkinson,s disease in rats

Jalali M[1], Saki Gh[2] , Sarkaki A[3], Farbood Y[3], Azandeh S[2]

1. Physiology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2. Department of Anatomical Sciences, School of Medicine, Cellular and Molecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3. Physiology Research Center, Dept. of Physiology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Background and Objective: Parkinson's disease (PD), an age dependent neurodegenerative disorder caused by a progressive death of dopaminergic neurons projected from substantia nigra pars compacta (SNc) to striatum. In addition to the typical motor symptoms of PD, non-motor symptoms like depression, anxiety, olfactory disturbances are sources of considerable burden in people with PD. The aim of this study was to assess the effects of Levodopa/Carbidopa on olfactory function, depression and anxiety -like behaviors in rats with 6-Hydroxydopamine (6-OHDA)-induced PD.

Materials and Methods: Male Wistar rats were divided into 3 groups. 1)Sham operated animals received vehicle. 2) PD received 6-OHDA (16 µg/2 µl) in right medial forbrain(MFB). 3) Treated PD (10 mg/kg/levodapa, 30mg/kg/carbiodapa PO, for 60 days after PD induction). PD was approved by apomorphine-induced contralateral rotation. Open field , elevated-plus-maze (EPM) and buried pellet test performed to evaluate the behavioral changes. Data analyzed statistically by one-way ANOVA and Tukey's post hoc test. P value less than 0.05 assign as significant alteration.

Results: Data showed that PD induction increased the latency to locate buried food with compared to sham ($p<0.05$). Horizontal locomotion (line crossings) in open field and the number of entries and time spent into the open arms of the EPM were also diminished ($P<0.01$). Levodopa/Carbidopa administration improved motor and non-motor behaviors versus to PD group ($P<0.001$).

Conclusion: Our results showed that long period treatment of PD with Levodopa/Carbidopa exhibits therapeutic potential to improve non-motor functions and has been considered in PD management.

Keywords: 6-OHDA; Parkinson's disease; Levodopa;Carbidopa; open-field; Elevated-plus-maze; Buried pellet test

P-163

The effect of intracerebroventricular infusion of Neuregulin1β on spatial memory in sporadic dementia model of Rats

Marzieh Jalilzad[1, 2], Parvin Babaei[1, 2], Adele Jafari[2]

1. Cellular & Molecular Research Center, Guilan University of Medical Sciences, Rasht, Iran
2. Department of Physiology, Faculty of Medicine, Guilan University of Medical Sciences, Rasht, Iran

Background: Alzheimer's disease (AD) is one of the neurodegenerative disorders which is characterized by deposition of β-amyloid protein (Aβ) and extensive neuronal cell death. Recent research has focused on the use of various neuropeptides in AD treatment. Neuregulin-1 (NRG1) is one of the candidates to improve cognitive function in AD. Therefore, the goal of this study was to evaluate the effect of NRG1β on improving cognitive deficit in AD model of rats.

Methods: : Fifty six adult male Wistar rats were randomly divided into Saline, Aβ and Aβ+ NRG1β, Aβ+ PBS , Aβ+ NRG1β + Erk1/2 Ant, Aβ+ NRG1β + Saline, Saline+Erk1/2 Ant (n=8). The AD model was established by injecting beta-amyloid protein (Aβ1-42, 4µg/2µl) stereo tactically into the right lateral ventricle, Then NRG1β (5µg/kg) was injected twice for two weeks, one week after Aβ injection. PD98059, Erk1/2 Antagonist (5µg/2µl) was injected 15 minute before injection of NRG1β. The cognitive performance of rats was evaluated using MWM and passive avoidance.

Data were analyzed using one way Anova test and $p<0.05$ was considered as significance.

Results: The cognitive functions in AD group were decreased compared with control group ($p=0.001$), and significantly restored after treatment with NRG1β ($p=0.001$). ERK1/2 antagonist of PD98059 failed to reverse NRG1β induced improvement in cognitive ability ($P < 0.05$).

Conclusion: Our findings indicate that NRG1β improves both spatial and associative learning and memory in Aβ-induced AD independently of ERK1/2 signaling.

Key words: NRG1β, Amyloid Beta, Rats, Alzheimer disease, Erk1/2 antagonist, Spatial memory

P-164

Effect of acute administration of quinidine, dextromethorphan and combination of dextromethorphan/quinidine on pentylenetetrazole (PTZ)-induced clonic and tonic seizure thresholds in mice

Hassan Jamali[1,2], Azhdar Heydari[2,3], Sayyed Morteza Vaghefi[1,2]

1. Student Research Committee, Kashan University of Medical Sciences, Kashan, I.R. Iran
2. Physiology Research Center, Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, I.R. Iran
3. Department of Physiology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, I.R. Iran

Background and Objective: Dextromethorphan (DM) as a non-opioid antitussive has neuroprotective effects. Combination of DM with quinidine decreases rapid metabolism of DM to dextrorphan (DX). The aim of the current study was to investigate the effects of acute administration of quinidine, DM and combination of dextromethorphan/quinidine (DM/Q) on pentylenetetrazole (PTZ)-induced clonic and tonic seizure thresholds in mice.
Materials and Methods: Male NMRI mice (25-30 g) were used in this study. Different doses of DM (5, 10, 25 and 50 mg/kg), quinidine(10, 20, and 30 mg/kg) and DM/Q (5/20, 10/20, 25/20, and 50/20) were administrated 30 min before the seizure induction. Intravenous infusion of PTZ was used to induce seizure induction and latencies to the occurrence of general clonus and tonic hind limb extension were recorded and converted to the seizure threshold dose.
Results: Quinidine at dose of 30 mg/kg significantly increased the threshold of tonic seizure ($P<0.05$). DM at doses of 25 and 50 mg/kg significantly increased threshold of clonic ($P<0.05$) and tonic($P<0.001$) seizures. DM/Q at dose of 50/20 mg/kg significantly decreased the threshold of clonic and tonic seizures ($P<0.001$).
Conclusion: The results of the present study confirm the previous reports that some doses of DM have anticonvulsant effect. Different effect of DM on clonic and tonic seizure thresholds may represent the different sensitivity of forebrain and hindbrain seizure circuitry to DM. Also, decreased effect of DM in the presence of quinidine may also be due to a change in the metabolism of DM.
Keyword: Dextromethorphan, Quinidine, Pentylenetetrazole, Seizure

P-165

Study of molecular Changes in the CA1 region following beta-amyloid injection in rat entorhinal cortex; Protective role of calcium blockers.

Hamid Gholami Pourbadie[1], Marzieh Joneidi[1], Fariba Khodagholi[2], Fatemeh Shaerzadeh[2]

1. Department of Physiology and Pharmacology, Pasteur Institute of Iran, Tehran, Iran
2. Neuroscience Research Center, Shahid Beheshti Beheshti University of Medical Sciences, Tehran, Iran.

Background and aims: Alzheimer's disease (AD) is a progressive brain disorder that is associated with dementia. The entorhinal cortex is one of the first brain regions affected in AD. High level of beta-amyloid proteins (Aβ) is seen in various brain regions, including the entorhinal cortex. Previous studies have shown that beta-amyloid causes calcium dyshomeostasis. In this study, molecular changes in the CA1 region following microinjection of beta-amyloid into the entorhinal cortex and the potential protective role of calcium channel blockers were investigated.
Methods: Beta-amyloid was injected into the entorhinal cortex of male Wistar rats under stereotaxic surgery, and then a guide cannula was planted in the right ventricle. Isadapine and Nemodipine (calcium channel blockers) were injected intraventricularly at 30 µg daily for 6 days. On the seventh day, the expression of Calpain 2, Caspase 12 and 3 in CA1 was measured by western blot technique. Pro-apoptotic changes were also assessed by Tunnel test.
Results: Our results indicated that beta-amyloid injection in the entorhinal cortex increased the expression of Calpain 2, Caspase 12 and 3 in the CA1 region. Apoptotic cells also increased in the CA1 region following amyloidopathy in the entorhinal cortex. Following the treatment of the rats with isradipine and nometidipine, the expression of Calpain 2, Caspase 12 and 3 decreased, and the number of apoptotic cells was returned to the control level.
Conclusion: injection of the beta-amyloid into the entorhinal cortex may change the molecular profile associated with apoptosis in neighbor regions such as CA1 and treatment with calcium channel blockers can prevent this change.
Key words: Alzheimer's disease, entorhinal cortex, calcium channel blockers, CA1

P-166

Evaluation and In vitro imaging of Amyloid-β Plaques in the Brain Sections of Alzheimer's Patients Using a Novel Peptide Radiotracer

Safura Jokar[1], Mostafa Erfani[2], Mohammad Sharifzadeh[3], Davood Beiki[4]

1. Department of Radiopharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
2. Radiation Application Research School, Nuclear Science and Technology Research Institute (NSTRI), Tehran, Iran.
3. Department of Toxicology and Pharmacology, Faculty of Pharmacy; Toxicology and Poisoning Research Centre, Tehran University of Medical Sciences, Tehran, Iran.
4. Research Center for Nuclear Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Background and Objective: Alzheimer's disease (AD) is recognized as one of the most prevalent causes of dementia that about 46 million worldwide people suffer from dementia (in 2015). Also, it is predicated, this number will arrive to quadruple by 2050. According to pathophysiology evidence, amyloid-β (Aβ) plaques are considered as one of the principal pathological hallmarks of AD in the brain. Therefore, the development of new radiotracers for Aβ plaques imaging can be useful for the detection of AD. With respect to these findings, we designed and synthesized a derived peptide of Aβ42 C-terminal sequence and radiolabeled with technetium-99m for imaging of Aβ plaques.
Materials and Methods: This peptide analog was successfully synthesized using the fmoc solid-phase method. The radiolabeling conditions were optimized and the stability studies were performed in plasma serum and cysteine. Moreover, binding affinity assay of the radio-peptide to formed Aβ aggregation was measured. To further assess and verify the affinity to Aβ plaques, autoradiography and imaging studies were applied in post-mortem AD brain sections.
Results and Conclusion: The candidate peptide was prepared with a high yield (more 95%). Radiochemical purity (more 95%) obtained at an optimal condition of a 50µg peptide and demonstrated high stability against ligand exchange after 24h. The obtained results of the affinity assay showed that this radio-peptide has a suitable affinity for Aβ aggregations as well as these findings were confirmed by autoradiography and imaging studies.
Conclusion: Our results illustrated that this radiotracer may be valuable in the diagnosis of Aβ plaques in AD animal models.
Keywords: Brain Imaging, Neurodegeneration, Peptide, Technetium-99m

P-167

Evaluating the Effects of Chronic Administration of Natural Honey on the Development of Morphine Dependence in Rats

Fazli Shojai E., Najafi M., Charkhpour M.

Background: According to the previous studies, the exact mechanism of dependence on opioids and withdrawal syndrome has not been fully understood.
Aim This study was aimed to evaluate the effects of chronic administration of natural honey on the development of morphine dependence in male rats.
Materials and methods: Honey was prepared from Tarom Oliya region in Zanjan province. Experiments were performed on male Wistar rats weighing 225-275 g, randomly divided into 6 groups (n=8). The study groups included morphine group, the three doses of morphine plus honey group (at doses of 200,400 and 800 mg/kg, i.p.), the morphine plus vehicle group, and the saline group. The subcutaneous injections of additive doses of morphine were used for 9 days to create morphinedependency. On the 9th day, one hour after the morning dose of morphine, naloxone (4mg/kg, i.p.) was injected, and symptoms of withdrawal syndrome were assessed for 60 minutes. Then, blood samples were taken to measure TNF-α. One-way ANOVA and Tukey tests were used to compare the results. P- Value of <0.05 was considered as statistically significant.
Results: The results of this study showed that intraperitoneal injection of honey at 3 doses (200, 400 and 800 mg/kg with $p<0.001$) could significantly decrease the total score of the symptoms compared to the morphine-vehicle control group. NHO could significantly decrease TNF-α at dose of 400 mg/kg.
Conclusion : The results indicated that chronic administration of NHO had beneficial effects in reducing symptoms of morphine withdrawal syndrome, and this effect is probably due to the anti-inflammatory effect caused by the flavonoids in honey.
Keywords: Morphine, Dependency, Withdrawal Syndrome, Natural Honey, Total Withdrawal Score, TNF-α

P-168

Investigating the anxiety like behaviour and Nrf2 gene expression during crystal meth addiction in male rats who were under treatment with buprenorphine

Akram sadat Kholghi[1], Hatami Homeira[1*], Hossein Pour Feizi Mohammad Ali[1], Nazli Khajenasiry[2]

1. Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.
2. Department of Biological Sciences, Faculty of Basic Sciences, Higher Education Institute of Rab-Rahid, Tabriz, Iran

Background and Objective: Anxiety is one of the most prominent psychiatric complaints of methamphetamine (MA) users. Buprenorphine has been shown to be a potent partial mu- (μ) receptor agonist and delta- (δ) receptor antagonist. Nuclear factor erythroid 2-related factor 2 (Nrf2), is a transcription factor. Nrf2 regulates the expression of antioxidant proteins that protect against oxidative damage triggered by injury and inflammation. Study the changes of Nrf2 level and investigating the effect of crystal meth and buprenorphine on anxiety like behaviors are the aim of this project.
Material and Methods: 49 male Wistar rats were randomly assigned into seven experimental groups (n=7): Control, Saline, Methamphetamine (10 mg/kg, i.p. for 5 days), Buprenorphine (6 and 10 mg/kg, i.p.), Methamphetamine + Buprenorphine (6 and 10 mg/kg for 14 days). Anxiety was studied by elevated plus maze. The tissue of cerebral hemisphere was assayed for the expression of Nrf2 receptor gene using RT- PCR.
Results: Administration of crystal meth decreased ($p<0.001$) and buprenorphine increased ($p<0.05$) open arm exploration in the elevated plus maze. The expression of the Nrf2 genes in the crystal meth group decreased ($p<0.001$). Gene expression of Nrf2 increased in buprenorphine ($p<0.05$).
Conclusion: Administration of crystal meth alone was anxiogenic in rats .The administration of buprenorphine was anxiolytic in rats. Alteration of Nrf2 gene expression during addiction indicating the oxidative condition of nervous system.
Key Words: Crystal meth, Buprenorphine, Nrf2 gene expression

P-169

Anti-nociceptive and anti-inflammatory effects of Ferulago angulata

Valiollah Hajhashem[1], Samira Rafieian Kopaei[1], Seyed Ebrahim Sajjadi[2]

1. Department of Pharmacology and Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Pharmacognosy, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Background and Objective: Ferulago angulata belongs to Apiaceae family and has high flavonoid content. This study was aimed to evaluate anti-nociceptive and anti-inflammatory effects of essential oil, hydro-alcoholic and phenolic extracts of Ferulago angulata aerial parts. Also analysis of the components of essential oil and measurement of total phenol and flavonoid contents of extracts were the other objectives.
Materials and Methods: Essential oil and plant's extracts were prepared according to standard methods. Acetic acid, hot plate and formalin tests were used to investigate anti-nociceptive effects. Additionally, carrageenan and croton oil tests were used to evaluate anti-inflammatory effects.
Results: Ferulago angulata aerial parts yielded 0.2% (v/w) yellowish essential oil. The Gas Chromatography/Mass Spectrometry (GC-MS) analysis of essential oil, identified 82 compounds which represented 98.9% of the essential oil. Thymol (7.9%), spathulenol (6.5%), trans-anethol (6.4%), myristicin (5.1%) and alpha-pinene (4.5%) were the main components. In acetic acid and formalin tests, the essential oil, hydro-alcoholic extract and phenolic extract showed significant ($P<0.001$) anti-nociceptive effect. In hot-plate test, morphine which was used as standard drug, revealed significant anti-nociceptive effect while the plant extracts and essential oil were ineffective. High dose of the extracts and essential oil in croton oil test ($P<0.001$) and high dose of hydro-alcoholic extract and phenolic extract in carrageenan test ($P<0.05$) reduced the inflammation.
Conclusion: Ferulago angulata extracts and essential oil have anti-nociceptive and anti-inflammatory effects. However, further studies are needed to clarify their mechanisms of actions.
Keywords: Anti-inflammatory, Anti-nociception, Essential oil, Ferulago angulate

P-170

The effects of thymoquinone on cognitive and hippocampal long-term potentiation in thioacetamide - induced hepatic encephalopathy in rat

Hajipour S[1], Sarkaki A[2], Farbood Y[2], Dianat M[2], Rashno M[3], Khorsandi LS[4]

1. Ph.D by Research Student of Neurosciences, Physiology Research Center.Ahvaz Jundishapur University of Medical Sciences, Ahvaz- Iran.
2. Dept. of Physiology, Physiology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz- Iran.
3. Department of Immunology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
4. Department of Anatomical Sciences, Cellular & Molecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz. Iran

Introduction. Hepatic encephalopathy (HE) is a severe neuropsychiatric syndrome associated with liver disease, impairment of cognitive function and decreased quality of life. The experimental model of HE was made by thioacetamide (TAA). Thymoquinone (TQ), the main active compound of Nigella sativa seeds has various pharmacological properties. The aim of this study was to assess the effects of TQ on spatial cognition and hippocampal long-term potentiation (LTP) in rats with hepatic encephalopathy.
Materials & Methods: male Wistar rats (200 ± 20 g) were randomized in six groups: 1) Control; received normal saline. 2) HE; received TAA (200 mg/kg). 3) HE + TQ5. 4) HE + TQ10. 5) HE + TQ 20 (mg/kg, i.p. for 7 days after HE induction. 6) the rats received antagonist of NMDA receptors. HE was induced by intraperitoneal injection of TAA (200 mg/kg) once every two days for consecutive 14 days. Spatial memory was evaluated in a Morris water maze (MWM), LTP was recorded from hippocampal dentate gyrus region. The data were analyzed using repeated measures two-way ANOVA followed by Tukey's post hoc test and $p < 0.05$ was assigned as significant difference.
Results. The data showed that HE weakens the brain LTP followed by cognitive impairment ($p<0.01$). TQ could improve significantly hippocampal LTP as well as cognition as dosage dependent ($p < 0.01$).
Conclusion: Our results confirm that TQ exhibits therapeutic potential to improve cognitive and brain electrical performance in an experimental model of HE which may be mediated through the combined antioxidant properties of TQ.
Keywords. Hepatic encephalopathy; Thioacetamide; Thymoquinone; Spatial memory; Rat

P-171

Changed Evoked Excitability of CA1 Pyramidal Neurons of Hippocampus in the Valproic Acid Rat model of autism

Razieh Hajisoltani[1,2], Narges Hosseinmardi[2], Mahyar Janahmadi[1,2]

1. Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Autism spectrum disorder (ASD) is a neurodevelopmental disorder which could be due imbalance of excitatory and inhibitory neurotransmission in certain part of brain including hippocampus. Considering the role of altered neuronal properties in neurodevelopmental disease including ASD, investigating the underlying the precise cellular mechanisms of alternation of the neuronal activity may help to develop possible novel targeted therapies for the treatment of ASD.
Materials and Methods: The evoked firing characteristics of CA1 pyramidal neurons in adult rats prenatally exposed to VPA (VPA, 500mg/kg, on embryonic day 12.5) were examined using whole cell patch clamp recording under current clamp condition and the results were compared with control groups.
Results: Prenatally exposed to VPA caused changes in evoked firing properties in response to 100-300 pA depolarizing current pulses. Our results showed that significant decrease in the peak amplitude of action potential, decay tau, and maximum rise slope when compared to control groups ($P<0.05$), as well as a significant increase in the half width, rise tau, and area under curve of action potential ($P<0.05$).
Conclusion: Prenatally exposed to VPA altered electrophysiolocal properties, our findings indicated that induction of autism was associated with change in evoked neuronal activity.
Keywords: Valproic Acid, Autism, Hyperexcitability, CA1 pyramidal neurons, Rat

P-172

Effects of lithium carbonate and ceftriaxone on recovery after spinal cord injury in rats

Bohloul Habibi Asl, Kiarash Fekri, Mohammad charkhpour, Moslem najafi, Sona Tabean

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Glutaminergic system is one of the important systems that is activated during spinal cord injuries (SCI). Ceftriaxone, a cephalosporin antibiotic, attenuates the activity of glutaminergic system. On the other hand, lithium carbonate, which is effective in mood stabilization, acts as a neuroprotective agent. The aim of this study was to investigate the effects of lithium carbonate and ceftriaxone on motor impairments induced by lumbar SCI in rats.
Materials and Methods: Fifty male rats were randomly divided into five groups as follows:
a) No surgical or pharmacological intervention; b) SCI treated by normal saline; c) SCI treated by lithium carbonate; d) SCI treated by ceftriaxone; e) SCI treated by ceftriaxone and lithium carbonate. After general anesthesia, SCI was induced by weight-dropping method. After finishing the period of pharmacological treatment, open field test was performed in order to investigate the motor impairments. Hind limb motor function was assessed using Basso, Beattie and Bresnahan (BBB) scale.
Results: The results indicated that ceftriaxone and lithium carbonate were effective in improving motor impairments on their own ($P<0.01$). But co-administration of these medications did not show any synergistic effects.
Conclusion: Although ceftriaxone and lithium carbonate seem to be effective in improving motor impairments but co-administration of them did not show any synergistic effects. These results are from an experimental model and validation is required for further investigation.
Keywords: Lithium Carbonate, Ceftriaxone, Spinal Cord Injury (SCI), Motor Impairments, Rat.

P-173

Irisin and neural differentiation in rat model of Parkinson’s disease

Hossein Hassanpour, Moslem Riyahi

Department of Basic Sciences, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran.

Background and Objective: Parkinson’s disease (PD) is a neurodegenerative disorder characterized by degeneration of the nigrostriatal dopaminergic neurons. Irisin is a novel myokine that produced by proteolytically processed from the FNDC5 (Fibronectin type III domain-containing protein 5). Our goal in this study was to investigate the effect of irisin on neural differentiation in the striatum of Parkinson's disease (PD) rats model. In this study, administration of irisin at 0.7 nmol/L significantly increased the nestin expression in the striatum of PD rats ($P<0.01$), so it could attenuate motor defects of the PD rats by increasing the number of dopaminergic neurons.
Materials and methods:Thirty adult Sprague Dawley male rats were randomly divided into 5 groups: control, positive control, irisin 7000 nmol/L, irisin 70 nmol/L, irisin 0.7 nmol/L. Irisin administration was peformed everyday for 12 weeks. PD was developed by unilateral intrastriatal microinjection of 6-hydroxydopamine (6-OHDA) in the striatum. PD induction was proved by elevated body swing test. The striatal expression of nestin was analyzed as the neural precursor marker by Real-time PCR.
Result: The expression of nestin gene as marker of neuron development significantly increased in irisin 0.7 nmol/L group compared with positive control ($p<0.01$) whereas other concentration of irisin did not differ with controls ($p>0.05$).
Conclusion: It seems that irisin through enhancing the expression of nestin gene as a neural and axonal development marker could expand the number of dopaminergic neurons and ameliorated the motor defects of the PD rats.
Keywords: Irisin, nestin, Parkinson’s disease, Real-time PCR

P-174

Activation of 5-HT1A receptors modulates hippocampal theta activity: Relevance to Alzheimer's disease

Soheila Hosseinzadeh[1,2*]

1. Neuroscience Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran
2. Department of Physiology, School of Medicine, Babol University of Medical Sciences, Babol, I.R Iran

Background and Objective: Hippocampal theta activity is related to spatial information processing. Serotonin from the medial raphe nuclei (MRn) desynchronizes theta activity through the modulation of synchronicity evoked in several relays of the synchronizing ascending system (SAS), a network of nuclei extending from the brain stem reticular formation to the septum and the hippocampus. Serotonin neurotransmission is tightly regulated by autoreceptors, 5-HT1A receptors, known to act through negative feedback inhibition at the cell bodies of the raphe nuclei.
Materials and Methods: We targeted the MRn with 5-HT1A receptor agonist, 8-OH-DPAT (4 µg/0.5 µl saline) during training testing in Morris maze. 192 IgG-saporin, a selective cholinergic immunotoxin, (1µl/ PBS) administrated 10 days before behavioral studies. hippocampal EEG activity was recorded through dorsal hippocampus. The theta band power (4–12 Hz) was divided into three sub-bands: low- (4–6.5), high- (6.5–9.5), and maximum-(9.5–12) frequency theta activity. The relative power were compared using an ANOVA and Tukey's test post hoc.
Results: 8-OH-DPAT injections in the animals trained under ICV administration of 192 IgG Saporin produced an increased expression of high-frequency theta activity concurrent with the facilitation of place learning in the Morris maze. Search strategies made by this groups predicted a 12% better performance as compared with the strategy choices made by 192 IgG-Saporin-lesioned animals.
Conclusion: Non-cholinergic septohippocampal neurons might be more important in serotonin-induced modulation of hippocampus-dependent memory processing and SAS-relay site may be a good candidate for the physiological mechanisms of the regulation of hippocampal rhythmicity and learning efficiency.
Keywords: Hippocampal EEG; 5-HT1A serotonin receptor; Learning; 192 IgG-saporin

P-175

Co administration effects of the cisplatin and vitamin E on anxiety behavior in male rats

Masoud Hoseinzadeh[1], Amir Alizadeh[2], Parniaan Heydari[2], Marzieh Kafami[3], Mustafa Ghanbarabadi[3], Batool Shakiba[2]

1. Department of Physiology and Pharmacology, School of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran.
2. Student Research Committee, Sabzevar University of Medical Sciences, Sabzevar, Iran.
3. Cellular and Molecular Research Center, Department of Physiology and Pharmacology, Faculty of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran

objectives: Cisplatin (cis-di ammine di chloro platinum (II)) is a widely-used platinum-based chemotherapeutic agent which has dose-limiting side-effects. Anxiety is one of its side effects that could disrupt the person's life. In present study we assess the protective effects of vitamin E (Vit E) on anxiety induced by cisplatin.
Methods: twenty-eight rats were randomly allocated to 4 groups (n=7 for each group) and were used as follows: (1) control, (2) cisplatin (2 mg/kg/7day, i.p), (3) cisplatin+ Vit E (200 mg/kg/7day, i.p), (4) Vit E (200 mg/kg/7day, i.p). The anxiety-associated behavior was evaluated by using elevated plus maze test after one week and data were analyzed using SPSS.
Results: Cisplatin significantly decreased the percentage of open arms entry (OAE) ($p < 0.01$), as well as decreased the time spent in the open arms (OAT) ($p < 0.05$) of the elevated plus maze. We evaluated the percentage of close arms entry (CAE) and time spent in the close arms (CAT). It has shown that cisplatin significantly increased close arms entry (CAE) in compare to groups supplementation with vitamin E ($p < 0.05$).
Conclusion: Our findings have shown that Vit E decline the anxiety behavior induced by cisplatin.
Key words: Vitamins E, Cisplatin, Anxiety, Elevated plus maze test

P-176

Comparison of duration time effects of systemic hypoxia on the hypoxic brain in rats

Fezzeh Hossienzadeh

Faculty of Medical Sciences Sarab, Sarab, Iran

Background and Objective: Hypoxia is one of the important factors that cause blood-brain barrier rupture and degeneration of tight junction proteins. This present study, designed to compare the duration of the effect of systemic hypoxia on tight junction proteins in the brain hypoxia.
Materials and Methods: Adult male Wistar rats were divided into acute and chronic control groups, acute and chronic hypoxia groups. Then control groups kept in the air room and hypoxic groups stayed in the normobaric hypoxic chamber (O2 11-10%) for two (acute) or ten (chronic) days. Effects of hypoxia on occludin, ZO-1 protein, MMP9 levels were assessed using western blotting.
Results: Western blot analysis revealed that occludin and Zo-1 protein expression significantly decreased in chronic hypoxia compared to acute hypoxia. The MMP9 protein levels significantly increased in acute hypoxia compared to chronic hypoxia.
Conclusions: Degeneration of tight junction proteins is time-dependent of hypoxia. It seems to increas MMP9 protein levels may be one of the important mechanisms responsible for this damage.
Key words: occludin, blood brain barrier, tight junction

P-177

The effect of cerebrolysin on recognition memory impairment and oxidative stress in D-galactose-Induced Senescence in Mice

Leila Hosseini[1,2], Ehsan Pourmemar[1], Alireza Majdi1, Morteza Haramshahi[1], Mahnaz Talebi[1], Pouran Karimi[1], Saeed Sadigh-Eteghad[*1]

1. Neurosciences Research Center (NSRC), Tabriz University of Medical Sciences, Tabriz, Iran
2. Student Research Committee, Tabriz University of Medical Sciences, Tabriz-Iran

Background and Objective: Cerebrolysin (CBL), a neurotrophic factor, is considered as pro-cognitive therapeutic approach for management of cognitive deficits. We aimed to investigate the effects of intranasal (i.n.) or intraperitoneal (i.p.) administration of CBL on the d-galactose-induced oxidative stress and memory impairment in mice.
Materials and Methods: CBL (1, 2.5 ml/kg/i.p.) or (1 ml/kg/i.n.) were administrated daily in d-galactose-received (100 mg/kg/subcutaneous) mice model of aging for eight weeks. Recognition memory was assessed by the novel object recognition task. Brain and blood of animals were analyzed for oxidative stress biomarkers including malondialdehyde, total antioxidant capacity, glutathione peroxidase and superoxide dismutase.
Results: we found that treatment with 2.5 ml/kg/i.p. and 1 ml/kg/i.n. doses reduced d-galactose impaired recognition memory. In addition, results showed an obvious increase in the antioxidant biomarkers and decrease in the malondialdehyde levels both in the blood and brain of aged mice in 2.5 ml/kg/i.p. dose, and only in the brain in 1 ml/kg/i.n. dose of CBL.
Conclusion: Our results showed that CBL could improve aging-induced oxidative stress and recognition memory deficit.
Keywords: Aging, Cerebrolysin, Oxidative stress, Memory, D-galactose

P-178

Simultaneous intrathecal injection of muscimol and endomorphin-1 alleviate neuropathic pain in rat model of spinal cord injury

Marjan Hosseini

Background and Objective: Due to the side effects of medications used for chronic pain, combination therapy seems to be an appropriate solution for the alleviation of chronic pain and reducing the side effects. The role of inhibitory GABA system is well proven in reducing neuropathic pain. Also, special attention has been focused on endogenous morphine in reducing chronic pain originate from damage to the nervous system. The purpose of this study is to investigate the analgesic effect of simultaneous administration of GABA agonist and endomorphinI. The role of oxidative stress, NR1 subunits of NMDA receptors and α2 subunits of GABA receptors in the spinal cord has also been investigated.
Materials and Methods: Spinal cord (T6-T8) was compressed. Three weeks after injury, drugs was injected individually or in combination. Mechanical and cold allodynia, thermal hyperalgesia and mechanical hyperalgesia were evaluated before injection and 15 and 60 min after injection. At the end, the spinal cords were prepared for histological evaluation. Results: Combination therapy significantly increased the pain threshold comparing to injection of endomorphinI or muscimol alone. Isobologram results showed that muscimol and endomorphinI additively increase the pain threshold. Histological studies indicate the increased expression of α2 subunits of GABA receptors and NR1 subunits of NMDA receptors in the spinal cord. The combination therapy also increased the glutathione and superoxide dismutase level and decreased the malondialdehyde levels in the spinal cord
Conclusion: Simultaneous administration of muscimol and endomorphineI could be a new candidate for alleviation of pain resulting from spinal cord injury.
Keywords: spinal cord injury, endomorphin-1, muscimol, chronic pain, central neuropathic pain

P-179

The effects of propranolol on cold allodynia, anxiety and nerve conductive velocity following L5 spinal nerve ligation in rats

Mehdi Hosseini[1], Mohammad Ali Zabihian[1], Zahra Bahari[*2], Farideh Bahrami[2], Zohreh Jangravi[3]

1. Students' Research Committee, Baqiyatallah University of Medical Sciences, Tehran, Iran
2. Department of Physiology and Medical Physics, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran
3. Department of Biochemestry, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran

Background and Objective: Neuropathic pain (NP) is one of forms of chronic pain and arises from peripheral or central nerve damage. One of an important complication of NP is an evoked pain sensation to innocuous stimuli (allodynia). Although ample studies have attempted to elucidate pathophysiological mechanisms of NP, however, the exact mechanism is far from clear. Adrenergic system has a critical role in modulation of NP. The purpose of the current study is to evaluate therapeutic potential of propranolol (β-adrenoceptors antagonist), on cold allodynia and anxiety in L5 spinal nerve ligation (SNL) model of NP. Additionally, we assay the effects of propranolol on sciatic nerve conductive velocity (NCV) in neuropathic rats.
Material and Methods: NP was induced by ligation of L5 spinal nerve. Intracerebroventricular injection (right side) of propranolol (20 µg/5µl) were started on day induction of NP and continued until 6 days' post-surgery. Cold allodynia (using acetone drop) and anxiety (using Elevated Plus Maze) evaluates on 2, 4 and 6 days' after SNL. NCV examines on day 10 after SNL (using extracellular field potential recording).
Results: In the present study QNP induced significant cold allodynia on 2, 4 and 6 days after neuropathy. Moreover, NP reduces NCV of sciatic nerve. Furthermore, microinjections of propranolol could significantly suppress cold allodynia and anxiety like behaviors on 4 and 6 days after neuropathy. Additionally, propranolol could significantly improve NCV of sciatic nerve.
Conclusion: Our findings indicate that propranolol and inhibition of β-adrenoceptors likely have a therapeutic effect against NP.
Key Words: Neuropatic pain, SNL, Adrenoceptors, Allodynia, Anxiety, NCV

P-180

The effects of crocin on long-term potentiation of the CA1 of hippocampus in rats under chronic restraint stress

AazadehAlsadat Hosseini Dastgerdi*, Maryam Radahmadi, Ali Asghar Pourshanazari

Department of Physiology, School of Medicine, Isfahan University of Medical Sciences

Background and Objective: Stress dramatically affects long-term potentiation (LTP) as cellular mechanism of memory. In addition, crocin indicated as the active constituents of saffron for enhancement of memory. This Study investigated effect of different dose of crocin on long-term potentiation in the CA1 of hippocampus in rats under chronic restraint stress.
Materials and Methods:32 male Wistar rats were randomly allocated to four different groups (n=8): Control, Stress (restraint stress as emotional stress; 6h/day for 21 days), two groups receiving daily intraperitoneal injections of crocin (30 and 60 mg/kg) accompanied by a period of 21 days restraint stress. The LTP was recorded from the CA1 while stimulating the schafer colatral pathway. LTP was induced by 100 Hz tetanization and field excitatory postsynaptic potential (fEPSP) slope and amplitude were measured 120 minutes after LTP induction in experimental group.
Results: Results revealed that stress significantly ($P<0.001$) decreased the slope and amplitude of fEPSP after LTP induction. In addition both doses 30 and 60 mg/kg of crocin significantly ($P<0.001$) improved these LTP parameters in stressed group. Although, the dose of 30 mg/kg crocin no significantly showed more beneficial effects than dose 60 mg/kg in stressed group.
Conclusion:It is concluded that doses 30 and 60 mg/kg of crocin had beneficial effects on improvement of LTP as cellular mechanism of memory in emotional stress conditions. Moreover, it seems that the low dose (30 mg/kg) of crocin was found capable of reversing the harmful effects of chronic emotional stress slightly better than high dose (60 mg/kg) of crocin.
Keywords: Stress, CA1, Long-term potentiation; Crocin, Rat

P-181

The effect of crocin and exercise on long term potentiation in rats under chronic unpredicted stress

Hajaralsadat Hosseini Dastgerdi, Maryam Radahmadi, Parham Reisi

Department of Physiology, School of Medicine, Isfahan University of Medical Sciences

Background and Objective: Unpredicted stress is one kind of destructive emotional stress that disturbs brain functions such as memory. Also, both crocin (as the main component of saffron) and exercise have been benefit effects on memory. The present study investigated the effect of crocin, exercise and crocin-accompanied exercise on long-term potentiation (LTP) as cellular mechanism of memory in rats under chronic unpredicted stress.
Materials and methods:40 male rats randomly allocated to five groups (n=8) containing: control, stress, stress-exercise, stress-crocin, and stress-crocin-exercise groups. Different kinds of stress (2h/day) was used for inducing of unpredicted stress for 21 days. Crocin (30 mg/kg) was injected intraperitoneally. Rats were forced to run on a treadmill (1h/day, 20-21 m/min). For evaluation of memory, the slope and amplitude of field excitatory postsynaptic potential (fEPSP) were measured for 90 minutes by using electrophysiological (such as LTP) method in experimental groups.
Results: Results showed that the slope and amplitude of fEPSP significantly decreased in the stress group. While crocin could significantly increase those in the stress-crocin and stress-crocin-exercise groups compared to the stress group. Also, the slope and amplitude of fEPEP after inducing of LTP decreased in the stress-exercise group compared to the stress-crocin group, whereas those increased in the stress-exercise-crocin group compared to the stress-exercise group.
Conclusion: It concluded that chronic unpredictable stress severity impaired memory. In addition, crocin treatment acted better than exercise on memory improvement in unpredictable stress conditions. Also, it is possible that memory improvement in crocin-accompanied exercise group was due to crocin but not exercise.
Keywords: Unpredictable stress, Crocin, Memory, LTP, Exercise, Rat

P-182

The effect of Acetyl L-Carnitine on ultrastructure of motoneuron synapses in adult rats with compressive spinal cord injury

Marjan Heshmati, Maryam Shareyeli, Mehran Jamali

Department of Anatomy and Pathology, Shahed University

Introduction: In this study, the effect of acetyl L-carnitine on ultrastructure of motoneuron synapses after spinal cord injury in adult rats was studied.
Materials and Methods: In this experimental study 16 adult Sprague Dawley rats weighing 250 to 300 grams were devided in to 4 randomized groups namely, A:laminectomy with daily intraperitoneal injection acetyl L-carnitine. B: laminectomy with daily intraperitoneal injection by saline ,C: group A + mechanical compression and D: group B+ mechanical compression. After 4 weeks they were sacricified for morphology study by light microscope and ultrastructure of synaptic zone of motoneurons by electronic microscope. The results statistic were analysed through commonly used methods and softwares.
Results: The morphological results indicated compression causes reduction of spinal cord motoneurons. Acetyl L-Carnitine decreased this reduction of motoneuron after spinal cord compression and preserved motoneurons ultrastucture in synaptic zone and mitochondria.
Conclusion: In this study acetyl L-carnitine was effective on preservation of ultrastructure of motoneuron synapses after mechanical compression on spinal cord. Of course, the measure of these changes in means of decreasing the effect of mechanical compression after spinal cord compression needs to further researches.
Keywords: Acetyl L-Carnitine, Spinal cord compression, synapse, ultrastructure, rat

P-183

Dexmedetomidine attenuates the induction and reverses the progress of 6-hydroxydopamine- induced Parkinsonism; involvement of KATP channels, alpha 2 adrenoceptors and anti-inflammatory mechanisms

Hashem Haghdoost-Yazdi, Azita Minaei

Cellular and Molecular Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

Corresponding author: Hashem Haghdoost-Yazdi. PhD, Cellular and Molecular Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

Background: Studies have shown that dexmedetomidine (DEX), a potent α2-adrenoceptors agonist provides neuroprotection through suppression of inflammatory response. In present study, we examined effect of DEX and its underlying mechanisms on the induction and progress of 6-OHDA- induced Parkinsonism in rat.
Material and Methods: The 6-OHDA was injected into the medial forebrain bundle of right hemisphere by stereotaxic surgery and then, behavioral tests carried out within second, fourth, sixth and eighth weeks post-surgery. All treatments were started before the toxin and continued to eight weeks afterwards. Striatal levels of dopamine, TNF-α and IL-6 were measured within the eighth week after the toxin by enzyme-linked immunosorbent assay kits.
Results: DEX at dose of 50µg/kg attenuated significantly the intensity of 6-OHDA- induced behavioral symptoms in the second week post-surgery. DEX also attenuated remarkably 6-OHDA- induced reduction in striatal dopamine level. These effects were also observed in rats treated by both DEX and yohimbine (YOH), a selective α2-adrenoceptors antagonist but were not observed in rats treated by both of DEX and glibenclamide (Glib), an ATP-sensitive potassium (KATP) channels blocker. DEX also reversed the progressive increase in intensity of the behavioral symptoms and reversed 6-OHDA- induced overproduction of TNF-α and IL-6. These effects were reversed by YOH but not Glib.
Conclusion: Our findings indicate that DEX attenuates the induction and reverses the progress of 6-OHDA- induced Parkinsonism through activation of KATP channels and α2-adrenoceptors, respectively. Through activation of α2-adrenoceptors, DEX also exerts anti-inflammatory effect which is possibly another mechanism underlying the DEX's antiparkinsonism effect.
Keywords: 6-OHDA, dexmedetomidine, KATP channels, α2-adrenoceptors, TNF-α, IL-6

P-184

Hepatocyte growth factor attenuates the severity of status epilepticus in kainic acid-induced model of temporal lobe epilepsy by targeting apoptosis and astrogliosis

Sobhan Haghani*[1], Nida Jamali-Raeufy[1], Tourandokht Baluchnejadmojarad[1], Mehrdad Roghani[2]

1. Department of Physiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Neurophysiology Research Center, Shahed University, Tehran, Iran

Objectives:Although drug therapy is the most common treatment for epilepsy,proper seizure control is not achieved with current medications.The present study was conducted to evaluate the protective effects of hepatocyte growth factor(HGF) in a rat model of temporal lobe epilepsy(TLE) and explore possible molecular mechanisms.
Materials and Methods: A rat model of temporal lobe epilepsy was established using intra-hippocampal injection of kainic acid(4 µg).Intra-cerebrovascular injection of HGF(6 µg)was performed 30 min before injection of kainic acid. Learning and memory impairment were investigated by behavioral tests.ELISA assay was used to determine astrogliosis and DNA fragmentation.Changes in neuronal density and mossy fiber sprouting were evaluated by Nissl and Timm staining,respectively.
Results: Behavioral assessments indicated that kainate treated rats showed spontaneous seizure and their alternation percentage scores in Y-Maze test were lower ($P<0.001$). Likewise,the passive avoidance test confirmed learning disability in Kainate treated rats($P <0.001$).HGF administration reduced the number of spontaneous seizures, alternation percentage score ($P<0.001$), and cognitive disturbances ($P<0.001$).The histopathological results also showed that HGF administration protected contributed to reduction of neuronal loss in the CA3 subregion of hippocampus and inhibited formation of aberrant mossy fiber sprouting (MFS) ($P<0.01$). Also, ELISA assay showed a significant decrease in GFAP ($P<0.01$), and DNA fragmentation ($P<0.05$) following HGF administration.
Conclusion: Our findings demonstrate the validity of HGF in protection against progression of the kainate-induced TLE in rats by improvement of learning, cognitive disturbances and inhibiting of apoptosis and astrogliosis.
Keywords: Hepatocyte growth factor; Temporal lobe epilepsy; Astrogliosis; Apoptosis; memory impairment

P-185

Okadaic acid attenuates short-term and long-term synaptic plasticity of hippocampal dentate gyrus neurons in rats

Background and Objective: Protein phosphorylation states have a pivotal role in regulation of synaptic plasticity and long-term modulation of synaptic transmission. Serine/threonine protein phosphatase 1 (PP1) and 2A (PP2A) have a critical effect on various regulatory mechanisms involved in synaptic plasticity, learning and memory. Okadaic acid (OKA), a potent inhibitor of PP1 and PP2A, reportedly leads to cognitive decline and Alzheimer's disease (AD)-like pathology. The aim of this study was to examine the effect of OKA on electrophysiological characteristics of hippocampal dentate gyrus (DG) neurons in vivo.
Materials and Methods: Male Wistar rats were divided into two control and OKA groups. OKA was injected intracerebroventricularly (i.c.v.) into lateral ventricles and after two weeks the longterm potentiation (LTP) and paired-pulse responses recorded from hippocampal perforant path-DG synapses in order to assess short-term and long-term synaptic plasticity.
Results: Results of this study revealed that OKA-induced inhibition of PP1 and PP2A activity drastically attenuates the field excitatory postsynaptic potential (fEPSP) slope and population spike (PS) amplitude following paired pulse and high frequency stimulation (HFS) of hippocampal DG neurons indicating pre- and post-synaptic involvement in electrical activity of these neurons. Administration of OKA impaired the short-term and long-term spatial memories conducted by Y-maze and passive avoidance tests, respectively. OKA-induced attenuation in electrophysiological activity and consequent memory deficits also provide a beneficial tool for studying neurodegenerative disorders such as AD.
Keywords: Okadaic acid, Protein phosphatase, Synaptic plasticity, Dentate gyrus

P-186

Cobalamin modulate neurotoxic effects of trimethyltin chloride on hippocampus neural cells and cognitive function

Zeinab Hamidizad[1] , Shima Ababzadeh[1,2], Fatemeh Heidari[1,2], Narges-al-Sadat Haeri[1], Mohsen Eslami Farsani[1,2], Mehdi Sadegh[3]

1. Cellular and Molecular Research Center, Qom University of Medical Sciences, Qom, Iran.
2. Department of Anatomy, School of Medicine, Qom University of Medical Sciences, Qom, Iran.
3. Department of Physiology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran.

Objective: Cobalamin (vitamin B12) is essential for metabolism of the nervous system and its supplementation attenuate neuropathic and neuroinflammatory diseases. We designed to investigate the neuroprotective effects of Cobalamin against the trimethyltin chloride (TMT) induced structural and functional damages in the hippocampus.
Methods: Adult male Wistar rats were divided into four groups: 1) control: received saline; 2) TMT: received a single dose of TMT (8mg/kg; ip) to induce hippocampal damages; 3) Cobalamin: received Cobalamin (18mg/kg; ip) for five consecutive days and 4) TMT+Cobalamin: received single ip injection of TMT then were treated with Cobalamin for five consecutive days. In day six of the experiments, behavioral effects of TMT and Cobalamin were evaluated through shuttle box and novel object recognition task. After the behavioral tests, animals were perfused transcardially and Nissl staining was used on hippocampus to assess neural cell damages.
Results: Novel object exploring time was significantly decreased in TMT treated rats and treatment with Cobalamin after TMT injection significantly recompensed this effect of TMT. In passive avoidance, TMT significantly decreased latency to enter the dark box, while Cobalamin administration after the TMT injection significantly abolished this effect of TMT. Neural cell counted in the areas of hippocampus was significantly decreased in the TMT group and Cobalamin treatment after the TMT injection significantly prevented neural cell loss.
Conclusion: These results indicate a neuroprotective role for Cobalamin against the TMT induced memory impairment and hippocampal neuronal loss.
Keywords: Avoidance memory, Neurotoxin, Novel Object, Vitamin B12

P-187

The role of orexin receptor 1 of basolateral nucleus of amygdala in the orexin-induced analgesia

Soghra Bornedeli[1], Roghaieh Khakpay[1], Fatemeh Khakpai[2], Mohammadali Hosseinpour-Feizi[1]

1. Department of Animal Science, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.
2. Cognitive and Neuroscience Research Center (CNRC), Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

Background and Objective: Orexin A, a hypothalamic neuropeptide, modulates pain sensation and perception via orexin receptors type 1 and 2 (OXR1 and OXR2). OXR1s and OXR2s have been identified in the amygdala. Furthermore, the amygdala plays a key role in the pain modulation. Therefore, this study was designed to investigate the role of OXR1s of basolateral nucleus (BLA) of amygdala in the inflammatory pain modulation via orexin A in the male rats.
Materials and Methods: In this study, male Wistar rats in the range of 230-270 gr were used. In order to study the effect of intra-BLA microinjection of orexin A in the pain modulation, cannulation of BLA nucleus was performed. Primarily, vehicles and/or drugs were injected into the right BLA nucleus, and 10 minutes later 50 µl of 2.5% formalin was injected into the left rat's hind paw; and then, formalin-induced flinches, flexing and licking behaviours were recorded for 60 min.
Results: The results of the current study showed that intra-BLA injection of orexin A attenuated both the first and the second phases of formalin-induced flinches and licking behaviours. Pretreatment of BLA nucleus by orexin 1 receptor antagonist (SB334867) counteracted the antinociceptive effect of orexin A on the formalin-induced licking behaviour in the both phases of formalin test; and even induced hyperalgesia in the second phase of licking behaviour.
Conclusion: According to the results of this study it can be concluded that the intra-BLA injection of orexin A induces moderate analgesia which is probably mediated by orexin receptor 1.
Keywords: Analgesia, Basolateral nucleus of amygdala, Orexin receptor 1, SB334867.

P-188

Investigating the effects of estrogen on physical or psychological stress-induced learning and memory impairments, explorative and anxiety like behaviours in female rats

Mina Khaleghi[1], Mohammad Khaksari[1], Mohammad Shabani[2], Hamideh Bashiri[1], Mohammad Amin Rajizadeh[1]

1. Department of Physiology and Endocrine and Metabolism Research Center, Kerman University of Medical Sciences, Kerman, Iran.
2. Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.

Background and Objective: Stress is a common problem in daily life affecting different aspects of individual lives. Stress plays an important role in the development of cognitive impairment. Many studies have reported that women are more susceptible to stress than men. On the other hand, the protective role of female sex hormones, especially estrogen, has been proven in stress disorders. Although some of the beneficial effects of estrogen on stress-related disorders have been studied, there are few studies on its effects on physical and psychological stress in laboratory animals. Therefore, in this study we seek to determine whether the different models of stress (physical and psychological) can act differently on ovariectomised rats (OVX) with low levels of estrogen and the effect of estrogen on physical or psychological stress-induced learning and memory impairments, explorative and anxiety like behaviors in female rats.

Method: Intact and OVX female rats were used in the present study. The rats were anesthetized combining dosage of Ketamine and Xylosine. Then, both ovaries were eliminated and two weeks after surgery the animals entered the study. Then, animals were exposed to physical and psychological stress for 1h/7 days and the cognitive function was evaluated using passive avoidance (PA) tests. Open field test was performed for evaluation of anxiety-like behaviors and motor function.

Result: Intact and OVX female of both physical and psychological stress had an increased anxiety- like behavior and decreased explorative behavior in open field test in comparison to female control rats. Female of both physical and psychological stress had an impaired PA learning and memory in shuttle box in comparison to the control group. Estrogen increased explorative behavior, learning and memory and decreased anxiety-like behavior.

Conclusion: In general, it can be concluded that estrogen can reduce physical and psychological stress-induced cognitive impairments.

Key words: Anxiety; Explorative behavior; Learning and memory; Estrogen; Physical stress; Psychological stress

P-189

Nicotine administration during adolescence alters the pain perception and neural response of ventrolateral periaqueductal gray matter to formalin injection

Fatemeh khaluzade, Hossein Azizi, Saeed Semnanian

Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.

Background and Objective: Nowadays tobacco smoking is recognized as a leading risk factor for morbidity and mortality worldwide. The initiation of smoking primarily occurs during adolescence which is a critical developmental phase characterized by specific alterations in neurobehavioral features. The ventrolateral periaqueductal gray (vlPAG) constitutes a major descending pain modulatory system. In this study, the long lasting effects of adolescent nicotine exposure on pain perception and vlPAG neuronal responses to formalin injection were investigated during adulthood.

we aimed to investigate long lasting effect of adolescent nicotine exposure on pain perception and the effect of adolescent nicotine treatment on vlPAG neuronal responses to formalin injection during adulthood.

Method: In this regard adolescent rats, postnatal days 28-42, received nicotine or saline and after 30 days of washout period formalin test performed. In the next part of study in vivo extracellular single-unit recording was used for investigating vlPAG neuronal responses to formalin injection.

Results: The results demonstrated that adolescent nicotine exposure amplifies pain related behaviors in formalin test. Nicotine administration also diminished the extent of inhibitory response of vlPAG neurons to formalin injection into the hind paw. It also changed the histogram pattern of inter-spike intervals in recorded signal.

Conclusion: Collectively, this study demonstrates long lasting effect of nicotine exposure on pain related behaviors and vlPAG neuronal response to formalin injection. So, this may alter the pain modulatory systems and subsequent response to painful stimuli.

Keywords: Adolescent nicotine exposure, Formalin test, Extracellular single unit recording, vlPAG, Rat

P-190

The anti-inflammatory effects of Saliva macrosiphon methanol extract in experimental model of acute inflammation

Aryan khani[1] ,Sara khani[2], Najmeh Sadghi[3],Hassan ali abedi[4], Afsaneh Ranjbar[5*]

1. Medical student , Tehran university of medical science , Tehran , Iran
2. Medical student , Shiraz university of medical science , shiraz , Iran
3. Dep of physiology , Jahrom university of medical science , Jahrom , Iran
4. Dep of physiology ,Jahrom university of medical science , Jahrom , Iran
5. Dep of physiology , Jahrom university of medical science , Jahrom , Iran

Introduction: There are several reports on the therapeutic effects Saliva macrosiphon in traditional medicine such as anti inflammatory , antiromathid , antinocieptive , antimicrobial and diuretic. This study investigated the anti inflammatory effects of this Plant in experimental model of acute inflammatory as compare to Sodium Salicylate.
Methods: The paw edema of rats was induced by subcutaneous injection of 0.1 ml of 5% carrageenan .The anti inflammatory activity was assessed with paws volume changes four hours after injection of carrageenan. Saliva macrosiphon extract were prepared using percolation method. Different doses of extract (500/1000/2000 mg/ kg i. p) and sodium Salicylate (300 mg/kg i. P) were given .
Findings:The result indicated that dose 2000 mg/ kg i. p of extract and sodium salicylate had anti inflammatory effect than control group ($P<0.05$).
Conclusion: It seems that Saliva macrosiphon could inhibit acute inflammatory response.
Key words: Saliva macrosiphon extract- anti- inflammatory effect - Sodium Salicylate

P-191

The analgesic effects of Saliva macrosiphon methanol extract in presence and absence of Atropine & Naloxone in male rat

Aryan khani[1] ,Sara khani[2], Najmeh Sadghi[3],Hassan ali abedi[4], Afsaneh Ranjbar[5*]

1. Medical student, Tehran university of medical science , Tehran , Iran
2. Medical student , Shiraz university of medical science , shiraz , Iran
3. Dep of physiology , Jahrom university of medical science , Jahrom , Iran
4. Dep of physiology , Jahrom university of medical science , Jahrom , Iran
5. Dep of physiology , Jahrom university of medical science , Jahrom , Iran*

Background and Objective: In this study the effects of Saliva macrosiphon methanol extract on pain in presence and absence of atropine (muscarinic receptor antagonist)and naloxone (opioid receptor antagonist)were investigated.
Methods: The methanol extract of Saliva macrosiphon were prepared using percolation method. Various doses of extract (500/1000/2000 mg/ kg i. p) and sodium salicylate (300 mg/kg i. P) were injected . The analgesic activity was assessed using formalin test in presence and absence of atropine (2mg/kg i. P)and naloxone (1.6mg/kg i. P).
Results: Dose 2000 mg/ kg i. p of Saliva macrosiphon methanol extract and Sodium Salicylate had analgesic effect than control group in formalin test ($P<0.05$).Also, the analgesic effect of this extract was decreased by atropine and naloxone ($P<0.05$).
Conclusion: These finding suggest that saliva macrosiphon methanol extract induces its inhibitory effect on pain that may be via muscarinic and opioid receptors.
Key words: Saliva macrosiphon extract- pain- sodium salicylate, atropine , naloxone

P-192

ANRIL potentially regulates NTF3 expression level in hypoxia

Fatemeh Khani-Habibabadi[1], Mohammad Javan[2], Mohammad Ali Sahraian[3], Mehrdad Behmanesh[1*]

1. Genetics Department, Biological Science Faculty, Tarbiat Modares University, Tehran, Iran
2. Physiology Group, Medical Science Faculty, Tarbiat Modares University, Tehran, Iran
3. Multiple Sclerosis ResearchCenter, Tehran University of Medical Sciences, Tehran, Iran

Background: Multiple sclerosis is an autoimmune disorder mediated by activated lymphocytes leads to myelin sheet degradation and physical disabilities. Hypoxia is related to Multiple sclerosis pathogenesis. In Hypoxia HIF-1a activation leads to triggering inflammatory pathways by induction of TNF expression. This hypoxia-inflammatory condition leads to disease aggregation and further damages. Accumulating data suggest regulatory roles for lncRNAs. For instance, by binding to the YY1 transcription factor, ANRIL lncRNA could regulate gene expression. In the promoter region of Neurotrophin 3 (NTF3), there are two conserved transcription factor binding sites for YY1. NTF3 controls the survival and differentiation of neurons. Hence, a correlation could be considered between these two genes. Here, the role of hypoxia on the regulation of ANRIL and NTF3 was surveyed. Methods: U-87 cell line, which is derived from microglioma tumor, were treated by 150 µM CoCl2 for 24 hours to induce hypoxia. Then, RNA was extracted and the first strand of cDNA was synthesized using M-MLV Reverse Transcriptase. The gene expression level was analyzed by qRT-PCR. Results: In microglia, ANRIL lncRNA was upregulated significantly under the hypoxia condition (4.7 fold, p= 0.0008). Consistently, hypoxia induction leads to upregulation of NTF3 mRNA level (10.2 fold, p= 0.001). Discussion: In hypoxic milieu, upregulation of ANRIL is simultaneous with a rise in NTF3 level. Considering the regulatory role of ANRIL in gene expression through binding to YY1 transcription factor and the existence of YY1 binding site on NTF3 promoter region, probably ANRIL could regulate the NTF3 expression in hypoxia condition.
Keywords: ANRIL; NTF3; YY1; Hypoxia

P-193

The effect of nobiletin on behavioral and histological alterations in a model of Parkinson's disease induced by intranigral injection of lipopolysaccharide in the rat

Maryam Khorasani[1], Marzieh Fakour[1], Reihane Ghasemi Tarei[1], Sedigheh Keshtkar[1], Zahra Kiasalari[2], Mehrdad Roghani[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran Iran
2. Neurophysiology Research Center, Shahed University, Tehran, Iran

Background and Objective: Anti-inflammatory property of nobiletin, a compound in citrus fruit's peel, has been shown. Besides, neuroinflammation is involved in triggering and progression of neurodegenerative disorders such as Parkinson's Disease (PD). The purpose of this study was to determine the effect of nobiletin on behavioral and histological changes in an experimental model of PD induced by intranigral injection of lipopolysaccharide (LPS) in rats.
Materials and Methods: In this study, to generate PD model, 5µg of LPS was injected into right midbrain of rats through stereotaxic surgery. Nobiletin was administrated daily for one week after the surgery at a dose of 10 mg/kg p.o. via gavage. Behavioral changes were evaluated by Y maze, Elevated plus maze, Passive avoidance, Novel object recognition, Forced swimming, and Rotational tests. For histological assessments, number of dopaminergic neurons was counted.
Results: Findings of this study demonstrated that administration of nobiletin to parkinsonian rats induced by LPS resulted in a significant decrease in the number of rotations and immobility time, and an insignificant decrease in percentage of alternation and significant increase of novel object discrimination and insignificant increase in the percentage of open arm spending time. Also, nobiletin treatment prevented loss of dopaminergic neurons.
Conclusion: Nobiletin treatment alleviated motor asymmetry and caused improvement of learning and memory and depressive like disorder in PD model induced by LPS and part of its beneficial effect is mediated via its neuroprotective effect.
Keywords: Parkinson Disease, Nobiletin, Behavioral changes, Lipopolysaccharide, Dopaminergic

P-194

Potential role of intra-accumbal orexin-1 receptors in the acquisition of methamphetamine-induced conditioned place preference in the rats

Elahe Khosrowabadi, Abbas Haghparast

Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Background and Objective: Studies have shown the role of nucleus accumbens (NAc) in reward-related behaviours and also orexinergic system is critically involved in reward processing. In the present study, we tried to investigate the effects of bilateral administration of SB334867, as an orexin-1 receptors antagonist into the NAc on the acquisition of methamphetamine-induced conditioned place preference (CPP) in the rats.
Materials and Methods: Thirty-three adult male Wistar rats (220–250 g) were entered in a CPP paradigm. Bilateral microinjections of different doses of SB334867 (1, 10 and 30 nM/0.5 DMSO) into the NAc were done 10 min before subcutaneous injection of methamphetamine (1 mg/kg) during 5-day conditioning (acquisition) phase. The CPP scores and locomotor activity of animals were recorded by video tracking system and Ethovision software.
Results: The results demonstrated that intra-accumbal microinjections of 10 and 30 nM solutions of SB334867 markedly decreased the acquisition of methamphetamine-induced CPP in a dose-dependent manner.
Conclusion: It seems that orexin-1 receptors in the NAc are involved in the development of methamphetamine-induced CPP and might be a potential therapeutic role in development of drug seeking behaviors in the rats.
Keywords: Reward, Orexin receptors, Nucleus accumbens, Methamphetamine, Acquisition, Conditioned place preference, Rat

P-195

Current trends of Mesenchymal Stem Cells in regenerative medicine; an efficacious treatment

Mahsa Bazargan

Background and objectives: Regenerative medicine is related to tissues or organs renewal. Human stem cells identifying as a potentiated cell that has the ability to proliferate, regenerate or repair damaged tissue. Mesenchymal stem cells (MSCs) are multipotential stem cell which can differentiate into multilineage cells that can be derived from adipose, muscle, placenta, skin and etc. MSCs have abundant features to regulate many acts in the immune system for the treatment of many diseases.
Research method: Published articles were accomplished from PubMed, Google Scholar, Wiley, Springer, Science Direct and Elsevier from 2012 to March 2019. Entirely, 45 articles were found and reviewed.
Results: MSCs acquire distinguish features, for instance, multilineage potential, secretion various anti-inflammatory mediators and have an immunoregulatory effect in the immune system. These properties distinct MSCs from other stem cells in cell replacement therapy and degenerative disorders. Nowadays MSCs application for many aspects of tissue engineering and regenerative medicine like bladder tissue, Muscle and dental tissue regeneration. Also, orthopedic injuries healing and Hear scar repair after the attack is another aspect of cell therapy application.
Conclusion: Current breakthrough investigation in MSCs and varied properties in proliferation, differentiation, Safety, and secretion many immunomodulatory mediators have made these cells as a favorite choice for future cell therapy in regenerative medicine.
Key Words: Regenerative medicine, Mesenchymal stem cell, cell therapy, Immunomodulation.

P-196

The effect of ointment containing Honey and Achillea millefolium and Nigella sativa oil on the process of treatment of wound and scald

Sina Jamali[1], Reza Aghaei[2]

1. DVM and the Club of Young Scientists Academician of Islamic Azad University of Shabestar Branch
2. Assistant Professor and Faculty Member of Islamic Azad University,Shabestar Branch

Background and purpose: Based on the recent researches,treatment and restoration of wounds remains one of the major challenges. The current stady was carried out based on styptic,antiinflammatory,antioxidant and antimicroorganism proved properties of the intended compounds used in the intended ointment.
Materials and Methods: In this experimental study,48 male Wistar rats with the average weight of 250-300gr were selected. Initially,the rats were anaesthetized with ketamine and xylazine , and at the back of 24 rats , grade2 circle scald to a diameter of 2cm and at the back of 24 rats , the wound to a diameter of 2 cm in size ,were created.Then each group was divided into control group(healing process to normal state)and treatment group(healing process with the mentioned ointment),which measurement of the wound surface and quantification of the level of Hydroxyproline in the urine was done randomly on days 7,14,21.The data were analyzed using the SPSS software
Results: Based on the results,the diameter of the wonds in the treatment group was significantly reduced compared to the control group.So that in the time span of 14-21,the tretment group had a meaningful difference with control group, and the amount of Hydroxyproline in the treatment group has a meaningful differece with cotrol group.
Keywords:wound,scald,Honey,Achillea millefolium , Nigella sativa

P-197

Wound healing potency of PCL/GEL nanofibers containing biologically produced Te NPs

Mohsen Doostmohammadi[1], Hamid Forootanfar[1*], Alieh Ameri[1], Elham Jafari[2], Hamid Reza Rahimi3, Mojtaba Shakibaie[1]

1. Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
2. Pathology and Stem Cells Research Center, Kerman University of Medical Science, Kerman,Iran

Background and Objective: Production of wound dressing materials with special charactersitics such as good 3D dressing, drug delivery potency, antibacterial effects, ability to moisture the wound are of great interest. Here in this study we developed a scaffold with ECM like stracture containing tellurium nanoparticles (Te NPs) with antioxidant effects and investigate the healing potency of as prepared nanofibers on wistar rat.
Materials and Methods: Nanofibers were prepared by electrospinning of polycaprolactone/gelatin solutionscontaining different concentrations (1, 1.5, 3%) of biologically produced Te NPs. Thirty rats were randomly devided to 5 groups: negative control, positive controle received CICALFATETM, and treatment groups receiving PCL/GEL/Te NPs 1%, 1.5% and 3%. The animals were sacrificed with chloroform after 14 days and the wounds with peripheral tissues were removed, fixed in formalin 10% and used for antioxidant tests analysis and histopathological examination.
Results: According to oxidative stress tests, the as prepared scaffolds showed dose dependant antioxidant effects. MDA level of group receiving PCL/GEL/Te NPs 3% was significantly lower than control. The treated groups have scanty of granulation tissue regarding to the dose of Te NPs (table 1). The inflammation state of PCL/GEL/Te NPs treated fibers was nearly equal to the positive control group. Also it was showed that the produced fibers had positive effects on collagen formation and horizentalization of collagen fibers.
Conclusion: Our results strongly demonstrate the wound healing potency of nanofibers containing 3% Te NPs by improving collagen formation and horisentaliation, reducing inflammation and induction of antioxidant effects.
Keywords: Wound healing; Nanofibers; Electrospinning; Oxidative stress

P-198

Trigonelline ameliorates liver dysfunction and neutrophil infiltration following a challenge of carbon tetrachloride in the mouse

Amir Rostami[1], Vahid Khodashenas[2], Mehrdad Roghani[3]

1. School of Medicine, Shahed University, Tehran, Iran.
2. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
3. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective: Liver damage is a prevalent complication due to viral infection and anti-pyretic agents. Carbon tetrachloride (CCl4) challenge is associated with liver injury. Trigonelline could protect tissues against some toxins. This study was conducted to evaluate protective effect of trigonelline following a challenge of CCl4 in the mouse.
Materials and Methods: NMRI mice were allocated to control, CCl4, and CCl4 groups pretreated with trigonelline at doses of 25 or 100 mg/kg. For induction of liver injury, CCl4 (10 ml/kg, i.p.) was used. After 1 day, mice were deeply anesthetized and measurement of liver biomarkers including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) was performed in addition to measurement of myeloperoxidase activity (MPO) as a valid index of neutrophil infiltration.
Results: Our findings showed that trigonelline at a dose of 100 mg/kg (not at a dose of 25 mg/kg) significantly reduces serum ALT and AST and lowers hepatic activity of MPO following CCl4 challenge.
Conclusion: It is concluded that trigonelline could reduce liver dysfunction and neutrophil infiltration following a challenge of carbon tetrachloride in the mouse.
Keywords: Liver injury, Carbon tetrachloride, Trigonelline, Neutrophil infiltration

P-199

Use of Mesenchymal Stem Cells as a suitable model for tissue engineering of rat kidney

Samira Shahraki[1], Abolfazl Khajavi Rad[1,2], Maryam M.Matin[3], Alireza Ebrahimzadeh Bideskan[4], Mohammad Aslzare5, Sara Hosseinian[1,2], Zahra samadi noshahr[1], Somayyeh Mahzari[1] , mahnaz allahyari[1]

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
3. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
4. Department of Anatomy and Cell Biology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
5. Urology and Nephrology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

The aim of this study was to acquire an effective method for preparation of rat decellularized kidney scaffolds capable of supporting proliferation and differentiation of Adipose tissue derived mesenchymal stem cell (Ad-MSCs) into kidney cells. We compared two detergents, the Sodium dodecyl sulfate (SDS) and triton X-100 for decellularization. The efficiency of these methods was assessed by Hematoxylin and Eosin (H&E), 4', 6 diamidino-2-phenylindole (DAPI) and immunohistochemistry (IHC) stainings. In the next step, Ad-MSCs were seeded onto the SDS-treated scaffolds were assessed after 3 weeks of culture. Proliferation and differentiation of Ad-MSCs into kidney-specific cell types on these scaffolds were then analyzed by H&E and IHC stainings. The histological examinations revealed that SDS was more efficient in removing kidney cells at all times plants as compared with triton X-100, in the SDS-treated sections the native extracellular matrix was more preserved than the triton-treated sections. The expression of laminin was completely preserved during decellularization procedure using SDS. cell attachment in the renal scaffold was observed after reccelularization. Furthermore, differentiation of Ad-MSCs into epithelial and endothelial cells was confirmed by expression of Na-K ATPase and Vascular endothelial growth factor receptor 2 (VEGFR-2) in seeded rat renal scaffolds respectively. Our findings illustrated that SDS was more effective detergent for decellularization of rat kidney compared with triton X-100 and indicate optimized method for decellularization and recellularization of rat kidneys to create functional renal natural scaffolds. These natural scaffolds supported the growth of Ad-MSCs and could induce their differentiation into epithelial and endothelial cells.
Key words: kidney, extracellular matrix scaffold, decellularization, recellularization, mesenchymal stem cells

P-200

Evaluation of antioxidant potential and wound healing activity of topical formulation of Heliotropium bacciferum extract in rat

Hadis Fathalipour[1], Hamid Forootanfar[2], Payam Khazaeli[2], Atefeh Ameri[2], Mohsen Doostmohammadi[2], Mira Mehrabani[2], Elham Jafari[3]

1. Sudent Research Committee, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran
2. Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
3. Pathology and Stem Cells Research Center, Kerman University of Medical Science, Kerman, Iran

Background and Objective: Wound healing is a dynamic process that happens in tissue under skin. Research shows a relationship between stress oxidative and wound healing, in inflammation, NOX activation is intensified which makes it to able produce excessive of ROS and finally inflammation and cellular damage is exacerbated. Also these factors make wound healing process delay. In this study, the medicinal plant which is called Heliotropium bacciferum has antioxidant effect and because of that and some anti-bacterial, anti-inflammatory effects, these factors make healing process happen sooner.
Materials and Methods: The herbal plant was collected and identified by pharmacognosist. The plant was then dried and hydroalcoholic extract was prepared by maceration method. The typical phytochemical tests were done and the related topical formulation was prepared by incorporating 2.5%, 5% and 10% of the prepared extract to suitable vehicle base. The wound healing activity was investigated on rats divided into
five groups of CICALFATE (standard), Sham, and three test groups of 2.5%, 5%, and 10% w/w of extract (formulation) after induction of wound. After 14 days, tissue was removed and analyzed for histopathological change and evaluation of oxidative stress. Data were analyzed using SPSS software.
Results: In histopathological examination, the group under treatment of formulation 5% concentration is better than standard. The prepared formulation represented suitable stability and released profile.
Conclusion: The obtained results of the present work showed suitable wound healing effect of topical formulation of Heliotropium bacciferum which need further investigations to found about related molecular mechanisms.
Keywords: Heliotropium bacciferum, stress oxidative, wound healing

P-201

Effect of Caw vitreous humour on wound healing in diabetic wistar rat

Mohammadimehr Sara[1], Lari Roya*[2], Fereidoni Masoud[3]

1. M.Sc. Student, Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad,
2. Iran.
3. Assistant Professor, Department of Biology, Faculty of Science, Ferdowsi University of Mashhad,
4. Mashhad, Iran.
5. Professor, Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran.

Background and Objective: The characteristic of diabetic ulcers is delayed wound healing due to persistent inflammation and excessive production of reactive oxygen species. In this study, the vitreous humour of Cow eyes was used as a biological dressing. The reasons for using the Cow vitreous humour are the availability of this tissue, its resistance to microbial contamination and, most importantly, being a source of collagen and hyaluronic acid, which their effects on wound healing are well known. Currently, vitreous has been considered as biological waste.
Materials & Methods: 35 streptozotocin-Induced diabetic rats (Wistar, male) were randomly divided into five groups. At the back of each mice, three of 6 mm diameter wounds were created. In each mouse, wounds were treated with; betadine as a control group, central and posterior vitreous dressing. Macroscopic and microscopic studies of wounds were performed on days 1, 3, 5, 8 and 14.
Results: Macroscopic studies indicated that at day 1 there were no significant effects on the vitreous treated wounds compared to the control group. On the third day, both central and posterior vitreous significantly reduced the diameter of the wounds ($p<0.05$), but such effect was not observed on the fifth, eighth and fourteenth days.
Conclusion: Although, the effects of collagen and hyaluronic acid are visible in the first stage of wound healing, in the phase of angiogenesis, the effect of vitreous dressing is not observed. It can be due to the presence of relatively high vitamin C in the vitreous.
Keyword: Vitreous humour, diabetic wound healing, hyaluronic acid, collagen

P-202

The efficacy of a traditional medicine preparation on second-degree burn wounds in rats

Nasser Ebrahimpour[1,2], Mehrnaz Mehrabani[1], Maryam Iranpour[3], Zeinab Kordestani[1], Mitra Mehrabani[4], Mohammad Hadi Nematollahi[5], Mahboobeh Raeiszadeh[6], Mehrzad Mehrbani[4*]

1. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Department of Traditional Medicine, Faculty of Traditional Medicine, Kerman University of Medical Sciences, Kerman, Iran
3. Pathology and Stem Cell Research Center, Kerman University of Medical Sciences, Kerman, Iran
4. Herbal and Traditional Medicines Research Center, Kerman University of Medical Sciences, Kerman, Iran
5. Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
6. Department of Traditional Pharmacy, Faculty of Traditional Medicine, Kerman University of Medical Sciences, Kerman, Iran

Objective: Aim of present study was evaluating the healing effect and related underlying mechanisms of Lime Salve in a model of deep second-degree thermal burn in male Wistar rats.
Materials and method: L.S was made up of a combination of refined calcium hydroxide powder, beeswax and sesame oil and its quality control was assessed. A deep second-degree burn was created by a hot plate in 48 male Wistar rats. Afterwards, they were randomly divided in four groups including normal saline (C group), L.S (T group), basement of formulation (B group) and silver sulfadiazine (S group). On days 5, 10, 17 and 24, the wounds were digitally photographed and after sacrifice of the rats, skin samples were obtained for performing qRT-PCR, immunohistochemistry staining and histological examination.
Results: L.S prominently augmented the wound closure rate, neovascularization on day 10 and collagen formation on day 17 and 24 in comparison with the C group. Furthermore, the Salve-exposed specimens showed a significant higher epithelialization with a peak on day 24. qRT-PCR also showed that on day 10, VEGF and TGF-β1 genes were significantly higher in the T group as compared with the C group. Also, MMP-9 and MMP-2 had a significant peak of expression on day 17 and rapid reduction of expression on day 24. Expression levels of IL-6 and TNF-α peaked on day 10 in the T group, followed by a progressive reduction until the end of the examination.
Conclusion: L.S could effectively accelerate the healing process of deep second degree burn wounds.
Keywords: Lime Salve; Rat; Burn Wound; Traditional Iranian Medicine; Calcium Hydroxide

P-203

The Combination of ATP and Trolox Improves human Sperm Quality after Cryopreservation

Bahareh Ebrahimi, Sara Keshtgar

Department of physiology, Medical school, Shiraz University of medical Sciences, Shiraz, Iran

Introduction: Cryopreservation of human spermatozoa in liquid nitrogen is usually used for long-term sperm storage. Unavoidably this process is accompanied by a reduction of viable and motile sperm, acrosomal lost and decrease of fertilization potential. Other disadvantages are damage to the cell and mitochondrial membrane, reduction in ATP production, and excess ROS production. In this study, we investigated the effects of Trolox and ATP combination on sperm quality.
Materials and methods: Forty human semen samples were washed with Ham's F10 and diluted (10 × 106 sperm/ml). The samples were divided into fresh and cryopreserved groups. Each group was allocated to control, vehicle, Trolox and ATP (2.5 mM and 200µM, respectively). Sperm motility was assessed by sperm analyzer, the percent of live sperm and membrane integrity was evaluated by eosin staining and hypoosmotic swelling test, respectively. ROS production was estimated using the luminescent method.
Results: Sperm cryopreservation reduced sperm quality, however, ROS production was decreased and total and progressive sperm motility increased after addition of Trolox and ATP. Sperm straight-line velocity, the percent of viable sperms, and sperm with intact membranes were increased by this treatment in cryopreserved-thawed sperm.
Conclusion: Trolox and ATP have no effect on normal fresh sperm, but thawed sperm quality improved by the effect of Trolox and ATP combination. Prevention of oxidative stress and sperm stimulation by ATP are two proposed mechanism for these findings.

P-204

The antidiabetic activities of new 1,2,3 triazol compounds as dipeptidyl peptidase-4 (DPP4) inhibitor in a rat diabetes model

Melika Ebrahimi, Samaneh Hosseinpour, Seyyed Abbas Tabatabai, Nima Naderi

School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Diabetes mellitus is becoming the main severe public health problem. Amongst antidiabetic medications affect hormone secretion, inhibitors of dipeptidyl peptidase type 4 (DPP-4 inhibitors) showed a good hypoglycemic effect along with an acceptable safety and tolerance. In this study, the effect of a newly synthesized DPP-4 inhibitor (confirmed by enzyme studies, encoded HF) was evaluated using a subacute model of type 2 diabetes.
Materials and Methods: Twenty-four male wistar rats (200-250 g) were fed with high fat diet for two weeks. A single administration of streptozocin (STZ; 35 mg; i.p.) followed another two weeks high fat diet caused a fasting blood sugar (FBS) above 140 mg/dl in the rats. Then, rats were randomly divided into four groups (n = 6 in each group). In two treatment group, HF (5 or 10 mg/kg) was administered once a day by oral rout (gavage) and a positive control group received sitagliptin (2 mg/kg p.o.) and the control group received saline solution (1 ml/kg) daily for 14 consecutive days. FBS levels were measured at the onset of therapy, one week and two weeks after treatment was initiated.
Results: The results show that HF (both 5 and 10 mg/kg) and also sitagliptin significantly reduced FBS compared with the control group. No significant difference in FBS was found between the three treatment groups.
Conclusion: Our results suggest that the compound HF could be considered as a hypoglycemic agent act through DPP-4 inhibition.
Keywords: DPP-4 inhibitor, diabetes mellitus, sitagliptin, rat

P-205

Modification of curcumin by lysine amino acid and encapsulation in nano-niosomes for its use in cancer treatment

Najmeh Alsadat Abtahi[1*], Fardin Rahimi[2], Bibi Fatemeh Haghiralsadat[3],javad zavar reza[2]

1. Department of Biochemistry and Molecular Biology Faculty of Medicine ShahidSadoghi University of Yazd.
2. Research Center for New Technologies in Life Science Engineering, University of Shahed, Tehran, Iran.
3. Medical Nanotechnology&Tissue Engineering Research Center, Yazd Reproductive Sciences Institute,Shahid Sadoughi University of Medical Sciences, Yazd.

Introduction: Cancer, also known as a malignant tumor or malignant neoplasm, is a group of 150 diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body(1). It is known that breast cancer is the most common cancer for women worldwide(2). To date, chemotherapy has been the most frequently used treatment for breast cancer. Although chemotherapy may suppress of cancer cells, its acute toxicity, poor solubility and adverse side-effects limited its usage (3). Natural anticancer drug has significantly lower toxicity, safe and easily available. Curcumin (Cur) is one of such products. Curcumin, an active component of turmeric, is also an anticancer agent which was reported to be able to suppress and treat various types of malignancies.
Curcumin (C21H20O6) is a natural yellow compound which typically found in Curcuma longa that is regarded as a natural polyphenolic antioxidant presented in many kinds of herbs. Curcumin has been exhibited multiple therapeutic relevance including Anti-cancer, Anti-Inflammatory, Antioxidant, Antimicrobial, Anti-Rheumatic, and Hepatoprotective activities. In addition, poor absorption and rapid metabolism of curcumin severely limit its bioavailability (4,5,6). Niosomes are the particles that can solve the problems like that (7). The purpose of this research is to synthesize nano system that containing curcumin and modified by Lysine aminoacid with the aim of affecting Breat cancer MCF-7 cell line.
Materials & Method: We optimized Noisome formulations in terms of surfactant and cholesterol content. Afterward, the Novel Cationic Niosomal that were synthesized by Lysine aminoacide in ordre to attaining better transfection efficiency and improved stability. Then, new noisome and the effects of nanoniosome formulations on cytotoxicity were evaluated.
Results: Curcumin Encapsulation in nanoniosomes was more than 98% and the drug release rate from nanocarriers showed a controlled and acceptable profile. The mean Diameter of noisomes was smaller than 100nm and the Zeta potential of them was positive after modified by Lysine. Drug release rate from nanocarriers showed controlled and time dependent profile was 33% in 48h in normal cell situation (37c and PH7.4)
MTT result showed that noisome effect on cancer cell was more than normal cell in 4h.
Conclusion: In this study, a significant amount of curcumin encapsulated in niosomes and modified by Lysine .This carrier get more positive and healthier than used DOTAP. Cationic potential shows that nanocarriers can entire cells easily.
Keywords: Breast Cancer, Regeneration and therapeutics therapy, Nanobiotechnology

P-206

Effect of Losartan as AT1-Angiotensin II receptor antagonist on renal function and tissue changes after renal ischemia reperfusion in male and female rats.

Saeedeh Ahmadi[1], Aghdas Dehghani[2], Samin Nahavandi[2]

1. Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2. Department of Physiology, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Background and objective: Renal ischemia reperfusion (RIR) is a clinical injury. According to the regulatory sex-dependent effects of renin–angiotensin system (RAS) on renal function, Administration of losartan can improve post-ischemic renal function by inhibition of Angiotensin 1(AT1) receptor. Therefore, this study evaluates the effects of losartan on renal injury caused by renal ischemia reperfusion in male and female rats.
Material and Method: 60 male and female Wistar rats were divided into 6 groups (3males and 3 females) including ischemic group in the absence (Isch group) and presence of losartan (Lisch group) and sham group. Bilateral ischemia was performed for 45 minutes in all the groups except sham group. Lisch group received losartan interaperitoneally 2 hours before ischemia and after 24 hours of reperfusion, blood samples were collected for serum analysis. Also, left kidney was hemogenated to evaluate NO and MDA and right kidney was placed in formalin (10%) in order to assess pathological tissue changes.
Results: Serum level of BUN and creatinine In Lisch and Isch groups increased significantly compared to sham group but in male Lisch rats, inhancement of BUN was more than females compared with Isch group. Also, serum NO increased in Lisch group in comparison with Isch group. However, serum level of MDA exhibits no difference in all groups. Ischemia results in renal injury in both sexes.
Conclusion: Losartan in Isch group could alleviate renal function in female which indicated the protective effect of NO system in female rats during ischemia.
Keywords: Renal ischemia reperfusion (RIR), renin–angiotensin aldosterone system (RAS), angiotensin II receptor type 1(AT1)

P-207

Effects of Nitroglycerin on Renal Ischemia-Reperfusion Injury in adult male Rats

Saeed Hajihashemi[1], Fatemeh Ahmadi[2], Ali Rahbari[3], Fatemeh Ghanbari[4]

1. Assistant professor of Physiology, Department of Physiology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran
2. MSc in Physiology, Arak University of Medical Sciences, Arak, Iran
3. Assistant Professor of Pathology, Department of Pathology, Arak University of Medical Sciences, Arak, Iran
4. Assistant Professor of Pharmacology, Department of Pharmacology, Islamic Azad University of Arak, Arak, Iran

Background and Objective: Ischemia-reperfusion (I-R) leads to acute kidney injury (AKI). The present study investigated effects of nitroglycerin (NG) on improving renal dysfunctions caused by I-R in rats.
Materials and Methods: Twenty-four rats were equally divided into four groups: (1) the control group, (2) the sham group, (3) the I-R group, and (4) NG-treated groups (50µg/kg) which were treated with NG after induction of IRI. AKI by I-R was induced through bilateral renal artery and vein clamping of both kidneys for 20 minutes followed by 24 hours of reperfusion.
Results: NG significantly increased creatinine clearance levels and renal blood flow rate (which was reduced by I-R). NG also significantly improved serum electrolytes (sodium and potassium) that were disordered by I-R. In addition, NG significantly offset impaired antioxidant defense mechanism and inhibited lipid peroxidation.
Conclusion: These results show that post treatment use of NG had a protective effect on renal tissue against AKI caused by I-R. Antioxidant activity and decreased lipid peroxidation can be the main factors responsible for the protective effect of NG on renal function.
Key words : Nitroglycerin, Renal Ischemia-Reperfusion Injury, Rat

P-208

The Effect of Sodium Cromoglycate on Acetic Acid-induced Ulcerative Colitis in Rats

Gholamreza Houshmand[1], Jafar Nikbakht[2] , Sara Bayat[3], Zahra Ghafouri[4], Sara Assadpour[5]

1. Department of Pharmacology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
2. Department of Physiology and Pharmacology, School of Medicine, Yasuj University of Medical Sciences, Yasuj, iran.
3. Department of Internal medicine, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
4. Department of Biochemistry, Biophysics and Genetics, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
5. Molecular and Cell biology Research Center , Faculty of Medicine , Mazandaran University of Medical Sciences , Sari , Iran.

Background and Objective: Ulcerative colitis (UC) is a type of inflammatory bowel disease that involves the colon. Glucocorticoids and amino-salicylate have been used for UC treatment. In order to assess drugs with less side effects, we evaluated the effect of sodium cromoglycate (SCG) on acetic acid (AA) - induced ulcerative colitis in rats.
Materials and Methods: Animals were randomly divided into six groups and treated three days by oral gavage. Group I (control): received 1 ml saline intra-rectally, II: 1 ml saline intra-rectally following SCG (100mg/kg). G-III (UC control): 1 ml AA intra-rectally. G-IV and G-V: 1 ml AA intra-rectally following SCG (100mg/kg). G-VI: 1 ml AA intra-rectally following SSZ (100 mg/kg). On the 5th day, 1 ml of AA was instilled into the colon. After 72 hours (8th day), clinical activity scores were measured and sacrificed by cervical dislocation and colon was dissected out. Colon was flushed with saline and weighed. It was used for macroscopic scoring and histopathological estimations. The same procedure was performed in the remaining groups in 20th day.
Results: Treatment with SCG (100 mg/kg) significantly decreased macroscopic scores compared to the UC group ($P<0.05$) on the eighth day. SCG (100mg/kg) significantly decreased clinical activity score, gross lesion score, percent affected area and wet colon weight when compared to AA-induced controls on 7th day.
Conclusion: the present data suggests that the pre-treatment of SCG prevents AA-induced UC in rats and this protective effect may at least in part be due to its mast cell stabilizing properties.
Keywords: Sodium cromoglycate, Ulcerative Colitis, Acetic acid

P-209

Introducing a new protocol for immunofluorescence imaging of islets and Akt-2 and cAMP assay of beta cells in mice

Tohid Vahdatpour[1,2*] and Ali ashraafian[1]

1. Department of Physiology, Faculty of Animal and Veterinary Sciences, Shabestar Branch, Islamic Azad University, Shabestar, Iran
2. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Background and Objective: There are several techniques for the analysis of the beta cells indices and imaging. This research presents a new method based on the trial and error. Materials and Methods: Islets were isolated from the dissected pancreas and after being washed in Krebs-Ringer bicarbonate buffer solution with 0.2% BSA. Then, islets were digested with 0.025% trypsin for 5 min at 37°C and passed through a 400-mm wire mesh. The cells were then plated on coverslips that were coated with poly-l-lysine and maintained at 37°C in a 5% CO2 incubator for 24 h. After incubation in 5% BSA and 0.15% Triton X-100 blocking solution, the cells were incubated by primary antibodies for 1 h at 4°C, washed with PBS, and incubated again with the appropriate fluorochrome-conjugated antibodies for 1 h. Antibodies included guinea pig anti-insulin antibody, mouse anti-glucagon and anti-somatostatin antibodies. After being thoroughly washed with PBS, immunofluorescence images of islets were obtained base on minimal background under a total internal reflection fluorescence microscope. The extracted biomass were diluted in 10×volume of 0.1 M HCl, homogenized and centrifuged at 10000 rpm for 5 min. After incubation, the surface liquid used for cAMP lysates was measured using the direct cAMP EIA kit and then Akt2 according to the manufacturer's instructions. Results: This method is an efficient protocol with high transparency of imaging compared to the other methods. Conclusion: presented protocol can be implemented as a more effective method for monitoring secretory function and intracellular beta cell enzymes.
Keywords: Beta cells, Pancreas, Diabetes, Animal modeling

P-210

The effects of morphine on cultured mouse Sertoli cells: A possible mechanism of infertility in addicted men.

Fatemeh Asgharzadeh[1], Shiva Roshan-Milani[2,3], Kimia Ahmadi[2], Amin Abdollahzadeh fard[2], Morteza Motazakker[4], Ehsan Saboory[2,3] , Mohammad Amini[2]

1. Student Research Committee, Urmia University of Medical Sciences, Urmia, Iran
2. Physiology Department, Medical Faculty, Urmia University of Medical Sciences, Urmia, Iran
3. Neurophysiology Research Center, Urmia University of Medical Sciences, Urmia, Iran
4. Cellular and Molecular Research Center, Physiology Department, Urmia University of Medical Sciences, Urmia, Iran

Background and objective: The opioid system may exert positive direct and/or indirect effects on spermatogenesis at the levels of the central nervous system and at the testes/sperm levels. However, long term opioid use could be associated with several reproductive complications that place the users at risk of hypogonadism and even infertility. Nevertheless, less is known about the effect of exogenous opioids such as morphine on Sertoli cells. Therefore, the purpose of this study was to investigate the effect of different concentrations of morphine on Sertoli cells viability after 24 or 48 hours exposure periods.
Material and methods: The mouse TM4 Sertoli cells were cultured in DMEM-F12 medium. TM4 cells (5000/per well) were incubated in 100µL of the medium on a 96-well plate. TM4 cells were then exposed to 0.01, 0.1,1,10 and 100µM morphine for 24 or 48 hours (triplicate). The cellular viability was then assessed using MTT method.
Results: In the morphine-exposed cells, cellular viability decreased compared to control cells. The cellular viability in control cells was 100±1%, which significantly reduced to 72±3% in cells exposed to 100µM morphine($P<0.05$). Both of 24 and 48 hours exposure period decreased cell viability compared to control in a concentration-dependent manner but the results did not differ significantly depending on exposure duration.
Conclusion: Exposure to morphine significantly decreased Sertoli cell viability in a concentration-but not time-dependent manner. Therefore, morphine-induced Sertoli cell death, may be involved, at least in part, in infertility associated with opioid abuse. However more studies are needed to clarify this finding.
Keywords: Morphine, Sertoli cell, TM4, cell viability

P-211

Bee venom derived BBB shuttle and its correlation with oligodendrocytes proliferation markers in mice model of multiple sclerosis

Fatemeh Emami[1], Tannaz Daneshseta[1], Mohammad Hossein Nasr Esfahani[2], Kamran Ghaedi[3], Nazem Ghasemi[4], Mehdi Aliomrani[5*]

1. School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences and Health Services, Isfahan, Iran.
2. Department of Cellular Biotechnology, Cell Science Research Center, Royan Institute for Biotechnology, ACECR, Isfahan, Iran.
3. Cell and Molecular Biology Division, Biology Department, School of Sciences, University of Isfahan, Isfahan, Iran
4. Department of Anatomy, School of Medicine, Isfahan University of Medical Sciences and Health Services, Isfahan, Iran
5. Department of Toxicology and Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences and Health Services, Isfahan, Iran.

Introduction: Multiple sclerosis is a demyelinating disease with a functional disturbance in the immune system. It was shown that Apamin as a blood-brain-barrier shuttle acts as a Ca2+ activated K+ channels (SK channels) blocker. In this study, the effects of Apamin on oligodendrocytes differentiation markers were evaluated on an induced model of MS.
Material and Methods: Forty-four 8 weeks C57BL/6 male mice (22±5g) except normal control group subjects were fed with 0.2% (w/w) cuprizone pellets for 6 weeks. After cuprizone removal, mice were divided randomly into six groups. Apamin (100µg/kg/BW) was administered intraperitoneally as a co-treatment during phase I (demyelination) or post-treatment phase II (remyelination) twice a week. Mice were anesthetized, perfused with phosphate buffer saline (PBS) and fixed brain was coronally sectioned and the changes in oligodendrocytes markers such as Olig2, PDGFR-α, and BrdU incorporation were assessed by immunohistochemistry (IHC) method. Results were analyzed by one-way analysis of variance (ANOVA).
Results: The most preventive effect of Apamin was observed in co-treatment administration as compared to the post-treated group (95% of CI diff: 30.6-49.3, P value: 0.0001). Apamin exposure enhanced the immunoreactivity to Olig2 and PDGFR-α as a marker of oligodendrocyte precursor cells. In addition, cell proliferation due to BrdU incorporation was significantly elevated during the 2 weeks after cuprizone removal (P value= 0.01).
Conclusion: This study highlights the potential therapeutic effects of Apamin as a bee venom derived peptide on oligodendrocytes proliferation and elevation in myelin content in an oxidative induced multiple sclerosis model due to cuprizone exposure.
Keyword: Multiple sclerosis, Apamin, Olig2, Cuprizone, Apitherapy, BrdU, PDGFR-α

P-212

The protective and anti-apoptotic effects of zinc on morphine induced-Sertoli cells apoptosis: A probable therapeutic role for zinc

Fatemeh Asgharzadeh[1] , Shiva Roshan-Milani[2,3], Kimia Ahmadi[2], Amin Abdollahzadeh fard[2], Morteza Motazakker[4], Leila Chodari[2,3] , Mohammad Amini[2]

1. Student Research Committee, Urmia University of Medical Sciences, Urmia, Iran
2. Physiology Department, Medical Faculty, Urmia University of Medical Sciences, Urmia, Iran
3. Neurophysiology Research Center, Urmia University of Medical Sciences, Urmia, Iran
4. Cellular and Molecular Research Center, Physiology Department, Urmia University of Medical Sciences, Urmia, Iran

Background and objective: Morphine enhances apoptosis in testicular germ cells. Zinc reduces morphine-induced apoptosis of somatic cells. However, little is known about the effects of morphine on testicular Sertoli cells and the effects of zinc on morphine-induced testicular injury. This study, therefore, aimed to investigate the effect of zinc on cell viability in morphine-induced Sertoli cell toxicity.
Material and methods: The mouse Sertoli cells (TM4) were cultured in DMEM-F12 medium. TM4 cells were incubated in 100 µL of the medium on a 96-well cultured plate. The TM4 cells investigated in four main groups: morphine (23µM), zinc (8µM), pretreatment and control, in which cells were exposed to treatment containing medium for 24 hours. In pretreatment group, cells were incubated with zinc before morphine and in control group were only incubated with free medium. Their effects on TM4 cell viability was then investigated by MTT assay.
Results: Cell viability decreased in cells exposed to morphine, while exposure to zinc showed opposite effects. Pretreatment with zinc before morphine recovered morphine-induced anti-proliferative effects. The cellular viability of control cells was 100±1%, which significantly increased to 113± 5%, in cells exposed 8µM zinc ($P<0.01$). The cellular viability in cells exposed to morphine reduced to 86±2%, however, pretreatment with zinc recovered it to approximately control levels.
Conclusion: Zinc reduces the toxicity and pro-apoptotic effects of morphine on Sertoli cells. Inhibition of spontaneously or pathologically-induced apoptosis of Sertoli cells by zinc, suggesting a probable clinical importance and therapeutic effects of zinc on infertility in addicted men.
Keywords: Sertoli cell,TM4, Morphine, Zinc, apoptosis

P-213

Effects of Injections of Loratadine and Steroid Hormones into Hippocampus on Learning and Passive Avoidance Memory in the Rats

Zahra Azardar*, Homayoun Khazali, Abdolkarim Hosseini

Master Student of Physiology- Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Aims: Study of the effect of histamine antagonist on memory and learning, showed that the antihistamines have a different effect on memory and learning. Loratadine is a long acting antihistamine, that is H1 histamine receptor antagonist, and since the neurotransmitters in the steroid environment have a different physiological function, steroid hormones with Loratadine were used for a wider study.
Materials & Methods: Twenty mature male rats weighing 250g were randomly divided into four experimental groups. Rats were anesthetized with intra-peritoneal injection and placed in a stereotaxic apparatus. There were placed two cannuales, 0.2 mm above hippocampus. A week after the surgery, As the memory criteria, the rats latency in entrancing to black box was measured. One-way analyses of variance (ANOVA) followed by Tukey's post hoc test, were used for analysis of the data.
Result: The collected information from pharmaceuticals showed that intra-hippocampus administration of Loratadine (2µl) immediately after training, decreased avoidance memory on the test day. Co-administration of Estradiol (1µl) and Loratadine (2µl) significantly decreased the inhibitory avoidance memory. Co-administration of Progesterone (1µl) and Loratadine (2µl) significantly decreased the avoidance memory and administration of Estradiol (1µl), Progesterone (1µl), and Loratadine(2µl), reduced the avoidance memory to about half of the memory of the control group.
Conclusion: Loratadine is involved in the mechanism(s) modulating avoidance memory. There is an interaction between Loratadine and steroid hormones in the modulation of avoidance memory consolidation in the hippocampus.
Keywords: Loratadine, Steroid Hormones, Learning, Avoidance Memory

P-214

Neuroprotective effects of clarithromycin on the neurological scores, brain edema and blood brain barrier disruption after severe traumatic brain injury in male rats: a behavioral and biochemical study

Farahnaz Babayan Mashhadi[1], Ali Siahposht- khachki[2] *, Fatemeh Babayan Mashhadi[3]

1. Medical Students, Mazandaran University of Medical Sciences, Ramsar campus, Ramsar, Iran
2. Department of Physiology, Mazandaran University of Medical Sciences, Sari, Iran
3. Cellular and Molecular Microbiology, basic sciences collage, Islamic Azad University of Mashhad

Background and Objective: Clarithromycin (CAM) is a member of the macrolide family and is a strong antibiotic for the treatment of microbial infection. Other effects including changes in inflammatory factors, migration, and cell proliferation are metalloproteinase matrix. Therefore, in this study, we investigated the effects of clarithromycin on neuronal protection after induction of cerebral infarction in rats.
Materials and Methods: The male Albino wistar rats received different doses of Clarithromycin (25, 50, 100 mg/kg, i.p.).All animals were intubated before surgery. In the TBI groups, diffuse TBI was induced by Marmarou method using a TBI induction device. The severe TBI was induced using a weight 450 gr.In the sham groups, all stages of induction of TBI were performed except dropping weight on the head. The disruption of Blood brain- barrier (BBB) was evaluated 6 h post- TBI. The neurologic score(VCS) and brain water content, the beam-walk –balance task (WB) were determined before trauma, on trauma time (D0), and 1 day(D1) and 2 DAy (D2) and 3 Day (D3) After TBI anaesthetized animals were sacrificed and the brain was removed and then analaysis MMP-9 with Elisa assay.
Results: Our results showed that traumatic brain injury led to significant brain edema and disrupt of blood brain-barrier and neurological defect and vestibulomotor dysfunction in the rat brain and decrease mmp in serume.Clarithromycin (25,50mg/ kg) could attenuated brain edema, improved BBB and vestibulomotor dysfunction in compare with TBI control group ($P<0.001$) but in 50 dose results were better.
Conclusion: These findings showed that Clarithromycin has a prominent role in TBI outcome's and perhaps protect neurons through modulating inflammatory and antioxidant pathways.
Keywords: Clarithromycin, TBI, neuroprotective, MMP-9, rat

P-215

Effects of Green Tea Catechin, Doxorubicin and their combination on Human Neuroblastoma Cell Line BE(2)C cell cycle progression

Zahra Bakhtiarie, Ladan Delphi, Houri Sepehri, Nasrin Motamed

School of Biology, College of Sciences, University of Tehran, Tehran, Iran

Background and Objective: Green tea contains 30 percent polyphenolic flavonoids by weight, with antioxidant and therapeutic properties. It includes large amounts of catechin that help cell damage prevention, anti-propagation, anti-angiogenesis, and anti-inflammation. Catechin is a natural antioxidant contains anti-cancer properties on several cancers. Neuroblastoma is the third types of childhood cancers showed severe side effects of by chemotherapy. Thereafter, it is necessary to plane targeted treatments with low toxicity which improves quality of life. In the present experiment, the effect of Catechin in combination with doxorubicin on Neuroblastoma cell line is studied.
Materials and Methods: Effective doses of catechin, doxorubicin, and their combination were assayed with MTT. Afterward, the flow cytometric analysis based on propidium iodide was performed to analysis cellular DNA content and cell cycle distribution.
Results: MTT assay revealed the effective doses of the drugs after 48h incubation. It was determined that the cells are sensitive to the high concentration of doxorubicin. The cell cycle distribution showed the effective dose of Catechin caused a distinctive peak in sub-G1 and arrest in G2/S phase. Doxorubicin caused a G2/S arrest, while ineffective doses combination caused a significant aggregation of cells in sub-G1.
Conclusion: Our results showed simultaneous treatment of catechin and doxorubicin showed cytotoxic effects on Neuroblastoma cancer cells. It was also revealed that this mode of combination followed with a distinct peak of subG1which maybe reflected apoptosis induction.
Keywords: BE(2)C, Cancer, Catechin, Cell cycle, Doxorubicin, Neuroblastoma

P-216

Role of the Ventromedial Hypothalamic D2 Receptor Antagonist (sulpiride) In Regulation Of Food Intake In 24 Hours Food Deprived Rat

Shiva Bakhshi

Neuroscience Research Center and Department of Physiology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Introduction: Doamine play an important role on the central nervous system to modulate food intake.
The dopamine receptors are distributed within the hypothalamus, and expression of D(1,2) receptors is greatest in the ventromedial nucleus. Therefore, we hypothesized that ventromedial hypothalamic D(1,2) receptors may be involved in the control of food intake.
Methods: Male Wistar rats were implanted with stereotaxic method to the VMH. Drugs or vehicle was injected in a volume of (0.001 , 0.005 , 0.01 µg/ml) into the VMH respectively. The weight of food pellets was measured over a 3 hours period. Feeding trials normally occurred between 9:00 and 12:00 h.
Results: sulpiride (D2 antagonist) (0.001 , 0.005 , 0.01 µg) were microinjected and food intake was assessed. The VMH injections of D2 receptor antagonist, sulpiride, were associated with food intake decrease (dose dependently) .
Conclusion: We conclude that sulpiride effect on the VMH inhibit food intake. This inhibitory effect is mediated by D2 receptors. This could be concerned as a goal for further therapeutic plans.
Key Words: Ventromedial hypothalamus; food intake; dopamine; D2 receptor antagonist.

P-217

The effect of oral administration of hydroalcoholic extract of quercus, crisium vulgare and falcaria vulgaris on preventing gastric ulcer induced by ethanol on inflammatory parameters in rat

Ali Mohammad Basatinya, Javad Sajedianfard, Said Nazifi

Department of Basic Sciences, School of Veterinary Science, Shiraz University, Shiraz, Iran.

Background and Objective: Gastric ulcer refers to open ulcers in the gastric mucosa due to the failure of the gastric defenses against the damaging factors. In recent years, treating gastric ulcer with herbal medicines has been a major success. The present study was carried out to investigate the effect of hydroalcoholic extracts of these plants on inflammatory factors in gastric ulcers induced by ethanol.
Materials and Methods: 30 male rats were randomly allocated into 6 groups: Control group (intact animals), Sham group (distilled water was gavaged for 14 days. Negative control group (omeprazole was administered at for 14 days (20 mg/kg)). Experimental groups (hydroalcoholic extracts were gavaged for 14 days (500 mg/kg)); gastric ulcer was induced by ethanol gavage 1 ml/200 g/kg. Then inflammatory parameters were measured by using Elisa. Data were analyzed by using SPSS.
Results: Administration of ethanol to rats of sham group resulted in severe lesions in their stomachs otherwise mucosal lesions in negative control group as well as groups treated with ethanolic extract of considerable plants (especially quercus) were very mild with regard to analyzed inflammatory parameters, ulcer area and number.
Conclusion: In conclusion, hydroalcoholic extracts of quercus, falcaria vulgaris and crisium vulgare has a gastroprotective effect against ethanol-induced gastric ulcer in rats.
Keywords: Quercus, Cirsium vulgare, Falcaria vulgaris, Gastric ulcer, Rat, inflammatory parameters

P-218

Evaluation of skin absorption of the Citrullus colocynthis in treatment of Type II diabetic patients

Akram Ahangarpour[1], Rafie Belali[2*], Fatemeh Bineshfar[3], Shokoh Javadzadeh[3], Leila Yazdanpanah[1]

1. Diabetes Research Center, Health Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
2. Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3. Department of Education Ahvaz, Khuzestan, Iran.

Background and Objective: Today, among the herbal Medicines used to treat diabetes, Citrullus colocynthis (CCT), due to its reducing effect on blood glucose (BG) and stimulating insulin secretion, is highly noticeable. But long-term oral consumption of this herbal medicine has often been associated with digestive complications, in this study, skin absorption of CCT as a new therapeutic approach in the treatment of type II diabetic patients, has been surveyed.
Materials and Methods: 40 type II diabetic patients (aged 45-65) were selected. Participants were asked for placing their metatarsus daily in a decoction containing a pack of 20 ± 2 gr of dry CCT fruit powder and one liter of water for 40-60 minutes each day and continuing that for 10 days. Blood and urine samples of patients collected at the beginning and the end of the study were examined for the BG levels, serum insulin content, lipid profiles, hepatic enzymes, urea, creatinine and microalbuminuria, (QUICKI), (HOMA-IR), (HOMA-β) and (DI) indicators were also calculated.
Results: local treatment of CCT could significantly decrease BG levels, stimulate insulin secretion and improve the function of pancreatic beta cells. It also decreased serum urea levels comparing to pre-treatment levels ($p < 0.05$) but there was no significant change in creatinine levels, lipid profiles, hepatic enzymes, microalbuminuria and other insulin sensitivity indexes.
Conclusion: This study showed that the CCT plant can also have systemic therapeutic effects on type II diabetic patients through dermal absorption.
Keywords: Citrullus colocynthis, Type II diabetes, skin absorption

P-219

Expression changes of TLR-2 and TLR-4 in gentamicin induced nephrotoxicity in rats

Zahra Pakfetrat[1], Zainab Karimi[*1], Sahar Janfeshan[2]

1. Shiraz nephro-urology research center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Department of Biology, Zarghan Branch, Islamic Azad University, Zarghan, Iran

Introduction: Gentamicin is an antibiotic of aminoglycoside family that causes nephrotoxicity in human and animal models and induced oxidative stress. Tool like receptors are part of innate immune system and participate in inflammatory responses so in this survey we investigated the effect of inflammation and oxidative stress induced by gentamicin on expression of TLR-2 and TLR-4 in rat models.
Methods: Rats were randomly divided in to two groups (Control (n: 10) and Gentamicin (100 mg/kg, for 10 days, i.p), n: 10). We examined the level of anti-oxidative enzymes in kidney tissue, BUN/Cr in serum, pro-inflammatory cytokines (IL-6, IL-1β, MCP-1, TNF-α) and TLR-2, TLR-4 by using real time-pcr method.
Results: Our functional and pathological results showed that gentamicin induced nephrotoxicity (necrosis in proximal convoluted tubules, increased the level of BUN/Cr in serum), in gentamicin treated group the level of MDA significantly increased and the real time pcr results revealed that the expression level of pro-inflammatory cytokines and TLR-2,TLR-4 increased.
Conclusion: Our results confirmed that gentamicin could effectively induce nephrotoxicity in rats, cause oxidative stress and increased expressions of TLR-2, TLR-4 and pro-inflammatory cytokines.
Key words: Gentamicin, Oxidative stress, TLR-2, TLR-4, Nephrotoxicity

P-220

Effects of trans-anethole on serum homocysteine and histological changes of ovary, uterus and adrenal in estradiol valerate induced-PCOS rat model

Peyravi Z, Jelodar G.A

Department of Basic Sciences School of Veterinary Medicine, Shiraz University

Background and Objective: Fennel has phytoestrogenic properties. One of the components of this plant is trans-anethol, which is phytoestrogenic and may be effective in treating of PCOS.
Materials and Methods: 48 female rats (220±30 g) with regular sexual cycle (monitored for two weeks) were divided in 6 groups.: Control (gavage with distilled water) Treatment control (healthy gavage with trans-anethol), Patient (after induction of PCOS gavage with distilled water) The treatment groups 1, 2, 3 were gavaged orally at 20, 40 and 80 mg / kg trans-anthol after PCOS induction. To induce PCOS (estradiol valerate 4 mg dissolved in 0.2 sesame oil) was injected intramuscularly and after seven weeks, the estrous cycle of rats was studied and the animals treated for 30 days. On the last day of experiment blood samples were taken and serum homocysteine was measured. The ovaries, uterus, and adrenals were isolated and after tissue processing sections were stained with hematoxylin and eosin. The status of follicles and thickness of tissue layers in ovaries and uterus and the ratio of cortex to medulla in adrenal glands were evaluated.
Result: There was a significant difference in the number of cystic follicles in the treatment groups with control group and patient group and there was no significant difference between groups in other ovarian follicles and ovarian layers. Results of uterine and adrenal layer thickness and serum homocysteine levels showed no significant differences between groups.
Conclusion: Our results showed that trans-anethole can reduce the number of cystic follicles caused by PCOS.
Keywords: trans-anethole, PCOS, homocysteine, Uterine, ovarian and adrenal tissue

P-221

Impact of chronic administration of orexin type 1 receptor antagonism on hematologic parameters in morphine dependent rats

Piri Zahra [1,2], Kourosh Arami Masoumeh [2,3*], Shahidi Minoo[4], Najaf zadeh Parvaneh[1]

1. Department of Pharmacology & Toxicology, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University, Tehran - Iran
2. Neuroscience Research Center, Iran University of Medical Sciences, Tehran, Iran
3. Department of Basic Sciences, Allied Medical College, Iran University of Medical Sciences, Tehran, Iran
4. Department of Hematology, Allied Medical College, Iran University of Medical Sciences, Tehran, Iran

Acknowledgements: The authors thank Iran University of Medical Sciences for the support of this study.
Orexin peptides produced in the hypothalamic nuclei are involved in opioid dependency. This study was carried out to find whether injection of orexin-A receptor antagonist have effect on hematologic factors in morphine dependent rats. Male Wistar rats were rendered morphine dependent by subcutaneous injection of morphine sulfate (10 mg/kg) at an interval of 12 h for 7 days. In control and treatment groups, SB-334867 vehicle (DMSO) and SB-334867 respectively, was injected during P1-P30 daily and then before each morphine injection during 7 days. SB-334867 reduced several hematologic factors of morphine dependent rats including mean corpuscular hemoglobin concentration (MCHC) and white blood cell count (WBC) but increased platelet cells count. Conclusion: It may be concluded that orexin, via orexin type 1 receptor (OX1R) may change hematologic factors in morphine dependent rats.
Keywords: SB-334867, Morphine, Dependent Rat, Hematologic Factors

P-222

Study the effects of hydroalcholic extract of Arum orientale on hemodynamics and neutrophil's activity in isoproterenol-induced myocardial infarction in rats

Asal Javidmehr, Samin Abbaszadeh, Hamid Soraya

Department of Pharmacology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran

Background and Objective: Arum orientale is a medicinal plant which wildly grows in northwest of Iran. In the present study, the effects of hydro-alcoholic extract of A. orientale on isoproterenol-induced myocardial infarction (MI) were evaluated.
Materials and Methods: Thirty adult male wistar rats were used in this study. A subcutaneous injection of isoproterenol (150 mg/kg/day) for 2 consecutive days at an interval of 24 h was used for the induction of myocardial infarction in rats. Hydroalcoholic extract of Arum orientale was injected ip at doses of 40, 80, and 160 mg/kg/day 20 min before each isoproterenol injection. Then, different parameters were evaluated.
Results: Induction of MI significantly ($P<0.001$) increased necrosis, neutrophil infiltration and MPO activity in heart tissue, peripheral neutrophil percent and MDA level and CPK activity in the serum. While administration of A. orientale significantly reduced necrosis, neutrophil infiltration and MPO activity in the heart (at dose 160 mg/kg) ($P<0.05$, $P<0.01$ and $P<0.05$ respectively). Also treatment with A. orientale significantly ($P<0.05$, $P<0.05$ and $P<0.001$ respectively) decreased peripheral neutrophils in blood, MDA levels and CPK activity in serum. Hydroalcoholic extract of A. orientale had no significant effect on hemodynamic parameters but improved the ECG pattern.
Conclusion: Our results for the first time reported cardioprotective effects of A. orientale that partially can be through suppression of inflammatory responses and reduction of lipid peroxidation following MI. Our findings may lead to discover novel herbal-origin drugs in order to prevent and treat MI and various ischemic heart diseases.
Keywords: Arum orientale, Myocardial Infarction, Neutrophil, Lipid Peroxidation, Creatine

P-223

Study the effect of Gensing extract following epilepsy model induction by Penicillin on cognitive behaviour in adult male rat

Sanaz Janati[1], Zohreh Ghotbeddin*[1], Mahnaz Taherian Fard[2], Zabiholah Khaksar[2]

1. Department of Physiology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.
2. Department of Physiology, Faculty of Veterinary Medicine, Shiraz University, Shiraz, Iran.

Background and Objective: Penicillin injection into the neurocortex is the model of experimental epilepsy and cause brain toxicity and cognitive problem by damaging the target neurons which have a high density of glutamate receptors. Ginseng has been used in traditional Chinese medicine to improve brain functions like memory, behavior and mood. So, in this work we assessed the effect of gensing extract following epilepsy model induction by Penicillin on cognitive behaviour in adult male rat.
Materials and Methods: In this study, 50 male rats (Wistar) were divided into 5 groups: control, sham, penicillin, Gensing and Gensing-treated penicillin groups. Penicillin (1500ul dosage) was injected by ICV method to the neocortex of Adult rats (230-280 g). 7 days after recovery period Gensing was injected 100 mg / kg for 7 days in treatment groups. Cognitive-behavioral study was performed by using Morris water maze test.
Results: Penicillin injection could affect the animal's descriptive memory and skills to find appropriate strategy reach to the target platform and increase unusual behaviors of swimming, such as swimming along the wall ($p<0.05$), the uncertain movements of the circular ($p<0.01$) and random movement ($p<0.01$) compared to the control and sham groups and Gensing treatment can reduce unconventional behaviors and increase the search-seeking behavior in order to reach the target platform in the shortest time.Conclusion: These results suggest that Gensing has been effective on cognitive behavior in epileptic rat by penicillin injection.
Keywords: Gensing extract, epilepsy model, Cognitive behavior, Rat.

P-224

The role of G-protein receptor 30(GPR30) in spatial learning and memory task in aged female rats receiving marijuana

Mohadeseh Chahkandi[1], Gholamreza Sepehri[2], Gholamreza Komeili[3], Mohammad Khaksari Hadad[4]

1. Dept. Physiology, Kerman University of Medical Science, Kerman, Iran
2. Dept. Physiology, Kerman University of Medical Science, Kerman
1. Dept, physiology, Zahedan University of Medical Sciences, Zahedan, Iran
3. Dept. Physiology, Kerman University of Medical Science, Kerman, Iran

Background and objective: Alzheimer's have a great impact in today's aging society and is somewhat commonly listed as a potential qualifying condition for medical marijuana. There is an unknown effect of marijuana in neurological functions in old people when taken in chronically . Animal stadies have shown that stradiol can prevent age-related cognitive decline. Recently, a novel G-protein coupled receptor (GPR30) was described to mediating estrogen signaling in various cell lines.
Materials and Methods: fifty-four rats were randomly allocated to 9 groups. The E2,G1 and G15(every 4 days) and marijuana(every day), either individual and combine, were given intraperitoneally for 21 days and Morris water maze (MWM) test were performed after end of the injections. All groups were compared to control and vehicle.
Results: In this study the role of GPR30 were investigated in spatial learning and memory task in aged female rats receiving marijuana. The results indicated that marijuana and marijuana plus G1(GPR30 agonist), significantly increase spatial learning and memory than in control and vehicle, however G1 alone, decreased it. The result of intra-peritoneal injection of estrogen and G1 and G15(GPR30antagonist),either individual and combine, shown estrogen individual and estrogen plus G15, both of them improve spatial learning and memory task but G1 injection didn't show any effect.
Conclusion: marijuana and estrogen either individual improve spatial learning and memory task in old age female rats, but the effect of estrogen, doesn't apply to the membrane receptor(GPR30).
Keywords:GPR30, spatial learning and memory, marijuana, old age rats

P-225

Cytotoxic effects of Hesperidin, hesperidin/carvacrol nanoemulsion and hesperidin/carvacrol combination on human breast cancer cellular model

Sara Hadidi[1], Houri Sepehri*[1], Ladan Delphi[1], Hassan Rafati[2]

1. Department of Animal Biology, School of Biology, College of Sciences, University of Tehran, Tehran, Iran
2. Medicinal Plants and Drug Research Institute, Shahid Beheshti University G. C., Tehran, Iran

Background and Objective: Nanoemulsions, offer several advantages in drug efficiency. Also, a combination of two or more therapeutic agents could target key pathways in different manners. Natural compounds phytochemicals like flavonoids contain anti-cancer properties. Hesperidin is a citrus flavonoid with various biological effects including anticancer activity. In the present study, hesperidin cytotoxic effect is under-investigated. To reach this goal hesperidin, a nanoemulsion of hesperidin/carvacrol formulation and hesperidin/carvacrol combination cytotoxic effects on the cellular model of breast cancer was assessed.
Material and Methods: MDA-MB-231, the metastatic human breast cancer cells, and MCF7, the invasive breast carcinoma cells were cultured in RPMI1640 medium. The cells were treated with the above-mentioned modes for 24h. Cytotoxic effects of the drug were assessed with MTT assay. Afterward, the cells' morphological changes and cell cycle distribution were analyzed.
Results: In both cell lines equal concentration of hesperidin caused more than 50% cell death after 24h. In combination mode, carvacrol promoted hesperidin cytotoxic effects while their nanoemulsion formulation did not contain any significant effect. Concurrently, the cells lost their normal morphological shapes though some of them detached and floated. The cell cycle analysis indicated different patterns of cell distribution in the mentioned model.
Conclusion: These results indicated the hesperidin cytotoxic effects on breast cancer cells could reinforcement in combination with carvacrol. Yet, nanoemulsion of hesperidin in carvacrol did not support its effects in breast cancer cells.
Keywords: Breast cancer, Combination mode, Hesperidin, Nanoemulsion

P-226

Protective effect of crocin the paracetamol-induced renal toxicity in rats

Jalal Hassanshahi[1,2], Ayat Kaeidi[1,2], Mohammadreza Rahmani[1,2], Elham Hakimizadeh[1]

1. Physiology-Pharmacology Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
2. Department of Physiology and Pharmacology, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Background and Objective: Acetaminophen as an analgesic and antipyretic drug is widely available without a prescription. An overdose of acetaminophen can induce kidney damage and crocin has antioxidant and anti-oxidative stress effects. Accordingly, in this study, we evaluate the renoprotective effect of crocin against paracetamol-induced nephrotoxicity in rats.
Materials and Methods: Forty male Wistar rats were randomly divided into four groups including control, acetaminophen (650 mg/kg), crocin (200 mg/kg), acetaminophen+crocin. The rat has received a single dose of acetaminophen orally, the treated with crocin (orally) daily for 3-day. Blood and kidney samples were collected after three days of treatment. To evaluate the oxidative stress status, superoxide dismutase (SOD), glutathione peroxidase (GPx) activity levels and malondialdehyde (MDA) level were measured. The hematoxylin and eosin method was applied to evaluate the kidney tissue damage score (KTDS). Data were analyzed using GraphPad Prism.
Results: acetaminophen significantly increased MDA level and KTDS ($P<0.01$), and also significantly decreased SOD, and GPx activity levels ($P<0.01$) in kidneys and crocin significantly attenuates the renal toxicity induced by acetaminophen ($P<0.05$).
Conclusion: Our findings showed that crocin has a renoprotective effect against paracetamol. The mechanism underlying the observed effects may be related to reducing renal oxidative stress.
Keywords: Paracetamol, Renal toxicity, Oxidative stress, Crocin, Rat

P-227

The antidiabetic activities of a newly synthesized quinazoline compound with dipeptidyl peptidase-4 (DPP-4) inhibitor activity in a murine diabetes model

Samaneh Hosseinpour, Melika Ebrahimi, Seyyed Abbas Tabatabai, Nima Naderi

School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Amongst antidiabetic medications affect hormone secretion, inhibitors of dipeptidyl peptidase type 4 (DPP-4 inhibitors) showed a good hypoglycemic effect along with an acceptable safety and tolerance. A series of DPP-4 inhibitors have been already synthesized and evaluated by in vitro enzyme studies in this lab. In the present study, the effect of a newly synthesized DPP-4 inhibitor – carboximidamide - was evaluated using a subacute model of type 2 diabetes.
Materials and Methods: Twenty-four male wistar rats were initially fed with high fat diet for two weeks. Then, a single administration of streptozocin (35 mg; i.p.) followed by another two weeks of high fat diet caused a fasting blood sugar (FBS) above 140 mg/dl in the rats. The rats were then randomly divided into four groups (n = 6 in each group). In two treatment group, the carboximidamide compound (10 or 15 mg/kg) was administered once a day p.o. for 14 consecutive days. A positive control group received sitagliptin (5 mg/kg p.o.) and the control group received saline (1 ml/kg) daily for 14 consecutive days. FBS levels were measured at the onset of therapy, one week and two weeks after treatment with drugs.
Results: The results show that a two-week treatment with quinazoline compound (both 5 and 10 mg/kg) and also sitagliptin significantly reduced FBS compared with the control group. No significant difference in FBS was found between the three treatment groups.
Conclusion: Our results suggest that the newly synthesized carboximidamide compound could be considered as a hypoglycemic agent by DPP-4 inhibition.
Keywords: DPP-4 inhibitor, diabetes mellitus, sitagliptin, rat

P-228

Exposure to cell phone radiofrequency changes corticotrophin hormone level and histology of brain and adrenal gland in male Wistar rat

Sima Shahabi [1,2], Iman Hassanzadeh Taji[3], Maedeh Hoseinnezhaddarzi[3], Fateme Mousavi[3], Shermineh Shirchi[3], Atena Nazari[2], Hooman Zarei[4], Fereshteh Pourabdolhossein[5,1,2] *

1. Physiology Departments, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran
2. Neuroscience Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
3. Student Research Committee, Babol University of Medical Sciences, Babol, Iran
4. Anatomy Departments, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
5. Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

Objective(s): Nowadays, the electromagnetic field-emitting devices have been used in our daily routine lives. Controversial reports exist concerning the effects of mobile radiofrequency (RF) on different parts of body, especially stress hormones. The main goal of the present work was to study the long-term effects of mobile RF900 MHz exposure with special focus on the adrenal gland pathophysiology and function.
Material and Methods: Adult male Wistar rats were exposed to Mobile RF 6 hours daily for 4-8 weeks. Intact and switched-off exposed animals were considered as control. Plasma ACTH and cortisol level was measured by ElISA method. At the end of the experiment, a histological study was done on adrenal gland and brain tissue by hematoxilin and eosin staining. The thickness of fasciculate layer of adrenal gland, its cell number and perimeter were measured by Fiji software.
Results: An enhanced plasma ACTH and cortisol level was found after prolonged exposure to mobile RF. The fasciculata layer of adrenal cortex eventually thickened following mobile RF radiation. While the number of cells in zona fasciculata remained constant, the cell size and perimeter increased during RF exposure. Finally, we found that vacuolization in brain tissue and the number and size of vacuoles considerably increased during two months of RF exposure.
Conclusion: Cell phone RF exposure induced significant hormonal and structural changes in adrenal gland and brain tissue. Therefore, the public should be aware and limit their exposure as much as possible.
Keyword: Cell phone, Radio-frequency, Corticotropin hormone, Cortisol, Adrenal glands, Hypertrophy

P-229

Protective effect of melatonin against chemicals-induced cardiotoxcity

Simin Zare [1], Fatemeh sadat Heydari [1], A. Wallace Hayes[2], and Gholamreza Karimi [1, 3]

1. Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
2. University of South Florida College of Public Health, Tampa, FL USA
3. Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

Cardiovascular diseases can refer to a number of conditions including atherosclerosis, hypertension, and ischemia/reperfusion (I/R), which are the leading causes of death among men and women in well-developed countries. There are some drugs and chemicals induce cardiotoxicity, mainly by generating free radicals. Reactive oxygen species (ROS) play a critical role in the pathogenesis of cardiac tissue injuries. This highlights a need for novel paradigms for prevention of cardiotoxicity by scavenging free radicals. Numerous researches support that melatonin act as a protector against various conditions in which free radicals cause molecular and tissue injury. Some of the mechanisms by which melatonin operates as a free radical scavenger and antioxidant have been identified. The importance of endogenous melatonin in cardiovascular health and the benefits of melatonin supplementation in different cardiac pathologies and cardiometabolic disorders has been proven. In accordance with all these studies melatonin has attracted a lot of attention to itself for reducing heart injuries. In the present communication, we review the therapeutic potential of melatonin in the treatment of cardiotoxicities caused by various chemicals along with its molecular mechanism of actions.

P-230

The protective effect of voluntary exercise on type 2 diabetes-induced alteration of sperm parameters

Uldouz Kharazi[1, 2], Saber Ghaderpour[1, 2], Gholamreza Hamidian[3], Rana Keyhanmanesh[*1, 2], Rafighe Ghiasi [1, 2]

1. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
2. Department of Physiology, Tabriz University of Medical Sciences, Tabriz, Iran.
3. Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.

Background and Objective: The most of diabetic men experience infertility or sub-fertility. It is well established that regular physical activity can improve blood glucose control in type 2 diabetic patients. This study was designed to determine the effect of voluntary exercise (VE) on quality and quantity parameter of sperm in type 2 diabetic male rats.
Materials and Methods: Thirty-two adult male Wistar rats were randomly divided into control, diabetic, VE and diabetic-VE groups. Diabetes was induced by a high-fat diet and 35 mg/kg streptozotocin. VE was performed for 10 weeks by placing the animal in a rotary wheel cage. At the end of the experiment, animals were euthanized and their left epididymis was removed and dissected in Ham's F10 and incubated at 37°C. Total count, motility, viability and morphology of sperm as well as teratozoospermia (TZI) and sperm DNA fragmentation index (SDFI) were assessed according to the WHO standard methods. Data were analyzed by one-way ANOVA and Tukey's posthoc.
Results: Results showed that diabetes decreased sperm total count, motility, viability and percentage of sperm with normal morphology and also increased TZI and SDFI significantly compared to control. Our results indicated that VE could increase the total count of sperm but this change was not significant compared to the diabetic group. It was revealed that VE increased motility, viability, normal morphology and reduced TZI and SDFI significantly compared to the diabetic group.
Conclusion: VE can be considered as a suitable protective strategy for improvement of infertility or subfertility in diabetic males.
Keywords: Diabetes, Voluntary exercise, Sperm analysis, Male infertility

P-231

Olanzapine prevents chemotherapy induced nausea and vomiting in patients with cancer : A randomized clinical trial

Atefeh Khani[1], Hamid Reza Khalkhali H[2], Ali Eishy Oskuyi [3], Hamdollah Sharifi H1[2]

1. Department of Pharmacology, Pharmacy Faculty, Urmia University of Medical Sciences, Urmia- Iran
2. Inpatient's Safety Research Center, Urmia University of Medical Sciences, Urmia, Iran
3. Department of internal medicine, Faculty of Medicine, Urmia University of Medical Sciences, Urmia-Iran.

Background and Objective: Nausea and vomiting caused by chemotherapy are important side effects of anti-cancer treatment, and its full prevention is a potential challenge. This study was conducted to determine the effect of olanzapine on the prevention of chemotherapy-induced nausea and vomiting in patients undergoing chemotherapy.
Materials and Methods: This randomized, double-blind, clinical trial, was done in 70 patients with no previous chemotherapy. All patients in intervention group received on the day of chemotherapy, day 1, an antiemetic regimen consisting of dexamethasone 8 mg and granisetron 1mg TDS and received olanzapine 5mg (B.W: 60kg or less) or 10 mg (B.W: more than 60kg) PO one day before chemotherapy and continued for days 1–5 following chemotherapy administration. Patients in control group received placebo instead of olanzapine. Early and delayed nausea and vomiting prevention were the primary and secondary end points; complete response (CR) in the whole period of chemotherapy was the third end point. Response to treatment evaluated by questionnaire completion in first, third and fifth of chemotherapy.
Results: Percentage reduction of nausea , vomiting, nausea and vomiting in acute phase (first day) in the intervention group compared to the control respectively were 72/46%, 16/50%, 81/42% ($p<0.001$). For the delayed phase (third and fifth day) were 56.23%, 57.2%, 55.23%;($p<0.001$), for the overall phase (first to fifth), respectively, were 51.47%, 68.6% ;($p<0.001$).
Conclusion: Olanzapine is effective in improving CINV in the acute, delayed and overall periods of chemotherapy

P-232

In vitro effects of Capparis spinosa extract on sperm function, DNA fragmentation, and oxidative stress in normozoospermia

Motahareh Khojasteh Rad[1], Esmaeel Ghani[2], Asker Ghani[3]

1. Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2. Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
3. Department of Horticultural Sciences, College of Agriculture, Jahrom University, Jahrom, Iran.

Background and Objective: Oxidative stress is one of the main causes of male infertility. Medicinal plants have many benefits, and may be useful for treating infertility in men. In the present study, the effects of Capparis spinosa extract were evaluated on sperm function, DNA fragmentation, and oxidative stress.
Materials and Methods: Polyphenol compounds and antioxidant effect of the extract were determined by HPLC and DPPH method respectively. Semen samples (n=50) were divided into control and experimental (15, 30 and 45 ppm of Capparis spinosa extract). Motility, viability, lipid peroxidation, and DNA fragmentation were evaluated at 0 and 24 hours after incubation.
Results: The antioxidant effect of leaf extract was 6 times greater than fruit. Progressive and total motility at concentrations of 30 and 45 ppm were significantly higher than control group. Viability in all treatments was significantly higher than control group. There was no significant difference in lipid peroxidation. DNA fragmentation at 45 ppm concentration was significantly lower than control.
Conclusion: Our results indicate that leaf extract of Capparis spinosa can protect sperm from oxidative stress. Using the extract or its effective compounds in sperm medium may be useful.
Keywords: Capparis spinosa, infertility, oxidative stress, sperm

P-233

The high risk of hydration process with saline-furosemide, dextrose and mannitol in female gender in cisplatin induced nephrotoxicity rat model

Mohammad-Sedigh Khosravi[1], Bahar Mazaheri[1], Farzaneh Ashrafi[2], Ardeshir Talebi[3], Mehdi Nematbakhsh[1,4,5]

1. Water and Electrolytes Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Internal Medicine, Hematology/Oncology Division, Isfahan University of Medical Sciences, Isfahan, Iran
3. Department of Clinical Pathology, Isfahan University of Medical Sciences, Isfahan, Iran
4. Department of Physiology, Isfahan University of Medical Sciences, Isfahan, Iran

Background: Cisplatin (CP) is widely used for cancer therapy in clinic, however its most side effect of nephrotoxicity is gender related. Hydration process may limit the CP induced nephrotoxicity while the side effect is gender related and female is more sensitive to cispelatin induce nephrotoxicity Accordingly, this study was designed to determine the best hydration methods in female during CP therapy.
Materials and Methods: Female Wistar rats were randomized into 7 groups of animals (6 in each group) treated with saline alone, CP alone and CP with one of the protocols of hydrations including: saline, mannitol, dextrose hydration, saline & furosemide, saline & mannitol The serum levels of blood urea nitrogen (BUN) and creatinine (Cr) were measured using commercial kits. The kidney tissue damage score (KTDS) was determined by H&E tissue staining.
Result: The mannitol and dextrose supplementation decreased survival time significantly ($p<0.05$). Furosemide and dextrose supplementations did not show a protective effect against CP induced nephrotoxicity. In addition, normal saline supplementation accompanied by CP increased the serum level of BUN and Cr and decrease body weight change significantly when compared with CP alone treated group ($p<0.05$). Pathology findings indicated that the KTDS were greater in CP treated group received normal saline, dextrose¸ mannitol or furosemide supplementation than the control group.
Conclusion: It is concluded that hydration with mannitol and dextrose worsen CP induced nephrotoxicity in female gender. Possibly sex hormones play an important role for such findings.
Keywords: Hydration, Mannitol, Furosemide, Nephrotoxicity, Cisplatin, Rats, Female

P-234

The beneficial effects of progesterone on electrophysiological alterations is mediated through GABA-A receptor in a chronic constriction injury model of neuropathic pain in rats

S. khajemahalleh, M. Jarahia[1,2], H. A. Safakhaha[1,2], A. Rashidy-Poura[1,2]

1. Laboratory of Neuropathic Pain and Electrophysiology, Research Center of Physiology, Semnan University of Medical Sciences, Semnan, Iran
2. Departmentof Physiology, school of Medicine, Semnan University of Medical Sciences, Semnan, Iran

Background and Objective: Many evidences support the neuroprotective effects of progesterone (PROG) against a variety of damage to nervous system. Recently, we reported that PROG (6 or 12 mg/kg) is effective against electrophysiological deficits induced by chronic constriction injury (CCI) of the sciatic nerve in rats, but the underling mechanism is not elucidated. The current study examined the role of GABA-A receptor in the beneficial effects of PROG on electrophysiological alterations in a CCI model of neuropathic pain in rats.
Materials and Methods: Male rats were administered daily by PROG (6 and 12 mg/kg, i.p.), 12 days following CCI generation, and maintained until day 26. The GABA-A receptor antagonist bicuculin (2mg / kg, i.p.) was injected half an hour before every PROG administration in all rats. Behavioral tests were accomplished before surgery (day 0) and on days 12, 26, 28, and 35 post-CCI, and were pursued by electrophysiological evaluations in the last day.
Results and Conclusion: Our data indicated that PROG administration at doses of 6 or 12 mg/kg recovered electrophysiological alterations induced by CCI. Bicuculin administration before PROG prevented the beneficial effects of PROG in electrophysiological level, suggesting that PROG action may be done, at least, partly through GABA-A receptors. These results may offer new strategies for the treatment of neuropathic pain.
Key words: Neuropathic pain, Peripheral neuropathy, Progesterone, Bicuculin, Neuroprotection

P-235

Beta Boswellic Acid enhances spatial learning and memory by reduction of tau phosphorylation level in the hippocampus regions of Alzheimer's model

Marzieh Dehghan Shasaltaneh[1], Nasser Naghdi[2], Sadrollah Ramezani[3], Gholam Hossein Riazi[4]

1. Department of Biology, Faculty of Science, University of Zanjan, Zanjan, Iran.
2. Department of Physiology and Pharmacology, Pasteur Institute of Iran, Tehran, Iran.
3. University of Sistan and Baluchestan, Zahedan, Iran.
4. Laboratory of Neuro-organic Chemistry, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran.

Background and objective: Learning and memory retention are processes that involve a permanent change in species' behavior based on environmental adaptation. One of heterocyclic compounds that plays an inhibitory role on protein kinases, is beta boswellic acid (BBA). To assess the effect of BBA on hyperphosphorylated tau protein in Alzheimer's disease, several approaches were investigated.
Materials and method: Three rat groups were selected which received destructive and effective doses of STZ and BBA intracerebroventricularly, respectively. Their spatial learning and memory, histological analysis and phosphorylation of tau protein were assessed.
Results: Our results showed spatial learning, memory and the disappearance of dark neurons were significantly effective in BBA+STZ group and STZ+BBA group comparison to Alzheimer's model, but these findings in the prevention group was higher than treatment group. The level of phosphorylated tau in hippocampus was declined upon BBA injection prior to STZ administration.
Conclusion: Antioxidant and antiinflamatory activity of BBA is associated with the increase of glutathione content and the reduction of malondialdehyde level as well as the inhibition of 5-lipoxygenase. BBA inactivate several enzymes involving in the hyperphosphorylated tau protein like GSK-3β and PKCs isoforms. Since our results in the state of BBA+STZ were satisfied, so it can be an effective lead compound for decrease of hyperphosphorylated tau protein in the brain using the effect on the enzymes.
Keywords: Spatial Memory; Boswellic acid; Hyperphosphorylated tau; Immunohistochemistry.

P-236

Effect of radio frequency wave (900 MHz) on brain serotonin levels and homocysteine in sreum and some of the tissues in rats

Radmard F, Jelodar G.A, Azimzadeh M

Department of Basic Sciences School of Veterinary Medicine, Shiraz University

Background and Objective: considering the fact that many people are exposed to radio frequency wave for a long time the damaging effects of radio frequency wave on biological systems has been widely discussed. The aim of the present study was to evaluate the levels of serotonin and homocysteine in brain, serum, adrenal, testicular and pancreas exposed to 900 MHz electromagnetic waves.
Materials and Methods: 30 adult male rats (190±20 g) were divided in 3 groups: control group (without exposure to waves) experimental group I and II exposed to 900 MHz daily for 2 and 4 hours respectively. The irradiation period was 30 days consecutive. At the end of experimental period, blood was collected through heart puncture and testis, pancreas and adrenal were isolated from all animals to determine the level of serotonin and homocysteine. Data were analyzed by one way ANOVA test.
Results: The results showed that exposures to radio frequency wave significantly increase serotonin levels in the brain and serum of group 3 (4 hr exposure) compare to control group, while it decreased in the pancreas tissue. Level of homocysteine in the brain and testis increased significantly in the third group compare to control group ($P<0.05$). There was no significant difference between second group (2hr exposure) and control group in the mentioned parameters.
Conclusion: Exposure to radio frequency waves can significantly alter serotonin and homocysteine level of serum and tissues in a time dependent manner
Keywords: radio frequency wave, serotonin, homocysteine, Brain, Testis

P-237

Evaluation of xanthine oxidase (XOX) in patients with arrhythmia in hospitals of Abadan city

Esmat Radmanesh*, Asma Mohammadi, Ali Reza Balizadeh Karami, Vahid Dehghan mashtani, tooba Sahraei, zeinab bandani tarashoki, Ehsan Khataviyan, Hossein moradi Kazerouni

Abadan faculty of medical sciences, Abadan, Iran

Background and Objective: Arrhythmia is the most common cause of sudden death in patients with cardiovascular disease. Reactive oxygen species (ROS) factors play an important role in cardiovascular diseases. XOX is one of these types of factors. Oxidative stress plays a major role in the development of various diseases.
Considering the prevalence of cardiovascular disease in Abadan, the aim of this study was to evaluate the diagnostic marker such as XOX in cardiovascular patients for better diagnosis.
Materials and Methods: In this study, 20 patients with arrhythmia referring to Taleghani and Beheshti hospitals in Abadan and 20 healthy individuals were studied and Ethical considerations were observed. The control group has a normal electrocardiogram, no history of heart disease, hypertension, diabetes, liver and kidney disease, malignancy, pregnancy, surgery, or acute medical problems during the three months prior to sampling. Blood samples are taken after centrifugation and plasma preparation for the measurement of XOX by Elisa reader. Results were analyzed using GraphPad Prism6 and expressed as mean ± SEM. Comparisons between groups were performed using T- test.
Results: The results of this study showed a significant increase ($P <0.005$) in the amount of Xanthine oxidase in patients with arrhythmia than the control group.
Conclusion: The present study showed that in the group with arrhythmia, the level of xanthine oxidase enzyme is far higher than the control group. It seems that controlling and inhibiting this enzyme in arrhythmic patients can be effective in reducing the incidence of cellular changes and arrhythmia complications.
Keywords: Arrhythmia, Xanthine oxidase, Abadan

P-238

Long noncoding RNAs XIST and MEG3 are dysregulated in rituximab treated Pemphigus patients

Mahbubeh Rojhannezhad[1], Abdorreza Naser Moghadasi[2], Abbas Nikravesh[3] , Mehrdad Behmanesh[4]

1. PhD student of genetics department of genetics, faculty of biological sciences, Tarbiat modares university
2. Tehran University of Medical Sciences, Department of Neurology
3. Department of Medical Biotechnology & Molecular Sciences, Faculty of Medicine, Bojnord University
4. Department of genetics, faculty of biological sciences, Tarbiat modares university

Background and Objective: Pemphigus is a group of IgG-mediated autoimmune diseases of stratified squamous epithelia, such as the skin and oral mucosa. The pathophysiological roles of T cells and B cells have been characterized in mouse models of pemphigus and patients, revealing insights into the mechanisms of autoimmunity.
Rituximab is a monoclonal anti-CD20 antibody that targets CD20+ B cells. Previously, prospective, open-label trials of rituximab and meta-analyses have supported the remarkable efficacy of rituximab in pemphigus, with 59–100% of patients achieving complete clinical remission after treatment, and a median remission duration of 15–19 months. Nowadays, studies demonstrate the increasing impact of lncRNAs on the regulation of molecular processes and the expression of genes.
Materials and Methods: In this study we have analyzed microarray data (GSE90152) for detecting differential expression focusing on lncRNA profile of rituximab treated patients with complete remission and patients with incomplete remission in CD4+ T-Cells and CD19+ B-cells.
Results: Analysis of the data showed that, expression of lncRNAs XIST and MEG3 altered about 8 fold and 3 fold respectively between patients with complete remission and incomplete remission in CD19+ B-cells.
Conclusion: Since lncRNA XIST act as scaffolding for protein recruitment, it may play epigenetic roles in different pathological conditions. MEG3 is a maternally expressed, imprinted long non-coding RNA gene. Among MEG3 related pathways are LncRNA-mediated mechanisms of therapeutic resistance, thus it may have a key role in the time of remission. Further experiments with more sample size is needed to validate this data.
Key words: Pemphigus, Rituximab, lncRNA XIST, lncRNA MEG3

P-239

Synthesis and Optimization of nano-niosome for Targeted delivery of Trachyspermum (Ajowan) with aim the Treatment of Fungal Infections

Fardin Rahimi[1,2], Ghassem Amoabediny [3], Hossein Sabahi[1]

1. Department of Life Science Engineering, Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran.
1. Research Center for New Technologies in Life Science Engineering, University of Shahed, Tehran, Iran
2. Faculty of Chemical Engineering, College of Engineering, University of Tehran, Iran

Background and Objective: Niosomes are One of the promising medication carriers that have the two-layer structure. Fungal infections are one of the most common fungal infections.Plant essential oils are very useful sources for preventing the growth of microbes and fungi.The aim of this study was to investigate the effect of Trachyspermum (Ajowan) Essential oil on the candidate fungal strain through loading in lipo-niosome.
Materials and methods: compounds of chemical were analyzed by GC/GC-MS apparatus. Liponiosome vesicles containing essential oil were prepared using nanoliponiosomal device.
The components of the system include: phospholipid phosphatidylcholine 80% soy, cholesterol (with a molar ratio of 70: 30), tween, PEG, and lipid ratio to essential oil is 60:1.After separation Ajowan essential oil release through dialysis bag .Determination of the mean and size distribution of essential oil nanoparticles was performed using DLS. nanosizer.nano-Carriers containing essential oil in the dialysis bag at 37 ° C and pH = 7.4, according to the physiological conditions of the body and its release rate.
Results:In the present study, loading of ajowan essential oils into nano-Carrier of lipo-niosome in order to reduce the dose of chemical drugs and increase the effect on Candida fungus strain, reduce the side effects of chemical drugs, increase stability, increase solubility, improve performance and thus a way to reduce or Replacement of drugs with high side effects. The effective concentrations of essential oil were 0.5, 1, 2 and 3 µl, respectively, which had the highest effect on the concentration of 3 µl 89% , and The nano-carrier encapsulation efficiency is more than 80%.
Conclusion:The results of the study showed that the amount of ajowan essential oil in the liponiosome carriers was 35/6±7/4 and the size of the nanoparticles was about 145.6 nm. The synthesized nano-carrier releases essential oil to treat fungal diseases. In this study, using a nano carrier niosomal for delivery of essential oil, a new method for treating patients with fungal infections was reported.
Therefore, the synthesized formulation is slow release and can be considered as an appropriate coating for chemical and essential oils of ajowan against oxidation, persistence and reduction of complications and toxicity to other organs of the body.
key words:nano-niosome vesicles, Fungal diseases,ajowan essential oils, encapsulation

P-240

Effects of Injections of Oxybutynin and Steroid Hormones into Hippocampus on Learning and Passive Avoidance Memory in Rats

Mostafa Rahimi Nasrabad[1] , Homayoun Khazali[2] , Abdolkarim Hosseini[3]

1. Master Student of Physiology, Faculty of Life Sciences and Biotechnology , Shahid Beheshti University Tehran, Iran
2. Associate professor Shahid Beheshti University - Faculty of Life Sciences and Biotechnology, Shahid Beheshti University Tehran, Iran
3. PhD. Candidate Shahid Beheshti University - Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Backgrounds and Objectives: It has been found that various neurotransmitters, including histamine H1 and acetylcholine, play a role in increasing and decreasing memory. Since neurotransmitters with a medium neuron and in the steroid environment, have a different physiological function, the purpose of this study is to investigate the effects of injection of oxybutynin (muscarinic antagonist) and steroid hormones into hippocampus and their interaction on memory and learning in rats.
Materials and Methods: Twenty adult male Wistar rats weighing 250-300g were randomly divided into four groups. Rats were anesthetized by intraperitoneal injection of ketamine hydrochloride plus xylazine. They were placed in the stereotaxic apparatus and two cannulas implanted in 2mm above the left and right hippocampus. After a week of recovery, Oxybutynin and oxybutynin plus steroid hormones were injected through the cannulas after successful training. Passive avoidance memory of rats was evaluated by shuttlebox apparatus. The data were analyzed using one-way ANOVA and then the tukey's post hoc test.
Results: The data collected from groups suggests that intrea-hippocampus injection of oxybutynin(2µl) reduced Passive avoidance memory on the test day and using of estrogen(1µl) with oxybutynin(2µl) reduced the inhibitory Avoidance Memory .Co-administration of progesterone(1µl) and oxybutynin(2µl) reduced the inhibitory Avoidance Memory. with applying simultaneously estrogen(1µl), progesterone(1µl) and oxybutynin(2µl), The inhibitory avoidance memory reduced the equilibrium to the control group nearly 50 %.
Conclusion: There is an interaction between oxybutynin and steroid hormones in the modification of the inhibitory avoidance memory in the hippocampus area.
Keywords: Oxybutynin, Hippocampus, Memory, Rat.

P-241

Metronidazole consumption is associated with reduced progeny production and development in Drosophila melanogaster

Zahra rostami

BACKGROUND: it seems that similar mechanisms are involved at molecular level in the induction of reproductive function in Drosophila melanogaster and vertebrates. Recently, there has been published reports indicate the use of metronidazole (MTZ) for the treatment of infections during pregnancy thus, increasing the need to fully understand its effect on fecundity. The objective of the present study was to investigate the effect of oral consumption of MTZ on the fecundity of Drosophila melanogaster.
METHODS: Wild-type flys were kept for 3 day in media containing MTZ concentrations of 1, 2 mg/ml. When larvae completed their development, the emerging flies were counted and examined for morphological abnormalities.
RESULTS: The analysis of 100 flies for each concentration, MTZ-treated flies show an incidence of malformations above control values, ($p < 0.005$, chi2 test). On the other hand, the 1, 2 mg/ml MTZ-treated series presented higher frequencies of total abnormalities than did concurrent and historic controls ($p < 0.05$, chi2 test), indicating an MTZ effect both parents fertility and larvaes during developmental morphogenesis.
CONCLUSIONS: The results of this study indicate that use of MTZ for 3 day before intercourse caused a harmful effect on fertility in fly. These findings confirmed the preliminary report of metronidazole on reproduction, which are widely used, especially in underdeveloped countries.
Keywords: Drosophila melanogaster, metronidazole, fertility

P-242

Anxiolytic Effect of Hyssopus officinalis L. Hydroalcoholic Extract on Ovariectomized Wister Rats

Maryam Rashidi[1], Shahrbano oryan[1], Delaram Eslimi Esfahani[1], Akram Eidi[2], Adel Salari Esker[1,*]

1. Department of Animal Science, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran
2. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran

Background and Objective: Ovariectomy in rats has been proposed as an experimental model of surgical menopause. Estrogen deficiency makes alteration at the level of the affective behaviour faculty, and it is restricted to the certain periods of age after ovary removal. The main constituents of Hyssopus officinalis L. (Hyssop) include several polyphenolic compounds, primarily flavonoids, such as apigenin, quercetin, diosmin, luteolin, and their glucosides. The objective of this study was to assess the potential anxiolytic activity of above-mentioned flavonoids on ovariectomized wister rats.
Materials and Methods: Forty-eight rats were randomly divided into six groups: control, receiving saline, control under treatment with hyssop extract (100 mg/kg), and the Ovx rats received hyssop extract, made of the aerial parts of plant [25, 50 and100 mg/kg, Intraperitoneal (I.P.)]. The extract injection was performed thirty minutes before testing. The level of anxiety was tested by elevated plus maze (E.P.M.). Data were analyzed using SPSS.
Results: Treatment with hyssop extract in Ovx female rats significantly increased the number of enterings, and time spent on the open arms compared to the control group.
The higher doses of hyssop extract made a dramatic increase in the open arm exploration.
Conclusion: These results demonstrated that hyssop extract had a marked anxiolytic effect on the experimental model of Ovx rats.
Keywords: Ovariectomy, Anxiety, Hyssopus officinalis, Elevated plus maze

P-243

Dose prepregnancy chronic valproate administration affect offspring electrophysiological properties of hippocampus

Tina Rahjoo, Mehdi Sadegh

Department of Physiology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran

Purpose: Valproate is a histone deacetylases (HDACs) inhibitor. HDACs are involved in the epigenetic processes and in some cases epigenetic modifications are inheritable. We designed to investigate, if pre-pregnancy chronic valproate might induce intergenerational consequences and affect offspring?
Methods: Twelve female Wistar rats were included as parents and divided in two groups. (1) Control group received saline daily via intraperitoneal (i.p.) injection for 30 days; (2) Valproate group received sodium valproate 300 mg/kg i.p. daily for 30 days. Two weeks thereafter one male rat was used for mating. After pregnancy and nursing, one males and one females pup were randomly selected from each mother and placed in the following groups for future experiments: (1) male offspring from control mother (male cnt, n=6); (2) female offspring from control mother (female cnt, n=6); (3) male offspring from valproate mother (male valp, n=6); (4) female offspring from valproate mother (female valp, n=6). These rats were used to evaluate electrophysiological properties of population spikes (PS) of the dentate gyrus.
Results: Pre-pregnancy valproate consumption did not significantly changed basic synaptic responsiveness of dentate gyrus, paired pulse indexes and synaptic potentiation of the offspring, when compared with offspring of control.
Conclusion: These data show no intergenerational consequences due to pre-pregnancy chronic valproate consumption.
Keywords: Epigenetic, Intergenerational, Histone deacetylases, Synaptic potentiation.

P-244

Effects of Injections of Pramipexole and steroid Hormones in to Hippocampus on passive avoidance learning and memory in male Rats

Marzieh zaferani, homayoun khazali, Abdolkarim Hosseini

Master student of animal physiology - Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Background and objective: In recent years, many studies have shown that different dopamine agonists have different effects on learning and memory. Pramipexole is a dopamine agonist used to treat Parkinson's disease and reduces memory and learning in rats. By activating mediator neurons or in steroid environment, neurotransmitters produce different physiological effects. Therefore, the aim of this study was to determine the effects of Pramipexole hippocampal injection with steroid hormones on passive avoidance memory and learning in rats.
Materials and Methods: In this experiment, twenty mature male rats weighing 200-250g were randomly divided into four experimental groups. After successful training, the rats were stereotaxic surgery and after one week the hippocampal injections of pramipexole individually (2µl), Pramipexole (2µl) plus estradiol (1µl) and Pramipexole (2µl) plus progesterone (1µl) and Pramipexole (2µl) along with Estradiol (1µl) and progesterone (1µl) ware done. As the memory criteria, the animal's latency in entrancing to dark house was measured. data were analyzed by SPSS software and appropriate statistical tests.
Results: The collected data showed that hippocampal injection of Pramipexole decreased passive avoidance memory. Also, estradiol injection along with Pramipexole and progesterone along with Pramipexole and co-injection of estradiol, progesterone and Pramipexole significantly decreased the passive avoidance memory.
Conclusion: The results Indicate the effect of modifying Pramipexole on passive avoidance memory. Also, there is an interaction between Pramipexole and steroid hormones in modulating of passive avoidance memory in the hippocampus.
Keywords: Pramipexole, Estradiol, progesterone, passive avoidance memory

P-245

In vitro Antibacterial Effects of Aqueous Extracts of Pistacia Vera L. Hulls on Gram–Positive and Gram–Negative Bacteria of Upper respiratory tract Diseases

Malek Zarei[1], Yasamin Hajiani[2]

1. Department of Pharmacology, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Pharmaceutical sciences, Islamic Azad University, Tehran, Iran

Background and Objective: Pistachio, containing about 11 different species, is a member of Anacardiaceae family, grown in Iran and different parts of the world. Upper respiratory tract infections are common in humans and finding a cheap available herbal medicine with fewer adverse effects, compared to synthetic medicines, is valuable. We aimed to investigate the antibacterial effect of aqueous extracts of Pistachio hulls on upper respiratory tract bacteria.
Materials and Methods: In this study, Pistacia Vera L. (pistachio) fruits were collected on August and shells were peeled off and dried under the sun and aqueous extracts were obtained by decoction, and maceration method, respectively. The antibacterial effects of extracts were studied by minimum inhibitory concentration (MIC) and disc diffusion methods. After soaking Blanc discs in total extracts and putting them in Mueller–Hinton agar environment, bacteria were incubated with 0.5 density McFarland and the diameter zone inhibition was investigated. Results: Diameter of inhibition zone for aqueous extract of shell was as follows: Strep Sanguis 20 mm, Strep Mutans 15 mm, lactobacillus 11 mm, Staph. Aureus 15 mm, Enterococcus faecalis 20 mm, Strep group A 13 mm, Candida 16 mm, and Pseudomonas aeruginosa 15 mm, and for
Conclusion: Pistachio hull extracts had satisfactory inhibitory effects on upper respiratory tract bacteria with the greatest effect on Enterococcus faecalis and Strep Sanguis, while they had no antibacterial effects against E. coli, which confirms aqueous extracts of Pistachio hull as a cheap and available substance for oral bacteria.
Keywords: Pistachio; Anti–Bacterial Agents; Nasopharyngeal Diseases; Iran

P-246

Does the oxidant-antioxidant status affect suicide behavior?

Mahin Oshnokhah [3], Maryam Bagheri[1,2], Hori Ghaneialvar [3], Karimeh Haghani [3], Ali Khorshidi [4], Ali Shahbazi [5], Sajjad Salari[1,2]

1. Department of Physiology, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran.
2. Psychosocial Injuries research center, Ilam University of Medical Sciences, Ilam, Iran.
3. Department of Clinical Biochemistry, Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran.
4. Department of Epidemiology, Ilam University of Medical Sciences, Ilam, Iran
5. Department of Neuroscience, Iran University of Medical Sciences, Tehran, Iran

Objective: Oxidative stress plays critical role in aging and pathogenesis of neurodegenerative and neuropsychiatric disorders. However, its role in suicidal behavior is not clear. Consequently, we aimed to evaluate the oxidant-antioxidant status in the serum of suicide attempters in Ilam city.
Methods: In this study, 50 suicide attempters and 40 control subjects (volunteers) aged 18-35 years were studied. In order to assess the oxidant-antioxidant status, serum levels of malondialdehyde (MDA), nitric oxide (NO), superoxide dismutase (SOD) and the total antioxidant capacity (TAC) were measured.
Results: Serum levels of SOD enzyme and TAC were significantly lower in suicide attempters group compared to the controls. Furthermore, serum NO level was significantly higher in the suicide attempters in compare with the controls. Interestingly, the serum level of MDA was significantly lower in the suicide attempters compared to the controls.
Conclusion: presence of oxidative stress in the absence of MDA elevation has been detected in suicide attempters can be considered as a hallmark in suicide behavior.
Keywords: suicide behavior, oxidative stress, TAC, MDA, SOD

P-247

Cyanidine 3 glucoside attenuates oxidative stress in a model of acute kidney injury induced by lipopolysaccharide in the mouse

Sepide Salari[1], Atefeh Ghorbanpour[1], Tourandokht Baluchnejadmojarad[2], Mehrdad Roghani[3]

1. School of Medicine, Shahed University, Tehran, Iran.
2. Department of Physiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
3. Neurophysiology Research Center, Department of Physiology, Shahed University, Tehran, Iran.

Background and Objective: Acute kidney injury (AKI) is a common sepsis-related complication and accompanies loss of kidney function. Lipopolysaccharide (LPS) is used to induce AKI. Cyanidine 3 glucoside (C3G) is an anthocyanin that is found in pigmented fruits with multiple protective effects in various tissues. This study was done to evaluate the protective effect of C3G in a model of AKI induced by lipopolysaccharide in the mouse and to assess possible involvement of oxidative stress.
Materials and Methods: Male mice (C57BL/6 strain, n=32) were randomly divided into 4 groups, i.e. control, LPS, and LPS groups receiving C3G (5 or 30 mg/kg). For induction of AKI, lipopolysaccharide was injected i.p. at a dose of 10 mg/kg. After 24 h, mice were killed and serum BUN and creatinine and oxidative stress parameters including reactive oxygen species (ROS), superoxide dismutase SOD, and catalase were determined.
Results: Our findings indicated that C3G significantly reduce serum BUN and creatinine and lower ROS and increase SOD activity and did not significantly affect catalase activity.
Conclusion: It is concluded that C3G is able to alleviate systemic LPS-induced AKI and part of its beneficial effect is via mitigation of oxidative stress and also through potentiation of defensive antioxidants.
Keywords: Acute kidney injury, Lipopolysaccharide, Cyanidine 3 glucoside, Oxidative stress

P-248

The effects of honey syrup and mixture of Cyperus rotundus, Crocus sativus L, Piper nigrum and Boswellia Serrata on memory impairment and oxidative stress parameters in hypothyroid rats

Shiva Saeri[1], Mosalreza Hajzadeh[1,2,3], Mahmoud Hosseini[1,2,3], Sara Hoseinian[1,2], Zohreh Arab[1]

1. Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences
2. Division of Neurocognitive Sciences, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences
3. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences

Background: Thyroid hormone deficiency is associated with increased risk of cognitive disorders. This study evaluated the impact of a combination of four memory enhancer herbs and honey on memory and their effects on oxidative stress parameters. The aim of using herbs in form of combination was enhancing the therapeutic effects. Meanwhile a comparison was performed between donepezil, and the herbals combination.
Material: Seventy Wistar rats 21 days old, were divided to seven groups: control, control-Honey (600mg/kg), PTU, PTU-Honey(600mg/kg), PTU-HZPSF (640mg/kg), PTU-HZPSF(1280mg/kg) ,PTU-Donepezil (0.5mg/kg). All groups except the control groups received 0.05% PTU in their drinking water for six weeks. To make the herbal combination, 5 grams of every constituent were powdered and mixed with 50 gram honey and the doses were daily administered by gavage. Donepezil also was administered the same method. To evaluate memory abilities MWM and PA tests were performed. Oxidative stress parameters were measured too.
Results: Both doses of herbals combination, and donepezill decreased latency time and increased delay in entering the dark compartment .Both doses reduced MDA and NO metabolites in the brain while raised the thiol content, SOD and catalase activities.
Conclusion: The results showed that treatment with both doses of combination and donepezil posse neuroprotive effects, but the high dose (HZPSF1280mg/kg) seems to be more effective.
Keywords:
HZPSF abbreviation for: Honey, Saffron, Pepper, Sage, Frankincense.

P-249

The effects of injection of Amlodipine and Steroid Hormone into Hippocampus on Learning and passive Avoidance memory in the rats

Hossein Salmani*, Homayoun Khazali, Abdolkarim Hosseini

Master Student of Physiology- Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

Aims: In the present study, the effect of Calcium Dihydropyridine antagonist and steroid hormones and their interaction in the inhibitory avoidance memory consolidation was investigated. Experiments showed blocking the calcium channels affecting memory and learning. Amlodipine (calcium dihydropyridine antagonist) by blocking the calcium channels of the nerve cells and affecting the synapses have a different effect on memory and learning, and since the steroids have a protective function on the central nervous system, steroid hormones with Amlodipine were used for a wider study.
Materials & Methods: In this experimental study, twenty male wistar rats weighing 220-250 g in 4 groups Received Amlodipine, Amlodipine and estrogen, Amlodipine and progesterone, Amlodipine and progesterone and estrogen, respectively, via the hippocampus and in final volume of 3µl. Rats were anesthetized with intra-peritoneal injection and placed in a stereotaxic apparatus. There were placed two cannuales, 2 mm above hippocampus. A week after the surgery, as the memory criteria, the rat latency in entrancing to black box was measured. Data were analyzed by SPSS software version 24 and appropriate statistical tests.
Result: The collected information from pharmaceuticals showed that intra-hippocampus administration injection of Amlodipine reduced passive avoidance memory. Also, estrogen injection with Amlodipine and progesterone with Amlodipine and simultaneous injection of estrogen, progesterone and Amlodipine significantly reduced the passive avoidance memory.
Conclusion: Amlodipine is involved in the mechanism(s) modulating avoidance memory. There is an interaction between Amlodipine and steroid hormones in the modulation of avoidance memory consolidation in the hippocampus.
Keywords: Amlodipine, Steroid Hormones, Memory, Passive Avoidance Memory, rat

P-250

The effect of methadone and haloperidol combination on anxiety induced by morphine withdrawal in male mice

Ashkan Sanaie Rad[1*], Mohsen Khalili[2], Elham Zahedi[3], Elham Esmail Jmaat[1]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Shahed University, Tehran, Iran.

3. Department of Physiology, Medical University of Tehran, Iran.

Background and Objective: Regarding inefficiency of common drugs used for alleviation of anxiety due to narcotics withdrawal, the present study was evaluated methadone and haloperidol co-drugs therapy on anxiety due to morphine withdrawal.
Materials and Methods: Ninety eight NMRI male mice were divided into acute and chronic experimental groups. Then, each group was divided into 7 subgroups: saline, morphine (control), methadone, haloperidol, methadone+haloperidol, methadone+haloperidol with 2/1 and 1/2 ratio, respectively. Mice were addicted chronically (over 8 days) by receiving escalating doses of morphine and acute (morphine was applied only on 8th day) procedures. Anxiety was induced by naloxone application in addicted mice. Elevated plus-maze and open field tests were used for evaluation of anxiety.
Results: Obtained data showed that in both chronic and acute groups, treatment with co-drugs methadone and haloperidol could markedly alleviate anxiety signs produced by interruption of morphine consumption.
Conclusion: We found out that the anxiety as a major sign of morphine withdrawal sign could be diminished by methadone+haloperidol therapy versus drugs alone.
Key Words: Morphine, Anxiety, Methadone, Haloperidol, Mice

P-251

Resveratrol attenuates angiotensin II–induced interleukin-6 expression through activation of sirtuin1 in hypertrophied H9c2 cells

Fariba Akhondzadeh[1] , Akram Astani[2,3], Razieh Najjari[1], Fatemeh Safari[1,4*]

1. Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Zoonotic Diseases Research Center, Faculty of public health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
3. Department of Microbiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
4. Biotechnology Research Center, International Campus, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Background and objective: Interleukin (IL)-6 is a proinflammatory cytokine that involves in the pathogenesis of cardiac hypertrophy. Recent studies have documented that resveratrol shows multiple cardioprotective effects. This study evaluated the ability of resveratrol's anti-inflammatory effects on IL-6 in hypertrophied H9c2 cardiomyoblast through histone deacetylase, sirtuin (SIRT)1.
Materials and Methods: To induce hypertrophy, the cells were incubated with angiotensin II (Ang). Treatment groups were treated with different doses (1, 10, 25, 50, 75, and 100 μM) of resveratrol (R). Cell viability was measured using MTT assay. Cell size was determined using crystal violet staining. Gene expression was assessed by real time PCR (RT-PCR) technique. ELISA assay was used to measure IL-6 concentration.
Results: Cell area and atrial natriuretic peptide mRNA levels decreased significantly in R25+Ang, R50+Ang, and R100+Ang groups, as compared to Ang group. Therefore, 10, 20, 30, 40, and 50 μM of resveratrol were used to to evaluate its anti-inflammatory effects. The results revealed that Ang II upregulated IL-6 at both mRNA and protein levels ($P<0.001$ vs. normal) and resveratrol (50 μM) decreased IL-6 mRNA ($P<0.01$) and protein ($P<0.05$) significantly in comparison to Ang group. However, in groups in which the cells were pre-treated with SIRT1 inhibitor, EX-527, the response of resveratrol was partially reversed. Transcription levels of IL-6 receptor components (gp-130 and gp-80) did not change significantly among the experimental groups.
Conclusions: Our results showed that one of the possible mechanisms for anti-hypertrophic effect of resveratrol is through downregulation of the inflammatory responses through activation of SIRT1.
Keywords: Cardiac hypertrophy. Cardiac inflammation. H9c2. Angiotensin II. Resveratrol. ANP. IL-6. gp130. gp80

P-252

Maintaining of plasma lysyl oxidase level in patients with atherosclerosis following by MgSo4 treatment

Fariba Azarkish[1], Aghdas Dehghani[1], Nepton Soltani[2], Hossein Farshidi[3], Ebrahim Eftekhar[1], Seyed Alireza Sobhani [4], Mahdiye Eslami[3]

1. Molecular Medicine Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

2. Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

3. Cardiovascular Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

4. Department of Pathology, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Background and Objective: Down regulation of lysyl oxidase (LOX) in early stages of the atherosclerosis causes endothelial dysfunction and plaque instability. Also, Magnesium deficiency progresses atherosclerosis. So, this study designed to evaluate the therapeutic effect of magnesium sulfate, MgSo4, on the plasma levels of LOX in moderate coronary artery disease (moderate CAD).
Materials and Methods: 80 moderate CAD patients were included in a randomized double blind placebo-controlled clinical trial. During 6 months, along with their routine treatment, patients received either oral placebo or 300 (mg) MgSo4 daily. Then, they located into four groups, MgSO4-treated- patients with one atherosclerotic vessel (MgSo4-treated-VR1, n=13), MgSO4-treated- patients with tow atherosclerotic vessel (MgSo4-treated-VR2, n=19), placebo-treated-CAD patients with one and two atherosclerotic vessel (Control-VR1, n=13 and Control-VR2, n=19). Every three months, LOX, Hemocystein, ESR, and lipid profiles levels were measured. The study was approved with IRCT20151028024756N3 code.
Results: The base levels of cholesterol, triglyceride (TG), LDL, VLDL, ESR and hemocystein were higher in Control-VR2 and Mg-treated-VR2 groups than Control and Mg-treated-VR1 groups. After Three month of treatment with MgSo4, lysyl oxidase maintained in high levels but this factor reduced significantly in the control groups after three and six months. In addition, MgSo4 decreased hemocystein level after three and six months compare to base- MgSo4-treated groups. Considering the effect of magnesium on lipid profiles, this element decreased TG, VLDL and ESR levels significantly compare with placebo groups
Conclusion: an appropriate dosage of MgSo4 can decelerate atherosclerosis by improving lysyl oxidase and decreasing lipid profiles and hemocystein level.
Keywords: Atherosclerosis, Lysyl Oxidase, Magnesium Sulfate, Lipid Profile

P-253

Does increased Nitric Oxide production and oxidative stress due to high fat diet affect cardiac function after myocardial infarction?

Marjan Aghajani[1], Alireza Imani[1], Mahdieh Faghihi[1], Mohammad Reza Vaez Mahdavi[2], Maryam Belaran[3], Kaveh Tabrizian[4], Mozhgan Aghajani[5]

1. Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

2. Department of Physiology, Faculty of Medicine, Shahed University, Tehran, Iran.

3. Department of Physiology, Faculty of Medicine, Zabol University of Medical Sciences, Zabol, Iran.

4. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Zabol University of Medical Sciences, Zabol, Iran

5. Rasool-e-Akram Hospital, Iran University of Medical Sciences, Tehran, Iran.

Background and Objective: High fat (HF) diet by affecting the oxidative stress and nitric oxide (NO) production may lead to different effects on function of the heart after myocardial infarction (MI). In the present study we aimed to address the hypothesis that high release of NO by activated macrophages affects LV function after MI.
Materials and Methods: The animals were randomly divided into four groups comprising each of 10 rats: 1) Sham; 2) MI; 3) Sham+ HF diet; 4) MI+ HF diet. Animals fed with HF diet 30 days before sham and MI surgery. MI was induced by permanent ligation of left anterior descending coronary artery (LAD). Nitric oxide (NO) production of peritoneal macrophages, the concentrations of MDA in the heart and the infarct size were measured.
Results: Our study indicated that HF has adverse effects on myocardium and it may increase NO production as well as oxidative stress ($p < 0.05$), resulting in augmentation of infarct size ($p < 0.05$).
Conclusion: Our results add to our knowledge that HF diet was associated with overproduction of NO by peritoneal macrophages and ROS that lead to development of infarct size and adverse remodeling.
Keywords: High fat diet, Myocardial Infarction, Nitric Oxide, Oxidative Stress, Peritoneal Macrophages

P-254

The effects of oral administration of beetroot juice on blood pressure and its interaction with adrenergic system of male hypertensive rat

Zahra Aghaei Fard, A. Bahaoddini, J. Vatanparast and A. R. Khosravi

Department of Biology, Shiraz University, Shiraz, Iran

Background and Objective: beetroot juice is used as antihypertensive agent traditionally in Iran. To evaluate the effects of oral administration of beetroot juice on the blood pressure of hypertensive rats and its probable mechanism the present study was performed by the following procedure:
Materials and Methods: 18 adult male rats were divided into 3 groups: control, sham (water gavage) and experimental (beetroot juice gavage). Hypertension induced by injection of 25mg/kg of deoxycorticosterone acetate twice a week for 4 consecutive weeks. During this time, rats drank water with 1% NaCl. The rats of sham and experimental groups one week before surgery, 1 cc of water and beetroot juice were gavaged. Then rats were anesthetized by IP injection of urethane. After tracheostomy the femoral vein and artery were cannulated for drugs injection and blood pressure and heart rate recording respectively. Blood pressure and heart rate were recorded at baseline and after adrenaline injection by power lab system. The data was analyzed using One-way-ANOVA at $P \leq 0.05$ as significant level.
Results: Mean arterial, systolic and diastolic pressure were decreased significantly in experimental group with compare to control and sham groups. However, in beetroot juice gavaged groups no change of blood pressure was recorded after adrenaline administration.
Conclusion: Beetroot juice is suggested as antihypertensive agent via inhibition of adrenergic system.
Keyword: Beetroot, Blood pressure, Adrenergic system.

P-255

Effect of Ischemic Postconditioning on Myocardial Function and Infarct Size Following Reperfusion Injury in Diabetic Rats Pretreated With Vildagliptin

Goltaj Bayrami[1], Pouran Karimi[2], Fariba Agha-Hosseini[1], Saeid Feyzizadeh[3], Reza Badalzadeh[1]

1. Physiology Laboratory, Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
2. Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
3. Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

BACKGROUND: Diabetic hearts are resistant to cardioprotection by ischemic-postconditioning (IPostC).This study has investigated the combined effects of IPostC and vildagliptin (Vilda) on myocardial function and infarct size (IS) against I/R injury in diabetic myocardium.
METHODS: Diabetes was established by high fat diet/low dose of streptozotocin and lasted for 12 weeks. The diabetic rats received Vilda (6 mg/kg/day, orally) for one month before I/R. Myocardial regional ischemia was induced through the ligation of left coronary artery, and IPostC was applied immediately at the onset of reperfusion. Myocardial hemodynamic was measured throughout the experiment. The IS was assessed by triphenyltetrazolium chloride staining method. The myocardial contents of troponin-I (cTnI), interleukin-6 (IL-6), and 8-isoprostane were measured in the homogenate from ischemic zone of left ventricles by enzyme-linked immunosorbent assay kit.
RESULTS: Pretreatment of the diabetic rats with Vilda significantly recovered the diabetes-induced reduction in left ventricular developed pressures and contractility at the baseline ($P < .05$ to $P < .01$). After I/R injury, IPostC could not significantly improve the myocardial function, cTnI content, and IS of the diabetic hearts. In Vilda-treated hearts, concomitant application of IPostC significantly recovered the heart functions, returned cTnI content as well as myocardial IL-6 and 8-isoprostane levels back to the control values ($P < .01$ to $P < .001$), and reduced IS more effectively (by 45%) in comparison to the diabetic group ($P < .001$).
CONCLUSION: Besides its glycemic and lipid profile controlling effects, Vilda has a protective effect on heart function and tends to restore cardioprotective effects of IPostC on diabetic hearts.
KEYWORDS: cardioprotection; diabetes; infarct size; ischemic postconditioning; reperfusion injury

P-256

Cytoprotective and antioxidant effects of Evolocumab against H2O2-induced oxidative stress in human endothelial cells (HUVECs)

Leila Safaeian[1], Shahryar Bahrizade[1], Mina Mirian[2]

1. Pharmacology and Toxicology Department , University of Medical Sciences , Isfahan , Iran

2. Pharmaceutical Biotechnology Department , University of Medical Sciences , Isfahan , Iran

Background: Evolocumab, an inhibitor of proprotein convertase subtilisin/kexin type 9 (PCSK9) has recently been approved for treatment of hypercholesterolemia. In the present study, we investigated the protective and antioxidant effects of Evolocumab on H2O2-induced oxidative stress in human vascular endothelial cells (HUVECs).
Materials and Methods: HUVECs were pretreated by (1.25-100 µg/ml) Evolocumab for 24 h and then exposed to 0.5 mM H2O2 for 2 h. Cell viability was assessed by 3-(4, 5- Dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay. The intra and extra-cellular hydroperoxides concentration and ferric reducing antioxidant power (FRAP) were determined in pretreated cells.
Results: Pretreatment of HUVECs with Evolocumab at the concentrations of 10-100 µg/ml significantly reduced the cytotoxicity of H2O2 in a concentration-dependent manner using MTT assay. Evolocumab pretreatment at different concentration ranges also decreased the hydroperoxides level and augmented the FRAP value in both intra- and extra-cellular assay.
Conclusion: These findings revealed antioxidant and cytoprotective effects of Evolocumab against H2O2-induced oxidative stress in HUVECs. With regard to the beneficial vascular activity of Evolocumab, further investigations are suggested for understanding its clinical value in human endothelial dysfunction and prevention and/or treatment of CVDs.
Key Words: Evolocumab, HUVECs, oxidative stress, antioxidant

P-257

Anti-arrhythimic effects of the potassium channel blocker, dalfampridine in isolated rat atria

Azam Bakhtiarian[1], Nahid Ghebleh Zadeh[2], Zahra Mousavi[3], Vahid Nikoui[4]

1. Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
2. Department of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran.
3. Department of Pharmacology-Toxicology, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University (IAUPS), Tehran, Iran.
4. Razi Drug Research Center, Iran University of Medical Sciences, Tehran, Iran.

Background and Objective: Cardiac arrhythmias are life-threating condition, which need for serious management. This study was aimed to investigate the possible antiarrhythmic effects of dalfampridine in ouabain-induced arrhythmia in rats.
Materials and Methods: Male rats including the control and dalfampridine-incubated (100 µM to 10 mM) ouabain-stimulated (40 µM) groups were used. After induction of anesthesia, the atria were isolated and the time of onset of arrhythmia and asystole were recorded. The contractile force of atria was also measured. Unpaired Student's t-test was used to compare the time of onset of arrhythmia or asystole as well as atrial beating rate and contractile force between treatments and control groups. Paired Student's t-test was carried out to find the effects of ouabain on atrial beating rate and contractile force within groups. P values less than 0.05 were considered statistically significant.
Results: Dalfampridine (1 mM) significantly delayed the onset of arrhythmia and asystole compared to control group ($P \leq 0.05$). Ouabain significantly boosted the atrial beating rate in control group ($P \leq 0.05$), while pretreatment of isolated atria with dalfampridine reversed this effect. Incubation of isolated atria with ouabain did not change the contractile force in both control- and dalfampridine-treated groups ($P > 0.05$).
Conclusion: It is concluded that dalfampridine might exert antiarrhythmic effects in reducing the atrial arrhythmias.
Keywords: Dalfampridine, Arrhythmia, Potassium channel blocker, Isolated atria

P-258

The influence of intermittent fasting on expression of antiaging proteins and blood pressure in rats of different ages

Firuzeh Badreh[1,4], Siyavash Joukar[2,3,4], Mohammad Badavie[6], Mohammad Rashnog[8], Tania Dehesh[9]

1. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
3. Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
4. Department of Physiology and Pharmacology, Afzalipour Faculty of Medicine, Kerman University of Medical Science, Kerman, Iran
5. Department of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
6. The Persian Gulf Physiology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
7. Department of Immunology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
8. Cellular and Molecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
9. Department of Epidemiology and Biostatistics, School of public health, Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: Intermittent fasting can be effective in reducing metabolic disorders and age-related diseases. However, there remain questions about the effects of fasting with respect to the age in which fasting begins, the chronic mild and severe fasting models and the mechanisms involved. We investigated the effects of age of beginning fasting and two models of fasting on blood pressure, insulin/glucose profile and expression of klotho, SIRT1 and SIRT3 in male Wistar rats.
Materials and Methods: Young (3 months), middle-aged (12 months) and old (22 months) animals were randomly divided into three subgroups and fed as ad libitum (AL), ad libitum with fasting 1 day per week (FW), and ad libitum with fasting every other day (EOD) respectively for three months.
Results: The FW reduced the weight gain in young animals ($P<0.001$ vs. AL), while EOD induced weight loss in all three age categories ($P<0.001$). Aging was associated with high blood pressure, high glucose and insulin levels. Both FW and EOD feeding decreased blood pressure and blood glucose level ($P<0.001$) and EOD decreased insulin level ($P<0.05$ vs. AL) in old animals. Parallel to aging the expression of SIRT1 and klotho significantly decreased in plasma and EOD feeding recovered this defect. Both FW and EOD feedings increased the expression of SIRT3 in middle-aged and old rats.
Conclusion: Age is a determining factor for the effectiveness of fasting and old animals respond more desirably to fasting. The effect of EOD fasting is more effective than FW fasting in improving the metabolic factors, partly through the recovery of SIRT1 and klotho.
Keywords: Fasting models; Age; Blood pressure; Insulin/glucose profile; Klotho; Sirtuins

P-259

Evaluating the effects of Silybum marianum extract on cardiac expression of farnesoid-X-activated receptor (fxr), ucp2 and ucp3 genes in the rat model of cirrhosis

Gholamreza Bayat[1,2], Roham Mazloom[1], Azadeh Khalili[1,2], Seyed Ali Hashemi[3], Parviz Fallah[4], Leila Beikzadeh[4], Mohammad Mahdi Ahmadian-Attari[2], Vahid Jamshidi[5]

1. Department of Physiology and Pharmacology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran
2. Evidence-based Phytotherapy and Complementary Medicine Research Center, Alborz university of medical sciences, Karaj, Iran
3. Department of Pathology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran
   Department of Medical Laboratory Sciences, Faculty of Para-Medicine, Alborz University of Medical Sciences, Karaj, Iran
4. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, Iran

Background and Objectives: According to clinical and experimental findings, cirrhosis could negatively affect the cardiac function and/or structure. The present study has been designed to answer the question of whether Milk Testile has the ability to reverse cardiac complications due to liver cirrhosis.
Materials and Methods: Forty two male Wistar rats allocated into 5 random groups (n=7 in each) including control, Sham-operated, Bile duct ligated (BDL), and two bile duct ligated groups which received oral Milk Testile extract at 300 and 600 mg/kg/day (MTE300 and MTE600) for 28 days. Besides liver enzymes and histopathological assessment, cardiac fxr, ucp2 and ucp3 gene expression, have been quantified using real-time RT-PCR technique.
Results: The liver enzymes of ALT, AST, LDH, GGT and ALP were significantly higher than that of the values in control group. The histopathological assessment also exhibited drastic liver damage in the BDL group. In addition, bile duct ligation also was associated with the significant down-regulation in cardiac expression of fxr, ucp2 and ucp3 mRNA genes. Administration of the MTE300 or MTE600 was not associated with significant reduction in the ALT and AST plasma levels however, interestingly the levels of LDH (MTE600), GGT and ALP showed significant elevation in MTE-treated than that of BDL group. Cardiac expression of fxr, ucp2 and ucp3 genes were significantly restored in MTE600 compared to BDL group.
Conclusion: Cardiac complication secondary to bile duct ligation such as alteration in cardiac gene expression, could be restored by chronic administration of 600 mg/kg/day MTE for 28 days.
Keywords: Milk Testile, Bile duct ligation, Cirrhosis, Farnesoid receptor (FXR), uncoupling Protein 2 (UCP2), Uncoupling Protein 3 (UCP3)

P-260

Perillyl alcohol ameliorates monocrotaline-induced pulmonary artery hypertension in rats

Ahmad Beik[1], Hamid Najafipour[2], Soodeh Rajabi[3]

1. PhD candidate, Department of Physiology and Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Science, Kerman, Iran
2. Distinguished Professor of Physiology, Department of Physiology and Cardiovascular Research Center, Institute of Basic and Clinical

Physiology Sciences, Kerman University of Medical Science, Kerman Iran

3. hD candidate, Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of medical science, Kerman, Iran

Background and objective: pulmonary artery hypertension is a disastrous disease with an unpromising prognosis that the current treatments cannot prevent its progression. The present study investigated the effects of Perillyl alcohol (P-OH), a natural monoterpenoid, on experimental pulmonary artery hypertension (PAH) in rats.
Materials and methods: 42 male NMRI rats weighing 250±30 grams were included in 7 groups: saline, monocrotaline, vehicle, P-OH (30, 40, 50, and 60 mg/kg). To induce PAH, a single dose of monocrotaline 60 mg/kg was injected subcutaneously. During days 28-42 animals were treated daily with an intraperitoneal injection of P-OH or vehicle. On day 43, animals were anesthetized with ketamine and xylazine. A polyethylene catheter was inserted into the right ventricle via the right jugular vein to record right ventricular pressure by PowerLab system. Right ventricular systolic pressure (RVSP) was used as an index of pulmonary artery systolic pressure. Furthermore, the ratio of the right ventricle to septum plus left ventricle weight was used as an index of the right ventricle hypertrophy (RVH).
Results: Monocrotaline significantly raised RVSP (89.2±2.1 mmHg vs 29.5±1.2 mmHg) ($p<0.001$) and caused RVH (0.59±0.01 mg/mg vs 0.3±0.01 mg/mg). RVSP and RVH in the vehicle group had no differences with the monocrotaline group. P-OH 50 mg/kg (best dose) significantly reduced RVSP and RVH compared to vehicle (32.8±2 vs 91.8±2.9 mmHg and 0.34±0.01 vs 0.54±0.01 mg/mg) ($p< 0.001$). Histologic and biochemical findings also supported the physiological data.
Conclusion: P-OH,50 mg/kg significantly attenuated RVSP and RVH and may be used in the treatment of PAH.
Keywords: pulmonary artery hypertension, rat, monocrotaline, Perillyl alcohol

P-261

Central GABA-A receptors are involved in cardioprotection against ischemia/reperfusion injury

Hoda Parsa[1], Alireza Imani[1, 2], Mahdieh Faghihi[1]

1. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Occupational Sleep Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran

Background and Objective: Gamma-amino butyric acid (GABA) is a neurotransmitter that modulates sleep and affects cardiac functions. Since sleep is considered as a physiological regulator in the body, we evaluated effects of acute sleep deprivation (SD) on cardiac hemodynamic parameters and expression of pro-inflammatory cytokines.
Materials and Methods: Male Wistar rats were bilaterally cannulated in the central nucleus of amygdala (CeA) which effects on cardiac function through GABA projections to nucleus tractus solitaries (NTS). Saline or bicuculline was injected 24 hours prior to induction of 30 minute ischemia following 120 minute reperfusion (IR). Forty-eight animals were randomly divided into four groups: Control (CONT), Bicuculline (BIC), acute sleep deprivation (SD) and bicuculline + acute sleep deprivation (BIC + SD). Animals in SD and BIC + SD groups were put in an aquarium for inducing 24 hours sleep deprivation.
Results: Our results showed SD attenuated pro-inflammatory cytokines (IL-6 and TNF-α) ($p<0.001$) and improved cardiac hemodynamic parameters ($p<0.001$). Administration of bicuculline increased pro-inflammatory cytokines and reduced cardiac hemodynamic parameters as compared to CONT ($p<0.001$). Furthermore, bicuculline administration prior to acute sleep induction decreased SD effects on cardiac hemodynamic parameters and pro-inflammatory cytokines ($p<0.001$).
Conclusion: Induction of sleep deprivation prior to ischemia/reperfusion induces cardioprotection through suppressing inflammatory responses, which it seems that GABA pathways may involve.
Key words: GABA, Cardioprotection, Acute sleep deprivation, pro-inflammatory cytokines

P-262

Pretreatment with vildagliptin boosts ischemic-postconditioning effects on experession levels of Micro_RNA's in rats with type 2 diabet following in-vitro myocardial ischemic reperfusion injury

Lale Pirzeh

Background and objective: The burden of myocardial ischemia/reperfusion (IR) injury is 2-3 folds higher in diabetic patients,so protecting diabetic hearts is clinically important. In this study, the effect of combined therapy by

vildagliptin and IPostC on the cardiac injury and experession levels of Micro_RNA's have been studied in the diabetic heart which suffers from IR injury.
Material and methods:. Type-2 diabetes was induced through high-fat diet and streptozotocin protocol in Wistar rats. Vildagliptin was orally administered to diabetic rats 5 weeks before IRinjury. Myocardial-IR injury was modeled by ligation of left coronary artery for 30minutes followed by 60minutes reperfusion, on a Langendorff-perfusion system.IPostC was applied at early reperfusion as 6 alternative cycles of 10 seconds reperfusion/ischemia. Creatine-kinase levels were measured spectrometrically, and infarct size was evaluated by TTC staining method. The expression level of microRNA-125b and microRNA-140 In the left ventricle was examined using the real-time PCR method.
Results: Induction of diabetes significantly increased creatine-kinase release in comparison to healthy rats, and all treatments significantly reduced the release of enzyme toward control levels($p<0.05$). Only the combination therapy(IPostC+vildagliptin) could significantly reduce the infarct size of diabetic hearts as compared to untreated diabetic-IR group ($p<0.01$) Finally, the combination therapy prevents from microRNA-140 expression rising which caused by IR injury in the diabetic heart and it increased the expression of microRNA-125.
Conclusion:Application of this combination therapy could overcome the diabetes-induced failure of cardioprotection by individual treatments and improve mitochondrial dynamic and autophagy flux.
Keywords: combined cure, heart protection, Myocardial infarction, post-readiness, mitochondria, autophagia

P-263

Cardioprotective effects of memantine "an NMDA receptor antagonist" in myocardial infarction in rats

Kosar Jannesar[1], Malekinejad Hassan[2], Soraya Hamid[2]

1. Pharmacy student, Student Research Committee, Department of Pharmacology and Toxicology, Urmia university of medical sciences , Urmia, Iran
2. Department of Pharmacology and Toxicology, School of Pharmacy , Urmia University of Medical Sciences , Urmia, Iran

Background: In addition to central nervous system (CNS), NMDA glutamate receptors also exist in peripheral tissues such as the heart. The stimulation of these receptors in the heart cells can increase the production of reactive oxygen species and lead to cardiac remodeling. The present study investigated the effect of memantine, an antagonist of NMDA receptors on hemodynamic parameters, cardiac hypertrophy, lipid peroxidation, Myeloperoxidase (MPO) activity and level of TNFα.
methods: Male wistar rats were randomly assigned into 5 groups of control, MI and pretreated ip with 5, 10 and 20 (mg/kg/day) of memantine for 7 days. For induction of MI, isoproterenol 100 (mg/kg) was injected subcutaneously at 8th day for 2consecutive days. The hemodynamic parameters (MAP), lipid peroxidation, myeloperoxidase (MPO) activity and TNF α levels were measured.
Results: The heart weight to body weight ratio was significantly decreased in memantine pretreated groups (10 and 20 mg/kg/day; $p<0.05$, $p<0.001$ respectively) in comparison to MI group. Hemodynamic parameters were improved significantly in memantine 20 (mg/kg/day) in comparison to MI group ($p<0.05$). Additionally the level of malondialdehyde and also MPO activity were decreased significantly in all pretreated groups in comparison to MI group ($p<0.001$, $p<0.05$ respectively). The level of cardiac TNFα was lower significantly in the memantine 20 mg/kg group in comparison to MI group ($p<0.05$).
Conclusion: The results of study showed that memantine can be cardioprotective in myocardial infarction at least in part through reduction in cardiac hypertrophy, oxidative stress and inflammation.
Key words: Memantine, Myocardial infarction (MI), Isoproterenol, Oxidative stress, Inflammation

P-264

Protective effects of Ferula Assa-Foetida on myocardial ischemic-reperfusion injury in diabetic rats

Faezeh Jafari Nezhad, Hossein Azizian*, Mohammad Ebrahim Rezvani, Zeinab Farhadi, Mansour Esmailidehaj

Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Objectives: Cardiovascular disease is the leading cause of morbidity and mortality in patients with diabetes mellitus. Assafoetida (AF) commonly consumed as a healthy beverage has been demonstrated to have various biological activities, including antioxidation and anti-obesity. The aim of this study is to investigate the effects of Assafoetida investigated on ischemic–reperfusion injury in isolated diabetic rat heart.
Methods: Thirty-two male Wistar rats were divided into 4 groups of eight. Group I, sham-control (Sham-Con); group II, diabetes (Dia); group III, Dia+AF25 mg/kg; group IV, Dia+AF50 mg/kg. Rats received AF through orally once a day for four weeks. Then their hearts were subjected to 30 min global ischemia and 90 min reperfusion under Langendorff apparatus.
Results: Results show that; AF50 reduces fasting blood glucose and improved lipid profile. Hemodynamic parameters decreased in Dia group, while AF50 prevented LVESP, LVDP, and ±dp/dt decrement. Also, the infarct size was decreased by AF50. The significant decrement in the levels of lactate dehydrogenase and creatine phosphokinase observed in Dia group and this effect was abolished by AF50. Also, treatment with AF50 resulted in improved oxidative stress. Although diabetes resulted in, an increment of sustained ventricular fibrillation and decrement heart running, AF50 reduced SVF and increased heart running.
Conclusion: Our results indicated that AF protects against diabetic cardiovascular dysfunction and is a potential source of natural antidiabetic and cardioprotective products.
Keywords: Cardiovascular, Diabetes, Assa-Foetida, Ischemia, Reperfusion, Rat.

P-265

Computational prediction of microRNAs targets for Myocardial Infarction Associated Transcript (MIAT) long non-coding RNA

Saeideh Jafarinejad[1], Maryamm Moazam-Jazi[*2], Morteza Hadizadeh[3]

1. Physiology Research Center, Kerman University of Medical Sciences, Kerman, Iran
2. Cellular and Molecular Research Center, Research Institute for Endocrine Sciences,Shahid Beheshti University of Medical Sciences
3. Student Research Committee, School of Medicine, Kerman University of Medical Science, Kerman, Iran

Background and Objective: Long non coding RNAs (lncRNAs) are a new layer of post/translational regulation which act as miRNAs sponges and protect the target mRNAs. Considering that lncRNAs are poorly conserved, prediction of any intra-species similarity in lncRNA functions would reliably connect animal model experimental observations to understanding of human diseases. We analyzed miRNAs binding affinity for myocardial infarction associated transcript (MIAT), a cardiovascular disease (CVD) related lncRNA, in human, mouse and rat for prediction of functional similarity in orthologs.
Materials and Methods: In silico analysis was performed using miRanda, the microRNA target prediction tool. The miRNA datasets of human, mouse and rat were downloaded from the miRBase as query. Only matched miRNA-lncRNA pairs with the total score of more than 150 and the minimum free energy of < -20 kcal/mol were considered as the significant pairs.
Results: MIAT showed 40% identity in human, mouse and rat. Only 7, 24, and 48 miRNAs had 100% identity in rat, mouse and human, respectively. Based on our finding, miR-760 was the only common miRNA with 100% identity in rat, mouse and human. miR-760 relates to hypoxic cardiomyocyte apoptosis and proliferation of hypoxic human pulmonary artery smooth muscle cells (hPASMCs).
Conclusion: Collectively, this intra-species exploration showed the less conservation of MIAT lncRNA, unlike to micRNAs, which should be considered in the studies. Furthermore, miR-760 as the common target among the human, mouse, and rat indicated the evolutionary conserved pathway in which MIAT-miR760 axis involved.
Keywords: MIAT, Long non coding RNA, MicroRNA, Ortholog

P-266

Combined effect of exercise and genistein on expression of miR-29, miR-133, Igf-1, and bcl-2 in the heart of ovariectomized diabetic rats

Parisa Habibi

Background and Objective: The aims of the present experiments were to investigate the effects of genistein and exercise as an estrogen therapy on the expression changes of miR-133, miR-29, IGf-1, and Bcl-2 in the heart of diabetic ovariectomized rats.
Materials and Methods: Seventy animals were divided into seven groups of control, sham, ovariectomy (OVX), diabetic ovariectomized (OVX.D), and diabetic ovariectomized with 8 weeks of genistein administration (OVX.D.G) and with 8 weeks of swimming training (OVX.D.E) and with 8 weeks of both of them (OVX.D.G.E). High fat nutrition and low dose Streptozotocin (STZ)-induced diabetic female rats received genistein or/and exercise treatment for 8 weeks after ovariectomy. The effect of these treatments was evaluated by measuring lipid profiles, miR-133, miR-29, Bcl-2 and IGF-1 expression levels in the cardiac tissue. Grafts were analyzed by Real-time-polymerase chain reaction for Bcl-2 and IGF-1 mRNA, miR-133 and miR-29 and H&E and PAS method for histological studies and western blot for Bcl-2 protein and elisa for caspase 3.
Results: Ovariectomy down-regulated miR-133, miR-29, Bcl-2, and IGF-1 genes and Bcl-2 protein expression levels and up regulated caspase 3 activity in the cardiac tissue and diabetic OVX rats showed further decrease in the expression of these genes. Genistein administration and swimming training significantly up regulated these genes and Bcl-2 protein expression levels and down-regulated caspase 3 activity in the heart ($p<0.05$).
Conclusion: Our results showed that genistein or /and exercise as a natural replacement therapy could prevent and improve estrogen deficiency effects in the heart.
Keywords: Ovariectomy, diabetes, miRNAs, exercise, genistein.

P-267

The relationship between heart rate variability and metabolic alterations in conscious rats with hemorrhagic shock

Fatemeh Khodadady[1], Farzaneh Ketabchi[2], Aminollah Bahaodini[1]

1. Department of Biology, Faculty of Science, Shiraz University, Shiraz (Iran)
2. Department of Physiology, School of Medicine, Shiraz University of Medical Sciences – Shiraz (Iran)

Background and Objective: Hemorrhagic shock (HS) is a common cause of death in trauma patients. Recently, special attention has been paid to the heart rate variability (HRV), as a useful way for identification of a wide spectrum of diseases. The aim of this study, was to determine whether HRV is linked to metabolic changes in compensated HS.
Materials and Methods: Conscious male Sprague Dawley rats were randomly divided into the sham and HS groups. After anesthesia, the tail artery and femoral vein were cannulated and fixed. Then, conscious animals were located in a small and dark chamber. After 1 hour of recovery period, HS was induced by blood withdrawal until blood pressure decreased to 40±5 mm Hg. Next, blood withdrawal was stoped. The arterial blood pressure and heart rate were recorded by Powelab system throughout the experiments. Furthermore, HRV was analyzed during three phases of compensation. At the end, the blood borne variables was measured.
Results: HRV parameters increased in the first phase of compensation in HS group and amplified in the second phase. However, HRV values were returned back to the values of sham group during the third phase of compensation in the HS group, while, blood glucose and plasma lactate levels in the HS group remained higher than the ones in the sham group. Also, there was a marked decrease in vein oxygen content without any significant alterations in pH.
Conclusion: This study indicated that the metabolic alterations in hemorrhagic shock may occur independent of heart rate variability.
Keywords: Conscious rats, Hemorrhagic shock, HRV, Lactate.

P-268

p- Coumaric acid protects cardiac function against LPS-induced acute lung injury by attenuation of oxidative stress

Maryam Kheiry[1], Mahin Dianat[1], Mohammad Badavi[1], Seyyed Ali Mard[1], Vahid Bayati[2]

1. Department of Physiology, Physiology Research Center, Faculty of Medicine,Ahvaz Jundishapur University of Medical Sciences, Ahvaz,

Iran

2. Cellular and Molecular Research Center, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Background and Objective: Acute lung injury (ALI) a high mortality rate is characterized by damage to pulmonary system giving rise to symptoms such as histological alteration, lung tissue edema and production of cytokine. p-coumaric acid (pCA) as a phenolic compound which found in fruits and vegetables, has been reported to exhibit a therapeutic effect in inflammatory disorders. The aim of our study was evaluation of pretreatment with pCA against heart dysfunction following LPS-induced ALI.
Materials and Methods: The rats were divided into four groups: Control, Lipopolysaccharide (LPS, 5 mg/kg, it), p-CA (100 mg/kg, ip), and LPS+pCA. Inflammatory response (IL-6, TNF-α) and oxidative stress (MDA) were measured in heart tissue. For evaluation the effect of LPS on cardiac response, ECG and hemodynamic parameters were recorded.
Results: A significant increase in lipid peroxidation, cytokine parameters, gene expression of Nrf2 demonstrated in heart tissue of ALI rats. LPS can impair cardiac function (in in vitro measurement of hemodynamic data by using Langendorff setup), and in in vivo measurement of ECG parameters, and pretreatment with p-CA recovered these data to control levels in heart. Pretreatment with p-CA causes modulation of cytokines and MDA level that protected cardiac injury caused by LPS in ALI model.
Conclusion: Our results showed anti-inflammatory and antioxidative effect of p-CA on LPS induced ALI.
Keywords: LPS, p-coumaric acid, ALI, ECG, Nrf2, Hemodynamic parameters

P-269

Investigation of the effect of resveratrol on serum and cardiac levels of angiotensin II and its receptors transcription in the rat cardiac hypertrophy model

Fahimeh Dorri Mashhadi[1], Javad Zavvar Reza[2], Mohabbat Jamhiri[1], Zeinab Hafizi[1], Fatemeh Zare Mehrjardi[1], Fatemeh Safari[1]

1. Department of Medical Physiology, Faculty of Medicine,Shahid Sadoughi University of Medical Sciences, Yazd, Iran

2. Department of Clinical Biochemistry, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Background and Objective: Angiotensin II plays an important role in the pathophysiology of cardiovascular disease. Resveratrol protects the heart against hypertrophic injuries but the responsible cellular and molecular mechanisms are still unknown.This study investigated the effect of antihypertrophic dose of resveratrol on serum and cardiac tissue levels of Angiotensin II as well as transcription level of angiotensin receptors in left ventricle tissue.
Materials and Methods: Male Wistar rats (170-220gr) were divided into control (Ctl), hypertrophied (Hyp), hypertrophied rats pretreated with resveratrol (H+R), resveratrol only (R), and the DMSO groups. Cardiac hypertrophy was induced by abdominal aortic banding. Arterial pressure (BP) was recorded directly via left carotid artery cannula connected to a pressure transducer. Fibrosis was confirmed by mMasson trichrome staining. The serum and tissue levels of angiotensin II were measured with ELIZA test. The rate of genes expression was assessed by real time RT-PCR tecnique. Statistical analysis was performed using Prism software (version 5).
Results: We observed that in H + R group BP and heart weight/body weight were decreased significantly ($p<0.001$, $p<0.05$, respectively vs. Hyp). The cardiac levels of angiotensin II and AT1a mRNA were increased in Hyp group ($p<0.01$ vs. Ctl). In H+R group AT1a mRNA level was decreased significantly ($p<0.05$ vs. Hyp).
Conclusion: It could be concluded that resveratrol protect the heart against hypertrophy progression in part by affecting angiotensin II and I its receptors in heart.
Keywords: myocardial hypertrophy, angiotensin II, resveratrol, AT1a, AT1b, AT2

P-270

Crocin attenuates oxidative stress and inflammation in myocardial infarction induced by isoprenaline via the PPARγ pathway in diabetic rats

Neda Dashtbozorgi[1,2], Mohammad Badavi[1,2], Seyyed Ali Mard[1,2], Mahin Dianat[1,2]

1. Department of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

2. Ahvaz Physiology Research center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Background and Objectives: Hyperglycemia induced oxidative stress and inflammation resulting in development of diabetic cardiomyopathy. The current study investigated the involvement of PPARγ activation in effects of crocin as a natural carotenoid in cardiac infarction in diabetic rats.
Materials and Methods: Diabetes was induced in male wistar rats by streptozotocin (STZ) injection after the administration of nicotinamide. Then saline, crocin and GW9662 were injected for 28 days. Isoprenaline (ISO) was administrated on 27th and 28th days for induction of myocardial infarction.
Results: Isoprenaline and STZ reduced antioxidant enzymes content in myocardial tissue and increased inflammation and lipid peroxidation, while crocin significantly decreased lipid peroxidation and inflammatory cytokines levels and also improved cardiac injury marker level and antioxidant capacity. However, GW9662 (PPARγ antagonist) administration reversed the positive effects of crocin
Conclusion: The results indicated the involvement of PPARγ pathway in the cardioprotective effects of crocin.
Keywords: Crocin, Myocardial Infarction, Inflammation, Isoprenaline, PPARγ

P-271

Ellagic Acid Improves Testis Weight Following Isoproterenol-Induced Myocardial Infarction in Diabetic Male Rats

Ali Rajabi Mohammad Abad, Hamid Reza Kazerani

School of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran.

Background and objective: Several diseases interfere with spermatogenesis including diabetes mellitus (DM), coronary heart disease, and chronic liver diseases. Diabetes mellitus has adverse effects on the fertility of diabetic patients; for instance, it causes abnormal spermatogenesis with sperm deformities and decreases testis weight. The purpose of this study was to evaluate the effects of ellagic acid on testis weight following isoproterenol-induced myocardial infarction in diabetic male rats.
Materials and methods: Male Wistar rats (295±25 g) were randomly divided into 5 experimental groups (n=10, each). The first group was the non-diabetic control. Diabetes mellitus was induced in all other groups using streptozotocin (55 mg/kg, i.p.). Group II the diabetic control. Group III was gavaged with ellagic acid (50 mg/kg) for 21 days. Myocardial infarction was induced in groups IV and V via injection of isoproterenol (100 mg/kg, i.p.) for two consecutive days. However, group V was further treated with ellagic acid (50 mg/kg) for 21 days. On day 21, testis weights were recorded in all rats.
Results: Streptozotocin caused significant reductions in testis weights in all diabetic groups ($p<0.05$). Co-administration of ellagic acid significantly increased this parameter in both infarcted and non-infarcted groups ($p<0.05$).
Conclusion: This study suggests beneficial effects for ellagic acid in improving testis weights in diabetic male rats. This effect seems to be independent of myocardial infarction.
Keyword: ellagic acid, isoproterenol, myocardial infarction, diabetic, testis weight

P-272

Effects of hydroalcoholic extract of Rosa damascena mill on the cardiac angiogenesis in diabetic male rats

Shiva Nosrati[1], Mohammad Zarei[*1], Iraj Salehi[1], Sara Soleimani Asl[2], Alireza Komaki[1], Shirin Moradkhani[3], Masoumeh Taheri Azandaryani[1] , Ghazaleh Omidi[1]

1. Department of Physiology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

2. Department of Anatomy, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

3. Department of Pharmacognosy, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran

Background and Objective: Diabetes as a widespread chronic metabolic disorder is increasing that known as persons' death factor by making severe complications in body. The changes in tissues' angiogenesis such as cardiac angiogenesis, is one of the damage following diabetes disease. Rosa damascena mill, known medical plants, has potent antioxidants properties and the antioxidants can make changes in angiogenesis. In this study, effects of hydroalcoholic extract of Rosa damascena mill on the cardiac angiogenesis in diabetic male rats was investigated.
Materials and Methods: Forty eight adult male Wistar rats were randomly assigned to eight groups: control, extracts (200, 400, and 1000 mg/kg), diabetic and diabetic + extracts (200, 400 and 1000 mg/kg). Extract doses was gavaged for 1 month. Immunohistochemistry (IHC) technique was used for investigating capillary density and enzyme-linked immunosorbent assay (ELISA) technique was used for measurement of vascular endothelial growth factor (VEGF) in serum of rats.
Results: Results of this study showed that the used doses of hydroalcoholic extract of Rosa damascena mill had no significant effect on cardiac capillary density and vascular endothelial growth factor levels in serum. However, there was no significant difference between control and extract groups and also diabetic and diabetic + extract groups on the blood glucose levels.
Conclusion: According to our results, the hydroalcoholic extract of Rosa damascena mill had no effect on cardiac angiogenesis in the normal and diabetic subjects. These findings were probably due to the insufficient amounts effective ingredients, especially flavonoids, in this plant or the duration of extract administration.
Keywords: Angiogenesis, Diabetes, Rat, Rosa damascena mill, Vascular endothelial growth factor

P-273

Hepcidin Peptide Inhibitor as Cardioprotection by Targeting Oxidative Stress and Inflammation in Type 1 Diabetic

Motahareh Zeinivand, Arezo Nahavandi

Department of Physiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Background and Objective: Hepcidin peptide is the dominant regulator of systemic iron metabolism. Studies suggest a dual role of hepcidin in neuronal iron load and inflammation. Furthermore, manipulation of hepcidin activity has recently been used to recover heart damage due to inflammation in Type 1 diabetic animal models.
Materials and Methods: In order to induce type 1 diabetic model, streptozotocin (STZ) was used. Animals were divided into groups of control (C), diabetic (D), diabetic + Iron (ID), and diabetic + dalteparin (DD). Then, 100mg/kg of dalteparin (anti-hepcidin) was administered intraperitoneally, and 12 mg/kg of iron administration P.O in rats once a day after diabetes for 8 weeks. At the end of the experiment, animals were randomly perfused and their heart tissue was prepared to measure serum iron level, ferritin, inflammatory cytokines such as IL-6, serum C-reactive protein (CRP), oxidative stress markers such as membrane lipid peroxidation (MDA), and hepcidin peptide gene expression.
Results: After inhibiting hepcidin by dalteparin treatment, serum levels of IL-6, CRP, glucose levels, iron and tissue levels of MDA and ferritin were remarkably reduced ($p<0.05$). Likewise, inhibiting hepcidin peptide improved cardiac function 8 weeks after induced type 1 diabetic ($p<0.05$).
Conclusion: Manipulation of hepcidin peptide by dalteparin could ameliorate diabetic cardiomyopathy (DM) in streptozotocin-diabetic rats through appropriate modulation and mitigation of oxidative stress and inflammation and this may expand the existing library of therapeutics to lower the complications of diabetes.
Keywords: Hepcidin peptide, Diabetic cardiomyopathy, Oxidative stress, Inflammation.

P-274

Ferula assa-foetida gum attenuates ischemia/reperfusion-induced arrhythmias in type 2 diabetic rats

Mahdiah Salari, Mansour Esmailidehaj, Hossein Azizian, Zeinab Farhadi, MohammadEbrahim Rezvani

Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Introduction:People with diabetes run a high risk of cardiovascular diseases and mortality. Recently,herbal drugs such as Ferula assa-foetida have been used as a complementary and alternative medicinal care.The present study was designed to explore whether FAFeffectson cardiac arrhythmias in the ischemic isolated diabetic rats heart.
Methods:Male diabetic rats were divided into five groups:1-control,2-Diabetes,3-Dia+FAF(25 mg/kg),4-Dia+FAF(50mg/kg) and 5-Dia+FAF(100 mg/kg).T2D was induced by High-Fat Diet and low doses of STZ.FAF was administrated for four weeks after the establishment of T2D. In the end, the animal hearts were removed and quickly mounted on a Langendorff apparatus.The ECG was analyzed to determine the total number of returnable ventricular fibrillation,sustain ventricular fibrillation and heart run.
Results:Results showed that percent of reversible and irreversible ventricular fibrillation in the Dia group were respectively, 34% and 17% that in groups 3 and 4 were reduced to 0%. Percent of Heart run was 50% in the Dia group and that increased to 100% in groups 3 and 4, and 67% in group 5. Percent Mortality was reduced from 53% to 0% in groups 3 and 4, and 25% in group 5.
Conclusion:Our study suggested that FAF protects against diabetic CVD and probably, antioxidant and antidiabetic activity of asafoetida may involve in these protective effects.
Keywords:Type 2 diabetes, ischemia/reperfusion, Ferula assa-foetida, arrhythmias, Infarct size.

P-275

Role of LAMP2 and PCNA genes in patients with type 2 diabetes and coronary artery disease

Seyedeh Fatemeh Sajjadi[1], Homa Hamledari [1], Mehrdad Behmanesh[1], Mohammad ali Boroumand [2], Mehdi Najafi [2]

1. Department of Genetics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran
2. Department of Pathology, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran

Background and Objective: Coronary artery disease (CAD) is the main complication for type 2 diabetes mellitus (2TDM) and one of the most important causes of mortality in the world. Recent studies have confirmed that autophagy plays a pivotal role in diabetes and its complications. Autophagy plays essential roles in cell survival, differentiation, and proliferation and homeostasis. Defects in autophagy lead to the etiology of many diseases, including diabetes, cancer, neurodegeneration, and cardiomyopathy. LAMP2 is a membrane protein located in the late endosome and lysosome, which has been used as a marker for autophagy. PCNA plays an important role in cellular processes such as proliferation and regulated with autophagy. The aim of the present study was to compare the expression levels of LAMP2 and PCNA on PBMCs, in CAD+ versus CAD-patients with T2DM.
Materials and Methods: Blood samples were obtained from 53 patients with T2DM (24 CAD+ and 29 CAD_ individuals confirmed by angiography). The expression levels of LAMP2 and PCNA genes were examined with Real time PCR method.
Results: Significant down-regulation of the LAMP2 (P=0.04) and PCNA (P=0.003) genes was observed in patients with T2DM and CAD. In a ROC curve analysis the area under the ROC curve for LAMP2 gene reached 0.66 (P=0.045), which indicates a potential biomarker for identifying patients with T2DM and CAD.
Conclusion: Our results showed that reducing the expression of genes involved in autophagy may play an important role in increasing the risk of cardiovascular diseases in type 2 diabetes patient.
Keywords: T2DM, CAD, Autophagy

P-276

Effect of aqueous fraction of Ziziphus jujuba on cardiovascular responses in Goldblatt hypertensive rats

Mohammad Naser Shafei[1*], Yasamin Kamkar-Del[2], Reza Mohebbati[3], Mahmoud Hosseini[1,2]

1. Division of Neurocognitive Sciences, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Iran
3. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: The antihypertensive effect of Ziziphus jujuba (Z. jujuba), Annab in Iran has been shown previously. For further investigation, we examined the antihypertensive effect of aqueous fraction(AQ) of the Z. jujuba in Goldblatt hypertensive rats
Materials and Methods: Animal assigned to five groups: 1- Control, 2- Goldblatt hypertensive (two kidney- one clip(2K1C)), 3) Losartan (Los) + Goldblatt, 4 and 5) AQ of Z. jujuba (150, and 300 mg/kg) + Goldblatt. Hypertension induced by clipped renal artery of one kidney. After confirmation of hypertension, rats were treated with Los and two doses of AQ by gavage for 28 days. In 28th day, the femoral arty cannulated and systolic blood pressure (SBP), mean arterial pressure (MAP) and heart rate (HR) were measured by power lab system. In end of experiment oxidative stress markers in the heart tissue were evaluated.
Results: In 2K1C hypertensive rats, SBP and MAP significantly increased ($P<0.01$-$P<0.001$) than control but HR did not change. All parameters significantly decreased by Los ($P<0.01$). Both doses of AQ significantly decreased SBP and MAP than 2K1C ($P<0.05$-$P<0.01$). The increased MDA level in 2K1C group ($P<0.001$) significantly reduced by Los ($P<0.01$) and both doses of AQ ($P<0.05$-$P<0.01$). Total thiol content, SOD and CAT activities in the heart tissue of 2K1C group significantly decreased ($P<0.05$-$P<0.001$) and these parameters significantly increased by both doses AQ and Los ($P<0.01$-$P<0.001$).
Conclusion: AQ fraction of Z. jujuba by inhibitory effect on RAS and antioxidant properties has a beneficial antihypertensive effect.
Keywords: Hypertension, Goldblatt hypertension, Ziziphus jujuba, Aqueous fraction, Oxidative stress.

P-277

The effect of nesfatin-1 on the fibrosis in the rat model of the cardiac ischemia-reperfusion injury

Nahid Aboutaleb[1], Masuomeh Sharifi[2], Behnaz Mokhtari[2], Yaser Azizi[3], Kamran Rakhshan[4], Somayeh Dashti [2]

1. Physiology Research Center, Physiology Department, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Ph.D. candidate of medical physiology, Physiology Department, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran.
3. Ph.D. of Physiology, Department of Physiology, Iran University of Medical Sciences, Tehran, Iran.
4. Ph.D. of Physiology, Physiology Research Center, Iran University of Medical Sciences, Tehran, Iran.

Background and Objective: Ischemic heart disease is one of the major causes of death worldwide. Despite the fact that reperfusion reduces mortality, but it can cause further complications such as tightening the walls of the heart resulting in tissue damage and even cell death. Nesfatin-1 (Ns-1) an anorexic nucleobindin-2-derived hypothalamic peptide, controls appetite and energy metabolism. There are solid evidences that Ns-1 is also expressed in the heart and acts as a peripheral cardiac modulator. In this study Ns-1was administered for its effects on fibrosis and cell death induced by cardiac ischemia-reperfusion injury in the male rat .
Materials and Methods: The animals (n=30; male rats) were randomly allocated to 3 groups: sham, myocardial infarction (MI) and MI with treatment by Ns-1. All animals were anesthetized with Ketamine and xylazine and then underwent tracheotomy. In the two last groups, LAD artery was ligated by silk 6/0 for 30 minutes and in treatment group Ns-1 was administered(10µg/Kg, i.p.) before reperfusion. 28 days later, echocardiography was done and animals were sacrificed under deep anesthesia. Data were analyzed using Prism by One Way ANOVA test.
Results: Collagen deposition in Masson trichrome staining that indicates fibrosis formation, demonstrated significant difference between groups; 40% in MI vs 21% in treatment($p<0.001$). Hematoxylin and Eosin staining showed score 2 (41%) in treatment, 3 MI(60%) and 1 in sham(15%). However there was no significant differences between treatment vs MI group.
Conclusion: Our results indicated Ns-1 may be used as a potentially effective treatment to reduce myocardial fibrosis formation.
Keywords: nesfatin-1, cardiac ischemia-reperfusion, Masson trichrome staining

P-278

Curcumin coated gold nanoparticles attenuates Doxorubicin Induced Cardiotoxicity via improved cardiac function

Yaser azizi, Zeynab sharifi aghdam

Department of Physiology, Faculty of Medicine, Iran university of Medical Sciences, Tehran, Iran

Background and Objective: Doxorubicin is a highly effective anticancer agent. However, it is associated with cardiotoxicity. Curcumin as a natural compound; can be used as reducing agent in synthesis of gold nanoparticles. It has been proved that conjugation of Curcumin to gold nanoparticles improve curcumin bioavailability. In this study, we investigated effects of curcumin coated gold nanoparticles on cardiotoxicity-induced by doxorubicin.
Materials and Methods: Here, we report synthesis of gold nanoparticles coated with curcumin. The formation of Cur-GNPs has been confirmed by UV-Vis absorbance spectroscopy; Dynamic Light Scattering and Fourier transform infrared. The cytotoxicity of Cur-GNPs on H9c2 heart cells was defined by MTT test. Then, we tested cardiac effect of Cur-GNPs in acute DOX-intoxicated mices. For this purpose, 40 male BALB/c mices were randomly divided into 4 groups: Control, cardiotoxicity (DOX), curcumin treated group (DOX + Cur) and Curcumin coated gold nanoparticles treated group (DOX + Cur-GNPs). At the end, Effect of Cur-GNPs on heart weight, body weight and heart weight to body weight, Serum parameters (LDH, CK-MB, cTn-I, ALT and AST), and histological examination (H&E) were measured.
Results: Statistical analysis showed that, treatment with Cur-GNPs could ameliorate cardiac functional parameters and serum levels of cardiac damage enzyme and liver injury markers were decreased. In addition, prevented body weight and heart weight decrease compared with DOX. Treatment with Cur-GNPs caused improved tissue damage induced by DOX.
Conclusion: The results revealed that, Cur-GNPs are a new effective way to reduce Dox-induced cardiotoxicity through improved cardiac injuries and function.
Keywords: Doxorubicin, Curcumin, Gold nanoparticles, Cardiotoxicity

P-279

Investigation on combination effects of gallic acid and cyclosporine A during ischemia/ reperfusion on rat electrocardiogram parameters and arrhythmia

M.Badavi[1, 2], N.Sadeghi[3*], M.Dianat[1], A . Ranjbar[3], Kh. Dehghani[4]

1. Physiology Research Center, Department of Physiology, Faculty of Medicine
2. Ahvaz Jundishapour University of Medical Sciences, Ahvaz, Iran
3. Arteriosclerosis Research Center, Golestan Hospital, Ahvaz Jundishapour
4. University of Medical Sciences, Ahvaz, Iran
5. Research center for non.Communicable Diseases, Jahrom University of Medical Sciences, Jahrom, Iran
6. Department of cardiology, Jahrom University of Medical Sciences, Jahrom, Iran

Background: At present, Cardiovascular disease (CVD) accounts for nearly half of no communicable diseases NCDs) in the world. Myocardial ischemia is the common disorder of CVD that lead to electrical disturbance in the heart due to reactive oxygen specious(ROS).
Objective: the aim of this study was the investigation of gallic acid and cyclosporine A(CsA) effects alone or together on Electrocardiogram(ECG) parameters changes in myocardium after ischemia - reperfusion in isolated hearts.
Method: Wistar rats weighing 250-300- g were used in this experimental study. Animals were randomly divided into the following groups:
The control and sham group that received saline(1ml), six groups that pretreatment with different doses of gallic acid (7.5, 15 and 30 mg/kg, 1ml) for 10 days by gavage alone or in combination with CsA (0.2µM), for 10 minutes before the induction of ischemia, and 10 minutes at the start of reperfusion
All groups experienced protocol included (30 minutes' global ischemia was induced following 60 minutes' reperfusion) on langendorff apparatus. except the control group. Electrocardiographic parameters such as RR, PR, QT, TpeakTend, JT and QTcB interval, ST elevation, R, P, Q, S, T amplitude and heart rate were computed at pre-ischemia, ischemia, and reperfusion period. Comparisons between groups were performed using one-way ANOVA or repeated-measurement ANOVA test.
Result: Data of this study showed that RR, JT, interval, p duration, ST elevation and PVC numbers during ischemia period increased compared with pre ischemia but decreased using gallic acid (7.5, 15 and 30 mg/kg) in combination with CsA, ($P<0.05$). In addition, P, R, S, T amplitude during the ischemia decreased in comparison with pre ischemia or sham group and increased with gallic acid (15 mg/kg) in combination with CsA ($P<0.05$).
Conclusion: In conclusion, the combination of both drugs was more efficient than each one alone. And doses of 15 and 30 mg/Kg of gallic acid acted better and protected the cardiomyocytes against ischemia induced electrical changes in ECG parameters and premature beats
Key words: Gallic acid, CsA, Rat, Ischemia Reperfusion injury

P-280

In vitro proangiogenic activity of evolocumab as a PCSK9 inhibitor

Leila Safaeian[1], Golnaz Vaseghi[2], Hedieh Jabari[1], Nasim Dana[2]

1. School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.

2. Applied Physiology Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

Background and Objective: The proprotein convertases family is involved in several physiological processes such as cell growth, migration and angiogenesis, and also in different pathological conditions. Evolocumab, an inhibitor of proprotein convertase subtilisin/kexin type 9 (PCSK9) has recently been approved for treatment of hypercholesterolemia. This study aimed to investigate the effect of evolocumab on angiogenesis in human umbilical vein endothelial cells (HUVECs).
Materials and Methods: Cell proliferation and migration were evaluated using 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and Transwell methods. In vitro angiogenesis was assessed by tube formation assay. VEGF secretion by HUVECs was also determined using an enzyme-linked immunosorbent assay (ELISA) kit. Data were analyzed using SPSS.
Results: Evolocumab significantly increased HUVECs viability at 100 µg/ml. Significant enhancement in cell migration, and average tubules length and size was observed at the concentrations of 10 and 100 µg/ml and also in mean number of junctions at the concentration of 100 µg/ml. Administration of evolocumab at the concentration of 10 µg/ml increased VEGF release into supernatants of HUVECs.
Conclusion: Findings of this investigation provided in vitro evidence for pro-angiogenic activity of evolocumab through promoting cell proliferation, migration, tubulogenesis and VEGF secretion in HUVECs.
Keywords: Angiogenesis, Cell Proliferation, Cell Migration, HUVEC, PCSK9, Evolocumab

P-281

Study of Gallic Acid Effects on Serum Parameters of Streptozotocin-Nicotinamide Diabetic Male (Animal Model of Type 2 Diabetes)

Hasanali Abedi[1,2], Mihan Jafari Darabjerdi[3] , Najmeh Sadeghi[1,2] , Hossein Kargar Jahromi[1,2]

1. Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran

2. Research Center for Non. Communicable Diseases, Jahrom University of Medical Sciences, Jahrom, Iran

3. Student Research Committee, Jahrom University of Medical Sciences, Jahrom, Iran

Background and Objective: Diabetes is a risk factor for cardiovascular disease. According to anti-hypoglycemic, antioxidant, anti-inflammatory and antiarrhythmic effects of gallic acid, the purpose of this study was to investigate the effects of gallic acid on serum parameters of diabetic male rats (type 2).
Materials and Methods: In this experimental study, forty male Wistar rats with an average weight of 220 ± 10 g were randomly assigned to four groups of ten as follows: Control and three experimental groups that were diabetic by nicotinamide and streptozotocin. After confirmation of diabetes, the control group received one cc normal saline for 10 weeks, preventive and treatment groups received a daily dose of 15 mg/kg of gallic acid for 10 and 3 weeks, respectively. On day 71, blood samples were collected from the heart and lipid profile, MDA, total antioxidant capacity, glycosylated hemoglobin were measured. The results were analyzed by one way ANOVA and Duncan post hoc test at the level of 0.05.
Results: Ten weeks after induction of type 2 diabetes, mean fasting blood glucose, heart weight, glycosylated hemoglobin, MDA, TAC, TC, TG, VLDL and LDL increased in the sham group compared to control group. In addition, the effects of prevention were significantly better than treatment.
Conclusion: Gallic acid with antioxidant, antihyperlipidemic, and anti-diabetic properties, has the ability to protect the heart against cardiovascular complications caused by diabetes.
Keywords: Gallic acid, Heart, Rat, Diabete

P-282

Memantine, an NMDA receptor antagonist, attenuates cardiac remodeling, lipid peroxidation and neutrophil recruitment in heart failure

Samin Abbaszadeh[1,2], Asal Javidmehr[1], Behnam Askari[3], Hamid Soraya[1]

1. Department of Pharmacology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran.

2. Department of Pharmacology, Faculty of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran.

3. Department of Cardiovascular Surgery, Seyyed-al-Shohada Heart Center, Urmia University of Medical Sciences, Urmia, Iran.

Introduction: In addition to their role in the central nervous system (CNS), N-Methyl-D-Aspartate (NMDA) receptors activation contributes to myocardial pathogenesis. This study sought to determine the potential cardioprotective effects of memantine, an NMDA receptor antagonist, in heart failure (HF).
Method: A subcutaneous injection of isoproterenol (5 mg/kg/day) for 14 days was used for the induction of heart failure in rats. Memantine was injected ip at doses of 5 and 20 mg/kg one week before isoproterenol injection for 21 days (n=8 each group). Then, hemodynamic, electrocardiogram and histopathological changes as well as lipid peroxidation, myeloperoxidase (MPO) and AMPK activity were evaluated.
Results: Histopathological analysis showed a marked attenuation of myocyte necrosis and fibrosis in memantine 20 mg/kg pre-treated group ($P<0.001$) in comparison to heart failure group. Pre-treatment with memantine 20 mg/kg significantly reduced myocardial edematous, MPO activity and MDA levels in comparison to HF group ($P<0.05$, $P<0.05$, $P<0.01$ respectively). Memantine had no significant effect on hemodynamic parameters and AMPK activity but improved the ECG pattern.
Conclusion: Our results for the first time showed cardioprotective effects of memantine in HF through reduction in cardiac remodeling, lipid peroxidation and neutrophil infiltration. In addition, these effects are through an AMPK-independent Pathways.
Keywords: Memantine, Heart failure, Isoproterenol, Cardiac remodeling, Lipid peroxidation, Neutrophil

P-283

Toxic effects of aluminum chloride on viability and membrane integrity of human lymphocytes

Mahmood Alidadi[1], Hamid Reza Momeni[1], Ghasem Mosayebi[2], Majid Komijani[1]

1. Department of Biology, Faculty of Science, Arak University, Arak, Iran

2. Department of Immunology, Arak University of Medical Sciences, Arak, Iran

Background and Objective: Aluminum, as an environmental pollutant, exerts its adverse effects on various human systems, including blood. Lymphocytes play important roles in the immune system. This study was preformed to investigate the effect of aluminum chloride on viability and membrane integrity of human lymphocytes.
Materials and Methods: Blood samples were taken from 18 healthy individuals and their lymphocytes were isolated using Ficoll solution. The lymphocytes were suspended in RPMI medium and transferred to 96 wells sterile plate (1×106 cells per ml). The cells were then divided into 3 groups: 1) lymphocytes at 0 hour, 2) control lymphocytes and 3) lymphocytes treated with aluminum chloride (1mM). The treatments were carried out for 24 hours in a CO2 incubator at 37°C. The samples from the different groups were used for evaluating vital parameters of lymphocytes. To evaluate cell viability, trypan blue staining and MTT (3(4,5-dimethylthiazol-2-yl)2,5-diphenyl tetrazolium bromide) assay were used. In order to study membrane integrity, propidium iodaide and acridine orange stainig were used. Data were analyzed using one way ANOVA and Tukey's test and $p<0.05$ was considered signifcant.
Result: Lymphocytes treated with aluminum chloride for 24 hours showed a signifcant reduction in cell viability while this pollutant had no effect on membrane integrity as compared to the control group.
Conclusion: Aluminum chloride exerts harmful effects on vital parameters of human lymphocytes, but has no effect on membrane integrity.
Key words: Lymphocyte, Membrane integrity, Viability, Aluminum chloride

P-284

A Comparative study on the equine and camelid antivenoms upon cardiovascular changes induced with Hemiscorpius lepturus venom in rats

Ramin Seyedian[1], Hossein Fatemikia [2]

1. Department of Pharmacology, Bushehr University of Medical Sciences, Bushehr, Iran

2. Department of Physiology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Background and Objective: In this study, the neutralizing abilities of the equine and the recently introduced camelid antivenoms on the hemodynamic parameters (inotropism, chronotropism and arrythmogenicity) were assessed following envenomation by Hemiscorpius lepturus venom in rats.
Materials and Methods: At first, the electrophoretic profiles of both products were obtained by using SDS-PAGE method (12.5%) stained with Coomassie blue and silver nitrate. Secondly, different doses of the camelid antivenom (10, 50 and 100µl) were given intravenously at 10 minutes before venom injection (400µg/rat). The neutralizing potencies of the camelid and the equine antivenoms were measured by preincubation (100µl) with the Hemiscorpius lepturus venom for 30 minutes at room temperature. Finally, the equal amounts of the antivenoms were injected intravenously to observe the hemodynamic changes.
Results: Based on the electrophoretic profile, it was evident that undesired proteins significantly decreased in equine antivenom, owing to impurities. Pretreatment with the camelid antivenom (100 µl), neutralized the elevation of the mean arterial pressure evoked with scorpion venom injection (88.15±4.56 versus 10.2±1.23 percent at the 8th minute). The Incubation of the venom and the camelid antivenom counteracted the hemodynamic changes, but the equine product had no effects. The intravascular injection of the equine antivenom transiently increased the mean arterial pressure same as the vehicle (108.67±8.63mmHg versus 52.67±1.93mmHg at the 10th minute).
Conclusion: The most obvious finding emerged from this study was that the camelid antivenom neutralized the hemodynamic changes in rats significantly,but in comparison,the equine antivenom had just a minor ability.
Keywords: Camelid antivenom; Envenomation;Hemiscorpius lepturus;Equine antivenom;Cardiovascular

P-285

The investigation of gallic acid on electrophysiology parameters in STZ- nicotinamide induced diabetic rats

Faraji F[1*], Abedi H[2], Sadeghi N[3]

1. Department of Physiology, Faculty of Medicine, Iranshahr University of Medical Sciences, iranshahr,Iran
2. Research center for non.Communicable Diseases, Jahrom University of Medical Sciences, Jahrom,Iran
3. Zeonoose Research Center, Department of microbiology, Faculty of Medicine Jahrom University of Medical Sciences, Jahrom, Iran

Introduction: The use of effective herbal medicines can help to the reduce of complications of diabetes for cardiovascular disease. This study aimed to investigate the effects of Gallic acid on cardiac electrocardiography in rats with type 2 diabetes.
Methodology: Forty adult rats were provided and were randomly divided into four groups of ten. 1-control (CTRL), 2 - sham (type 2 induced diabetes), 3 - prevention group (D2G10) who had induced diabetes and had received Gallic acid in the form of gavage for 10 weeks and 4 - Group therapy (D2G3) for 7 weeks diabetes, followed by gallic acid for 3 weeks. One day after the last gavage, the animals were weighed. Animals were then anesthetized with ketamine and xylazin, and the electrocardiogram strip was recorded. The results were analyzed by SPSS software, one way ANOVA and Duncan test at a significant level of $P \leq 0.05$.
Results: In this study, the mean QTC interval in sham prevention and treatment group significantly increased from control group ($P < 0.05$). Gallic acid in diabetic rats decreased PR interval versus the control group ($P = 0.12$) and there was no difference between the sham and control groups ($P > 0.05$). There were no significant differences in mean heart rate among different groups ($P > 0.05$). In terms of amplitude, the R wave was higher in all groups than the control group ($P < 0.05$). In the treatment group, the T-wave amplitude increased significantly compared to the control group.
Conclusion: Gallic acid has cardiac protection
Keywords: Gallic Acid, Diabetes, Rat

P-286

Mercury and Atherosclerosis: Cell Biology, Pathophysiology, and Epidemiological Studies

Tahereh Farkhondeh[1] , Reza Afshari[2,3], Omid Mehrpour[4], Saeed Samarghandian[5,6*]

1. Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran
2. BC Centre for Disease Control, British Columbia, Canada.
3. School of Population and Public Health, University of British Columbia, British Columbia. Canada
4. Medical Toxicology and Drug Abuse Research Center (MTDRC), Birjand University of Medical Sciences , Birjand , Iran

5. Noncommunicable Disease Research Center, Neyshabur University of Medical Sciences, Neyshabur. Iran.

6. Department of Basic Medical Sciences, Neyshabur University of Medical Sciences, Neyshabur, Iran

Background and Objective: Today atherosclerosis is considered as a main cause of death worldwide. A significant association between heavy metal exposure and atherosclerosis progression has been demonstrated. In this study, we discuss the scientific literature on the effect of mercury on the pathogenesis of atherosclerosis, and also considered epidemiological studies of mercury as a risk factor for atherosclerosis.
Methods: Web of Science, Google Scholar, Medline, PubMed, and Scopus were searched by using the following keywords: (cardiovascular diseases OR atherosclerosis OR endothelial dysfunction) AND (mercury) to 2019.
Results: Mercury has been found to have the potential to act as one of the novel risk factors for atherosclerosis development. The findings indicated the role of mercury in the pathogenesis of atherosclerosis: vascular endothelial dysfunction, oxidative stress, inflammation, and dyslipidemia.
Conclusion: Mercury may act as one of main risk factor in the progression of atherosclerosis. However, more studies are required to found the exact mechanisms involved in the pathogenesis of atherosclerosis induced by mercury.
Keywords: Mercury; atherosclerosis; inflammation, oxidative stress, dyslipidemia

P-287

Effect of Enalapril on myocardial capillary density in male diabetic rats

Fallahzadeh Ali Reza[1*], Khazaei Majid[2], Ghavipanjeh Gholamreza[3], Ramian Parvin[4]

1. Cellular and Molecular research center, Yasuj University of Medical Sciences, Yasuj, Iran

2. Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

3. Physiology Research Center, Institute for basic Sciences, Kashan University of Medical Sciences, Kashan, Iran

4. Department of Zoology, Faculty of basic Sciences, Shahrekord Univercity, shahrekord, Iran

Background and Objective: Diabetes is a metabolic disease that affects all systems of the body. It is one of the most important risk factors for cardiovascular disease. Enalapril is used in the treatment of some cardiovascular diseases. This study evaluates the effect of Enalapril on myocardial capillary density of diabetic rats.
Methods: In this study 24 Wistar rats randomly divided into three groups, control group, diabetic sham group and group of diabetic rats receiving enalapril (15 mg/kg) daily. Streptozotocin (60 mg/kg) was injected intraperitoneally to induce diabetes. After twenty one days the animals were sacrified, heart was removed and capillary density in the myocardial tissue was evaluated using immunohistochemical staining and is reported as capillaries per mm2.
Results: Cardiac muscle capillary density in diabetic sham group was significantly lower than enalapril group. In other words enalapril significantly increased capillary density in cardiac muscle in diabetic rats.
Conclusion: Based on the results of this study, it seems that enalapril increases capillary density in the cardiac muscle of diabetic rats.
Key words: Diabetes, Rat, Enalapril, Myocardial capillary density

P-288

Cerebrolysin Ameliorates Isoproterenol-Induced Myocardial Injury in Male Rats

Gholamreza Ghavipanjeh[1, 2], Abolfazl Ardjmand [1, 2]

1. Physiology Research Center, Institute for Basic Science, Kashan University of Medical Sciences, Kashan, Iran

2. Departments of Physiology, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran

Background and Objective: Myocardial injury (MI) is the principal cause of death from cardiovascular disease (CVD). The present study was conducted to investigate the ameliorative and antioxidant effects of cerebrolysin (CBL) on isoproterenol-induced MI in rats.

Materials and Methods: MI was induced in the rats by subcutaneously injecting 100 mg/kg of isoproterenol (ISO) in the first two days. The serum levels of creatine phosphokinase (CK-MB) and cardiac troponin I (cTnI) were measured on the third day to confirm MI. The post-treatment involved intraperitoneally injecting 5 ml/kg of CBL for 7 days. Nitric oxide (NO), malodialdehyde (MDA) in the heart tissue and catalase (CAT) and serum levels of superoxide dismutase (SOD) and glutathione peroxidase (GPX) were measured on the 10th day using the enzyme-linked immunosorbent assay (ELISA). Histopathological examinations of the heart tissue were also performed.
Results: The present results suggested significant increases in CK-MB, cTnI, MDA and NO. A significant decrease was also observed in the ISO-treated rats in certain antioxidant enzymes, including CAT and GPX. CBL administration showed a significant ameliorative increase against the oxidative ISO-induced damage. Moreover, the histopathological findings showed lower levels of the infiltration of inflammatory cells and edema and vascular proliferation in the CBL-treated rats.
Conclusion: The present histopathological and biochemical findings attributed antioxidant properties to CBL in the rat myocardium and suggested protective effects on ISO-induced MI.
Keywords: Myocardial injury, Isoproterenol, Cerebrolysin, Malondialdehyde, Nitric oxide,
Cardiac markers

P-289

Cerebral Ischemia/Reperfusion Injury in the Hypothyroid Rat

Somaye keshavarz[1,2], Dr Gholam Abbas Dehghani[2]

1. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences. Shiraz, Iran
2. Department of Physiology, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Background: Due to disturbance in fat metabolism and increased atherosclerosis, hypothyroidism is a well-recognized risk factor for cardiovascular disease, including stroke. Although studies have shown that hypothyroidism is associated with cerebrovascular dysfunction, stroke in hypothyroid patients or hypothyroid animals, can cause less neuromotor injuries. The present study is designed to demonstrate how cerebrovascular function after stroke can be affected by hypothyroidism.
Material and methods: In this study, two groups of euthyroid and hypothyroid (HO) rats of equal numbers (n=22) were studied. Hypothyroidism was induced by adding Methimazole (0/25 grams in 100 milliliters) for 4 weeks in drinking water. Transient cerebral ischemia was induced for 60 min by middle cerebral artery occlusion and reperfusion for 24 hours. Neurologic disability scores (NDS) evaluated after 24 h and cerebral infarct volume was measured using Triphenyl tetrazolium chloride (TTC) staining technique. Evans Blue (EB) extravasation technique was used to evaluate the cerebrovascular integrity disruptions.
Results: Thyroid hormones levels, T3 (72.5□□2 vs. 198±3 ng/dL;P=0.001) and T4 (1.03±0.05 vs. 3.08±0.07 µg/dL;P=0.001), were significantly lower in the HO group than in the controls. Furthermore, most clinical signs seen in hypothyroid patients were also present in the HO group. The results of cerebral ischemia of HO group compared to control showed significant decrease in NDS (1.57±0.11 vs. 2.23±0.09; P=0.03), cerebral infarct volume (129±15 vs. 266±17 mm3; P=0.001), but significant increase in EB extravasation.
Conclusion: Hypothyroidism, for unknown reasons, aggravates cerebrovascular integrity disruption after ischemia-reperfusion. Nevertheless, cerebral ischemia causes lesser neurological disability and infarct volume in hypothyroid animals.
Keywords: brain ischemia, hypothyroidism, blood-brain-barrier, brain infarction

P-290

Therapeutic effects of Ferula Assa-Foetida on metabolic parameters and cardiovascular disorders in type 2 diabetic rats

Mahboobe Kahtenaroon, Hossein Azizian, Zeinab Farhadi, Mohammad Ebrahim Rezvani, Mansour Esmailidehaj

Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Objectives: Type 2 diabetes (T2D) is one of the largest metabolic diseases in the world with severe cardiovascular complications. Assafoetida (AF) commonly consumed as a healthy beverage has been demonstrated to have various biological activities. The aim of this study was to investigate the effects of AF-enriched diet on vascular endothelial disorders caused by T2D. Methods: Thirty-two male Wistar rats were divided into 4 groups of eight. Group I, sham-

control (Sham-Con); group II, diabetes (Dia); group III, Dia+AF 0.5%; group IV, Dia+AF 2%. T2D was induced by nicotinamide and streptozotocin. Rats received AF AF-enriched diet for four weeks. In the end, after laparotomy, the abdominal aorta was removed and placed in modified Krebs-Ringer solution. Then contraction and relaxation responses in the presence of acetylcholine, sodium nitroprusside, phenylephrine, and calcium chloride were recorded. Results: The results showed that AF 0.5%, in addition to reducing the consumption of water and fasting blood glucose, improves lipid profiles, cardiovascular risk indices, and liver enzymes. Also, AF improves many vascular disorders caused by T2D, including decreasing vascular contractility in the presence of extracellular calcium through protein kinase C inhibition. Conclusion: The results of this study suggest that AF has dose-dependent effects on metabolic and vascular disorders caused by T2D. Also, AF is a potential source of natural cardioprotective products.
Keywords: Type 2 diabetes, Cardiovascular, Assa-Foetida, Vascular Tension, Metabolism

P-291

The Effect of Hydro-Alcoholic Extract of Ginger (Zingiber Officinale Roscoe) on Diabetic Cardiomyopathy in Streptozotocin-Induced Diabetic Rats

Maryam Mahmoudabady, Tara Abdi, Saeed Niazmand

Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Neurogenic Inflammation Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran
Background and Objective: Fibrosis and inflammation in the heart of diabetic patients alongside with increased production of free radicals and collagen are known as diabetic cardiomyopathy. Ginger Rhizome has anti-diabetic, antioxidant, and anti-inflammatory effects. In this study we investigated the effect of ginger extract on diabetes-induced cardiomyopathy in streptozotocin-induced diabetic rats.
Materials and Methods: Animals were divided into 7 groups: control, diabetic, diabetic treated with different doses of ginger extract, 100, 200 and 400 mg/kg (Z100, Z200 and Z400), metformin (Met, 200 mg/kg) and metformin-valsartan (Met/Val, 200 and 30 mg/kg, respectively). Serum glucose, AST, LDH and CK-MB were measured. Fibrosis and inflammation were determined by histologic assessment. Gene expression of TGF- β -1, TGF- β -3 and AT1 was evaluated by Real Time PCR in heart tissue.
Results: Serum glucose level in all treated groups, except of Z100, was significantly lower than diabetic group. Serum levels of AST, LDH and CK-MB were significantly reduced in all treated groups compared to diabetic control group. In the study of fibrosis, collagen amount in heart tissue of all treated groups, except of Z100 was significantly lower than diabetic group. Inflammatory cell infiltrates were decreased, and disarrangement was improved in cardiac tissues of all treated groups compared to diabetic group. The expression of AT1, TGF-β1 and TGF-β3 genes in all treated groups downregulated compared to diabetic group.
Conclusion: Treatment by ginger extract reduced myocardial fibrosis and inflammation, in the course of diabetic cardiomyopathy possibly through regulation the expression of genes involve in SMAD/TGF-β pathway.
Keywords: Diabetes, Ginger, Cardiomyopathy, Fibrosis, Inflammation

P-292

Effect of human amniotic membrane mesenchymal stem cells-condition medium on myocardial ischemia reperfusion injury in rats

Behnaz Mokhtari [1], Nahid Aboutaleb [2], Yaser Azizi [1]

1. Department of Physiology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Physiology Research Center and Department of Physiology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran

Background and Objective: Cardiac ischemic diseases are the leading cause of death in the world. Ischemia reperfusion injury (IRI) is a result of physical and biochemical disorders which occurs as a result of restoration of blood flow to the ischemic region. Stem cell therapy is a promising therapeutic target for improving myocardial injury. Human amniotic membrane mesenchymal cells (hAMCs) lead to the production and releasing of factors (condition medium) that are able to improve myocardial ischemic regions. But the exact mechanism of their therapeutic effects is unclear. Therefore, we investigated the effects of intra-myocardial injection of hAMCs-condition medium on myocardial interstitial fibrosis in IRI model in rats,

Materials and Methods: Male Wistar rats (15 rats weighing 200-250g) were randomly divided into 3 groups: sham, IRI and IRI + condition medium. MI animals were subjected to 30 minutes left anterior descending coronary artery (LAD) ligation and 28 days of reperfusion. 150 µl of hAMCs-condition medium were injected into 3 different sites of the infarct border zone after 30 minutes of ischemia in treatment group. Left ventricle was used to measure cardiac fibrosis by Masson's trichrome staining.
Results: Interstitial fibrosis in IRI group was significantly higher than sham group ($P < 0.05$). Intra-myocardial injection of hAMCs-condition medium significantly decreased myocardial interstitial fibrosis ($P < 0.05$).
Conclusion: The results of this study showed that hAMCs-condition medium has cardioprotective effects in IRI condition. Attenuation of myocardial interstitial fibrosis by hAMCs-condition medium plays significant role in this context.
Keywords: human amniotic membrane mesenchymal cells, condition medium, ischemia reperfusion injury, interstitial fibrosis

P-293

The effect of different digoxin concentrations on heart tissue and antioxidant status in iron-overloaded rats

Yaser Masoumi-Ardakani[1], Hamid Reza Nasri[2], Beydolah Shahouzehi[3]

1. PhD Candidate, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran.
2. Associate Professor, Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran.
3. Assistant Professor, Student Research Committee, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran.

Background and Objective: Thalassemia is a hereditary disorder and has an economic burden on patients and the government. The most prevalent complication in these patients is iron overload which is
followed by cardiomyopathy. Digoxin is considered as a treatment against heart failure in thalassemia. The present study evaluated the effect of two digoxin concentrations on iron content and antioxidative defense in cardiac tissue of iron-overloaded rats.
Methods: The study was conducted on 48 rats which were divided into 6 groups. Group 1 was the control group and did not receive any treatment and group 2 was the iron overload group. In addition groups 3 and 4 were the digoxin control groups which received 1 and 5 mg/kg/day of digoxin, respectively. Groups 5 and 6 received 1 and 5 mg/kg/day of digoxin plus iron-dextran, respectively. After 1 month, malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPX), and total antioxidant status (TAS) were assessed in cardiac tissues.
Results: Co-administration of iron-dextran and digoxin (1 and 5 mg/kg/day) significantly increased SOD and TAS levels ($P < 0.001$) and reduced MDA ($P < 0.001$) in heart tissue compared to control and iron overload groups. GPX levels significantly reduced in groups 5 and 6 (iron + digoxin 1 ($P < 0.05$) and iron + digoxin 5) ($P < 0.001$) compared to the iron control group.
Conclusion: Digoxin remarkably facilitates iron uptake by cardiomyocytes by affecting other channels such as L-type and T-type Ca2+ channels (LTCC and TTCC). Digoxin administration in the iron-overloaded rat model deteriorated antioxidative parameters and increased iron entry into heart tissue at higher doses. Therefore, in patients with beta thalassemia major, digoxin must be administered with great care and serum iron and ferritin must be regularly monitored.
Keywords: Digoxin, Iron Overload, Superoxide Dismutase, Glutathione Peroxidase, Heart Iron Content

P-294

Effect of Fish and Flaxseed Oil Supplementation on Isoprenaline-Induced Myocardial Infarction in Rats: Inhibition of Mitochondrial Permeability Transition Pore Opening

Seyd Hosein Abtahi Ivary[1], Najme Jajarmy[1], Mehedi Karimi Shahri[1], Majid Shokoohi[2], Hamed Shoorei[2], Abbas Ebadi[3], Maryam Moghimian[1], Faraz Sigaroodi[2]

1. Department of Basic Sciences, School of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran.
2. Department of Anatomical Sciences, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.
3. Department of Emergency Medicine, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

Background and Objective: Dietary n-3 polyunsaturated fatty acids have positive effects on the heart. The present study investigated the effects of pretreatment with fish oil (FO) and flaxseed oil (FLO) on the heart of the rat, which is associated with the isoprenaline (ISO)-induced myocardial injury.

Materials and Methods: The study was conducted on 40 male Wistar rats which were included in control, ISO, FO + ISO, and FLO + ISO groups (each containing 10 rats). In ISO rats, acute myocardial ischemia was induced by ISO while in FO + ISO group, the rats were pretreated with FO orally for 4 weeks. Finally, rats in the FLO + ISO group received pretreatment with FO and flaxseed oil orally for 4 weeks. Eventually, the histopathological examinations of the cardiac tissues and serum activity of creatine kinase-MB (CK-MB) were assessed. Moreover, mitochondria were isolated to examine the mitochondrial swelling.
Results: Based on the results, ISO administration significantly increased the serum CK-MB activity compared to the control group. In addition, severe muscular damage to the heart was observed in more than 70% of the rats in ISO group. However, a remarkable decrease in the intensity of heart tissue destruction, as well as the serum levels of CKMB was found in the FO + ISO group compared to the ISO group. Conversely, there was no significant decrease in the serum level of CKMB in FLO + ISO group compared to the ISO group.
Conclusion: In general, pretreatment with FLO significantly suppressed the intensity of heart tissue destruction compared to the myocardial ischemic group. FO and FLO led to a decrease in CaCl2-induced swelling in the mitochondria. Therefore, FO and FLO result in protecting against ischemia/reperfusion injury through inhibiting the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine.
Keywords: Isoprenaline, Myocardial Infarction, Fish oil, Flaxseed oil, Cardioprotection

P-295

Toxic effects of cadmium chloride on viability and membrane integrity of human lymphocytes

Mona Sadat Mirkamali[1], Hamid Reza Momeni[1], Ghasem Mosayebi[2], Majid Komijani[1]

1. Department of Biology, Faculty of Science, Arak University, Arak, Iran
2. Department of Immunology, Arak University of Medical Sciences, Arak, Iran

Background and Objective: Lymphocytes are one of the main White blood cells that their integrity are important for the body's defense system. Humans are exposed to heavy metals and environmental pollutant, including cadmium, via several ways. Cadmium exerts destructive effects on blood parameters by inducing oxidative stress. This aim of this study was to investigate the effect of cadmium chloride on viability and membrane integrity of human lymphocyte.
Materials and Methods: Blood samples were taken from 18 healthy individuals and their lymphocytes were isolated using Ficoll solution. The lymphocytes were suspended in RPMI medium transferred to 96 wells sterile plate (1×106 cells per ml). The samples were divided into three groups: 1) 0 hour lymphocytes, 2) control group and 3) lymphocytes treated with cadmium chloride (15µM). Groups 2 and 3 were incubated for 24 hours in a CO2 incubator at 37°C. To evaluate cell viability, trypan blue staining and MTT assay were used while for evaluating membrane integrity of lymphocytes stained by propidium iodide and acridine orange. The results were analyzed by one way ANOVA and Tukey's test.
Results: Treatment of lymphocytes with cadmium chloride for 24 hours could significantly decrease viability of lymphocytes. However, this pollutant had no effect on the integrity of the plasma membrane.
Conclusion: Cadmium chloride exerts negative effects on the lymphocyte viability for 24 hours, while at this time point had no effect on the membrane integrity.
Key words: Lymphocytes, Viability, Cadmium chloride, Plasma membrane integrity

P-296

Reveratrol decreases Interleukin-6 and soluble glycoprotein130 levels during mal-adaptive phase of cardiac hypertrophy in rats

Razieh Najjari, Fariba Akhondzadeh, Fatemeh Safari

Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Background: Cardiac hypertrophy is characterized by increase of cardiomyocytes size and extracellular matrix remodeling.Interleukin-6 (IL-6) has emerged as a pro-inflammatory cytokine involved in the pathophysiology of left ventricular hypertrophy progression. The aim of this study was to investigate the effect of polyphenole, Resveratrol, on hypertrophy related parameters and cardiac level of IL-6 and its receptor componenets (gp130 and gp80) in early (adptive) and late (mal-adaptive) phases of cardiac hypertrophy in rats.
Materials and Methods: Cardiac hypertrophy was induced two and ten weeks after aortic banding (H2W and H10W, respectively). Resveratrol-treated groups were given 1 and 10 mg/kg/day of resveratrol (R1 and R10, respectively).

Intact animals served as normal. Blood pressure was recorded by cannulating the carotid artery. Fibrosis and cell size were assessed by specific staining. IL6 and soluble gp130 (sgp130) concentrations were measured by ELISA method. Gene expression was evaluated by Real time RT-PCR.
Results: Resveratrol decreased IL6 level in H10W+R1 and H10W+R10 ($P<0.01$, $P<0.001$ vs. H10W, respectively). Resveratrol also downregulated cardiac IL6 mRNA in these groups ($P<0.001$ vs. H10W). The serum concentration of sgp130 was increased in H10W group ($P<0.01$ vs. normal) and resveratrol normalized it in H10W+R1 and H10W+R10 groups ($P<0.05$, $P<0.001$ vs. H10W). The transcription level of gp130 and gp80 was increased in H10W ($P<0.05$, $P<0.01$vs. normal) however it did not change in resveratrol-treated groups.
Conclusions: Our findings revealed a possible mechanism for anti-hypertrophic effects of resveratrol during progression of cardiac hypertrophy through down-regulation of inflammatory responses.
Keywords: Cardiac hypertrophy, IL-6, Resveratrol

P-297

Comparison selective phosphodiesterase 3 inhibitor and non-selective phosphodiesterase inhibitor effects on cardiac remodeling and hemodynamic parameters of heart failure in rat animal

Reza Shafiee-Nik[1], Mohammad Mahdi Vahedi[2]

1. Department of Pharmacology, School of Medicine, Mashhad University of Medical Science, Mashhad, Iran.
2. Department of Pharmacology, School of Medicine, Zahedan University of Medical Science, Zahedan, Iran.

Background and Objective: Selective phosphodiesterases3 (PDE3) inhibitors increases cAMP content and proposed for systolic heart failure treatment in short course. PDE3 inhibitors have positive intotropic and chronotopic effects but its effects on cardiac remodeling and hemodynamic parameters have not been adequately identified in comparison with non-selective PDE inhibitors.In this study, we assayed amrinon (PDE3 inhibitors) and IBMX (non-selective PDE inhibitor) effects on structural change by echocardiographic and hemodynamic pressure parameters by isolated heart langendorff in doxorubicin induced heart failure in rat.
Materials and Methods: sixty rats were randomly allocated to 6 groups: control, doxorubicin, IBMX, Amrinon, doxorubicin+IBMX, doxorubicin+Amrinon. At previous studies, animals treated with doxorubicin 2.5mg/kg/ip every other day for two weeks and PDE inhibitors 1 mg/kg/ip/BID for one week. Echocardiographic study evaluated functional and cardiac remodeling in all of rats. Hearts were removed and placed on langerdoff apparatus with added increasing doses isoproterenol (10-10- 10-5 M) to control and doxorubicin groups and same doses of isoproterenol and PDE inhibitors (10-4 M) to other groups. Data were analyzed using prism and dose – respnce curves were plotted to compare EC50.
Results:The results showed, increase ejection fraction, with decrease in Left Ventricular end systolic diameters and volumes, and shift to right EC50 curve of maximum contraction force and ventricular rate in amrinon compare to IBMX.
Conclusion: Our results showed that amrinon have protective effect on geometric remodeling and improve EF in heart failure due to doxorubicin toxicity but end systolic LV diameters and volumes did not decrease by IBMX.
Keywords: Amrinon, IBMX, Cardiac Remodeling, maximum contraction force

P-298

The effect of Astragaloside IV on myocardial infarction in rats

Haleh Vaez[1], Alireza Garjani[1], Nezhla Tamarzadeh[1], Doa Alsos[1], Fatemeh Fathiazad[2]

1. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran
2. Department of Pharmacognosy, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

Background and Objective: Astragaloside IV (AST) is a saponin derived from the roots of Astragalus plants which has been widely used in traditional medicine to treat cardiovascular diseases. However, the effect of AST on myocardial infarction remains unknown. Thus, we aimed to investigate the cardioprotective effects of AST on isoproterenol-induced myocardial infarction in rats.

Materials and Methods: Male Wistar rats were assigned to 5 groups of control, isoproterenol, and treatment with 2.5, 5 and 10 mg/kg AST given orally immediately before MI induction. Subcutaneous injection of isoproterenol (100 mg/kg) for two consecutive days was used to induce myocardial infarction. AST was given orally once daily for 4 days. On the fifth day hemodynamic parameters were assessed, and serum and tissue samples were used to evaluate histological and biochemical changes. We also used three doses of 0.1, 1 and 2 µM of AST in isolated heart model.
Results: AST administration increased mean arterial blood pressure and heart rate and improved the left ventricular contractility. AST had no effect on oxidative stress, but the peripheral neutrophil count, cardiac enlargement and cardiac ischemia was significantly decreased by AST. Also, histopathological evaluations showed that AST significantly diminished post MI necrosis and fibrosis in heart tissue and inhibited the inflammatory responses. The isolated heart studies hemodynamic factors showed no significant changes.
Conclusion: AST can protect heart against myocardial infarction by improving cardiac histology and ventricular contractility. Due to the lack of protection in the isolated heart, it is likely that the positive effects are more associated with the improvement of the oxidative stress markers in the systemic circulation.
Keywords: Astragaloside IV, Myocardial infarction, Isoprotrenol, Oxidative stress, Isolated heart

P-299

The Effect of 4-phenylbutyric acid on hemodynamic parameters on isoproterenol induced myocardial infarction in rat

Fatemeh Vatankhah[1], Alireza Garjani[2], Haleh Vaez[2]

1. Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
2. Department of Pharmacology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

It has been shown that myocardial infarction (MI) is related to misfolded and unfolded proteins. Chaperone mediated autophagy is one of the intracellular pathway which eliminates these proteins, therefore, it can be useful for post MI patients. The aim of this study was to investigate the effect of 4-phenyl butyric acid (4-PBA), a chemical chaperone, in rats with myocardial infarction.
Rats were divided into 5 groups (n=5): control group receiving subcutaneous (SC) normal saline (NS, day 1 and 2) + intra pritoneal (IP) NS (day 1-5), Isoproterenol (ISO) group receiving ISO 100 mg/kg (SC, day 1 and 2) + NS (SC, day 1-5), and 3 treatment groups of 4-PBA (P20 mg/kg, P40 mg/kg, P80 mg/kg; IP, day 1-5) +ISO 100 mg/kg (SC, day 1 and 2). At the end of experiment hemodynamic parameters were recorded and analyzed.
The results showed that ISO administration induced significant cardiac injuries demonstrated in hemodynamic changes and these damages improved by 4-PBA administration. The cardiac protection was dose-dependent in a way that low dose of 4-PBA (20mg/kg) showed more effective results. In other words, autophagy stimulation exceeded of a limitation may deteriorate the condition and the modulation of this pathway is needed.
KEYWORDS: 4-Phenylbutyric acid; heart; Isoproterenol; autophagy; myocardial infarction; hemodynamic parameters

P-300

The role of Atrial natriuretic peptide and Nitric oxide on antiarrhythmic effect of Oxytocin in rat

Fariba Houshmand[1], Mahdieh Faghihi[2]

1. Department of Physiology, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord
2. Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran

Background and Objective: A previous study showed that oxytocin (OT) has antiarrhythmic effect. The aim of this study is to determine the role of Atrial natriuretic peptide (ANP) and Nitric oxide (NO) in OT-induced antiarrhythmic protection in ischemia induced-arrhythmia in rat.
Materials and Methods: Rats were divided in six groups and all of them were subjected to 25 min regional ischemia. OT (0.01µg/rat) was administrated intraperitoneally 30 min before ischemia. The ANP receptor antagonist (anantin, 1.2 mg/kg, ip) and nitric oxide synthase inhibitor (L-NAME, 0.2 mg/kg, ip) were injected 10 min before OT. In the

other animals, anantin and L-NAME were administered alone 40 min prior to ischemia. Ventricular arrhythmias such as number of premature ventricular contractions (PVC), sum of episodes and durations of ventricular fibrillation (VF) and ventricular tachycardia (VT) were counted during the occlusion period.
Results: Compared with the ischemia group, severity of ventricular arrhythmia was attenuated and VF was abolished by OT treatment. These OT effects were eliminated by ANP receptor blockers and nitric oxide synthase inhibitor. Anantin and L-NAME alone had no significant effect on ventricular arrhythmias.
Conclusion: These findings demonstrate an important role of ANP and NO in OT protection against ischemia induced-arrhythmia in rat.
Key words: Oxytocin, Atrial natriuretic peptide, Nitric oxide, Arrhythmias, Myocardial ischemia.

P-301

The prevalence and 5-year incidence of low physical activity in 10,000 urban population in Kerman, Iran: Relationship with other cardiovascular risk factors

Yeganeh Mahboobeh[1], Najafipour Hamid[2], Baneshi Mohammad Reza[3], Kahnooji Massomeh[4], Ahmadi Milad[3], Shadkam Mitra[5], Mirzazadeh Ali[6]

1. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences Kerman University of Medical Sciences, Kerman, Iran
2. Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
3. Modeling in Health Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran
4. Iran Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
5. Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
6. Department of Epidemiology and Biostatistics, University of California San Francisco, CA, USA

Background: Because of high prevalence of cardiovascular diseases in Iran and their relationship with low physical activity (LPA), this study aimed to measure the prevalence of LPA, its 5-year incidence rate and its relationship with six other coronary artery disease risk factors among an urban population aged 15 to 80 years in Kerman, Iran.
Method: 10000 adults were randomly recruited through single-stage cluster sampling (KERCADR study, phase2). Demographic characteristics, smoking, opium use, mental status and physical activities were assessed. Adjusted odds ratio (AOR) was reported as a measure of the relationship between LPA and other coronary artery diseases (CAD) risk factors. LPA incidence rate was calculated according to the data from 2820 individuals who jointly participated in phases 1 and 2 of the study.
Results: The prevalence of low, moderate, and intense physical activity were 46.9%, 34.9% and 18.2% respectively. LPA showed a rise from 45.1% to 50.6% after the age of 25 years. Females had higher LPA than men (47.8% vs. 46.2%, P<0.01). Participants with LPA, had significantly higher chance AOR (95%CI), of cigarette smoking 1.51(1.25-1.80), diabetes 1.39 (1.08-1.79), overweight/obesity 1.32(1.16-1.50), hypertension 1.29(1.08-1.55), and opium addiction 1.18(1.02-1.43). 5-year incidence rate of LPA was 7.9 per hundred subjects per year (7.7% in males vs 8.1% in females).
Conclusion: Almost half of the studied population suffer from LPA being at risk for CAD. Such risky life-style pattern while worsened in the last five years, makes the emerging of CAD epidemic unavoidable, if appropriate timely interventions not being in place accordingly.
Keywords: physical activity, coronary artery disease, urban population, prevalence, incidence rate, Kerman, Iran

P-302

The Effect of Salvia Extract Supplementation on serum C-reactive protein following Eccentric Exhaustive Exercise in non-Athlete Women

Saeed Takhti[1], Mohammad-Ali Kohanpour[2]

1. Islamic Azad University, South Tehran Branch, Tehran, Iran
2. Islamic Azad University, Lamerd branch, Fars, Iran

Background and objective: The aim of this study was to investigate the effect of salvia extract supplementation on serum C-reactive protein (CRP) levels following an eccentric exhaustive activity in non-athlete women.

Materials and Methods: A sample of 30 women from 20 to 30 years old non-athletes in Tehran with a BMI greater than 18 but less than 25 were randomly selected and randomly divided into three groups: salvia, placebo, and control (each Group 10). Supplementation was done for two weeks. Salvia extract with a dose of 200 mg per day was used as capsule and placebo (flour powder) in the same manner (equal dose and similar capsule). The control group did not receive any supplement. Before and after the supplements, all three groups were taken in an eccentric exhaustive activity, and before and after the blood sample, they were taken.
Results: Serum CRP levels increased significantly in all three groups ($P<0.05$), but this increase was significantly lower in the salvia group than in the other two groups ($P<0.05$) and between the placebo and control groups There was no significant difference ($P>0.05$).
Conclusion: One area of eccentric exhaustive activity in non-athlete women may lead to increased inflammation of the acute phase. However, supplementation of the salvia extract for two weeks may significantly reduce the inflammation, although it does not completely eliminate it.
Keywords: Acute Phase Inflammation, Salvia Plant, CRP, Antioxidant Plants, Eccentric Activity

P-303

The effect of voluntary exercise on function and morphological structure of Leydig cells in type 2 diabetic rats

Hamed Heydari[1], Saber Ghaderpour[1], Rana Keyhanmanesh[1], Gholamreza Hamidian[2], Rafighe Ghiasi[1]

1. Department of physiology, Tabriz University of Medical Science, Tabriz, Iran.
2. Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.

Background and Objective: It is well known that diabetes and its complications can cause unexplained infertility in men. The voluntary exercise (VE) is performed under non-stressed condition and seems to have a satisfy role in control of diabetes side effects. This study was conducted to evaluate the effect of VE on volume and total number of Leydig cells and plasma level of testosterone in diabetic rats.
Materials and Methods: Thirty-two adult male Wistar rats were randomly divided into control, diabetic, VE and diabetic-VE groups. Diabetes was induced by high-fat diet and 35 mg/kg streptozotocin. VE was performed for 10 weeks by a rotary wheel cage. At the end of experiment, animals were anaesthetized and plasma samples were taken for measurement of testosterone. Testes were fixed in formalin, processed by standard paraffin embedding and tissue sections were stained by H&E. Mean volume and total numbers of Leydig cells were estimated by optical dissector and stereo-investigator software. One-way ANOVA and Tukey's post-hoc were performed for data analysis.
Results: Results showed that diabetes reduced volume and total number of Leydig cells as well as plasma level of testosterone significantly compared to control groups. It was also indicated that VE in normal rats did not change number of Leydig cells but increased volume of these cells and testosterone level compared to control. Results revealed that VE in diabetic rats improved morphology and function of Leydig cells compared to diabetic group.
Conclusion: VE is a suitable protective strategy for improvement of infertility in diabetic males.
Keywords: Dibetes, Voluntary exercise, Leydig cells, Testosterone

P-304

Effects of Immediate and Delayed Exercise on Motor disorder & Brain Edema in the Experimental Traumatic Brain Injury

Mohammad Khaksari Hadad, Zahra Soltani, Mohammad Pourranjbar, Sedigeh Amir Esmaeilei, Sara Shirazpour, Forouzan Rafie

Physiology and Pharmacology Departmaent, Kerman Medical Science University, Kerman, Iran.

Background and Objective: Brain trauma is one of the most common causes of death in the world. In this study, the effects of preconditioning, early and delayed exercise on motor performance and brain edema in the experimental traumatic brain injury (TBI) was investigated.
Materials and Methods: Eighty rats were randomly assigned to 2 groups (sham and TBI) and 5 categories: sedentary [(NE)], exercise [24A (1month 24 after trauma), exercise 1WA (1month1week after trauma), exercise 1mB (1month before trauma), exercise 1mBA (1month before 1month after trauma)]. The rats in the exercise group were trained to run on a treadmill 3 days a week for 45 min. Motor performance and brain edema were evaluated by Rotarod (RR), and brain water count percent (%BWC).
Results: The exercise groups showed a significant improvement in RR ($p<0.001$). Improvement of movement was observed in the 1MBA, 1WA, 24A, and 1MB exercise group respectively. There is no difference between 24A and 1wA exercise group ($P> 0.05$). The TBI 1MBA exercise group showed significantly enhanced RR than other exercises groups ($p<0.05$). In %BWC the exercise TBI group showed significant deterioration compared to control group ($p<0.001$). %BWC was significantly decreased respectively in the 1MBA, 1WA, 24WA, and 1MB groups ($p<0.05$).
Conclusion: Our results showed that Delayed session of treadmill exercise could prevent motor deficit and brain edema in the experimental TBI rats. However, prior exercise exacerbated this function. Therefore, the optimal timing of starting exercise is crucial in motor and brain recovery after TBI.
Keywords: TBI, Exercise, Motor disorder, Brain edema

P-305

Effects combined exercise training on levels of chemerin, omentin and insulin resistance in men with type 2 diabetes

Mehdi Zarei*, Amin Rashidlamir, Amir montazeri

Department of Physical Education and Sport Sciences, University of Neyshabur, Neyshabur, Iran

Background and Objective: Regular exercise training has been shown to be a useful option to treat and prevent type 2 diabetes. The purpose of this study was to investigate effects of 12 weeks of combined aerobic-resistance exercise training on levels of chemerin, omentin and insulin resistance in men with type 2 diabetes.
Materials and Methods: In this experimental research, 20 male patients with type 2 diabetes, were randomly divided into two groups combined aerobic-resistance training (n=10) and control (n=10). Subjects in training group performed 12weeks aerobic-resistance training, 3 weekly training sessions with given intensity (aerobic: intensity of 60-70% maximum heart rate–resistance: intensity 60-70% repetition maximum). Blood sampling for chemerin, omentin resistance and fasting glucose insulin measurement in the beginning and after 12 training protocol weeks were conducted.
Results: After 12 weeks, in combined training group chemerin($p=0.01$), resistance insulin($p=0.01$) and fasting glucose($p=0.001$) significantly decreased and Vo2max significantly increased ($p=0.001$) in the compared to the control group. Significant change were not observed at the levels of omentin($p=0.37$).
Conclusion: 12 weeks of aerobic-resistance training in men with type 2 diabetes decreases levels of chemerin, insulin resistance and fasting glucose, but does not affect the level of omentin.
Key words: Exercise, Diabetes Mellitus Type 2, Insulin resistance index, chemerin protein, Omentin protein

P-306

Therapeutic effects of physical activity against juvenile stress induced anxiety or depression like behaviors and BDNF levels in the prefrontal cortex of adult female rats.

Mohammad Saeedi[1], Nasroallah Moradi-Kor[2], Hadi Rashidipour[3], Ali Ghanbari[2], Ahmad Reza Bandegi[4], Ali Rashidy-Pour[2,5]

1. Student Research Committee, Semnan University of Medical Sciences, Semnan, Iran.
2. Laboratory of Learning and Memory, Research Center of Physiology, Semnan University of Medical Sciences, Semnan, Iran.
3. School of Veterinary Medicine, Islamic Azad University, Garmsar Branch, Garmsar, Iran.

4. Department of Biochemistry, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran.

5. Department of Physiology, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran.

Background: Exposure to stress during juvenile period has been demonstrated to impair mood related behaviors and BDNF changes in the prefrontal cortex. The present study investigated the protective effects of voluntary exercise (EX), against juvenile stress induced deficits in anxiety and depression like behaviors and BDNF levels in the prefrontal cortex in adult female rats.
Methods: Rats were subjected to restraint stress (2 h/day for 10 days, PND30-40). Then, the animals were subjected to treatment with voluntary exercise (running wheel, 15 days, PND41-55), followed by anxiety and depression testing and BDNF assessment in prefrontal cortex.
Results: The obtained results showed rats submitted to adolescent stress exhibited anxiety and depression like behaviors in adulthood. In addition, adolescent stress decreased BDNF levels in the prefrontal cortex. Treatment with EX alleviated both behavioral and biochemical deficits by juvenile stress, and even exerted the positive effects on BDNF changes in the prefrontal cortex.
Conclusion: Our findings provide important evidences that treatment with EX during pre-pubertal period can protect against juvenile stress induced behavioral and biochemical changes in adulthood.
Keywords: Anxiety, Depression, BDNF, Juvenile stress, Physical activity

P-307

Comparing the Effect of Air Pollution on Salivary Malondialdehyde and Total Antioxidant Capacity Response to a Semi-Soccer Protocol in Indoor Vs. Outdoor Environment

Vahab Khan Ahmadi[1], Ali Samadi[2*], Majid Hasan Pour Ezati[3]

1. Physical Education and Sport Sciences Department, Faculty of Humanities, Shahed University, Tehran, Iran.

2. Physical Education and Sport Sciences Department, Faculty of Humanities, Shahed University, Tehran, Iran.

3. Biology Department, Faculty of Basic Sciences, Shahed University, Tehran, Iran.

Background and Objective: Health benefitis of exercise have gained a wide recognition, which increased the popularity of indoor and outdoor exercises. Howerer, due to the augmentation of pullotants concentration in the air, and enhancement of ventilation during exercise increasing concern exists over the adverse effects of air pollution on health. So, the present study compared the effect of air polluton on salivary malondialdehyde (MDA) and total antioxidant capacity (TAC) response to a semi-soccer protocol in indoor vs. outdoor environment in adolescent male soccer players.
Materials and Methods: Nine male adolescent soccer players completed a soccer-specific Bangsbo protocol in two environments (indoor vs outdoor) at two air quality conditions (Air Quality Index 50-100 = Healthy, and 100 to 150= Unhealthy). Salivery samples were collectod before and immidiatly after performing the protocol in each condition. MDA and TAC were assesesd using specified kits. Data were analyzed using SPSS.
Results: Finding confirmed that completing the exercise protocol in unhealthy air - in both indoor and outdoor environments – leads to unfaroble changes in MDA and TAC levels ($p<0.05$) in comparison with healthy air condition. However, comparing the MDA and TAC changes after exercise in indoor vs. outdoor environments revealed that there was not significant difference between indoor vs. outdoor environments ($p>0.05$).
Conclusion: As oxidative stress is the main mediator of negative health effects of air pollution and based on findings of this study the general recommendation of shifting exercise to indoor environment at the time of air pollution needs to be reconsidered.
Keywords: outdoor, indoor, Oxidative stress, adolescent soccer players, air pollution

P-308

The effects of exercise on hippocampal inflammatory cytokine levels, brain oxidative stress markers and memory impairments induced by lipopolysaccharide in rats

Zahra Gholamnezhad[*1, 2], Zahra Jahangiri[1, 2], Mahmoud Hosseini[1,3]

1. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

2. Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

3. Division of Neurocognitive Sciences, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and Objective: The exercise effects on behavioral tests, hippocampal and cortical oxidative stress, and hippocampal inflammatory cytokines of lipopolysaccharide (LPS) administered rats were investigated.
Materials and Methods: The rats were divided into four groups (N=8): (1) control; (2) moderate training (MT, 15 m/min, 30 min/day, 9 weeks); (3) LPS (1 mg/kg LPS) and (4) LPS+MT (1 mg/kg LPS; 15 m/min, 30 min/day, 9 weeks). LPS was injected two hours before the behavioral experiments during the last week of training. Finally, the rats' brain were removed for biochemical assessments.
Results: LPS increased escape latency and traveled distance to reach platform in Morris water maze (MWM) test ($p<0.05$-$p<0.001$). In passive avoidance (PA) test, LPS decreased latency to enter dark compartment and time spent in light compartment and increased time spent in dark compartment ($p<0.01$-$p<0.001$), while MT improved the rats performances in MWM and PA tests ($p<0.01$-$p<0.001$). Additionally, LPS increased tumor necrosis factor α (TNF-α), interleukin 1 beta (IL-1β) and C-reactive protein levels in the hippocampal tissues, malondialdehyde (MDA) and nitric oxide metabolite in hippocampal and cortical tissues, and decreased thiol contents and catalase (CAT) and superoxide dismutase (SOD) activity in hippocampal and cortical tissues compared to the control group ($p<0.01$-$p<0.001$); while moderate training decreased the levels of TNF-α, IL-1β and MDA; increased thiol contents and SOD and CAT activity in the LPS+MT compared to the LPS group ($p<0.001$).
Conclusion: These results indicated that moderate training improved LPS-induced learning and memory impairments by attenuating the hippocampal cytokine levels and brain oxidative damage.
Keywords: Moderate training, Lipopolysaccharide, learning, Memory, cytokine, oxidative damage

P-309

Effects of L-citrulline supplementation on blood pressure response to an exhaustive exercise in healthy women

Atefeh Fereidooni[1], Fahimeh Kazemi[2], Parveneh Nazarali[2]

1. Faculty of Physical Education and Sport Sciences, Alzahra University, Tehran, Iran.
2. Department of Exercise Physiology, Faculty of Physical Education and Sport Sciences, Alzahra University, Tehran, Iran

Background and Objective: L-citrulline supplementation has been indicated to increase production of the vasodilator nitric oxide, reducing resting mean arterial blood pressure (BP) in humans. However, the study on the effect of L-citrulline on BP immediately after the exercise is limited. The purpose of the present study was to determine the effects of L-citrulline supplementation on BP response to an exhaustive exercise in healthy women.
Materials and Methods: The protocol of this study was approved by the Research Ethics Committee of Sport Sciences Research Institute (SSRI) in Iran (Identifier: IR.SSRC.REC.1398.050). After filling out the questionnaires related to health and exercise historty, 24 healthy women aged 24 to 29 years were randomly divided to 2 groups of L-citrulline (receiving daily a supplement of 6 grams L-citrulline powder, n=12) and control (receiving daily a placebo of 6 grams starch powder, n=12), and participated in 2 sessions with one-week interval. The subjects had no history of exercise for 6 months. In each session, Bruce exhaustive test was performed and BP (systolic and diastolic) was measured immediately after the exercise using a manual sphygmomanometer. Data were analyzed using 2×2 (groups versus sessions) repeated measures analysis of variance (ANOVA).
Results: Results revealed no significant difference in systolic and diastolic BP of two groups in two sessions ($P>0.05$).
Conclusion: The findings of the present study showed that IL-citrulline supplementation could not be effective on BP response to an exhaustive exercise in healthy women.
Keywords: IL-citrulline, Blood pressure, Bruce exercise test, Women

P-310

The Effects of Glycyrrhiza glabra L. extract Use with Aerobic Training on Inflammatory Factors and Cognitive state in Elderly with Mild Cognitive Impairment

Mohammad-Ali Kohanpour, Sayyed Mohammad Ahmadizade

Islamic Azad University, Lamerd branch, Fars, Iran

Background and objective: Our aim is to investigate the effect of a 12-week aerobic training protocol and treatment with Glycyrrhiza glabra extract on serum interleukin 1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α) levels and cognitive state in the elderly with mild cognitive impairment (MCI).
Materials and Methods: Forty people who attained scores 21-25 on the Mini–Mental State Examination (MMSE) were selected by purposive and convenience sampling and randomly assigned to four groups of 10 each: training, G. glabra-treated, training+G. glabra-treated, and placebo. All interventions were conducted within 12 weeks. Aerobic training protocol consisted of 8-minute running at an intensity of 75-85% maximum heart rate in the first session. One minute was added to the duration of running per two sessions so that after 12 weeks, the duration of running in two last sessions was 26 minutes. G. glabra extract was orally administered in 200 mg/kg body weight capsules per day.
Results: IL-1β and TNF-α levels significantly decreased in training and G. glabra-treated groups but their decrease was more marked in training+G. glabra-treated group ($p<0.05$). Cognitive state in three intervention groups significantly improved compared to placebo group, and this improvement was more marked in training+G. glabra-treated group ($p<0.05$).
Conclusion: Consumption of G. glabra extract with aerobic training for 12 weeks can slow down or stop the progression of MCI in the elderly through improving their cognitive states via decreasing inflammatory factors.
Keywords: Aerobic training, Glycyrrhiza glabra, cognitive state, inflammation, cognitive impairment

P-311

Influence of maternal high intensity training in preconception and pregnancy periods on the cardiac oxidative stress of adult male offspring

Reyhane mohamadkhani[1,2], Alireza Komaki[1], Iraj Salehi[1], Neda Khaledi[2], Hamid Rajabi[2]

1. Neurophysiology Research Center, Hamedan University of Medical Sciences, Hamedan, Iran.
2. Faculty of Physical Education and Sport Sciences, Kharazmi University, Tehran, Iran.

Background and Objective: It is well established the non-pharmacological role of exercise in promoting general health. The protection role of exercise can begin as early as fetal conditions. Maternal exercise in pregnancy periods has been shown to improve the long-term health of offspring in later life. We investigated if a treadmill exercise intervention could improve cardiac health and physical activity of offspring.
Materials and Methods:32 female rats were divided into 4 maternal groups according to the initiation time of maternal exercise: sedentary, exercise before pregnancy, exercise before and during pregnancy, exercise during pregnancy. After the birth process, the weight of offspring was recorded and the offspring was allocated in offspring groups according to the initiation time of maternal training. In adult male offspring groups, an open field test was used to evaluate the locomotor activity and also, the total oxidant status and the total antioxidant capacity were assessed in the heart tissue. One-way Anova was used to statistical analysis and an alpha level of 0.05 was carried out to denote result significantly.
Results: The birth weight of offspring was not affected by maternal exercise before or during pregnancy. Besides, the total antioxidant capacity and physical activity were significantly higher in offspring with maternal who exercise before and during pregnancy but maternal exercise could not be altered the total oxidant status.
Conclusion: These findings suggest that the positive intergenerational consequence of maternal exercise prior to and during pregnancy lead to enhance the cardiac total antioxidant capacity in the next generation.
Keywords: high-intensity-training, pregnancy, antioxidant capacity, stress oxidative, maternal exercise

P-312

Systemic introduction of mesenchymal stem cells conditioned media in repeated doses modified tracheal responsiveness and lung pathology in asthmatic rats

Mahdi Ahmadi[1,3], Rana keyhanmanesh[2], Reza Rahbarghazi[3], Hossein Heiran[2]

1. Tuberculosis and lung Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

2. Drug Applied Research Center, Tabriz University of medical sciences, Tabriz, Iran.

3. Department of Physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: It has been showed that systemic transplantation of MSC-CM could protect the lung architecture against inflammation. In contrary, we recently reported that systemic administration of MSC–CM in single dose has inert effects on IFN-γ/IL-4 balance in lung tissues of sensitized rats. In line with this issue, more investigations are necessary to uncover the therapeutic effect of CM administrated in repeated doses in comparison with single dose.
Material and Methods: Male rats were divided into four experimental groups (n=۶); control rats (C group), Sensitized rats (S group), sensitized rats received a single dose of 50 µl CM intravenously (S+SD group) and sensitized rats received repeated doses of 50 µl CM intravenously (S+SD group). Two weeks post-allergen challenge tracheal responsiveness to methacholine and pathological features were examined.
Results: Our results showed that Tracheal responsiveness to methacholine and pathological scores in the lung tissue of asthmatic groups were significantly higher than the control rats ($p<0.01$ to $p<0.001$). CM in repeated dosages could significantly reduce Tracheal responsiveness and pathological injures in lung tissues ($p < 0.001$ to $p < 0.05$). In contrary, CM in single dosage did not yield any beneficial effect.
Conclusion: Overall, this study showed that systemic administration of MSC-derived CM in repeated dosages, but not in single dose, could be effective in amelioration of asthmatic changes
Keywords: Asthma, Conditioned media, Tracheal responsiveness, pathological scores

P-313

The effect of aqueous-alcoholic extract of Berberis integerrima Bge on the basic tension of the isolated smooth muscle and its interaction of the adrenergic system

Plants are used as medicine sources in the health system of different countries. Berberis integerrima Bge. plant also contains vitamin C and polyphenol, and considering vitamin C plays a role in bronchoconstriction of the muscles, we decided to examine the effect of it on level of tension of trachea muscle. the sympathetic nervous system plays a role in the relaxation of the muscles, and the material in this plant is also likely to play this role, we also investigated the interaction of the extract with the adrenergic system. Fourteen male rats were kept under normal conditions in an animal room. Each of them was anesthetized by intraperitoneal injection of 1/2 g/kg of urethane, divided into 3 mm rings, and placed in an Organ bath. The tissues were connected to a power transducer. it was connected to a Bridge amplifier (to amplify the signal). the data was recorded by a system called Power lab. then 80 mg/kg of barberry after that epinephrine and propranolol were added respectively. The significant decrease was observed in trachea rings in the presence of the extract compared to the control group. This effect was fixed even after the addition of epinephrine as an agonist of the adrenergic system and propranolol as an β2 receptor antagonist.
Conclusion: Hydroalcoholic extract of Zarafshani barberry has an effect on the tension of smooth muscle and causes it to relax, and this effect interacts with the adrenergic pathway, but it is not likely to interact with β2 receptors

P-314

Systemic and lung changes due to inhaled parquet in rat

Fatemeh Amin[1*], Arghavan Memarzia[2], Hamideh Kazemi Rad[2], Mohammad Hossein Boskabady[2]

1. Department of Physiology, Faculty of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

2. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhsd, Iran

Background and Objectives: Paraquat (PQ) is an herbicide inducing inflammation and oxidative stress in various organs including lung. We aimed to investigate the effect of inhaled PQ on systemic and lung inflammation and oxidative stress in rat.
Methods: Control, exposed rat to inhaled PQ (27 and 54 mg/m3) in two series of each group were studied. Animals were exposed to for 8 times (on other days, totally for 16 days). Hematologic parameters as well as oxidant, anti-oxidand biomarkers, toala and differential WBC were measured both in the blood and broncho-alveolar lavage (BALF) were measured one day after last exposure to PQ, in one sery, 16 days after the last PQ exposure.
Results: PQ exposure increased total WBC, neutrophil, eosinophil, monocyte counts, malondialdehyde (MDA), nitrite (NO2) levels but decreased thiol content, superoxide dismutase (SOD) and catalase (CAT) activities ($p<0.05$ to $p<0.001$) in the blood and BALF in both condition. The percent change of total WBC, neutrophil, eosinophil and monocyte counts in the blood and BALF measured immediately after the end of PQ exposure were significant higher than those measured 16 after the exposure ($p<0.05$ to $p<0.001$).
Conclusion: Findings of current study indicated inhaled PQ induced systemic and lung inflammation and oxidative stress. Although most parameters measure immediately after PQ exposure were higher than 16 days after exposure, all markers were higher even in late measured condition than control group indicating a long-term effect of inhaled PQ toxicity.
Keywords: Paraquat, Immediate effect, late effect, Acute toxicity, Oxidative stress, Lung injury.

P-315

Anti-inflammatory and Anti-remodeling Effects of Myrtenol in the lungs of Asthmatic Rats: Histopathological and Biochemical Findings

Mohammad Abbas Bejeshk[1], Mitra Samareh Fekri[2*], Hamid Najafipour[3], Farzaneh Rostamadeh[4], Elham Jafari[5], Mohammad Amin Rajizadeh[6], Yaser Masoumi- Ardakani[7]

1. MSc of Physiology, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Associate Professor of Pulmonology, Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
3. Professor of Physiology, Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
4. Ph.D. of Physiology, Endocrinology, and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
5. Assistant professor of Pathology, Pathology and Stem Cells Research Center, Kerman University of Medical Science, Kerman, Iran
6. MSc of Physiology, Gastroenterology, and Hepatology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
7. Ph.D. by research student of Physiology, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

Introduction: Asthma is a chronic inflammatory disease of the airways. In this study, we evaluated the anti-inflammatory effects of Myrtenol on the inflammatory indices in the pulmonary parenchyma and airways and on the inflammatory and oxidative indices of the bronchoalveolar lavage fluid (BALF) of asthmatic rats.
Methods: The allergic asthma was induced by sensitization (2 weeks) followed by the inhalation of ovalbumin (4 weeks). Animals were divided into two main groups: 1) Histopathology and 2) Measurement of inflammatory and oxidative biomarkers in the BALF. Each main group was subdivided into four subgroups: Control, Asthma, Asthma+Dexamethasone and Asthma+Myrtenol. (-)-Myrtenol (50mg/kg) or Dexamethasone (2.5mg/kg) was administered intraperitoneally once a day for one week, at the end of inhalation period.. On day 50, lung histopathologic parameters and inflammatory indices in BALF including INF-γ, IL-10, IL-1β, and TNF-α and oxidative stress biomarkers (MDA, SOD, and GPX) were measured.
Result: In the Asthma group, leukocyte infiltration, the thickness of smooth muscle and epithelium of airways wall and the number of goblet cells increased. Myrtenol reduced all of the above-mentioned indices except the epithelium thickness. It also inhibited the increase in BALF IL-1β, TNF-α and MDA and increased the levels of INF-γ, IL-10 and SOD.
Conclusion: Our results suggest that Myrtenol reduced damages caused by experimental asthma by reducing the inflammatory indices, normalizing the level of interleukins and balancing oxidative stress in the lungs. It also prevented airways remodeling. Myrtenol may be suggested as a potent herbal medicine for the treatment of allergic asthma.
Keywords: Experimental asthma, Myrtenol, Oxidative stress, Interleukins, Histopathology

P-316

Nasal breathing enhances resting-state frontal and temporal lobes activity

Tannaz Parsazadegan[1], Mohammad Reza Raoufy[1], Alireza Salimi[2]

1. Department of Physiology, Faculty of Medical Science, Tarbiat Modares University, Tehran, Iran
2. Chronic Respiratory Disease Research Center (CRDRC), National Research Institute of Tuberculosis and Lung Disease (NRITLD), Shahid Beheshti University of Medical Science, Tehran, Iran.

Background and Objective: Olfactory bulb activity during nasal breathing generates respiration-coupled rhythms in widespread neocortical and subcortical regions. These oscillations are thought to be important in information processing and organizing distributed network activity in brain areas. However, the difference in cortical activity during nasal versus oral breathing is poorly understood. In this study, we assessed resting-state cortical activity using electroencephalography (EEG) during nasal and oral breathing in healthy subjects.

Materials and Methods: EEG signals were recorded by 22 electrodes from thirty right handed healthy subjects (age 18-40 years). Signals were sampled at 256 Hz with filter between 1Hz and 40Hz during 2 min resting state with eyes-open condition. Power spectral density (PSD) was calculated by means of Welch's periodogram (built-in MATLAB).
Results: Our results exhibited a significant increase in EEG power of frontal and temporal lobes at theta, beta and gamma frequency during nasal breathing compared with oral breathing. No significant differences were found at alpha and delta frequency in these regions.
Conclusion: We concluded that the difference in cortical activity between nasal breathing and oral breathing may be a possible neuronal mechanism for a direct impact of the respiratory cycle during nasal breathing on information processing.
Keywords: Nasal breathing, resting-state, frontal lobe, temporal lobe

P-317

Evaluation of the protective effects of curcumin and nanocurcumin against paraquat-induced lung injury in rats: the role of oxidative stress and gene expression

Asieh Hosseini[1], Danyal Rasaie[2], Sara Soleymani Asl[3], Amir Nili Ahmadabadi[4], Akram Ranjbar[5]

1. Razi Drug Research Center, Iran University of Medical Sciences, Tehran, Iran
2. Student Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran.
3. Anatomy Department, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
4. Toxicology and Pharmacology Department, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran
5. Medical Plants and Natural Products Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

Background and Objective: Paraquat (PQ) is a contact herbicide. Lung is one of the primary targets for toxicity of PQ. Mechanism of lung toxicity with PQ is accompanied by a redox cyclic reaction. The aim of the current study is comparison the protective effects of curcumin and nanocurcumin against lung injury induced by sub-acute exposure with PQ through modulation of oxidative stress and gene expression.
Materials and Methods: Rats were exposed to paraquat (5 mg / kg / day, orally) + curcumin or nanocurcumin (30mg/kg/day, orally) for 7 days. Then different groups of rats were anesthetized with ketamine and xylazine injection and lung tissues were dissected. After that, oxidative stress biomarkers, genes expression of GST, Nrf2, KEAP-1, HO-1 and NQO1 were assessed. Hydroxyproline content were measured in conjunction with histopathological examination to evaluate the fibrotic changes in lung tissue.Data were analyzed using SPSS.
Results: Pulmonary MDA level and KEAP-1expression were elevated and the TAC, TTG levels, GST, Nrf2, HO-1 and NQO1 expression was reduced by PQ. These changes were inhibited significantly by daily curcumin and nanocurcumin treatments. Histopathological examination also showed that curcumin and nanocurcumin ameliorated the increase in collagen deposition and fibrosis in the lungs exposed to PQ. We found nanocurcumin to be superior to curcumin in protective effects on mentioned factors.
Conclusion: The present results demonstrate that nanocurcumin had significantly more protective effect than curcumin to prevent the development of PQ-induced lung injury most probably via modulation of oxidative stress and gene expression.
Keywords: Curcumin, Nanocurcumin, Paraquat, Oxidative stress, Fibrosis, Lung

P-318

The role of endothelin-1 receptors on pulmonary hemodynamic in rats subjected to liver dysfunction

Maryam Khoramzadeh[1], Farzaneh Ketabchi[1*] , Amirreza Dehghanian[2]

1. Dep of Physiology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.
2. Dep of Pathology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

Introduction: Liver cirrhosis may lead to a wide spectrum of complications from hepatopulmonary syndrome to portopulmonary hypertension, though their mechanisms are not fully understood. The aim of this study was to investigate the effect of BQ-788, the ET-1 receptor antagonist, in the presence or absence of endothelial nitric oxide (NO) inhibition, L-NAME, on right ventricular systolic pressure (RVSP) in liver dysfunction.
Methods: Male Sprague Dawley rats were divided into three groups of control, partial portal vein ligation (PPVL) and common bile duct ligation (CBDL). 28 days after the first surgery, animals were anesthetized, the femoral artery

and vein, and the right ventricle cannulated. The right ventricular systolic pressure (RVSP) and systemic arterial blood pressure (mBP) were recorded during a slow intravenous injections of BQ-788 at before and after L-NAME.
Results: Mean RVSP in the PPVL and CBDL groups were higher than that in the Sham group. Injection of BQ-788, increased RVSP in the Sham group, with no change in the PPVL and CBDL groups. There was a significant increase in RVSP following injection of L-NAME only in the Sham and PPVL groups. Re-injection of BQ-788 increased RVSP in the Sham group, whereas, it decreased RVSP in the CBDL group. Besides, the first injection of BQ-788 and L-NAME resulted in the increase of mBP in the Sham group. However, mBP did not change by the first or second BQ-788 and L-NAME.
Conclusion: ET-1 receptors play a role in regulating the pulmonary hemodynamic, which may be partly linked to NO regulatory pathway

P-319

The effects of carvacrol hematological parameters, oxidative stress and pulmonary function tests in patients exposed with sulfur mustard

Mohammad Reza Khazdair[1], Azam Alavinezhad[2], Mohammad Hossein Boskabady[3*]

1. Clinical Research Development Unit, Torbat Jam Faculty of Medical Sciences, Torbat Jam, Iran.
2. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: Sulfur mustard (SM) is a vesicant agent which lead to injury in different organs including; lung, eyes, skin, heart, nervous and digestive systems. In this study, the effect of carvacrol (CAR) on pulmonary function tests (PFT), hematological indices and oxidant/antioxidant biomarkers in patients with sulfur mustard (SM)-induced lung disorders was examined.
Materials and Methods: Twenty patients exposed to SM 27-30 years ago, were divided into two groups and treated with either placebo (P) or CAR (1.2 mg/kg/day) (n=10 for each group). Forced vital capacity (FVC), peak expiratory flow (PEF), total and different white blood cell (WBC), hematological parameters and oxidant/antioxidant biomarkers were measured at the baseline (step 0), one and two months (step I and II, respectively) after starting the treatment.
Results: PEF was significantly increased in CAR-treated group in step II compared to step 0 ($P<0.01$). Total WBC ($P<0.01$) and neutrophil ($P<0.05$) count in CAR-treated were significantly decreased in group in step I and II ($P<0.01$ for both cases) compared to step 0. The levels of thiol, superoxide dismutase and catalase in CAR-treated group were significantly increased ($P<0.05$ to $P<0.001$) in step I and II; but, malondialdehyde significantly decreased in step II compared to step 0 ($P<0.01$). The percentage of total and differential WBC, oxidant/antioxidant biomarkers, FVC and PEF values following a two-month treatment period, were significantly improved in the CAR-treated group compared to the placebo group ($P<0.05$ to $P<0.001$).
Conclusion: Two-month treatment with CAR, reduced inflammatory cells and oxidant biomarkers, while increased antioxidant biomarkers and improved PFT tests in SM-exposed patients.
Keywords: Carvacrol, Sulfur mustard, hematological indices, Pulmonary function tests, Oxidative stress

P-320

Genistein preserves the lungs of ovariectomized diabetic rats: addition to apoptotic and inflammatory markers in the lung

Faeze Daghigh[1], Alireza Alihemmati [2], Pouran Karimi [3], Parisa Habibi [4], Naser Ahmadiasl [1*]

1. Tuberculosis and Lung Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
2. Department of Histology & Embryology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
3. Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
4. Department of Physiology, Hamadan University of Medical Sciences, Hamadan, Iran

Background and Objective: The role of isoflavones in pulmonary structure and function during menopause is not well studied. Moreover, the important role of estrogen in the physiological function of respiratory system has been revealed. Genistein, as an isoflavone, mimics estrogenic in diabetic rats. Here, we hypothesized that genistein would

reverse changes in the protein expression levels related to estrogen deficiency in the lung of ovariectomized diabetic rats.
Materials and Methods: Wistar female rats were assigned to four experimental groups (n=10 in each group): sham, rats underwent laparotomy without ovariectomy; OVX, rats that underwent ovariectomy; OVX.D, rats underwent bilateral ovariectomy and were fed a high-fat diet (HFD); OVX.D.G, ovariectomized diabetic rats with genistein administration (1 mg/kg /day). After ovariectomy, rats continued to feed HFD for a 4-week period. After 4 weeks of HFD feeding, a single dose of 30 mg/kg of streptozotocin was administered in the diabetic group. Genistein was administered for eight weeks. At the end of the experiment, lung tissue was removed and Western blotting technique and hematoxylin-eosin staining were used for evaluation of the lung.
Results: Genistein treatment significantly decreased inflammatory and apoptotic biomarkers in the ovariectomized diabetic rats compared to non-treated animals ($P<0.05$). Also, genistein exerted a protective effect in the lung architecture.
Conclusion: Genistein partly reversed ovariectomy-induced changes in apoptotic and inflammatory biomarkers in the lung. Our data suggest that genistein treatment as a natural replacement therapy may prevent the estrogen deficiency effects in the lung of diabetic menopausal women.
Keywords: Apoptosis, Diabetes, Genistein, Inflammation, Ovariectomy

P-321

Evaluation of the Effect of Human Amniotic Membrane Mesenchymal Stem Cells Conditioned Medium (hAM-MSCs-CM) on Ovalbumin-Induced Asthma in BALB/c Mouse Model

Nahid Aboutaleb[1], Fereshteh Dalouchi[1], Yaser Azizi[1]

1. Department of Physiology, Faculty of Medicine, Iran university of Medical Sciences, Tehran, Iran

Background and Objective: Asthma is a chronic inflammatory disease of the lung and accompanied by immune system imbalance. Chronic inflammation causes tissue damage and structural changes of the airways including goblet cell hyperplasia, increased airway smooth muscle mass and narrowing of the airway. In this study, hAM-MSCs-CM with immunomodulatory and anti-inflammatory properties was used to evaluate its effect on tissue damage of ovalbumin-induced asthma in mice.
Materials and Methods: 40 male BALB/c mice were randomly devided into 4 groups: control group (sensitized and challenged with saline), asthma group (sensitized with intraperitoneal injection of 20 µg OVA, 100 mg aluminum hydroxide and 1 mL saline on the 1st, 8th and 14th day and challenged with 3% OVA for 1 week), treatment groups (Intravenous injection of 50µl CM and DMEM). After anesthesia, lung tissue sections stained with H&E.
Results: In the control group, vascular smooth muscle, epithelial mucosa and bronchial lumen were normal. In the asthma group thickening of the bronchial wall and basement membrane, thichening of the bronchial smooth muscle and narrowing of the lumens were observed. These changes were reduced in the treatment group with CM. But morphologicaly significant difference wasn't observed between asthma group and asthma group treated with DMEM.
Conclusion: Our results showed that CM could improve lung tissue changes of OVA-induced asthma in BALB/c mice model.
Keywords: Mesenchymal Stem Cells, Human Amniotic Membrane, Conditioned Medium, Asthma

P-322

Allergen induces anxiety-like behavior and enhances activity of amygdala in rat model of asthma

Kolsoum Dehdar, Mohammad Reza Raoufy

Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Background and Objective: Asthma is a chronic inflammatory disease of the airways that affects not only the airways but also the central nervous system (CNS). Psychiatric disorders, such as anxiety, are common in asthma. However, no study to date provides direct experimental evidence for the effect of allergic inflammation on function amygdala, which is essential region for modulating anxiety behavior. We assessed the impact of allergic inflammation on the appearance of anxiety-like behavior and amygdala activity in a rat model of asthma.
Methods: We applied elevated zero maze test to estimate the level of anxiety in animals. To measure activity in the amygdala, we used local field potential recording technique in awake rats.

Results: Our findings indicated an increase in anxiety-like behavior in the OVA group ($p < 0.001$, $d = 1.75$). Spectral analysis of amygdala revealed a higher delta and theta activity in the OVA group compared to the control group ($p < 0.01$, $d = 1.44$; $p < 0.05$, $d = 1.14$, respectively).
Conclusions: Findings of the present study reports that disrupting the activity of amygdala appears to contribute to the induction of anxiety-related behaviors with asthma.
Keywords: Asthma; Anxiety; Amygdala; Local Field Potential; delta activity; theta activity

P-323

Anti-inflammatory and anti-oxidative effects of Myrtenol in the rats with allergic asthma

Mohammad Amin Rajizadeh[1], Hamid Najafipour[2*], Mitra Samareh Fekri[3], Farzaneh Rostamadeh[4], Elham Jafari[5], Mohammad Abbas Bejeshk[6] , Yaser Masoumi- Ardakani [7]

1. MSc of Physiology, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Professor of Physiology, Department of Physiology, Afzalipour Medical Faculty and Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
3. Associate Professor of Pulmonology, Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
4. Ph.D of Physiology, Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
5. Assistant professor of Pathology, Department of Pathology and Pathology and Stem Cells Research Center, Kerman University of Medical Science, Kerman, Iran
6. MSc of Physiology, Gastroenterology and Hepatology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
7. Ph.D by research student of Physiology, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

Introduction: To investigate the effect of Myrtenol, the active ingredient of Myrtle, on the oxidant and anti-oxidant indices and interleukins in the allergic asthma.
Methods: Allergic asthma was induced by ovalbumin (OVA) sensitization and inhalation in four groups of rats; Control, Asthma, Asthma+Dexamethasone and Asthma+Myrtenol. Myrtenol (50mg/kg) or Dexamethasone (2.5mg/kg) was administered intraperitoneally for 7 consecutive days after OVA inhalation. At the end, histopathological parameters and interleukins (INF-γ, IL-10, IL-1β, TNF-α) and oxidative stress biomarkers, Malondialdehyde, superoxide dismutase and glutathione peroxidase in the lung and serum were measured by hematoxylin & eosin staining and ELISA method respectively.
Results: Myrtenol reduced the pathological changes in the lungs and airway endothelium. The level of IL-1β and MDA in the serum and lung tissue, and also the level of TNF-α in the lung tissue decreased in the Myrtenol group compared to the asthma group. Myrtenol increased the level of IL-10 and the activity of GPX in the lung tissue and serum.
Conclusion: Myrtenol may improve asthma by increasing the ratio of antioxidants to oxidants and reducing the ratio of pro-inflammatory to anti-inflammatory interleukins in the lung. Myrtenol is presented as a potent herbal medicine ingredient for the treatment of asthma.
Keywords: Allergic asthma, Myrtenol, Malondialdehyde, Superoxide dismutase, Glutathione peroxidase, Interleukins

P-324

Perillyle alcohol ameliorates monocrotaline-induced pulmonary arterial hypertension with through PARP1-mediated miR-204 and its downstream pathway in rats

Soodeh Rajabi[1], Hamid Najafipour[2], Saeideh Jafarinejad Farsangi[1], Zeinab Kordestani[2], Ahmad Beik[3], Majid Askaripour[4]

1. Department of physiology and Physiology Research Center, Kerman University of medical science
2. Cardiovascular Research Center, Kerman University of medical science, Kerman Iran

3. Endocrinology and Metabolism Research Center, Kerman university of medical science, Kerman Iran

4. Gastroenterology and Hepatology Research Center, Kerman University of Medical Sciences, Kerman Iran

Background and Objective: Pulmonary arterial hypertension (PAH) is a vascular disease in lung that characterized by elevated pulmonary arterial pressure (PAP) due to small arteriole remodeling and vasoconstriction. Micro-RNAs are small non-coding RNAs that are dysregulated in many diseases. Many miRNAs play a role in the pathology of PAH. Perillyle alcohol (P-OH) is an antioxidant plant derivative that has anti-cancer effects. In this study we investigated the effect of P-OH on expression of PARP1, miR-204 and its targets, HIF1a and NFATc2.
Methods: Thirty six male NMRI rats, randomly divided into four groups: control, monocrotaline, vehicle and perillyle alcohol groups. Monocrotaline with single dose of 60 mg/kg injected subcutaneously in day 0. P-OH injected once a day with dose of 50mg/kg for last three weeks.
Lung tissue fixed in formalin %10 for pathology and evaluation of expression of miRNA and mRNA was performed with real time quantitative PCR and western blotting.
Results: Right ventricular systolic pressure in Vehicle rats was 91mmHg that reduced to 32mmHg in P-OH rats, significantly ($p<0.001$).
MiR-204 expression reduced in PAH vehicle rats compared to control rats (-9.4+1.9- fold; $p<0.05$). P-OH increased miR-204 expression compared to vehicle group (12.3+4.9- fold; $p<0.05$). mRNA Expression of PARP1(5.1±1.8-fold; $p<0.05$) and HIF1α (7.9+3.9-fold; $p<0.001$) increased in vehicle rats that reduced after treatment with P-OH ($p< 0.05$). Also, protein expression of PARP1(-1.1+0.18-fold; $p<0.01$), HIF1α (-1.6+0.2-fold; $p<0.01$), and NFATc2 (-1.09+0.12-fold; $p<0.01$) reduced with P-OH ($p< 0.05$).
Conclusion
P-OH improved pulmonary arterial hypertension possibly with effect on PARP1 and miR-204 and their downstream targets HIF1a and NFATc2 pathway.
Key words miR-204, Perillyle alcohol, Pulmonary Arterial Hypertension, PARP1, rat

P-325

The effect of quercetine on expression of miR-204 and its targets in monocrotaline induced pulmonary arterial hypertension in rats

Majid Askaripour[1], Hamid Najafipour[2], Soodeh Rajabi[3], Saeideh Jafarinejad Farsangi[1], Ahmad Beik[4]

1. Department of Physiology and Physiology Research Center, Kerman University of medical sciences, Kerman, Iran
2. Department of Physiology and Cardiovascular Research Center, Kerman University of Medical Sciences, Kerman, Iran.
3. Endocrinology and Metabolism Research Center, Kerman University of Medical Sciences, Kerman Iran.
4. Gastroenterology and Hepatology Research Center, Kerman University of Medical Sciences, Kerman Iran.

Background and Objective: Pulmonary arterial hypertension (PAH) is a chronic disease of vasculature that characterized by elevated pulmonary arterial pressure (PAP).Micro-RNAs are small non-coding RNAs with about 22 nucleotides in length and by binding to their target mRNAs, lead to the destruction of the mRNA or the suppression of the translation. Many miRNAs play a role in the pathology of PAH.
Quercetine is an antioxidant plant derivative that has anti-cancer and anti-inflammatory effects.
In this study we investigated the effect of quercetine on miR-204 expression and its targets, PARP1, HIF1a and NFATc2.
Materials and Methods: Thirty six male NMRI rats randomly divided into four groups: control, monocrotaline, vehicle and quercetine groups. Monocrotaline with dose of 60 mg/kg injected subcutaneously in day 0. Quercetine injected for last three weeks. miRNA and mRNA expression evaluated with real time quantitative PCR and western blotting.
Results: Right ventricular systolic pressure in Vehicle rats was 91mmHg that reduced to 54mmHg in P-OH rats, significantly ($p<0.05$).
miR-204 expression reduced in MCT induced PAH rats compared to control rats (-9.4+1.9- fold; $p<0.05$). Quercetine increased miR-204 expression compared to vehicle group (13.2+6.1-fold;$p<0.05$) .Quercetine reduced the mRNA expression of PARP1(-4.2+1.6-fold; $p<0.05$)and HIF1α (-3.2+2.8-fold; $p<0.05$), also protein expression of PARP1 (-1.12+0.19-fold; $p<0.01$),HIF1α (-1.18+0.19-fold; $p<0.001$)and NFATc2(-1.2+0.1-fold; $p< 0.001$) in PAH rats ($p<0.05$).
Conclusion : Quercetine with the effect on miR-204 and its downstream targets may ameliorate pulmonary arterial hypertension in rats.
Key words: Quercetine, Pulmonary Arterial Hypertension, miR-204, PARP1, NFATc2, Rat

P-326

Overactivation of resting brain networks is associated with lung function impairment in patients with asthma

Leila Gholami-Mahtaj[1], Mohammadreza Raoufy[1]

Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Background: Asthma not only impairs physical function of patients but also affect their psychological state and function of brain. However, changes of the functional alterations of brain network in asthma patients remain largely unclear. We used EEG to investigate functional brain organization in asthmatic patients.
Methods: EEG was recorded during the resting state with awake and eyes-open condition in thirty-eight sex and age-matched subjects. EEG power data were quantified for define default mode network (DMN) and salience network at different frequency bands. We examined lung function using spirometry. Correlation between EEG power and clinical parameters were calculated. Source localization and functional connectivity was evaluated using standard low-resolution brain electromagnetic tomography (sLORETA).
Results: EEG power in asthmatic patients significantly increased at all of frequency bands (delta, theta, alpha, beta and gamma) than controls. In asthmatic patient, EEG power had a positive correlation with lung function impairment, asthma duration and asthma control test. sLORETA analysis showed high activation at DMN and salience network in all of frequency bands and localized neural sources to the rostral anterior cingulate cortex, dorsomedial prefrontal cortex, posterior cingulate cortex, insula and dorsal anterior cingulate cortex.
Conclusion: Our findings indicated overactivation of resting brain networks which is associated with lung function impairment and severity of disease in asthmatic patients. These results provide important evidence to support the role of brain networks in the pathophysiology of asthma.
Keywords: Asthma, EEG, resting brain networks.

P-327

Muscarinic receptors blockade and nitric oxide production contribute in the relaxant effect of Berberis vulgaris extract on rat tracheal smooth muscle

Zahra Ghasemi, Farzaneh Naghdi[1,2], Saeideh Saadat [1,2], Zahra Gholamnezhad[1,2], Hassan Rakhshandeh[3], Mohammad Hossein Boskabady[1,2]

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
3. Pharmacological Research Center of Medicinal Plants, Mashhad University of Medical Sciences, Mashhad, Iran

Berberis vulgaris (Berberidaceae) has been demonstrated to possess multiple pharmacological activities. The current study evaluated the relaxant effect of B. vulgaris hydroalcoholic extract on rat tracheal smooth muscle (TSM) and its

possible molecular mechanisms. TSM were contracted by 10 μM methacholine or 60 mM potassium chloride (KCl) and the effects of cumulative concentrations of the extract (0.1, 0.4, 1.6, 6.5 mg/ml) and theophylline (0.2, 0.4, 0.6 and 0.8 mM) were examined. To examine the possible mechanism(s) of the relaxant effect of the plant, its effect was also examined on incubated tissues with atropine, chlorpheniramine, propranolol, diltiazem, glibenclamide, indomethacin, ω-nitro-L-arginine methyl ester (L-NAME) and papaverine. The results showed concentration-dependent relaxant effects for B. vulgaris in non-incubated TSM contracted by KCl and methacholine ($p<0.05$ to $p<0.001$). There was not any significant difference in the relaxant effects of B. vulgaris between non-incubated and incubated tissues with chlorpheniramine, propranolol, indomethacin, diltiazem, glibenclamide, and papaverine. However, the relaxant effects of 1.6, 6.5 mg/ml of B. vulgaris in incubated tissue with L-NAME ($p<0.01$ for both cases) and 6.5 mg/ml of the extract in incubated tissue with atropine were significantly lower than non-incubated tissues ($p<0.05$). The EC50 value of B. vulgaris in tissues incubated with chlorpheniramine was significantly higher than non-incubated TSM ($p<0.05$). A relatively potent relaxant effect of B. vulgaris comparable to the effect of theophylline was shown. Muscarinic receptors blockage and nitric oxide production were suggested as the possible mechanisms of the relaxant effect of the plant on TSM.

Keywords: Barberry; relaxant effect; trachea; smooth muscle; muscarinic receptors; nitric oxide

P-328

Relaxant effect of Urginea maritima through the beta-2 adrenergic, calcium and potassium channels pathway on the tracheal smooth muscle

Hamideh Kazemirad[1], Fatemeh Amin[2], Mohammad Hossein Boskabady[1]

1. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Department of Physiology, Faculty of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

Background and Objectives: Urginea maritima (U. maritima) plant has protective effects on the cardiovascular system and the respiratory system. Therefore, the present examined the relaxant effect of U. maritima on rat tracheal smooth mucle and its possible mechanism.
Methods: Male Wistar rats were divided to five group. Ttracheal smooth muscle (TSM) was contracted by KCl (60 mM) or methacholine (10 μM) for 5 min and cumulative concentrations of U. maritima extract (12.5, 25, 50, 100, 20, 400 μM/ml) were added to organ bath every 5 min. Theophylline (0.2, 0.4, 0.6 and 0.8 mM) as positive control, and saline (1 ml) as negative control were also examined in non-incubated tissues. The relaxant effect of the extract was examined on non-incubated and incubated TSM with glibenclamide, propranolol, diltiazem, and indomethacin.
Results: There was concentration-dependent relaxant effects of U. maritima on non-incubated TSM contracted by KCl (60 mM) or methacholine (10 μM), ($p<0.0001$). The relaxant effects of U. maritima in incubated tissues with glibenclamide, propranolol and diltiazem were significantly lower compared to non-incubated tissues ($p<0.0001$). In the indomethacin incubated group the relaxant effects of the extract was not significantly different from non-incubated tissues. EC50 values of U. maritima extract in incubated TSM with glibenclamide, propranolol, and diltiazem were significantly higher than non-incubated tissues ($p<0.001$).
Conclusion: The results also showed that beta2-adrenoceptor stimulation, potassium channel blocking, and calcium channel blocking are the possible mechanisms for the relaxant effects of the plant.

Keywords: Urginea maritima, Tracheal smooth muscle, Relaxant effect, Possible mechanism

P-329

Serum Levels of Visfatin, Sirtuin-1, and Interleukin-6 in Stable and Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Mohammad Reza Aslani[1], Sara Mokhtari[2], Hassan Ghobadi[3]

1. Lung Inflammatory Diseases Research Center, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.
2. Medical student, Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.
3. Internal Medicine Department (Pulmonary Division), Faculty of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

Background and Objective: Disturbance in the balance of inflammatory and anti-inflammatory factors are evident in the development of chronic obstructive pulmonary disease (COPD). The present study aimed to investigate serum visfatin, sirtuin-1 and interleukin-6 (IL-6) levels in patients with stable and acute exacerbation of COPD.
Materials and Methods: We measured serum visfatin, sirtuin-1 and IL-6 levels in 30 patients with stable COPD (SCOPD), 30 patients with acute exacerbation of COPD (AECOPD), and 30 control subjects and compared them with airflow limitation according to the COPD stage in the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) criteria, peripheral O2 saturation (SpO2), and COPD Assessment Test (CAT) score. We also tested the association of serum visfatin and sirtuin-1 levels with COPD patients' clinical parameters.
Results: Both serum visfatin and IL-6 levels increased in SCOPD and AECOPD groups compared with control group ($P < 0.01$ and $P < 0.001$, respectively). Moreover, visfatin and IL-6 levels increased in AECOPD patients compared with SCOPD group in GOLD stages III-IV ($P < 0.05$ and $P < 0.001$, respectively). On the other hand, serum sirtuin-1 levels significantly decreased in COPD patients compared with healthy subjects ($P < 0.05$). There was a significant negative correlation between serum visfatin and sirtuin-1 levels.
Conclusion: Elevated visfatin and IL-6 levels demonstrated their proinflammatory effects in patients with COPD, especially in AECOPD patients. In addition, there was negative association between serum visfatin and sirtuin-1 levels suggest that may be their pathophysiologic and therapeutic roles in COPD patients.
Keywords: Chronic Obstructive Pulmonary Disease, Visfatin, Interleukin-6, Sirtuin-1

P-330

Carvacrol Affected lung injury induced by inhaled paraquat

Arghavan Memarzia[1], Fatemeh Amin[2], Mahrokh Heydari[1], Mahmoud Hosseini[1, 3] and Mohammad Hossein Boskabady[1]

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Physiology and Pharmacology, School of Medicine, Physiology-Pharmacology Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran. 3Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: Paraquat (PQ) is a herbicide poison used in agriculture inducing oxidative stress. Carvacrol showed anti-spasmic, anti-inflammatory and anti-oxidant effects. The effect of carvacrol on lung injury induced by inhaled paraquat was examined.
Materials and Methods: Male rats were divided into 6 groups as: a control group exposed to normal saline aerosol, Two groups exposed to 27 and 54 mg/m3 doses of PQ aerosol (PQh and PQl respectively), two groups treated with two doses of carvacrol (20 and 80 mg/kg/d) and one group treated with dexamethasone (1.25 µg/ml) after the end of exposure to 54 mg/m3 for 16 days ($n = 6$). Oxidant, anti-oxidant markers, total and differential WBC counts in broncho-alveolar lavage (BALF) were assessed at the end of the study.
Results: There were significant increase in total WBC, neutrophil, eosinophil and monocyte due to both doses of PQ, significant increase in lymphocyte, nitrite and malondialdehyde levels and significant decrease in catalase and superoxide dismutase due to PQh but thiol level was decreased due to both doses of PQ ($p<0.05$ to $p<0.001$). Total WBC, neutrophil and eosinophil were significantly reduced due to both doses of carvacrol and dexamethasone, nitrite, malondialdehyde and catalase levels were improved due to high dose of carvacrol and dexamethasone and lymphocytes was reduced only due to high dose of carvacrol ($p<0.05$ to $p<0.001$).
Conclusion: Lung inflammation and oxidative were observed due to inhaled PQ and treatment with carvacrol improved lung inflammation and oxidative stress.
Key words: Carvacrol, Paraquat, Lung injury, Lung inflammation, Oxidative stress

P-331

Study of Microscopic Effect of Palmatine on Diabetic Wound Healing of Male wistar Rats

Amir hossien toozandehjani[1], Sahar Molzemi[1,2], amir hossien ashnai[2]

1. Department of medical radiation engineering, Islamic Azad University, Shahroud, Iran
2. School of Medical Sciences, Shahrood Branch, Islamic Azad University,Shahrood, Iran

Background: Diabetic foot is the most common cause for hospitalization among diabetic patients whose treatment is costly in the world. In developed countries, over 5% of diabetic patients are involved in diabetic foot, and if it is not

treated quickly and appropriately . The aim of this study was investigating the effect of palmatine on wound healing of diabetic male wistar rats.
Method: In this experimental study, 48 male Wistar rats with weight ranged between 180 and 240gr were selected and randomly divided into 4 groups of 12 animals. The Control group (healthy rats that received intraperitoneal citrate buffer along with induced diabetes of other groups), sham (streptozotocin induced diabetic rats with 55 mg/kg without treatment), first experimental (diabetic and treatment with eucerin) and second experimental (diabetic and treatment with palmatine). Wound healing process was investigated within 10 and 14 days after wounding using macroscopic and microscopic methods.
Results: Wounds in the group that become diabetic with streptozotocin (10/87± 0.01) showed delayed healing compared to healthy group (2/56±0.001) and wound healing in the second experimental group with palmatine treatment (2/56±0.001) was accelerated compared to control group(0/5±0.001).
Conclusion: The results showed that palmatein, which is twice daily, causes accelerated healing of skin lesions of healthy and diabetic specimens.
Keywords: Palmatine; Diabetic , Rat

P-332

Green Synthesis, production of Gold Nanoparticles Using Extract of Shilajit

Mandana Jafari[1], Mitra Mehrabani[1], Mehrnaz Mehrabani[2]

1. Herbal and Traditional Medicines Research Center, Kerman University of Medical Sciences, Kerman, Iran
2. Physiology Rresearch Center, Kerman University of Medical Sciences, kerman, Iran

Background and Objective: Green synthesis is now considered an alternative to chemical and physical synthetic procedures for nanoparticles by using sustainable and eco-friendly materials instead of harsh and toxic chemicals. This research aimed at synthesizing Gold nanoparticles using locally- sourced extract of Shilajit.
Materials and Methods: In the present study the capability of extract of shilajit (gathered from Bahraseman mountains (Jiroft 28°40'41"N and 57°44'26"E, Iran)) for biosynthesis of gold nanoparticles (Au NPs) was evaluated. The produced biogenic Au NPs were characterized using UV–visible spectroscopy, transmission electron microscopy (TEM), scanning electron microscopy (SEM) methods. To evaluate cytotoxic effects, MTT method was used and finally data were analyzed using SPSS.
Results: The related TEM and SEM images of biogenic Au NPs indicated spherical shaped and well dispersed nanostructures with the average particle size of 53.8 nm. Zeta potential analysis of as-synthesized Au NPs showed a peak at − 18.6 ± 1.8 mV. Cytotoxic activity of biologically synthesized Au NPs (assisted by MTT-based colorimetric assay) revealed IC50 (µg/mL) of 75.6 ± 1.6, 82.6 ± 2.3 and 61.5 ± 2.6, against three cancer cell lines of HT1080, MCF7, and A549, respectively. However, one normal cell of 3T3 inhibited by 85% in the presence of 500 µg/mL of the biogenic Au NPs.
Conclusion: Gold Nanoparticles produced by extract of shilajit are effective on cancer cell lines.
Key Words: Gold nanoparticles, Cytotoxic, Shilajit

P-333

Antioxidant effect of Hyssopus officinalis leaves extract in the model of Salmonella colitis

Hadi Cheraghi[1], Ehsan SoleimannejadBari[2]

1. Department of Clinical pathology, Faculty of Veterinary Medicine, Razi University, Kermanshah, Iran.
2. Young Researchers Club, Urmia Branch, Islamic Azad University, Urmia, Iran.

Background and Objective: Hyssopus officinalisis is traditionally used in folk medicine for various aims. In view of its anti-inflammatory, anti-bacterial and antioxidant potential, it could be beneficial for the treatment of colitis,

which is associated with interaction between genetic, environmental factors and intestinal microbiome leading to dysregulated immune responses. This study evaluates the antioxidant effect of hydroalcoholic extract of Hyssopus officinalisis Leaves (HOL) in Salmunella induces colitis in mice which resembles human colitis.
Materials and Methods: In this study, ethanolic extracts of H. officinalis were prepared. Also, MIC and MBC of these extracts were evaluated for Salmonnella spp. HOL (300, 150, 75 mg/kg) were administered orally for 14 days in salmonella-induced groups. Response to treatment was assessed with using disease activity index (DAI); macroscopic/histological damage; determining oxidative stress indicators: Total antioxidant Capacity (TAC) in serum, myeloperoxidase (MPO), Gluthathione Peroxidase (GPx) and malondialdehyde (MDA) level in colon tissues. The effect of these extracts Data were analyzed using SPSS.
Results: The results exhibited significant activity against MIC value in the range of 8-16 mm and 0.5-1 µl/ml, HOL treatment in colitic mices directed decreased DAI scores, macroscopic and histologic damage. It also reduced MPO and MDA levels in tissue. Whereas, prevented depletion of serum TAC and Gpx level in colon. The dose of HOL that produced most significant beneficial effect was 300 mg/kg.
Conclusion: HOL administration relieved the disease activity in colitis by decreasing oxidative stress.
Keywords: Hyssopus officinalis, Antioxidant, Colitis, Myeloperoxidase, Gluthathione Peroxidase

P-334

The effect of Buxus hyrcana on learning and memory and oxidative stress in the epileptic model of memory impairment in the rat

Abdolkarim Hosseini, Vahid Azizi, Farzin Allahyari

Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran.

Background and Objective: Pentylenetetrazol (PTZ) is a chemical substance which largely used for induction of seizure and epilepsy in the animal model, and it can also, disrupts free radicals balance and causes oxidative stress in the body with a negative impact on memory and learning. In this study, the medicinal plant Buxus hyrcana, was used to evaluate its effect on oxidative stress and memory deficit caused by PTZ in the rat.
Materials and Methods: Twenty-four rats were randomly allocated to 4 groups: control negative under treatment with PTZ (sub-threshold dose 35 mg/kg for one month), control positive under treatment with Phenobarbital (PB-30 mg/kg), and two PTZ groups under treatment with B. hyrcana extract (BHE-150, and -300 mg/kg). Standard passive avoidance test was used to evaluate retention and recall (evaluation of memory and learning). After behavioral evaluation, rats were anesthetized, brains were removed, and following preparation of hippocampal homogenates, oxidative stress (malondialdehyde (MDA), catalase, superoxide dismutase (SOD)) was evaluated using specified kits. Data were analyzed using SPSS.
Results: Step-through latency in passive avoidance test in PTZ group receiving BHE at a dose of 300 mg/kg was greater than PTZ group. In addition, hippocampal lipid peroxidation (MDA level) in BHE-300 treated PTZ group was significantly lower and catalase activity and SOD level were significantly greater versus PTZ group.
Conclusion: Our results showed that BHE could prevent memory deficit and ameliorate hippocampal oxidative stress in PTZ-kindled rats.
Keywords: Buxus hyrcana, Epilepsy, Oxidative stress, Neuroinflammation, Learning and memory

P-335

Investigation on the effect of hydroalcoholic extract of plantago lanceota leaf Compared to Phenytoin on wound healing on Diabetes rats whit streptozotocin

Hassanali Abedi[1], Hossein Kargar Jahromi[1], Zahra Ghazanfari[2], Hoda Haghshenas[2]

1. Research center for non.Communicable Diseases, Jahrom University of Medical Sciences, Jahrom, Iran
2. Student Research Committee, Jahrom University of Medical Sciences, jahrom, Iran

Background and Objective: Diabetes is one of the oldest known human diseases and one of the main problems of health systems in Iran. The most commonly occurring skin disorder in diabetics is the inability to tolerate local injuries that predispose people to wounds, especially diabetic foot. Plantago plant in Iranian traditional medicine is used as an antiseptic for wounds in gum and mouth and as a anti-inflammatory agent. Since the effects of Plantago on diabetic ulcers have not been studied yet, the aim of this study was to investigate the effects of this plant on rat diabetic ulcer.

Materials and Methods: This is an experimental study. Mice were injected streptozotocin to get diabetic (50 mg / kg). Animals were divided into 4 groups of 12 as follows: Group 1 (Right wound with ucerin), Group 2 (Right wound with phenytoin), Group 3 (Right wound with 5% extracts), Group 4 Right wound with 10% extract).
In all groups, the left wound was treated with normal saline as control ulcer. The percentage of wound healing in 2 mm on days 3, 7, 10 and 14 was calculated by shooting the wounds and Image J software. The results were analyzed by SPSS software using one way ANOVA and Duncan's post hoc test.
Results: On days 3, 7, 10, and 14, the use of bergamot and technetium had a significant increase in wound healing compared with ucerin.
Conclusion: According to the results of this study, it was found that the extracts of Plantago have an antioxidant and anti-inflammatory effect, respectively. Improve the dose of diabetic wounds.
Keywords: plantago lanceota, diabetes, wound, streptozotocin, rat

P-336

Evaluating the effect of Silybum marianum seed and Cichorium intybus root extracts on hepatic gene expression of Farnesoid X Receptors (FXR) in rat model of acetaminophen-induced hepatotoxicity

Azadeh Khalili[1,2], Gholamreza Bayat[1,2], Vahid Jamshidi[3], Roham Mazloom[1], Parviz Fallah[4], Mohammad Mahdi Ahmadian-Attari[2], Seyed Ali Hashemi[5], Leila Beikzadeh[4]

1. Department of Physiology and Pharmacology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran
2. Evidence-based Phytotherapy and Complementary Medicine Research Center, Alborz university of medical sciences, Karaj, Iran
3. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, Iran
4. Department of Medical Laboratory Sciences, Faculty of Para-Medicine, Alborz University of Medical Sciences, Karaj, Iran
5. Department of Pathology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran

Background and Objective: Bile acid receptors known as Farnesoid X receptors (FXR), are one of the nuclear superfamily receptor members which have a pivotal role in the bile acid regulation and liver protection against some hepatotoxic situations. The objective of the present study was to examine the possible role of FXR in modulating the hepatoprotective effects of silymarin and chicory extract in rat model of acetaminophen-induced hepatotoxicity.
Materials and Methods: Male Wistar rats allocated into five random groups including control, vehicle-treated, Acetaminophen-treated, two acetaminophen-treated received silymarin extract at 200 and 400 mg/kg/day and two acetaminophen-treated received chicory extract at 500 and 1000 mg/kg/day. The liver function and histology as well as hepatic FXR gene expression, has been evaluated using liver enzyme assay, tissue staining and Real-Time RT-PCR technique, respectively.
Results: The levels of AST, ALT and LDH of the acetaminophen-received group were significantly higher compared to that of the control group whereas those of extract treated groups was significantly lower than those of acetaminophen-received ones. Moreover, the Real-Time RT-PCR findings showed that administration of acetaminophen associated with a non-significant down-regulation pattern (-33%) of FXR gene expression. FXR up-regulation was seen in extract-treated groups of 200 mg/kg/day silymarin extract as well as in chicory received extract at 500 mg/kg/day.
Conclusion: The main findings of our study are that the hepatoprotective activity of silymarin and chicory extract at least in low doses, might be partly, directly or indirectly, mediated by FXR gene up-regulation.
Keywords: Farnesoid X Receptors (FXR), Acetaminophen, silymarin, chicory

P-337

In vitro evaluation of Cholinesterase inhibitory effects and metal chelating abilities of Asarum europaeum

Arezoo Rastegari[1], Mahnaz Khanavi[2], Mina Saeedi[1,3], Mahdieh Eftekhari[2], Yasaman Vahedi Mzdabadi[1], Tahmineh Akbarzadeh[1,4], Mahdieh Soleimani[2]

1. Persian Medicine and Pharmacy Research Center, Tehran University of Medical Sciences, Tehran, Iran
2. Department of pharmacognosy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
3. Medicinal Plants Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
4. Department of Medicinal Chemistry, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Background and Objective: According to Iranian traditional medicine references (ITM), A. europaeum has a warm and dry nature which was prescribed for neurological diseases such as epilepsy and seizures. Also, it was

recommended for memory enhancement and amnesia. In this study, different fractions of A. europaeum were investigated for some biological activities from anti-Alzheimer's point of view. In this respect, anticholinesterase activity, neuroprotectivity on pc12 cell line as well as metal chelating ability of different extracts and fractions were evaluated.
Materials and Methods: The aqueous and hydroalcoholic extracts of the rhizome of the plant were prepared by the maceration in boiling water and methanol (80%), respectively. The hydroalchoholic extract was fractionated using petroleum ether, chloroform, ethyl acetate via liquid-liquid extraction. The ChEI activity was performed using Ellman's method and the chelating ability was evaluated toward Fe2+, Cu2+, and Zn2+ ions. Also, their neuroprotectivity effect were also investigated on the pc12 cell line.
Results: It was found that ethyl acetate fraction showed the best AChEI activity (IC50 = 99.69 µg/ml), however, it depicted no activity against BChE. It also showed good chelating ability toward Fe2+, Cu2+, and Zn2+ ions and good neuroprotectivity in comparison to quercetin.
Conclusion: Our results revealed that ethyl acetate fraction of the rhizome of A. europaeum can be a potent alternative and complimentary approach against Alzheimer's disease and memory enhancement.
Keywords: Alzheimer's disease, Asarum, cholinesterase, metal-chelating, neuroprotectivity

P-338

Inhibition of Cyclooxygenase 2 in Breast Cancer Cell Line by Pistacia Atlantica Extract

AliReza Rafati[1*], Neda Fariborzi[2], Seyedeh-Sara Hashemi[3]

1. Division of Pharmacology & Pharmaceutical Chemistry, Sarvestan Branch, Islamic Azad University, Sarvestan, Iran.
2. Division of Food Science & Nutrition, Sarvestan Branch, Islamic Azad University, Sarvestan, Iran.
3. Burn & Wound Healing Research Center, Shiraz University of Medical Science, Shiraz, Iran.

Background and Objective: Globally, cancer is the second leading cause of death. Cancer-related inflammation plays an important role in malignant progression of several cancer types. Current therapeutic approaches are not completely effective for cancer therapy. In addition, they are associated with high side effects. Since medical herbs have fewer side effects than chemical drugs. Lots of attention has been paid to the use of herbal extracts in cancer treatment. Therefore, the present study aimed to investigate the effects of anti-tumor and anti-inflammatory of Pistacia atlantica extract in in vitro conditions.
Materials and Methods: In this study, MCF-7 cell line was treated with different concentrations of hydro alcoholic extracts of Pistacia atlantica (50, 100, 250, 500 µg/mL). After 48hours, the effects of the extract on tumor growth and COX-2 gene expression were analyzed by MTT and Real time PCR, respectively.
Results: The results revealed that the MCF-7 cell line growth significantly decreased in a dose dependent manner comparing to the control group ($P<0.05$). Moreover, Real time PCR results indicated that the expression of COX-2 significantly decreased in a dose dependent manner even at the low concentration of extract comparing to the control group ($P<0.05$).
Conclusion: Based on the results, Pistacia atlantica extract not only suppressed growth of cancer cell line, but also significantly reduced cancer-related inflammation. Therefore, it may be utilized as a new therapy against several types of cancer.
Keywords: Breast Cancer, MCF-7, Cyclooxygenase2, Pistacia atlantica extract

P-339

Evaluation of anti-inflammatory, antioxidant, and antibacterial effect of fractions of Punica granatum var. pleniflora extract

Mahboobeh Raeiszadeh[1,2], Mitra mehrabani[1], Alireza Poostforoush[3], Mojdeh Esmaeili Tarzi[4], Mehrzad Mehrabani[5,1], Mohammad Hadi Nematollahi[6], Sara Naghdi[1], Mehrnaz Mehrabani[4*]

1. Herbal and Traditional Medicines Research Center, Kerman University of Medical Sciences, Kerman, Iran
2. Department of Traditional Pharmacy, School of Persian Medicine, Kerman University of Medical Sciences, Kerman, Iran

3. Department of Chemical Engineering, Faculty of engineering, Shahid Bahonar University of Kerman, Kerman, Iran
4. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
5. Department of Persian Medicine, School of Persian Medicine, Kerman University of Medical Sciences, Kerman, Iran
6. Department of Biochemistry, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

Background and objective: Punica granatum has been widely used in traditional remedies for curing several medical conditions. However, studies addressing its detailed molecular mechanisms especially those involved in the inflammatory process are still limited. Hence, the current study was aimed to investigate the anti-inflammatory, antioxidant and antibacterial effect of fractions of P. granatum extract (PGE).
Materials and Methods: Firstly, total extract of P. granatum, petroleum ether, dichloromethane and ethyl acetate fractions were prepared. Total phenolic content of PGE was assessed by Folin–Ciocalteu method. The effect of PGE on the viability of J774A.1 macrophage was evaluated using MTT assay. To evaluate the anti-inflammatory effect of PGE on lipopolysaccharide (LPS)-stimulated J774A.1 macrophage, the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) at mRNA level was assessed using qRTPCR. Furthermore, in vitro antimicrobial and antioxidant activities of PGE were accomplished.
Results: The results showed that nontoxic concentration of PGE were ≤31µg/mL, except petroleum ether fraction (≤125 µg/mL). Total and ethyl acetate fractions at concentration of 15µg/mL had a tendency to decrease the expression of COX-2 and iNOS in macrophage J774A.1 cells. Ethyl acetate showed the most antioxidant activity (IC50=26.13µg/mL) and phenolic content (383 mg Gallic acid / g extract). Also the best antibacterial activity was for ethyl acetate and residual fraction.
Conclusion: The results showed that total and ethyl acetate fractions may show potential therapeutic effects and it might be driven by its phenolic compounds.
Keywords: murine macrophage J774A.1, Punica granatum var. pleniflora, anti-inflammation, antioxidant, antibacterial.

P-340

Protective effect of Silybum marianum L. on liver toxicity And tissue changes induced by acetaminophen

Mostafa Salari[1], Dr.Soheyla Ebrahimi[2]

1. Payam-e-noor University, International branch, Qeshm Island, Iran.
2. Department of biology faculty of science payame noor university iran

Background and Objective: Silybum marianum is an important herbal medicine that used in the treatment of liver and biliary disorders. In the present study, the protective effects of aqueous extract of Silybum marianumis on liver toxicity due to acetaminophen poisoning in adult male rats were investigated. Acetaminophen is a pain reliever and

overuse that it causes serious damage to the liver and kidneys. Since acetaminophen's liver damage leads to death, achieving compounds that neutralize the effect seems to be necessary.
This study was designed to determine the therapeutic effects of Silymarin protection against toxic liver toxicity acetaminophen was performed in mice.
Materials and Methods: In this study, 63 male Wistar rats with an approximate weight of 200 ± 10 g were used that In 9 groups (n= 7) included: Control group, Patient group (500 mg / kg intraperitoneal acetaminophen), Group without treatment (acetaminophen and saline intraperitoneally), Extract group 200 (200 mg / kg extract), Extract group 400 (400 mg / kg extract), Group 1 therapy (Acetaminophen and 200 mg / kg extracts), Group 2 therapy (acetaminophen and 400 mg / kg extract), Group 1 pre-treatment (200 mg / kg extract for one week before injection of acetaminophen), Group 2 pretreatment (400 mg / kg extract for one week before injection of acetaminophen) that Randomly grouped.
48 hours after the last injection, blood sampling was performed and serum levels of LDH, AST, ALT and ALP and total antioxidant capacity (FRAP) were measured. In order to study tissue changes, 0.5 micron thick sections were prepared and stained with Hematoxylin Eosin.
Results: ALT and AST enzymes are present in the liver cells, and in liver disease, the amount of these enzymes increases in the blood. In the present study, according to other researchers, the use of acetaminophen increased the levels of ALT, AST and LDH.
The results of this study showed that taking hydroalcoholic extract of Silybum marianum can eliminate the symptoms of acute poisoning with acetaminophen and improve the dose of 400 mg / kg in comparison with 200 mg/ kg dose.
Pre-treatment with Marilian extract has been able to protect against liver due to acetaminophen and 400 mg / kg dose compared to 200 mg / kg dosage. Histological studies in this study confirmed the results of the study of liver enzymes. Regarding the results of the study of total antioxidant capacity of serum, it seems that hydroalcoholic extract of marmalade is effective in increasing the antioxidant capacity in hepatic protection against acetaminophen.
Conclusion: The results of this study showed that taking hydroalcoholic extract of Silybum marianum can eliminate the symptoms of acute poisoning with acetaminophen and improve the dose of 400 mg / kg in comparison with 200 mg / kg dose. Histological studies in this study confirmed the results of the study of liver enzymes.
Keywords: Liver toxicity, Silymarin, acetaminophen, hepatotoxicity

P-341

Protective effects of Resveratrol against Bisphenol A induced Hepatotoxicity in rats

Hossein Bordbar[1□2□] Fatemeh Soleymani[1,2], Elham Nadimi[1,3], Seyedeh-saeedeh Yahyavi[2], Khatereh Fazelian-Dehkordi[1,2*]

1. Histomorphometry and Stereology Research Centre, Shiraz University of Medical Sciences, Shiraz, Iran.
2. Department of Anatomical Sciences, Shiraz University of Medical Sciences, Shiraz, Iran.
3. Department of Immunology, Shiraz University of Medical Sciences, Shiraz, IR Iran.

Background and Objective: Bisphenol-A (BPA) is a chemical substance with increasing exposure to it and applies toxic effects on the liver. Resveratrol (RES) is a medicinal plant that functions as protective properties. This study was designed to evaluate the protective effects of resveratrol on the liver after BSA administration in adult male rats.
Material method: Thirteen Sprague dawley male rats were divided into 5 groups, one group as control and others daily receiving, BPA (50 mg/kg/d), RES (100 mg/kg/d), and BPA plus RES and olive oil by oral gavages, respectively. After 8 weeks, the liver was removed and prepared for stereological study.
Results: The total volume and number of hepatocytes, absolute nucleus and cytoplasm volume were respectively decreased by 18%, 41%, 32% and 37% in the BPA group in comparison to the control animals ($P<0.05$). Also, the sinusoidal space was increased by 17%, 42%, 31% and 30% in the BP group compared to the control, RES+BP, RES and oil groups. RES-treatment due to increase by 11%,13% and 21% in total volume, absolute nucleus and cytoplasm volume compare to BPA group($P<0.05$). Histopathological studies showed that the vacuolization of hepatocytes and irregularities in the liver structure and sinusoidal dilatation in BPA treated rats.
Conclusion: This study demonstrated that BPA causes hepatotoxicity and resveratrol as an antioxidant substance can protect the toxicity effect of bisphenol-A in adult male rats.
Key word: Bisphenol-A, Resveratrol, Hepatotoxicity, Liver, Stereology

P-342

Clinical trials for controlling cancer complications based on principles of Persian medicine

Ghazaleh Heydarirad, Sajjad Sadeghi

Traditional Medicine and Materia Medica Research Center, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Cancer rates are increasing worldwide, and the number of cancer patients is expected to rise to 21 million by 2030. Studies have shown that cancer patients are increasingly inclined to use complementary and traditional medicine. Persian medicine (PM) as a holistic medical school which has several-thousand-year old history, is based on the theory of four humors comprising phlegm, blood, yellow bile, and black bile. The aim of this study was to investigate clinical trials conducted based on principles of Persian medicine for controlling cancer complications.
Materials and Methods: In this review study, the keywords "cancer", "cancer complication", "traditional medicine" and "Persian medicine" were searched in the Iranian Registration Center of Clinical Trials (IRCT). Also, current investigations on related subjects were considered through a search of the Pub Med and Google Scholar until the end of 2018.
Results: Most clinical trials were conducted to evaluate the effects of psycho-educational interventions, aromatherapy, Iranian herbal medicine, massage, reflexology, and acupuncture on cancer complications. Most of the cancers which were evaluated were breast, prostate, and gastrointestinal cancers, especially colorectal cancer. Most of the complications that were assessments include nausea and vomiting, anxiety, depression, sleep disorders, fatigue, hot flashes, pain and neuropathy.
Conclusion: The clinical trials which conducted based on principles of Persian medicine indicate that traditional interventions might have beneficial effects on improving cancer complications, but the evidences we found were few. Further large and randomized controlled studies are necessary to confirm the benefits of PM on cancer complications.
Key words: Persian medicine, clinical trial, Iranian, traditional

P-343

The effects of different doses of Nepeta menthoides in mice reserpine-induced depression

Sedighe Talebi[1], Batool Rahmati[1], Mohsen Naseri[1], Fatemeh Emadi[4], Masoumeh Jorjani[5]

1. Department of Traditional Medicine, School of Medicine, Shahed University, Tehran, Iran.
1. Neurophysiology Research Center, Department of Physiology, School of Medicine, Shahed University, Tehran, Iran(corresponder).
2. Traditional Iranian Medicine, Clinical Trial Research Center, Shahed University, Tehran, Iran.
3. Traditional Iranian Medicine, Clinical Trial Research Center, Shahed University, Tehran, Iran.
4. Department of Nanomedicine and Tissue Engineering, Department of Pharmacology & Neuroscience Research Center, Shaheed Beheshti Medical University, Tehran, Iran.

Backgroud: Nepeta Menthoides is an Iranian native plant with anti-depressant and sedative properties. This study was designed to search the effects of Nepeta menthoides aqueous extract pretreatment on reserpine induced depression
Material and Methods: 64 male mice were randomly divided into 8 groups of 8 mice. Control normal saline (10 ml/kg), flouxetin (20 mg/kg), imipramine (10 mg/kg), Reserpine (10 mg/kg normal saline), and treatment groups received different doses of the extracts (50, 100, 200, 400 mg/kg) for 7 days. In the 8th day all of the groups except control normal saline received reserpin (4 mg/kg) and were tested 24 hours later. Tests included forced swimming (FST), tail suspention (TST) and open field test (OFT).
Results: reserpine enhanced immobility time (64.37±5.93) in compared to normal saline (38.25±2.59) while Nepeta pretreatment were declined immobility time in a dose dependent manner [(25.75±5.90 (100 mg/kg)And 23.5±7.43(200 mg/kg)]. Also, Nepeta reduced immobility time dose dependently in tail suspension test $p<0.01$. Open field test showed that none of agents did not influence total motility.
Conclusion: Pretreatment with Nepeta menthoides could prevent of depression like behavior induced by reserpine better than fluoxetine and imipramine.
Keywords: Nepeta menthoides, Depression, Reserpin, Forced swimming, Tail suspension

P-344

Effect of nettle (Urtica Dioica) on quality of sleep in hemodialysis patients: A randomized clinical trial

Khadijeh Alizadeh[1], Seyed Afshin Shorofi[2], Nouraddin Mousavinasab[3], Fatemeh Espahbodi[4], Mousa Esmaeili[5], Ravanbakhsh Esmaeili[6*]

1. Student Research Committee, School of Nursing and Midwifery, Mazandaran University of Medical Sciences, Sari, Iran.
2. Traditional and Complementary Medicine Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran; Adjunct Research Fellow, Flinders University, Adelaide, Australia.
3. Department of Biostatistics, School of Health Sciences, Mazandaran University of Medical Sciences, Sari, Iran.
4. Department of Nephrology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
5. Mazandaran Cardiovascular Research Center, Mazandaran University of Medical Sciences, Sari, Iran.
6. Orthopedic Research Center, Mazandaran University of Medical Sciences, Sari, Iran.

Background: Sleep disorders are the common complication of end-stage renal failure. This study aimed to examine the effect of nettle (Urtica Dioica) on sleep quality in hemodialysis patients.
Materials and methods: This randomized clinical trial was conducted on 90 hemodialysis patients who were selected using the convenient sampling method and then randomly assigned into experimental and control groups. The experimental group received 400-mg nettle tablets three times a day for three consecutive months. The control group did not receive any intervention from the research team. The socio-demographic/ clinical characteristics were collected using a pre-structured questionnaire. Sleep quality was measured with the Pittsburgh Sleep Quality Index before intervention and after the first, second and third month of intervention.
Results: No statistically significant difference was found between the two groups for sleep quality before and after intervention ($p = 0.09$). The effect of nettle on sleep quality wasnot significantly differenet at the end of the first ($p = 0.14$), second ($p = 0.34$) and third ($p = 0.97$) month.
Conclusion: Our study showed that nettle did not significantly increase sleep quality in hemodialysis patients. Despite the use of hypnotics, sleep quality is commonly decreased in hemodialysis patients. However, nettle along with hypnotics helped maintain the stability of sleep quality in the present study. Nettle tablets in the hemodialysis patients decreased sleep latency and increased sleep duration.
Key words: Nettle, sleep quality, hemodialysis patients, clinical trial

P-345

Pancreatic lipase inhibitory activity of Burdock (Arctium lappa L.) extract

Narjes Farzin[1], Amir Mousavi[2], MohammadReza Naghavi[3], Kambiz Larijani[4]

1. Department of Horticultural Sciences and Agronomy, Science and Research Branch, Islamic Azad University, Tehran, Iran.
2. National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran.
3. Department of Agronomy and Plant Breeding, Faculty of Agriculture & Natural Resources, Karaj, Iran
4. Department of Chemistry, Science and Research branch, Islamic Azad University, Tehran, Iran

Background and Objective: Burdock (Arctium lappa) has a long history as a traditional medicine. The aim of this study was to evaluate the in vitro and in vivo ability of the burdock root extract to inhibit porcine pancreatic lipase activity as natural anti-obesity drugs.
Materials and Methods: The in vitro lipase inhibitory of extract was tested by para-nitrophenyl palmitate (pNPP) as substrate. In vivo study was conducted on five groups of 10 male Wistar rats including normal diet, fat diet, and fat diet along with 200 mg/kg Orlistat as well as 200 and 400mg/kg burdock extract. Weight of the rats was recorded at the beginning and the end of the second, fourth, sixth and eighth week of the experiment. Lipid level in the feces, lipid profile, and serum liver enzyme, fasting blood sugar (FBS), triglycerides and cholesterol were measured at the beginning and the end of the study.
Results: The in vitro results showed that burdock extract was noticeably effective to inhibit pancreatic lipase (IC50=20±3 µg/ml). In animal studies, burdock extract in both doses compared to fat control, significantly caused weight loss ($P < 0.05$). Lipid in feces was significantly more than normal control in burdock extract groups ($P < 0.05$). The effect of burdock extract on decreasing FBS, triglyceride as well as normalizing liver enzymes rates was also significant.
Conclusion: Our results indicated that burdock root extract can lead to lipase inhibition and weight loss and it may give us approaches to develop a new and effective drug for obesity treatment.
Keywords: Burdock extract, Obesity, Lipase inhibitor, Lipid profile.

P-346

Lupeol-containing Hawthorn hydroalcoholic extract regulated the polycystic ovarian syndrome-upregulated androgen receptors in rats

Malekinejad F[1], Alijanpour K[2], Rezaei-Golmisheh A[3], Malekinejad H[4*]

1. Department of Clinical Biochemistry, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran
2. Department of Pharmacology, School of Medicine, V. N. Karazin National University, Kharkiv, Ukraine
3. Department of Histology & Embryology, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran
4. Department of Pharmacology & Toxicology, School of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran

Background and Objectives: Hawthorn (Crataegus spp.) is traditionally used for preventing and treating of cardiovascular diseases and hypercholesterolemia. One of the bioactive components of Hawthorn is lupeol. We investigated the effect of lupeol on androgen receptor expression and testosterone concentration in rats with experimentally-induced polycystic ovarian syndrome (PCOS).
Methods: The healthy female rats were aliquoted into 5 groups including control and test groups. The control group received 0.25 ml/day sesame oil (IP) for 35 days. The test groups received 60 mg/kg B.W./day DHEA (for 3 weeks) for PCOS induction. The test groups were subdivided into 4 sub-groups and nominated as PCOS (received the DHEA solvent), HBE (received Hawthorn Berry hydroalcoholic extract, 100 mg/kg, orally), LPL (received lupeol, 10 mg/kg, IP) and MET (received Metformin, 500 mg/kg, oral) for 2-weeks. After the last treatment, serum testosterone level by ELISA method and the expression of androgen receptors in the ovary by PCR technique were determined.
Results: PCR analyses showed that the expression of AR mRNA in non-treated PCOS positive animals up-regulated significantly. HBE, Lupeol and MET down-regulated the AR mRNA expression. Lupeol induced down-regulation was found higher than HBE and lower than MET. All three compounds declined the testosterone level significantly with the highest reduction of HBE.
Conclusion: our data suggest that both HBE and Lupeol could be considered as potent compounds in the management of PCOS. Their capability attribute to the regulation of PCOS-induced up-regulation of AR expression and to the reduction of testosterone release.
Key Words: Androgen receptor; Hawthorn; Lupeol; Testosterone.

P-347

Chrysin attenuates hippocampal inflammation, electrophysiological activity and memory deficits, in cerebral hypoperfusion and reperfusion in male rats

Maryam Khombi Shooshtari[1], Alireza Sarkaki[1], Yaghoob Farbood[1], Seyed Mohammad Taghi Mansouri[1,2], Mohammad Badavi[1], Layasadat Khorsandi[3], Mohammad Ghasemi dehcheshmeh[4]

1. Department of Physiology, Faculty of Medicine, Physiology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2. Department of Anesthesiology, Columbia University Irving Medical Center, New York, NY 10032, United States of America

3. Department of Anatomical Sciences, Faculty of Medicine, Cell & Molecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

4. Department of Immunology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Background and Objective: Cerebral ischemia leads to neuronal damage in the hippocampus and cognitive decline. Here we investigated the neuroprotective potential of chrysin (CH), a well-known member of the flavonoid family, in an animal model of cerebral ischemia-reperfusion (I/R).
Materials and Methods: Adult male Wistar rats (250–300 g) were randomly divided in 5 groups and submitted to either I/R or a sham surgery after three-weeks of pretreatment with CH (10, 30, 100 mg/kg) and/or vehicle. I/R model induced by bilateral common carotid arteries occlusion for 20 min, followed by reperfusion. Subsequently, spatial cognitive performance was evaluated in a Morris water maze (MWM), an extracellular single unit was recorded from hippocampal dentate gyrus region, after then the hippocampal tissue content of IL-1β and TNF-α were assayed using ELISA kits.
Results: The results showed that I/R significantly reduced the spatial memory performance in MWM. As well as, I/R decreased the average number of spikes/bin and increased the level of IL-1β, TNF-α in the hippocampus of vehicle-pretreated groups as compared to the sham-operated Groups ($p<0.001$). Furthermore, 21 consecutive days' pretreatment with CH significantly restored the spatial memory, increased the average number of spikes/bin and decreased the levels of IL-1β, TNF-α in the hippocampi of the I/R rats ($p<0.01$).
Conclusion: Our data confirm that chrysin could prevent brain inflammation and thereby prevents cognitive and extracellular neuronal activity impairments due to cerebral ischemia. So it could be a promising neuroprotective agent against cerebrovascular insufficiency states.
Keywords: Ischemic stroke, Chrysin, Spatial memory, IL-1β, TNF-α, Rat

P-348

Effect of curcumin pretreatment on morphine-induced inhibitory memory impairment and nitric oxide in rat

Kharazmi K, Ardjmand A, Heydari A

Physiology Research Center, Institute for Basic Science, Kashan University of Medical Sciences, Kashan, I. R. Iran.

Background and Objective:Curcumin, as a polyphenolic compound in turmeric plant, has neuroprotective effect in the improvement of learning and memory. Curcumin has interaction with diverse molecules, e.g., nitric oxide (NO). The present study dealt with the effect of curcumin pretreatment on morphine-induced inhibitory memory impairment and nitric oxide metabolites (NOx) level in rat.
Materials and Methods:Forty rats were divided into 4 groups: Control (saline gavage for 35 days+posttraining saline (i.p.); Curcumin(curcumin gavage (10 mg/kg for 35 days)+posttraining saline (i.p.); Morphine (saline gavage for 35 days+posttraining morphine (7.5 mg/kg/i.p.); Curcumin+Morphine(curcumin gavage (35 days)+posttraining morphine (i.p.). The animal's memory was evaluated in an inhibitory memory apparatus in all groups, the memory of animals in the second day was reported as the time delay (Sec.) to enter the dark chamber. The locomotor activity was evaluated using the open field. After behavioral tests, the brains were removed under anesthesia for evaluating the NOx level using the Griess method. One-way anova test was used for the difference between the groups.
Results:The time delay to enter the dark chamber in Morphine and Morphine+Curcumin groups were decreased ($P<0.001$) and increased ($P<0.01$), compared to Control and Morphine groups, respectively. Tissue NOx levels in Morphine and Morphine+Curcumin groups were decreased ($P<0.05$) and increased ($P<0.001$), compared to Control and Morphine groups, respectively. Locomotor activity in open field did not show a significant difference in four groups ($P>0.05$).
Conclusion:Curcumin improves the morphine-induced inhibitory memory impairment in rat, probably via the NO signaling pathway.
Keywords:Memory, Learning, Curcumin, Morphine, Nitric oxide

P-349

Protective effect of alpha-pinene on blood-brain barrier damage and brain edema in a rat model of focal cerebral ischemia

Mahdieh Khoshnazar[1], Siavash Parvardeh[2], Mohammad Reza Bigdeli[*1]

1. Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran

2. Department of Pharmacology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Blood-brain barrier (BBB) disruption and consequent cerebral edema play a pivotal role in the pathogenesis of ischemic stroke. Alpha-pinene is a terpenoid molecule which possesses potent antioxidant

effects. Accordingly, the aim of this study was to investigate the effect of α-pinene on BBB permeability and brain edema in a rat model of ischemia stroke.
Materials and Methods: Focal cerebral ischemia was induced by utilizing middle cerebral artery occlusion (MCAO) method in male Wistar rats. The animals underwent 60 min focal cerebral ischemia followed by a 24-hour period of reperfusion. The rats were divided into sham, control, and α-pinene-treated groups (n=6). Single doses of α-pinene (25, 50, and 100 mg/kg, i.p.) were administered at the beginning of reperfusion. Alteration in brain vascular permeability was evaluated by tail vein injection of 2% Evans blue (EB) dye 30 min after MCAO. The tissue levels of EB in the brain samples were measured after 24 hours by using a spectrophotometer. To assess brain edema, dry weights of the brain samples were measured at the end of reperfusion and subtracted from brain's wet weight.
Results: Twenty four hours after the administration of α-pinene (50 and 100 mg/kg) a significant reduction in EB concentration was observed in the brain samples. In addition, α-pinene (50 and 100 mg/kg) could significantly decrease cerebral edema in rat brain.
Conclusion: It was ultimately attainted that α-pinene exerts neuroprotective effect in the rat model of focal ischemic stroke through the attenuation of BBB disruption and brain edema.
Keywords: Stroke; Alpha-pinene; Cerebral edema, Blood-brain barrier

P-350

Role of amygdala–medial prefrontal cortex circuitry in regulating the expression of fear memory extinction

Masoomeh Dadkhah[1,2], Abbas Ali Vafaei [2], Ali Rashidy-Pour [2]

1. Pharmaceutical Sciences Reserch Center, Ardabil University of Medical Sciences, Ardabil, Iran
2. Laboratory of Learning and Memory, Research Center of Physiology, Department of Physiology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran

Background and Objective: Fear extinction is an active learning process that allows the adaptive control of conditioned fear responses.The basolateral amygdala complex (BLA) and infralimbic region of the prefrontal cortex (IL) play distinct roles in the extinction of auditory fear conditioning. It's well-known that projections from IL to BLA, inhibits fear expression. Although the details of IL–BLA interaction are not still clear. Here, we investigated the role of functional interactions between BLA and IL the in mediating fear memory extinction.
Materials and Methods: The current study employed an auditory fear conditioning (AFC) paradigm to evaluate freezing behavior during extinction in male rats. Adult male rats (250-300 gr) were bilaterally implanted into the IL and BLA. After a week, animals randomly divided in to 4 groups: SAL/IL-SAL/BLA; SAL/IL-LID/BLA; CORT/IL-SAL/BLA; CORT/IL-LID/BLA. Using lidocaine, rats underwent inactivation of the BLA and then intra-IL infusion of corticosterone (20 ng/0.5 µl/ per side) as a glucocorticoid receptor agonist, prior to extinction training session.
Results: Using AFC approach, we found that inactivation of BLA prior to extinction training caused a significant reduction in freezing ($P < 0.05$). BLA inactivation and then corticosterone administration in IL before extinction training changed facilitatory effect of corticosterone on extinction ($P < 0.001$).
Conclusion: These findings provide evidence for the involvement of the BLA in facilitatory effect of CORT on memory extinction. Taken together, our findings provide further evidence for a critical contribution of the IL-BLA neural circuit to fear extinction.
Keywords: Auditory fear memory, Extinction, Inactivation, Infralimbic, Amygdala

P-351

Effects of Ritalin abuse on the changes of the prefrontal cortex dopamine beta hydroxylase, serum corticosterone and anxiety in rats

Homa Manaheji[1, 2], Samira Daniali[1, 2*], Vida Nazemian[1, 2]

1. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background: Mounting evidence has propounded that PFC plays a vitally important role in ADHD and is involved in the therapeutic actions of low-dose psychostimulants (p7). Catecholaminergic stimulants like Ritalin can execute impactful modulatory actions on neuronal activity of and prefrontal cortex-dependent behavior, for instance working memory, attention and anxiety. Most of the previous studies which were analyzing the impacts of Ritalin and other psychostimulants usage on the brain functions and behavior have utilized males as research subjects, maybe because of higher prevalence of ADHD in males versus females 1. It seems that females with ADHD and also sex differences have been neglected in research until recent years to a great extent 13. So, the wide ranges of research to define the impacts of Ritalin abuse on brain structures, dependent behaviors, expression of hormones and neurotransmitters and sex differences should be done.

P-352

Could treadmill exercise and sex hormones treatment improve learning, memory and hippocampal BDNF level in transient congenital hypothyroid rats?

Leila Derafshpour[1], Abbas Ali Vafaei[2*], Ali Rashidy-Pour[2], Ahmad Reza Bandegi[3], Ehsan Saboory[1], Hamidreza Sameni[4], Nahid Jashire Nezhad[4], Adel Kashefi[5]

1. Neurophysiology Research Center, Urmia University of Medical Sciences, Urmia, Iran
2. Laboratory of Learning and Memory, Research Center and Department of Physiology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran.
3. Dep. of Biochemistry, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran
4. Research Center of Nervous System Stem Cell, Department of Anatomical Sciences, Semnan University of Medical sciences, Semnan, Iran.
5. Laboratory of Neuroscience and Behavior, Department of Physiological Sciences, University of Brasilia, Brasilia, Brazil

Background and Objective: Transient thyroid function abnormalities at birth exhibit intellectual developmental and cognitive disorders in adulthood. Given the well-known effects of physical activity and sex hormones on cognitive functions and brain derived neurotrophic factor (BDNF), the present study examined the effects of treadmill exercise, sex hormones, and the combined treatment on learning and memory and hippocampal BDNF levels in transient congenital hypothyroid rats.
Materials and Methods: To induce hypothyroidism, 6-propyl-2-thiouracil was added to the drinking water from the 6th day of gestation to the 21st postnatal day (PND 21). From PNDs 28 to 47, female and male pup rats received 17β-estradiol and testosterone, respectively and about 30 minutes later, they were forced to run on the treadmill for 30 minutes once a day. On PNDs 48–55, spatial learning and memory of all rats tested in the water maze, which followed by measurement of BDNF in the hippocampus.
Results: Results showed that developmental hypothyroidism (DH) induced significant deficits in spatial learning and memory and hippocampal BDNF in both male and female rats. In both male and female hypothyroid rats, exercise alleviated learning deficits, and all treatments (exercise, hormone injections, and the combined treatment) improved memory retention, and hippocampal BDNF.
Conclusion: These findings highlight the impact of physical activity and sex hormones in improving biochemical and behavioral deficits induced by developmental thyroid hormone insufficiency.
Keywords: transient hypothyroidism, exercise, spatial memory, BDNF, rat, estrogen, testosterone

P-353

Activation of hippocampal glial glutamate transporter (GLT-1) reduces the naloxone-induced withdrawal signs in morphine dependent rats

Mahgol Darvish[1], Negin Saeedi[1], Narges Hosseinmardi[1], Mahyar Janahmadi[1], Soomaayeh Heysieattalab[2]

1. Department of Physiology and Neuroscience research center, Medical School, Shahid Beheshti University of Medical Sciences, Tehran,

Iran

2. Department of Psychology, School of Psychology, Neuroscience Lab, University of Tabriz, Tabriz, Iran

Background and Objective: Addiction is a chronic relapsing disorder. Addicted individuals persistently engage in drug seeking and using despite profound negative consequences. Repetitive administration of opioids initiate adaptive mechanisms, lead to addiction. Among these maladaptive responses to drug exposure, long-lasting alterations in the expression of proteins, which are responsible for maintaining glutamate homeostasis are noticeable. These alterations engender an aberrant potentiation of glutamate transmission in hippocampus. Glial glutamate transporter (GLT-1) makes up more than 80% of hippocampal glutamate transporters and removes 90% of extracellular glutamate. Since opioids alter the expression of GLT-1, we evaluated the effect of hippocampal GLT-1 activation on morphine dependence.
Materials and Methods: Morphine (10 mg/kg, s.c.) was administered at an interval of 12 hours for 9 days. Then, morphine withdrawal syndrome precipitated by naloxone (1.5 mg/ kg, i.p.) was evaluated in rats receiving morphine with or without ceftriaxone (0.5 mmol/0.5 µl) as a GLT-1 activator.
Results: Animals receiving intra-hippocampal microinjection of ceftriaxone 30 min before each morphine administration, demonstrated a significant reduction in several signs of morphine withdrawal syndrome, including activity, ptosis, head tremor and freezing (unpaired t-test or Mann–Whitney U test, $P<0.05$, $P<0.01$, $P<0.001$). Pretreatment with ceftriaxone reduced other signs of withdrawal such as diarrhea, penis-licking, chewing, scratching, sniffing and yawning. But the difference was not significant (unpaired t-test or Mann–Whitney U test, $P>0.05$).
Conclusion: Obtained results showed that GLT-1 alteration in the hippocampus may play role in different properties of morphine dependence.
Keywords: morphine dependence, GLT-1, glial cells

P-354

Monophosphoryl lipid A inhibits accelerated epileptogenesis in traumatic rat once administered immediately after trauma

Mozhdeh Radpour, Hamid Gholami Porbadie, Mohammad Sayyah*

Department of Physiology and Pharmacology, Pasteur Institute of Iran, Tehran, Iran

Background and Objective: Traumatic epilepsy includes 5% of all epilepsy cases. Monophosphoryl lipid A (MPL) is a toll-like receptor agonist and adjuvant component of prophylactic and therapeutic vaccines; with safe, well-tolerated and effective efficiency. Considering the role of neuroinflammation in traumatic epilepsy, we examined the impact of post-trauma injection of MPL on the rate of pentylentetrazole kindling (PTZ) in rat.
Materials and Methods: Trauma was exerted to temporo-parietal cortex of rats by Controlled Cortical Impact device. After 30 minutes, MPL (0.1 µg/ rat) were infused into the left lateral ventricle. After 24h, traumatic rats underwent pentylentetrazole kindling.
Results: Trauma significantly decreased number of PTZ injections required for kindling (12.6± 0.7 in control rats, 5.5±0.5 in traumatic rats, and 11.8 ±1.1 in sham-operated rats, $p<0.0001$). Rats received MPL after trauma needed number of PTZ injection similar to control group (14.8±0.6).
Conclusion: The post-trauma injection of MPL to rats prevents acceleration of kindling epileptogenesis by trauma.
Key words: PTZ Kindling,Post Traumatic Epilepsy,seizure

P-355

Effects of carvacrol and physical exercise on motor and memory impairments associated with Parkinson's disease

Ziba Rajaei[1], Leila Hamzehloei[2], Mohammad Ebrahim Rezvani[2]

1. Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
2. Department of Physiology, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Objective: Parkinson's disease (PD), a progressive neurological disorder, presents motor and non-motor impairments. Carvacrol is a naturally occurring phenolic monoterpene that is found in the essential oils of the Lamiaceae family. The present study was undertaken to investigate the effects of carvacrol and treadmill exercise on memory deficit, rotational behavior and oxidative stress biomarkers in a 6-OHDA-lesioned rat model of PD.
Methods: Wistar rats were treated with carvacrol at a dose of 25 mg/kg and/or ran on a treadmill for a week. Then, 6-OHDA was microinjected into medial forebrain bundle and treatments continued for 6 more weeks. Aversive memory, rotational behavior and oxidative stress biomarkers were assessed at the end of week 6.
Results: 6-OHDA-leasioned group showed a significant increase in rotational behavior and a decrease in step-through latency in passive avoidance test as compared with sham group. These behaviors were accompanied by increased lipid peroxidation levels and decreased total thiol concentration in the striatum and/or hippocampus of hemiparkinsonian rats. Moreover, treatment with carvacrol and exercise reduced rotational behavior and improved aversive memory deficit, which was accompanied by decreased lipid peroxidation levels and increased total thiol concentration in the striatum and/or hippocampus.
Conclusion: Treatment with carvacrol and treadmill exercise ameliorated motor and memory deficits by modulating oxidative stress in the striatum and hippocampus of hemiparkinsonian rats. Therefore, combination of carvacrol and treadmill exercise could be effective therapeutic tool for treatment of neurobehavioural deficits in PD patients.
Key words: Carvacrol, Treadmill exercise, Aversive memory, Motor behavior, Oxidative stress, Parkinson’s disease.

P-356

Neuroprotective effects of morin in the 6-hydroxydopamine model of Parkinson's disease in rats

Hossein Rajabi Vardanjani[1], Marzieh Pashmforosh[2]

1. Medical Plants Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran
2. Behbahan Faculty of Medical Sciences, Behbahan, Iran

Background and Objective: Morin as a natural flavonoid is used in traditional medicine and possess neuroprotective effects. Parkinson's disease (PD) as a neurodegenerative disease is associated with neuroinflammation and oxidative stress. The present study aimed to assess the effect of morin on 6- hydroxidopamine (6-OHDA) PD model.
Materials and Methods: Rats were randomly assigned to the following groups (n = 6): (1) Vehicle/Vehicle; (2) Vehicle/Morin; (3) 6-OHDA (16 µg/2 µl in normal saline) /Vehicle and (4) 6-OHDA/Morin (40 mg/kg/2 ml, PO). The Rats were subjected to stereotaxic microinjections of 6-OHDA or vehicle. Morin was administrated for 28 days. After that, the apomorphine behavior (1), rotarod test (2) and antioxidant markers were assessed in the striatum (3). Data were analyzed using GraphPad Prism 6 software.
Results: Morin treatment reversed the elevation of the number of rotations induced by 6-OHDA ($p < 0.05$). Morin treated showed the reduction of the latency in the fall resulted by 6-OHDA ($p < 0.05$). In addition, striatal lipid peroxidation (MDA level) in the Morin-treated group was significantly lower and superoxide dismutase (SOD) and glutathione peroxidase (GPx) activity were significantly greater versus the 6-OHDA group ($p < 0.001$).
Conclusion: Our results showed the neuroprotective effect of morin in the treatment of Parkinson's disease. The protective effect of morin against PD may be due to its antioxidant activity.
Keywords: Morin, Parkinson's disease, 6-hydroxidopamine, Oxidative stress, Rat

P-357

Protective effects of against glutamate-induced oxidative stress and apoptosis in PC12 and N2a cells

Rajabian A[1], Sadeghnia HR[2], Moradzadeh M[3], Hosseini A[1]

1. Pharmacological Research Center of Medicinal Plants, Mashhad University of Medical Sciences, Mashhad, Iran,
2. Department of Pharmacology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran,
3. Neurocognitive Research Center,Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran, Golestan Rheumatology Research Center, Golestan University of Medical Sciences, Gorgan, Iran

Background and Objective: Neurodegenerative diseases have been associated with glutamatergic dysfunction. Glutamate-mediated excitotoxicity has been widely used as a model for studying neurodegenerative disorders. The present study aimed to investigate the neuroprotective effect of Rheum turkestanicum against glutamate-induced oxidative damage and apoptosis. Materials and Methods: The cultured PC12 and N2a cells were pretreated (2 h) with varying concentrations of berberine (25-200 µg/ml), followed by exposure to glutamate (8 mM) for 24 hr. The cells viability, intracellular reactive oxygen species (ROS), lipid peroxidation, apoptosis were measured. Rutin as an antioxidant was used as positive control. Results: In both cell lines, pretreatment with R. turkestanicum significantly decreased ROS generation, lipid peroxidation in glutamate-injured cells. Moreover, R. turkestanicum showed anti-apoptotic effects by reducing apoptotic cells in sub-G1 area. Also the quantification of rutin in R. turkestanicum extract was achieved and was about 0.11% ± 0.01 w/w. Conclusion: The results of present study suggest that R. turkestanicum protects against glutamate-induced PC12 and N2a cells injury by decreasing oxidative stress and subsequently inhibiting apoptosis. This is relevant to R. turkestanicum treatment in neurodegenerative disorders.
Key words: Apoptosis, Neurodegeneration, Oxidative stress, R. turkestanicum

P-358

Effects of Cepo-Fc on recognition memory impairment and pain behavioral responses during persistent peripheral inflammation

Nasser Rahmani [1,2], Jalal Zaringhalam[1,2]

1. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran,Iran
2. Department of Physiology, School of Medicine, Shahid beheshti University of Medical Siences,Tehran,Iran

Background and objectives: Pain is connected to cognitive processing and may leads to memory impairments. Hippocampus is an important part of the brain was involved in learning and memory processing but many clinical studies have shown functional changes in the hippocampus of patients with pain. However physiological and pharmacological concept of these changes is still a matter of concern. In a part of our study we investigated CFA-induced inflammatory pain on recognition memory impairment with therapeutic effects of Cepo-Fc (carbamylated erythropoeteen) in treating pain related memory impairment.
Material and methods: inflammatory pain induced by CFA injection on day 0. Hyperalgesia and recognition memory were assessed on 0 and 7 days of the study via Hargreveage and Novel Object Recognition assay.
Results: Persistent peripheral inflammation induced hyperalgesia responses and recognition memory impairment on day 7 of the study. Administrating of Cepo-Fc significantly reduced hyperalgesia responses, whereas promoted recognition memory on day 7 of the study compared to day 0.
Conclusion: Regarding to our results it can conclude that persistent peripheral inflammation induced recognition memory impairment. Cepo-Fc reduced hyperalgesia wherase promotes Recognition Memory impairment, so Cepo-Fc may be an effective drug for in treating pain related memory impairment.
Key words: Cepo-Fc, Inflammation, Pain, Recognition Memory

P-359

Monoacylglycerol lipase inhibitor, JZL-184, like aspirin, has neuroprotective effects in the mice middle cerebral artery occlusion model of stroke

Mohammadreza Rahmania[1], Mohammad Allahtavakolia[1], Ali Shamsizadeha[1], Ayat Kaeidia[1], Jalal Hasanshahi[1], Mahdieh Azin [1], Elham Hakimi[1], Mahsa Hasanipoor[1], Gholamreza Bazmandegan[2], Iman Fatemi[1]

1. Department of Physiology and Pharmacology, School of Medicine, Physiology-Pharmacology Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

2. Non-communicable Diseases Research Center, Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Background and Objective: Investigators are searching to find new therapeutic strategies to reduce stroke secondary injury. JZL-184 (JZL) is an inhibitory factor for the production of arachidonic acid (AA). Thus, it suppresses of AA metabolites which are the cause of inflammation and tissue edema. Therefore, JZL may be considered for suppression of stroke secondary injury in mice middle cerebral artery occlusion (MCAO) model. Additionally, Aspirin is a known anti-inflammatory factor which is used to reduce pro-inflammatory secondary injury. The aim of this study was to determine the effects of JZL on the reduction of stroke secondary injury and to compare them with Aspirin effects.
Material and methods: MCAO model has been induced and accordingly 83 male MCAO induced mice have been introduced to the study. The animals were divided into seven groups including intact, controls, vehicle, Aspirin, JZL 4, 8 and 16 mg/kg administrated groups. Brain edema and infarction, behavioral functions and brain levels of IL-10, TNF-α and matrix metalloproteinase-9 (MMP9) have been examined in the evaluated groups.
Results: The results revealed that JZL reduced brain edema, infarction, brain levels of TNF-α and MMP9 and also increased brain levels of IL-10 as well as improved behavioral functions in all three concentrations. The therapeutic effects of JZL were observed as well as Aspirin.
Conclusion: Based on the results, it seems that JZL can be considered as a good candidate for inhibition of stroke secondary injury in the case of delayed treatment.
Keywords: Stroke, MCAO, JZL-184, Aspirin, Monoacylglycerol lipase

P-360

The intensity of LPGi neuronal responses to naloxone during the rest phase differs from the active phase

Fatemeh Rahmati-Dehkordi[1], Hossein Azizi[1], Behzad Garmabi[2], Saeed Semnanian[1]

1. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

2. Study and Treatment of Circadian Rhythms Research Center, Shahroud University of Medical Sciences, Shahroud, Iran

Background and Objective: Many biological events are controlled by the internal clock and exhibit circadian rhythm. Investigations have shown that the circadian rhythm can affect the mechanisms associated with opiate dependence. Lateral paragigantocellularis (LPGi) nucleus plays a pivotal role in opiate dependence. The aim of the current study was to assess the LPGi neuronal responses to naloxone in morphine dependent rats during the rest and active phase.
Method: Male Wistar rats (250-300 g) were administered 10 mg/kg morphine every 12 h, for 10 days. Control rats received saline with the same protocol. Thereafter, when they were made dependent on morphine, extracellular single-unit recording was used for investigating LPGi neuronal responses to naloxone in morphine-treated rats during day (8:00-12:00) and night (20:00-24:00).
Results: Results showed that the extent of excitatory responses of LPGi neurons to naloxone was higher during day (the rest phase) compared to night. Also, the baseline activity of excitatory responses was increased and the baseline activity of inhibitory responses was decreased during night.
Conclusion: We show for the first time that LPGi neurons have a circadian rhythm in their activity. It seems that the intensity of LPGi neuronal responses to naloxone is potentiated during the rest phase and this may affect the naloxone-induced withdrawal syndrome.
Keywords: Circadian rhythm, Morphine, Extracellular single unit recording, LPGi nucleus, Naloxone

P-361

Interaction between naloxone and silver nanoparticles in central amygdala

Mahnaz Rahimpour[3], Manizheh Karami[1]*, Ali Haeri Rohani[2]

1. Associate Professor Department of Biology, Faculty of Basic Sciences, Shahed University

2. Professor Faculty of Biology, College of Sciences, University of Tehran

3. Phd student Faculty of Biology, College of Sciences, University of Tehran

Background and Objective: Repeated injection of morphine can induce conditioned place preference (CPP) while naloxone, a selective competitive mu-opioid receptor antagonist, can reverse the effect of morphine. Silver nanoparticles (SNPs), one of the most commercially used nanomaterials, may be available in biological systems because of degradation and an environmental release of them. The purpose of this research was to study the effects of silver nanoparticles on naloxone induced conditioned place aversion (CPA) and withdrawal signs in morphine conditioned rats.
Materials and Methods: Male Wistar rats (300-350 g) were cannulated bilaterally by Stereotaxic apparatus for the CeA (Anteriorposterior= –2.12 mm posterior to bregma and lateral= ±4.1 mm; dorsoventral=7.8 mm, according to the atlas of Paxinos and Watson (Paxinos and Watson, 2003) coordinates. Morphine (0.5-7.5 mg/kg) was injected s.c. once a day throughout the conditioning phase of a CPP paradigm. On day of the testing, the naloxone (0.05- 0.4 µg/rat) was administered intra-CeA 10 min before of testing. SNPs (0.0001- 0.01 µg/rat) were intra-CeA injected 10 min before microinjection of naloxone dosages. Data in all groups were compared by ANOVA (one- and/or two-way analysis of variance).
Results: Naloxone (0.4 µg/rat) caused meaningful CPA in the morphine conditioning model, however, a microinjection of silver nanoparticles (0.001, 0.0001 µg/rat) caused meaningful change in naloxone induced CPA and had significant effect on the withdrawal signs. Conclusion: SNPs may have an impact on response in CPP animal model.
Keyword: morphine, naloxone, silver nanoparticles, withdrawal signs, CPP, CPA

P-362

The effects of cinnamaldehyde on acute or chronic stress-induced anxiety-related behavior and locomotion in male mice

Razieh Rahimi, Farshid Etaee, Nafiseh Faraji, Arezoo Rezvani-Kamran, Ghazaleh Omidi, Alireza Komaki*

Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

Anxiety and stress are considered as universal psychiatric exhibitions of the present societies and lifestyles. Several experiments have been conducted to examine natural anxiolytic agents to find out an alternative to synthetic anxiolytic drugs. The present study investigated the anxiolytic effects of cinnamaldehyde (Cin) on mice behavior in the elevated plus maze (EPM) and open field (OF) tests. Sixty male Swiss mice, weighing 20–30g, were divided into six groups including: acute stress+mazola oil; chronic stress+oil; acute stress+Cin (20mg/kg); chronic stress+Cin; non-stress+oil; and non-stress+Cin groups. The groups were administered for seven days (once a day). The acute stress+Cin group showed a meaningful rise in the percentage of entries into the open arms compared to the acute stress+oil group ($P<0.05$). The percentage of time spent in the open arms in the chronic stress+Cin group was significantly higher compared to the chronic stress+oil group ($P<0.01$). The percentage of entries into the open arms increased significantly ($P<0.01$) in the chronic stress+Cin group in comparison with the chronic stress+oil group. The Cin treated groups showed significant increases in the time spent in the center area and in the number of entries into the center area compared with the oil treated groups in OF test. The number of entries into the arms (total activity), as well as locomotor activity was not significant among groups. The results of the present study indicated that Cin, as a natural product, might have anxiolytic effects in mice behavior in the EPM and OF tests.
Keywords: Cinnamaldehyde; Acute stress; Chronic stress; Anxiety; locomotion; Mice

P-363

Effect of intracerebroventricular administration of MHY1485 and adiponectin on memory in experimental model of Alzheimer's disease

Samira Rashtiani[1,2], Kambiz Rohampour[2], Adele Jafari[2], Iran Goudarzi[1]

1. School of Biology, Damghan University, Damghan, Iran.

2. Neuroscience Research Center, Department of Physiology, Guilan University of Medical Sciences, Rasht, Iran

Background and Objective: There is a close relationship between Alzheimer's disease (AD) and insulin signaling dysfunction. Adiponectin (APN) is an adipocytokine that affects insulin sensitivity through binding to its receptors (AdipoR 1 and AdipoR2), which results in the activity of AMPK and PPAR-α. Leptin and APN diminish insulin resistance by activating AMPK and inhibiting mTOR. MHY1485, an mTOR activator, was used to assess the downstream signaling of adiponectin in memory improvement process in AD.
Materials and Methods: Fifty-six rats were randomly allocated to 7 groups: control, APN, STZ, STZ+APN and MHY1485 in three doses (0.01, 0.1 and 1 µM). Icv-STZ (3mg/Kg) on day 1 and 3 was used to induce dementia. After 2 weeks passive avoidance memory was assessed. Thirty minutes before retrieval tasks APN or MHY+APN were injected, intracerebroventricularly.
Results: The step through latency (STL), which was diminished by STZ, increased significantly ($p \leq 0.001$) in APN+STZ group. Administration of different doses of MHY before APN, reversed the memory improving effect of APN, significantly ($p \leq 0.01$). Total time spent in dark compartment (TDC) was decreased by APN, while MHY increased the TDC values to a significant level ($p \leq 0.01$).
Conclusion: Our results indicate that the memory improving effect of APN is mediated, at least in part, by the inhibition of mTOR, as reactivation of mTOR by MHY could reverse its effect in passive avoidance memory.
Keywords: Alzheimer's disease, Adiponectin, mammalian target of rapamycin (mTOR), Memory.

P-364

Neuroprotective consequences of postconditioning on embolic model of cerebral ischemia in rat

Rezazadeh H, Allahtavakoli M

OBJECTIVE(S): It has been reported that ischemic postconditioning, conducted by a series of brief occlusion and release of the bilateral common carotid arteries, confers neuroprotection in permanent or transient models of stroke. However, consequences of postconditioning on embolic stroke have not yet been investigated.
MATERIALS AND METHODS: In the present study, rats were subjected to embolic stroke (n=30) or sham stroke (n=5). Stroke animals were divided into control (n=10) or three different patterns of postconditioning treatments (n=20). In the first pattern of postconditioning (PC10, n=10), the common carotid arteries (CCA) were occluded and reopened 10 and 30 sec, respectively for 5 cycles. Both occluding and releasing times in pattern 2 (PC30, n=5) and 3 (PC60, N=5) of postconditionings, were five cycles of 30 or 60 sec, respectively. Postconditioning was induced at 30 min following the stroke. Subsequently, cerebral blood flow (CBF) was measured from 5 min before to 60 min following to stroke induction. Infarct size, brain edema and neurological deficits and reactive oxygen species (ROS) level was measured two days later.
RESULTS: While PC10 ($P<0.001$), PC30 and PC60 ($P<0.05$) significantly decreased infarct volume, only PC10 decreased brain edema and neurological deficits ($P<0.05$). Correspondingly, PC10 prevented the hyperemia of brain at 35, 40, 50 and 60 min after the embolic stroke ($P<0.005$). No significant difference in ROS level was observed between PC10 and control group.
CONCLUSION: Ischemic postconditioning reduces infarct volume and brain edema, decreases hyperemia following to injury and improves neurological functions after the embolic model of stroke.
Key words: Cerebral blood flow, embolic stroke, postconditioning

P-365

The effect of Tanacetum polycephalum on passive avoidance learning and memory against the pentylenetetrazol-induced model of memory impairment in the rat

Farnoosh Rezaali[1], Vahid Azizi[2], Farzin Allahyari[2], Abdolkarim Hosseini[2]

1. Department of Life Science Engineering, Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran.
2. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran.

Background and Objective: Large body of studies showed that the pentylenetetrazol (PTZ) can disrupt free radicals balance and causes oxidative stress in the body with a negative impact on memory and learning. The present study

was envisaged to study the effect of Tanacetum polycephalum extract (TPE) in the pentylenetetrazol (PTZ) kindling rat model and its associated learning and memory deficit.
Materials and Methods: Twenty-four rats were randomly divided to 4 groups: control negative under treatment with PTZ (sub-convulsant dose 35 mg/kg at an interval of 48 ± 2 h in 30 days (12 injections)), control positive under treatment with Phenobarbital (PB-30 mg/kg), and two PTZ groups under treatment with TPE (300, and 450 mg/kg). Standard passive avoidance test was used to evaluate retention and recall (evaluation of memory and learning). Data were analyzed using SPSS.
Results: The step-through latency (STL) of the kindled rats was significantly reduced compared with control ones. TPE improved passive-avoidance learning ability in PTZ-kindled animals.
Conclusion: From the results, it can be concluded that the TPE reduces seizure severity and improve cognitive functions in PTZ-kindled rats.
Keywords: Tanacetum polycephalum, Epilepsy, Passive avoidance, Pentylenetetrazol, Learning and memory

P-366

Effect of chondroitinase ABC I immobilization on porous silicon nanoparticles in myelin repair

S. Rezaei[1], B. Dabirmanesh[2], A. Golestani[3], M. Javan4 & K. Khajeh[1,2]

1. Department of Nanobiotechnology, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran
2. Department of Biochemistry, Faculty of Biological Sciences, Trabiat Modares University, Tehran, Iran
3. Department of Clinical Biochemistry, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
4. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Background and Objective: Failure of remyelination is a critical impediment to recovery in multiple sclerosis (MS). Following injury to the central nervous system (CNS), chondroitin sulfate proteoglycans (CSPGs) are upregulated by reactive glia which form a glial scar. Removal of CSPGs with chondroitinase ABC I (ChABC) has successfully improved recovery in various injury models. But ChABC loses its enzymatic activity rapidly at 37˚C, necessitating the use of repeated injections into the site of injury and this could lead to an immune response directed against ChABC.
Materials and Methods: At first ChABC was expressed and purified. Then all porous silicon (PSi) samples were prepared on p-type Si wafer. The etching time of the electrochemical process was 5 min in hydrofluoric acid: ethanol: H2O and after that ChABC immobilized on PSi. Animals were deeply anesthetized following cuprizone (CPZ)-induced demyelination and vehicle, PSi, ChABC or ChABC@PSi injected into corpus callosum (CC). The postoperative survival period of animals was 2 weeks.
Results: In the present study we have revealed that our nano formulation significantly reduced the expression of CSPGs. Moreover, CSPGs digestion by ChABC may reduce the extend of demyelination area as well as astrogliosis. Furthermore, ChABC@PSi treatment increased the number of newly generated oligodendrocyte which consequently enhanced myelin repair.
Conclusion: Our results showed that CSPGs digestion by immobilized ChABC on PSi enhances remyelination in CPZ model.
Keywords: Chondroitinase, Porous silicon nanoparticle, Remyelination, Chondroitin sulfate proteoglycan

P-367

The effect of sinomenine on intrahippocampal kainate-induced oxidative stress in the rat

Samira Ramazi[1], Tourandokht Baluchnejadmojarad[2], Mehrdad Roghani[3], Javad Fahanik-Babaei[4], Seyed-Mahdi Mohamadi-Zarch[1], Mahsa Tashkori[1], Morteza Nazari-Serenjeh[1], Davood Nourabadi[1]

1. Student Research Committee, Iran University of Medical Sciences, Tehran, Iran
2. Department of Physiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
3. Neurophysiology Research Center, Shahed University, Tehran, Iran

4. Physiology Research Center, Iran University of Medical Sciences, Tehran, Iran

Background and Objective: Oxidative stress is considered as one of the causes in the pathophysiology of temporal lobe epilepsy (TLE). Sinomenine has shown neuroprotective effects through oxidative stress counteracting. In this study, we decided to evaluate the effect of sinomenine on some oxidative stress markers in intrahippocampal kainate-induced rat model of TLE .
Materials and Methods: Male rats (n=28) were randomly divided into four groups: sham, lesion (intrahippocampal injection of kainic acid) and two lesion groups receiving sinomenine at doses of 30 or 50 mg/kg orally. Finally, brains were extracted for biochemical assessments of reactive oxygen species (ROS), malondialdehyde (MDA), superoxide dismutase (SOD) and glutathione (GSH).
Results: Our obtained data showed that intrahippocampal injection of kainate significantly increases the level of ROS and MDA and reduces the level of GSH and SOD. On the other hand, sinomenine administration at a dose of 50 mg/kg was able to successfully decrease ROS and MDA level and increase SOD but its effect on GSH level was not significant.
Conclusion: Sinomenine at a dose of 50 mg/kg could greatly diminish oxidative stress in a rat model of TLE.
Keywords: Sinomenine, Temporal lobe epilepsy, Kainic acid, Oxidative stress, Hippocampus

P-368

The role of GABAB receptors in cardiovascular and single unit responses in posterior insular cortex

Afsaneh Ranjbar[1] , Masoumeh Hatam[2], Ali Nasimi[3]

1. Dep of physiology, Jahrom university of medical science , Jahrom , Iran
2. Dep of physiology , Shiraz university of medical science Shiraz, Iran
3. Dep of physiology , Isfahan university of medical science , Isfahan , Iran

Introduction: The posterior part of insular cortex (PIC) is involved in cardiovascular , pulmonary and gastrointestinal functions. We have previously shown that microinjection of glutamate and agonist and antagonists of GABAA receptors into the posterior insular cortex of rat elicited cardiovascular responses. In this study we investigated the possible role of GABAB receptors of PIC in cardiovascular function.
Methodes : Experiments were performed on urethane anesthetized rats. GABAB receptors agonists and antagonists were microinjected into the PIC and arterial pressure, heart rate (HR) and single-unit responses were recorded simultaneously.
Results: Injection of baclophen (1000 pmol/150 nl), a GABAB agonist and phaclofen (1000 pmol/150 nl), a GABAB antagonist, produced no significant change in either mean arterial blood pressure or heart rat. Most neurons did not respond to baclophen or phaclophen, but some showed long excitatory or long inhibitory single-unit responses.
Conclusion: It seems that GABAB receptors in the PIC had no effect on cardiovascular responses, and GABAB receptors probably are involved in other functions.
Key words: Insular cortex ,GABAB receptors, cardiovascular ,single unit

P-369

Dopamine modulates synaptic plasticity in hippocampal CA1 region in control and kindled mice

Nahid Roohi, Javad Mirnajafi Zadeh, Yaghoub Fathollahi

Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Background and Objective: Hyperexcitability inducing factors such as seizure and epilepsy potentiate the synapses and impair learning and memory. Moreover, Dopamine (DA) as a neurotransmitter modulates synaptic plasticity and has an important role in cognitive functions. However, how the modulatory effect of DA on plastic properties of a neuron will change as a consequence of epilepsy is not well understood.

Materials and Methods: Here, we examined the effect of bath application of DA and optogenetically stimulation of DA neurons on synaptic currents in CA1 pyramidal neuron using whole cell patch clamp technique.
Results: Our results demonstrated that DA has a reversal role on LTP in intact and kindled mice such that application of DA prevented LTP induction in intact slices while rescued LTP in kindled slices.
Conclusion: Taken together, our results highlight the importance of DAergic modulation in normal and disease conditions.
Keywords: Dopamine, Plasticity, Optogenetic, LTP

P-370

The effect of quinpirole on anxiety level and freezing behavior in rats

Motahareh Rouhi Ardeshiri [1, 2], Esmaeil Akbari[1,2]

1. Immunogenetics Research Center, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
2. Department of Physiology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.

Background and Objective: Rats treated chronically with the dopamine D2/D3 receptor agonist quinpirole develop compulsive-like behaviors that resemble compulsive checking behavior of Obsessive Compulsive Disorder in patients. The present study was designed to investigate the effects of quinpirole on freezing behavior of rats.
Materials and Methods: Adult male wistar rats with the range of body weight 250 to 300 gram were used. Quinpirole was dissolved in normal saline, and injected at 0.5 mg/kg in a total volume of 1 ml/kg (subcutaneous injection in the neck). Control rats were infused by the same volume of normal saline. The dose of quinpirole (0.5 mg/kg) was chosen based on previous investigation.
Results: Our results demonstrated that quinpirole induced freezing and anxious behaviors in comparison to the control rats.
Conclusion: It seems that dopaminergic system of the rat brain was engaged in fear responses.
Keywords: Quinpirole; freezing behavior; anxiety

P-371

Interaction effects of intra-hippocampal injections of Escitalopram with estrogen and progesterone on conditional avoidance memory behavior in the male Wistar rats

Nazanin Zahra Roozkhosh, Homayoun Khazali, Abdolkarim Hosseini, Vahid Azizi

Department of Life Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran.

Introduction: Escitalopram, is an inhibitor for serotonin transportation, also it's reducing the symptoms of depression in patients. In addition, this drug has many effects on alleviating depression, also effects on memory, but

its concerning pathways are still unknown. The purpose of the present study was to investigate the interaction effect of intra-hippocampal injection Escitalopram of with estrogen and progesterone on conditional avoidance memory behavior in the male Wistar rats.
Materials and methods: The effect of Escitalopram on the hippocampus of male Wistar rats was evaluated using stereotactic surgery. To investigate the avoidance memory process the animal, undergo through the shuttle box avoidance memory device. Data analysis was performed by SPSS software and tukey follow-up test.
Research findings: The results of this study indicate that Escitalopram significantly increases the avoidance memory of male Wistar rats compared to the control group. But when it co-injected with estrogen or progesterone, it can modulates the avoidance memory.
Conclusion: Intra-hippocampal injection of Escitalopram increase the memory and learning in the rat that receiving the drug. On the other hand, Escitalopram, when combined with estrogen and progesterone, reduces the memory and we can suggests that the Escitalopram interacts with the pathway of estrogen and progesterone.
Keywords: Memory, Hippocampus, Male Rats, Escitalopram

P-372

Buprenorphine treatment changed the level of P2X4 receptor gene in the amphetamine addicted rats

Shima Roshani, Hatami Homeira*, Kholghi Akram, Azizi Hana

Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.

Background and Objective: P2X4 receptors are expressed on the cell surface of microglia. Methamphetamine intoxication results in a constellation of gene expression changes in neurons and microglia. Buprenorphine is an opioid used to treat opioid addiction. The primary outcome of this study was therefore to investigate the alteration of P2X4 receptor gene following methamphetamine addiction in male rats who were under treatment of buprenorphine.
Material and Methods: 49 male Wistar rats were randomly assigned into seven experimental groups (n=7): Control, Saline, Methamphetamine (10 mg/kg, i.p. for 5 days), Buprenorphine (6 and 10 mg/kg, i.p.), Methamphetamine + Buprenorphine (6 and 10 mg/kg for 14 days). Hippocampal tissue was assayed for the expression of P2X4 receptor gene using RT- PCR.
Results: amphetamine administration significantly decreased the level of P2X4 receptor gene in comparison to control group ($p<0.001$). The expression of P2X4 gene was decreased after the buprenorphine (10 mg/kg) administration in comparison to control group ($p<0.05$). In other two methamphetamine addicted groups, administration of buprenorphine with two doses for 14 days decreased the level of P2X4 gene expression in comparison to methamphetamine groups ($p<0.01$)
Conclusion: The present work shows that methamphetamine toxicity severally decreased the level of P2X4 gene expression. Treatment of buprenorphine gently reduced this reduction and tried to approach it to control level. So it seems, P2X4 receptor gene play a role in modulating methamphetamine addiction.
Keywords: Buprenorphine, Amphetamine, P2X4 receptor gene

P-373

Can Irisin affect the motor dysfunction of the rat model of Parkinson Disease (PD)?

Moslem Riyahi, Hossein Hassanpour, Mohammad shahverdi

Department of Basic Sciences, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran.

Background and Objective: PD is a common neurodegenerative disorder caused by progressive degeneration of dopaminergic neurons. Neuronal loss depleted striatal dopamine, which associated with motor disabilities like tremor, bradykinesia, rigidity. Irisin, a novel hormone with 112 amino acid residue that produced and secreted from muscle cells during exercise. The aim of this study was to evaluate the effect of Irisin on motor defections of the rat Parkinson model. The results of this study indicate that IP injection of irisin at 0.7 nmol/L significantly decreased asymmetrical behavioral in comparison with other PD rats.

Materials and methods: Thirty adult Sprague Dawley male rats were divided into Groups to five groups: control (intact animals), positive control (rats with PD), Irisin 7000 nmol/L, Irisin 70 nmol/L, Irisin 0.7 nmol/L (the last three groups rats with PD + Irisin IP injection). PD induction was developed by unilateral infusion of 6-hydroxydopamine (6-OHDA) into the striatum. Asymmetrical behavioral were determined by Elevated body swing test (EBST). It is performed to prove PD induction and assess the effect of irisin on PD motor defects. Recombinant Irisin was injected intraperitoneally every other day for 12 weeks.
Result: A significant increase in the biased swing was observed in PD rats, whereas it was significantly corrected after treating with 0.7 nmol/L Irisin for 12 weeks.
Conclusion: The results of this study indicate that infusion of 6-hydroxydopamine (6-OHDA) into the striatum caused asymmetrical behavior by striatal dopamine depletion and Irisin injection ameliorated the motor defections of the PD rats.
Keywords: Elevated body swing test, Irisin, Motor Dysfunction, Parkinson

P-374

Anti-cataleptic effect of L-Dopa is ameliorated by inactivation of Adenosine A2A receptors in 6-OH Dopamine lesioned rats

Siamak Reyhani-Rad[1], Javad Mahmoudi[2]

1. Department of Laboratory Sciences, Marand Branch, Azad University, Marand, Iran
2. Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Background and Objective: In Parkinson's disease (PD), prolonged exposure to L-3,4-dihydroxyphenylalanine (L-DOPA) results in motor fluctuations, such as the on-off phenomenon, and L-DOPA-induced dyskinesia. Previously, we found that inactivation of adenosine A2A receptors in the substantia nigra pars compacta (SNc) improves 6-OHDA-motor deficit and decrease catalepsy in parkinsonian rats. This study aimed to evaluate the effect of Adenosine A2A receptor antagonists (Caffeine and SCH 58261) on the anti-cataleptic effect of L-DOPA in 6-hydroxydopamine (6-OHDA)-lesioned male Wistar rats.
Materials and Methods: Catalepsy was induced by the unilateral infusion of 6-OHDA (8 μg/2 μl/rat) into the central region of the SNc and were assessed by using beam traversal test. After a 3-week recovery period, rats received L-DOPA intraperitoneally (ip; 15 mg/kg) twice daily for 20 days, and the anti-cataleptic effect of which was assessed by the beam test at days 5, 10, 15 and 20. Results: The results showed that L-DOPA had an anti-cataleptic effect only until day 15, and its effect was abolished on day 20. On day 21, these rats were co-treated with caffeine (30 mg/kg, ip) and SCH 58261 (2mg/kg, ip) as A2A receptor antagonists and L-DOPA (15 mg/kg, ip). At the mentioned dose, caffeine and SCH 58261 improved the anti-cataleptic effect of L-DOPA.
Conclusion: From these results, it may be concluded that adenosine A2A receptor antagonists ameliorate the ability of L-Dopa to relieve catalepsy in 6-OH Dopamine lesioned rats through inhibition of A2A presynaptic receptors in substantia nigra pars compacta.
Key Words: adenosine A2A receptor, L-Dopa, 6-OHDA, Parkinson's disease, rat

P-375

Effects of concurrent blockade of orexin receptor-2 and cannabinoid receptors-1 on the nicotine-induced enhancement of neuronal activity in the ventral tegmental area and the nucleus accumbens

Parham Reisi*, Fatemeh Azizi, Reza Fartootzadeh, Hojjatallah Alaei

Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

Background and Objective: The ventral tegmental area (VTA) and the nucleus accumbens (NAc) have role in the dependency on nicotine. Both orexin and cannabinoid systems are likely to play an important role in reward system. We aimed to evaluate the effect of orexin receptor-2 (OX2R) and cannabinoid receptor-1 (CB1R) blockade on the neural activity of VTA and NAc in response to nicotine in male rats.

Materials and Methods: Nicotine was injected subcutaneously and its effect on the firing of VTA and NAc neurons was evaluated, using in vivo extracellular single unit recording. Nicotine increased the neuronal activity of both VTA and NAc. AM251 (0.18, 0.9, 1.8 nmol/0.3 µL) and (5, 25, 125 ng/rat), as a selective cannabinoid CB1R antagonist, and TCS-OX2-29 (0.5, 1, 5 nmol/0.3 µL) and (1, 3, 10 ng/rat), as a selective OX2R antagonist, individually or simultaneously were microinjected into the VTA or the NAc respectively.
Results: The results revealed that blockade of OX2R and CB1R in both areas could prevent the increased firing rate, caused by nicotine. Concurrent blockade of the two receptors decreased neuronal firing rate, but not a greater response than their single application.
Conclusion: The blockade of OX2R and CB1R could prevent the increased firing rate, caused by nicotine; However, because there was no synergistic effect in the simultaneous blockade of these two receptors, therefore, to investigate the interactions of these two receptors, further studies are needed, especially in the field of intracellular signaling.
Keywords: Ventral tegmental area, Nucleus accumbens, Nicotine, Orexin receptors, Cannabinoid receptors, Extracellular single unit recording.

P-376

Effect of closed-loop low-frequency stimulation on seizure intensity and learning and memory impairment in pilocarpine model of epilepsy in rats

Meysam Zare, Mahmoud Rezaei, Amir Shojaei, Mohammad Reza Raoufy, Javad Mirnajafi-Zadeh

Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Introduction: Epilepsy is a common neurological disease which accompanies cognitive impairments such as learning and spatial memory deficits. Low frequency stimulation (LFS) is an effective deep brain stimulation pattern that is potentially a new therapeutic approach for drug-resistant epilepsy. In this study, pilocarpine was used to induce epilepsy and LFS was applied in a closed-loop system to study its effect on seizure severity, learning and memory and brain waves was studied.
Materials and methods: Epilepsy was induced by pilocarpine in male Wistar rats (5-6 weeks). After achieving stage 5 seizures, animals underwent stereotaxic surgery to implant a tripolar electrode in the CA1 region of the right ventral hippocampus and a monopolar recording electrode in medial prefrontal cortex (mPFC). One group of animals received LFS via a closed-loop system after online seizure detection. Spontaneous seizures were monitored by daily video recording when the local field potentials (LFPs) were recorded simultaneously. The seizure severity and LFP analysis were done in addition to evaluation the spatial learning and memory by Barnes maze test.
Results: LFS applying reduced the seizure severity and duration and restored the epilepsy-induced impairment in working and special memory. In addition, LFS reduced the increment in power of delta, theta, and gamma wave during seizure attacks. The coherences of delta, theta and gamma waves between ventral hippocampus and mPFC were increased during seizure occurrence, but, application of LFS decreased these kind of connections.
Conclusion: The results of this study revealed that applying LFS during seizure attacks reduced the seizure severity and improved the memory. In addition, the changes in power and coherence of the LFP waves returned toward normal situation in LFS-received epileptic animals.
Keywords: Closed-loop system, ventral hippocampus, medial prefrontal, low frequency stimulation, spatial memory

P-377

The effect of low and high doses of lead over one and two months on spatial learning and memory

Fatemeh Zare Mehrjerdi, Azadeh Shahrokhi Raeini

Neurobiomedical Research Center, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences and Health Services

Background and Objective: Acute and chronic exposure to lead causes major problems in the nervous system. Lead accumulates in various parts of the brain, including the hippocampus and cortex and causes cognitive and behavioral disorders. The aim of this study was to investigate the effect of different doses of lead on spatial learning and memory in lead poisoned rats over one and two months.

Materials and Methods: male Wistar rats were divided into 5 groups. 1- Sham. 4 lead groups: 1- 100ppm for one month (1M) 3- 100ppm for two month (2M) 4- 500ppm for 1M 5- 500ppm for 2M. Spatial learning and memory was tested using the Morris Water Maze. During the first 4 days, the time and distance required to reach the platform were compared. At the last day, the elapsed time in the target quadrant was compared.
Results: The time and distance to reach the platform in lead groups 500ppm; 2M and 1M and 100ppm; 2M showed a significant increase compared to control group. The lead group 100ppm; 1M had no significant increase vs control group. Time spent in the target quadrant in lead groups 500 and 100ppm; 2M showed significant decrease compared to the control group.
Conclusion: This study showed that exposure to low doses of lead for 1M had no effect on memory and learning. But exposure to low doses for 2M and high doses of lead both in 1 and 2M impairs learning and memory.
Keywords: Rat, Lead Acetate, Spatial Learning and Memory

P-378

Anticonvulsive effects of endocannabinoids; an investigation to determine the role of regulatory components of ndocannabinoid metabolism in the Pentylenetetrazol induced tonic- clonic seizures

Parisa Zareie, Mehdi Sadegh, Mohammad Reza Palizvan, Homeira Moradi-Chameh

2-Arachidonoylglycerol (2-AG) and anandamide are two major endocannabinoids produced, released and eliminated by metabolic pathways. Anticonvulsive effect of 2-AG and CB1 receptor is well-established. Herein, we designed to investigate the anticonvulsive influence of key components of the 2-AG and anandamide metabolism. Tonic-clonic seizures were induced by an injection of Pentylenetetrazol (80 mg/kg, i.p.) in adult maleWistar rats. Delay and duration for the seizure stages were considered for analysis. Monoacylglycerol lipase blocker (JJKK048; 1 mg/kg) or alpha/beta hydroxylase domain 6 blocker (WWL70; 5 mg/kg) were administrated alone or with 2-AG to evaluate the anticonvulsive potential of these enzymes. To determine the CB1 receptor involvement, its blocker (MJ15; 3 mg/kg) was administrated associated with JJKK048 or WWL70. To assess anandamide anticonvulsive effect, anandamide membrane transporter blocker (LY21813240; 2.5 mg/kg) was used alone or associated with MJ15. Also, fatty acid amide hydrolase blocker (URB597; 1 mg/kg; to prevent intracellular anandamide hydrolysis) were used alone or with AMG21629 (transient receptor potential vanilloid; TRPV1 antagonist; 3 mg/kg). All compounds were dissolved inDMSO and injected i.p., before the Pentylenetetrazol. Both JJKK048 and WWL70 revealed anticonvulsive effect. Anticonvulsive effect of JJKK048 but not WWL70 was CB1 receptor dependent. LY2183240 showed CB1 receptor dependent anticonvulsive effect. However, URB597 revealed a TRPV1 dependent proconvulsive effect. It seems extracellular accumulation of 2-AG or anandamide has anticonvulsive effect through the CB1 receptor, while intracellular anandamide accumulation is proconvulsive through TRPV1.
Keywords 2-Arachidonoylglycerol . ABHD6 . Anandamide . CB1 receptor .MAGL . Rat . TRPV1

P-379

Study of the effect of intracerebroventricular injection of kaempferol and its intraction with vanilloid type 1 receptor on pain in male rats

Mohammad Mahdi Zarei[1*], Zohreh Abdolmaleki[1], Siamak Shahidi [2]

1. Department of Pharmacology, Faculty of Veterinary Medicine, Karaj Branch, Islamic Azad University, Karaj, Iran
2. Department of Physiology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran Department of Pharmacology, Faculty of Veterinary Medicine, Karaj Branch, Islamic Azad University, Karaj, Iran

Background and Objective: Kaempferol is one of the most important herbal active constituent with nerve protection, anxiolytic, antinociceptive, and anti-inflammatory effects. The aim of this study was to evaluate the effect of intracerebroventricular injection of kaempferol and its interaction with vanilloid type 1 receptor on pain in male rat.
Materials and Methods: In this experimental study, 10 groups of rats (six animals in each group) weighting 200-250g were used. Groups included following saline (sham), DMSO, morphine, kaempferol at dosages of 0.5, 1, and 1.5 mg/rat, capcaisin, capsazepin, capcaisin plus kaempferol (1.5 mg/rat), capsazepin plus kaempferol (1.5 mg/rat). After surgery of rats, the cannula implantation was done and after recovery of rats during one week, the components have been injected to the rats through cannula. Then antinociceptive effects of components evaluated by writhing, tail flick, and formalin tests. Data were analyzed by one way ANOVA and Tukey as a post test.

Results: Our results in this study showed that administration of both kaempferol (1.5 mg/rat) and capsaicin had significant analgesic effects in comparison to the control groups at the pain assessment tests. Co-administration of capsaicin plus kaempferol (1.5 mg/rat) had significant analgesic effects compared to the control groups. Moreover, co-administration of capsazepin and kaempferol (1.5 mg/rat) decreased antinocceptive effects of kaempferol alone.
Conclusion: Our findings showed that kaempferol could attenuate the acute and inflamamatory pain. However, kaempferol ameliorates the acute and inflamamatory pain at least in part by activating type I vanilloid receptors.
Keywords: Kaempferol, Type 1 Vanillid Receptor, Pain, Central nervous system.

P-380

Investigating the effects of subchronic sesame and flaxseed oils consumption against seizure and depression in adult male mice

Raha Zalkhani[1], AhmadAli Moazedi [1,2] , Hossein Najafzadehvarzi [3,4]

1. Department of Biology, Faculty of science, Shahid Chamran University of Ahvaz, Ahvaz, Iran.
2. Stem cell and Transgenic Technology Research Center, Shahid Chamran University of Ahvaz, Ahvaz, Iran
3. Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
4. Department of pharmacology, Faculty of veterinary medicine, Shahid Chamran University of Ahvaz, Iran

Running title: Effects of Sesame and Flaxseed oils against seizure and depression
Objectives: Epilepsy is a highly debilitating disorder by unpredictable seizures associated with emotional disturbance. One potential treatment for seizure and depression is dietary therapy. So, this study evaluated effects of daily oral administration of sesame and flaxseed oils in depression and seizure.
Materials and methods: Twenty-one adult male mice were divided into the following groups: control (normal saline recipient, 1ml/kg) , sesame and flaxseed oils groups (8mg/kg bodyweight, for 21 days). At the 22th day, locomotor activity and depressive like behavior were assessed by open field and tail suspension tests. Also in 23th day, animals received a subcutaneous injection of strychnine for induction of seizure. The seizure latency and death time were recorded through observation of animal behavior immediately after injection strychnine.
Results: There were no significant differences in locomotor activity among control, sesame and flaxeed groups. But it has been shown a significant increase in latency to immobility ($p=0.027$) and decrease in total immobility ($p=0.001$) in flaxseed oil group compared to control group. Also sesame oil group showed a significant reduction in the duration of total immobility ($p=0.027$) and its latency to immobility wasn't significant. There were no significant differences in latency to seizure and death time in flaxseed oil groups compared to the control group. The subchronic consumption of sesame oil significantly increased the death time than the control group but the latency to seizure was not significant.
Conclusion: The results reveal that sesame and flaxseed may be considered as a food adjuvant for attenuating emotional problems in epilepsy.
Key words: Sesame, Flaxseed, Strychnine, Depression, Seizure, Mice

P-381

Effects of Memantine and Docosahexaenoic acid on Learning and Spatial Memory in Adult Male Rats model of Alzheimer's disease

Nastaran Zamani[1], Ahmad Ali Moazedi[2], Mohamad Reza Afarinesh Khaki[3], Mehdi Pourmehdi Boroujeni[4]

1. Department of Biology, Faculty of Science, Payame noor university, Tehran, Iran.
2. Department of Biology, Faculty of Science, Shahid Chamran University of Ahvaz, Ahvaz, Iran.
3. Kerman Cognitive Research Center and Kerman Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.
4. Department of Food Hygiene, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.

Backgrounds and Objectives: Alzheimer's disease (AD), the most common form of dementia, is a neurodegenerative disorder clinically characterized by progressive deterioration of cognitive and behavioral function. This study investigated the effect of coadministration Memantine(MEM) and docosahexaenoic acid (DHA) on learning and spatial memory in an experimental rat Alzheimer model.
Materials and Methods: In this study 63 adult male Wistar rats were divided into 9 groups: control, lesion which received bilateral electric lesions of nucleus basalis magnocellularis (NBM), sham (the electrode was entered into

the NBM with no lesion), lesion+3mg/kg MEM, lesion+1mg/kg DHA, lesion+3mg/kg MEM - 1mg/kg DHA, Memantine Vehicle (lesion+0.2 mL saline), DHA Vehicle (lesion+0.2mL Sesame Oil), lesion+0.2 mL saline - 0.2mL Sesame Oil. After one week, the rats were trained to perform the Y-maze task for five days.
Results: In this study, the results of analysis of variance with repeated measurements showed that the bilateral lesion of NBM impaired the spatial learning compared to the control and sham groups ($P<0.001$). No effect on spatial learning was seen in lesion+saline, lesion+Sesame Oil, lesion+saline - Sesame Oil groups compared with the lesion group. The treatment with Memantine and DHA in groups, lesion+3mg/kg MEM ($P<0.05$), lesion+1mg/kg DHA ($P<0.05$), lesion+3mg/kg MEM - 1mg/kg DHA ($P<0.01$), significantly improved spatial learning.
Conclusion: The results of this study indicate that coadministration Memantine - docosahexaenoic acid increases memory and spatial learning defects in electrical lesions model of NBM of Alzheimer's disease.
Keywords: Memantine, docosahexaenoic acid, Spatial learning, Nucleus basalis of magnocellularis, Alzheimer's disease

P-382

Effects of Brief Electrical Stimulation on Regeneration of Transected Sciatic Nerve

Hosein Samaram[1], Nadia Naghavi[1], Sareh Naseri[1], Morteza Behnam Rasouli[2]

1. Electrical Engineering Department, Faculty of Engineering, Ferdowsi University of Mashhad, Mashhad, Iran.
2. Biology Department, Faculty of Sciences, Ferdowsi University of Mashhad, Mashhad, Iran.

Background and Objective: In peripheral nerve injuries, electrical stimulations (ES) have been used to accelerate the nerve regeneration. In this study effects of brief voltage-controlled ES on the functional recovery in a transection model of the rat sciatic nerve has been investigated.
Materials and Methods: Fifteen adult male Wistar rats (250-350g) were anesthetized, their right sciatic nerve were transected and randomly divided in one control and two experimental groups (n=5). The proximal and distal ends of the transected nerve were sutured to a 10 mm-long silicone tube and then stimulated as follows; 10 and 30 min ES (20Hz, 3V, 100µs) in experimental groups and no ES in the control group. A hot plate test was done every two week and at the end of the experimental period (12 weeks) the relative nerve conduction velocity (NCV) was measured.
Results: Hot plate results indicate that at weeks 8 and 10, the withdraw time in experimental groups are shorter than the control group. However, the differences are not significant. Based on the electrophysiology test, the 10 min-ES group had a significantly higher NCV compared to the control group and the 30 min-ES group ($p<0.05$).
Conclusion: Results demostrated that brief ES can increase the speed of nerve regeneration and also a shorter ES protocol can be more effective while can reduce the chance of infection and the cost of keeping patients under anesthesia.
Keywords: Peripheral Nerve Regeneration, Voltage-controlled Electrical Pulses, Brief Stimulation

P-383

Effects of ethanolic extract of Artemisia persica on scopolamine-induced cognitive impairment and anxiety in rats

Mahbubeh Setorki*

Associate of professor, Department of Biology, Izeh Branch, Islamic Azad University, Izeh, Iran

Background and Objective: Artemisia persica is used as an antiseptic, appetizer, antiparasitic, and antipyretic agent as well as to relieve fascial pains, and in the past, was used to relieve neuropathic pain and facilitate uterine contractions during childbirth. In in vitro studies, the antioxidant, anticancer, antibacterial, antifungal and anti-malarial effects of this plant have been shown. The aim of this study was to investigate the antioxidant potential and effects of A. persica on scopolamine-induced cognitive impairments and anxiety.
Materials and Methods:In this experimental study, 50 male rats were randomly divided into 5 groups of 10 each, including control group, scopolamine (0.7 mg/kg, intraperitoneal injection) group, and three groups receiving scopolamine and ethanolic Artemisia persica extract (100, 200, and 400 mg/kg). After three weeks of treatment, behavioral tests including passive avoidance memory, plus maze test, and rotarod test were conducted. The level of malondialdehyde and the antioxidant capacity of the serum and brain in the rats were measured.

Results: Treatment with A. persica extract at 100, 200, 400 mg/kg in rats receiving scopolamine caused a significant increase in secondary latency in shuttle Box test. Treatment of rats receiving scopolamine with A. persica extract at 100, 200, and 400 mg/kg significantly decreased the time elapsed in closed arms and significantly increased the time elapsed in the open arms in plus maze test.
Conclusion: The results of this study indicate that A. persica can act as a potent neuropharmacologic agent against cognitive impairment by modulating cholinergic activity and neuritis in the rat hippocampus.
Keywords: Artemisia persica, avoidance memory, anxiety

P-384

Motion sickness in pets: a clinical case report

Shahin Hassanpour [1*], Seyyede Parastoo Rahimi [2], Sina Salajegheh Tazerji [3]

1. Section of Physiology, Department of Basic Science, Faculty of Veterinary Medicine, Science and Research Branch, Islamic Azad University, Tehran, Iran
2. Doctorate student of Veterinary Medicine, Faculty of Veterinary Medicine, Science and Research Branch, Islamic Azad University, Tehran, Iran
3. Young Researchers and Elites club, Science and Research Branch, Islamic Azad University, Tehran, Iran

Motion sickness occurs with sensitivity of central nervous system when an incongruity comes about between visually perceived movement and vestibular system's sense of bodily movement. Symptoms include dizziness, fatigue, depressed appetite, nausea and nausea-caused vomiting. The emetic chemoreceptor trigger zone (CTZ), located in the postrema of medulla oblongata, is responsible for vomiting in motion sickness. It seems a "motion vomiting substance" is secreted into the cerebrospinal fluid in the emetic process. Furthermore, certain therapeutic measures against motion sickness are aimed at preventing the presumed chemical stimulation of the CTZ in dogs and monkeys against motion-induced vomiting.
This study was done as the first report on pug breed dog (male, aged 8 months, 6.38 kg) suffering motion sickness in Iran. Motion sickness is a rare case and there are few reports only on small animals in veterinary medicine. The main complications for disease by owners are dehydration due to vomiting and lack of balance. Based on the medical clinical trials, it is postulated antihistamines can decrease symptoms of the disease. So, it is suggested to use Diphenhydramine (H1 histamine-receptor antagonist) 30-minutes in short intercity trips with car or public transport system. Also, air condition, pause after short periods was recommended in prevention and treatment process. This concept originated from reports in which ablation of the area postrema protected some dogs and monkeys against motion-induced vomiting. However, lesions of the area postrema were not effective in preventing motion sickness in cats. Based on the next owner report, the severity of disease decreased.
Keywords: Motion sickness, Small Animal

P-385

Evaluation of low dose of methamphetamine in the Astrocyte Model of Alzheimer's Disease Induced by Aβ1-42

Bita Soltanian[1], Marzieh Dehghan Shasaltaneh[2*], Gholam Hossein Riazi[3], Nahid Masoudiyan[1]

1. Department of Biology, College of Science, Damghan Branch, Islamic Azad University, Damghan, Iran
2. Department of Biology, Faculty of Science, University of Zanjan, Zanjan, Iran.
3. Laboratory of Neuro-Organic Chemistry, Institute of Biochemistry and Biophysics (IBB), University of Tehran, Tehran, Iran

Background and objective: AD is a chronic neurodegenerative disease that characterized by neurofibrillary tangles and Aβ. METH is a powerful, highly addictive stimulant that affects the central nervous system. We assessed the effect of low-dose of METH on learning and memory in Alzheimer's model
Materials and method: we have investigated the influence of the effective dose of METH on memory improvement, by evaluating Bax, Bcl-X, PKCα, GSK3β and Cdk5 gene expression. Phosphorylated tau (Ser396), p-GSK3β, GSK3β and GSK3α proteins were assessed by western blotting. Cell cycle and apoptosis were checked by flow cytometry and Hoechst staining

Results: Our results show that Bax/Bcl-x ratio was significantly lower in the prevention groups higher than the treatment group. In the prevention group, the expression of GSK3β, Cdk5 and PKCα genes is decreased. In the treatment group, GSK3β and Cdk5 are significantly increased. The level of protein GSK3α and GSK3β in the treatment and prevention groups are increased and decreased, respectively. The percentage of necrosis and early apoptosis in treatment and prevention groups are decreased. The results of cell cycle show that G1 is increased and G2 is decreased in the prevention group.
Conclusion: Investigating the various factors in cell signaling pathways associated with Aβ, apoptosis and cell cycle confirm the validity of our hypothesis, that the protective effect of low-dose of METH is higher than its treatment role in AD.
Keywords: Alzheimer's disease; Hyperphosphorylated tau; Methamphetamine; Apoptosis

P-386

Thoracic Spinal Cord Injury Causes alterations in Oscillatory Activity and Dopaminergic Markers in Rat Primary Motor Cortex Associated with Deficit in Forelimb Motor Skills

Omid Salimi[1,2], Parviz Shahabi[2], Hamid Soltani Zangbar[2], Ahad Karimzadeh[2]

1. Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
2. Neuroscience research center (NSRC), Tabriz University of Medical Sciences, Tabriz, Iran

Background and Objectives: The loss of spinal sensorimotor pathways following spinal cord injury (SCI) can promote retrograde neurodegeneration in the brain, especially the primary sensorimotor cortex. This study aimed to examine the effects of rat thoracic contusion SCI on oscillatory activity, dopaminergic biochemical markers in the hindlimb and forelimb areas (HLA, FLA) of primary motor cortex (M1) as well as motor skill learning of non-affected forelimb.
Materials and Methods: Sixteen male Wistar rats were equally and randomly subjected to only laminectomy (Sham) or contusion injury (SCI) in the thoracic cord at level T10. Oscillatory activity and motor skill performance for 6 consecutive days were evaluated using local field potential (LFP) recording and skilled forelimb reaching task, respectively. The level of dopamine and expression of D1 and D2 dopamine receptors were determined in HLA and FLA by ELISA and Western blot.
Results: The electrophysiological results showed a sustained increase of LFP power in the HLA (in rest) and FLA (in rest, and task condition) of SCI rats compared with uninjured rats. SCI rats had lower learning rate and performance scores in a skilled forelimb reaching task than uninjured rats. Biochemical analysis of HLA and FLA showed a reduction in the level of dopamine and expression of D1 and D2 receptors after SCI.
Conclusion: These findings suggest that thoracic SCI causes aberrant changes in oscillatory activity and dopaminergic markers of M1 that are not restricted to HLA but also found in FLA and appears as a deficit in forelimb motor skill performance.
Keywords: Spinal cord injury, Oscillatory activity, Dopamine, Motor skill

P-387

Impact of buprenorphine on learning and memory ability, oxidative status and inflammation in the hippocampus of rat

Mohammad Samini[1], Tahereh Farkhondeh[2], Mohsen Azimi-Nezhad[3], Saeed Samarghandian[3]

1. Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran
3. Department of Basic Medical Science, Neyshabur University of Medical Sciences, Neyshabur, Iran

Background and Objective: The impact of buprenorphine (BUP) on cognitive function is not fully understood. Therefore, this study was designed to investigate the association between BUP and learning and memory functions in an animal model.
Materials and Methods: For this reason, twenty four male Wistar rats were randomly allocated in to one control and two BUP-treated groups (0.3 and 1 mg/kg, SC), (n=8, for each group). After 4 weeks, learning and memory abilities were assessed by using Y-maze test. Then, oxidative stress indices [glutathione (GSH), malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT)] and inflammatory parameters [necrotic factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β)] were assessed in serum and hippocampus of rats.
Results: The present findings indicated that the memory and learning time was lengthened in BUP (1mg/kg)-treated rats versus control animals ($p<0.05$). Additionally, it was observed that BUP (1 mg/kg) significantly increased the

serum and hippocampal levels of MDA and TNF-α and also decreased GSH levels versus the control group ($p < 0.05$).
Conclusion: The present results reveal that BUP may cause learning and memory dysfunction via inducing oxidative stress and inflammation in hippocampus.
Keywords: buprenorphine; learning, memory, oxidative stress, inflammation

P-388

Role of 5-HT3 receptors Blockade in the entorhinal cortex on Spontaneous Alternation in Y- maze in the electerical amygdala kindled rat

Zeinab Sayyahi[1,2*], Javad mirnajafi-zadeh [3], Abdolrahman Sarihi [1,2], Alireza Komaki[1,2]

1. Department of Physiology, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
2. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
3. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Background: Epilepsy is a chronic neurological disorder characterized by frequent seizures. One of the important types of epilepsy from the clinical point of view is temporal lobe epilepsy, which is the most common topical epilepsy in adults that is resistant to commonly used treatments. Over the past two decades, there have been many advances in drug therapies for epilepsy and complications, but about one third of patients still have not responded to common medications. The aim of this study was to determine the role of 5-HT3 receptors Blockade in the entorhinal cortex on the Discrimination index in Novel Object recognition in the electerical amygdala kindled rats.
Materials and methods: Male Wistar rats (weighing 270–350 g) were used in this study. Animals were assigned to seven groups as control, sham, kindled, kindled + vehicle, kindled + Ramo. 1µg, kindled + Ramo. 10µg, kindled + Ramo. 100µg. In kindled + vehicle group, animals were injected with ramosetron vehicle and then received the kindling stimulations. In kindled + Ramo. 1 µg group, animals were injected with ramosetron 1µg / 0.5 µl (ICV) and then received the kindling stimulations 24 h after applying the vehicle injection. In kindled + Ramo. 10 µg group, animals were injected with ramosetron 10 µg / 0.5 µl (ICV) and then received the kindling stimulations 24 h after applying the vehicle injection. In kindled + Ramo. 100 µg group, animals were injected with ramosetron 100µg / 0.5 µl (ICV) and then received the kindling stimulations 24 h after applying the vehicle injection. At the end of each step, the Y-Maze Behavioral Test was performed.
Results: Main findings: The 5-HT3 receptor blockad was significantly increased by using the selective antagonist of this receptor in high and moderate doses in Y-maze test, compared to the Kindled + vehicle group.
Conclusion: In this study, it was observed that Kindling leads to dissfunction in the recognition and spatial memory, and acute injection of 5-HT3 receptor selective antagonist leads to improved spatial memory. Therefore, Ramosetron as 5-HT3 receptor antagonist , possibly with the release of acetylcholine at the synaptic space, can improve memory and learning disorders caused by electrical amygdala kindling. In general, it can be concluded that injection of selective 5-HT3 antagonist with 5-HT3 receptor block removes the inhibitory effect on acetylcholine release and improves acetylcholine release in the synaptic space of diagnostic and spatial memory. Based on the studies and the results of the present experiments, it can be concluded that injection of the selective antagonist 5-HT3 receptor improves spatial memory. On the other hand, electrical kindling of the amygdala and the resulting seizures impair spatial memory and learning.
Keywords: Epilepsy, 5-HT3 Receptors, electrical kindling, Seizure, Amygdala, Entorhinal Cortex, spatial memory

P-389

Neuroprotective effects of thyroid hormones on methamphetamine–induced cell death in primary hippocampal neurons

Seyedeh Masoumeh Seyedhosseini Tamijania[1], Elmira Beirami[2,3*], Abolhassan Ahmadiani[2], Leila Dargahi[2*]

1. Immunogenetics Research Center, Mazandaran University of Medical Sciences, Sari, Iran
2. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Animal Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran

Background: Methamphetamine (MA) induced-cognitive dysfunction is mainly attributed to neurotoxic effects in different brain area such as hippocampus. The thyroid hormones (THs), 3,5,3′-triiodo-l-thyronine (T3) and l-thyroxine (T4), possess neuroprotective effects on certain features of the pathophysiology of brain damage. The current study evaluates the neuroprotective effects of thyroid hormones on MA–induced cell death in primary hippocampal neurons (PHNs).
Materials and Methods: PHNs were isolated from hippocampus of E17-18 rat embryos, grown for 7 days and then treated with different MA concentrations (2–9 mM) for 72 hours. To investigate the effects of T4 (1, 2, 4, 6, 8, and 10 µM) and T3 (200, 400, 600, 800, and 1000 nM), cells were co-treated with MA and T4 or T3.

Immunocytochemistry against βIII-tubulin was performed to verify the purity of neuronal culture and MTT assay was used to assess cells survival.
Results: Our findings showed an almost pure population of pyramidal neurons with a low density of glia. Exposure of PHNs to 2–9 mM MA significantly reduced cell viability. T4 obviously increased the viability of MA-treated cells at a concentration of 8 µM and also T3 increased the viability of MA-treated cells at a concentration of 800 nM.
Conclusion: THs possess neuroprotective effects against MA-induced loss of cell viability in culture of primary hippocampal neurons and therefore can be potentially considered as an approach to combat MA neurocognitive effects.
Keywords: Methamphetamine; Thyroid hormones; Primary hippocampal neurons; Cell death

P-390

The relationship of GST-T1 and GST-M1 polymorphisms with oxidative stress in acetaminophen poisoned patients

Saeedeh Shojaeepour[1*], Motahare Jamalimehr[2], Zohreh Oghabian[2], Ali Mandegary[2], Leila Pourgholi[2]

1. Pathology and Stem Cell Research Center, Kerman University of Medical Sciences, Kerman, Iran
2. Department of Toxicology & Pharmacology, School of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: Acetaminophen poisoning is one of the most extensively drug overdose in Iran. It seems searching about acetaminophen toxicity risk factors is necessary due to its availability and widely use. With therapeutic dosing, acetaminophen is mainly metabolized via glucuronidation and sulfation and only small fraction is metabolized to a toxic metabolite NAPQI. Genetic variability, include those encoding enzymes important in acetaminophen metabolism, could predispose some individuals to a higher risk of acetaminophen-induced liver injury. For instance glutathione S-transferases constitute a superfamily multifunctional enzymes which play a key role in cellular detoxification. The purpose of this study was deletion determination of the GSTM1 and GSTT1 genes in acetaminophen poisoned patients and its relationship with liver injury.
Material and Method: Blood samples were obtained from 135 patients with acetaminophen toxicity who were treated at Loghman Hospital. Genomic DNA was extracted from blood samples using salting out method. Genetic polymorphisms of glutathione S-transferases were detected by polymerase chain reaction. Oxidative stress parameters were also measured by the TBARS and FRAP methods. Statistical analysis was conducted using the SPSS software and values of $P < 0.05$ were considered to be statistically significant
Results: Amount of MDA measured by the TBARS test was significantly higher ($p = 0.000$) in patients with acetaminophen toxicity. There was no relationship between the oxidative stress parameters and GSTT1 and GSTM1 gene polymorphisms.
Conclusion: Reduced glutathione S-transferase enzyme activity among individuals with null genotypes has no effect on oxidative stress parameters and liver injury that caused by it.
Keywords: Acetaminophen, Oxidative stress, Polymorphism, Glutathione S-transferase (GST)

P-391

Isoniazid inhibits morphine-induced incentive sensitization in mice using a conditioned place preference paradigm

Kamran Shahabi, Amir Abbas Barzegari

Department of Biology, Faculty of Basic Science, University of Maragheh, Maragheh, East Azerbaijan Province, IR Iran

Repeated intermittent exposure to morphine may induce sensitization to rewarding effects of this drug. This process (sensitization) plays important role in morphine addiction. Different brain regions and neurotransmitter systems including GABAergic system affect on sensitization. Therefore, the purpose of this study was to assess the effects of modulation of GABAergic systems by isoniazid on the morphine reward sensitization.
Methods: Conditioned place preference (CPP) method was used for assessing rewarding effects of drugs. First, CPP induced by morphine (0.5-10 mg/kg, s.c.) or isoniazid (25, 50 and 75 mg/kg i.p.). Sensation to the rewarding effects of morphine induced as follow: on three consecutive days the mice received morphine effective dose (5 mg/kg, s.c.); then after five days interval, induction of CPP commenced with the ineffective dose of morphine (0.5 mg/kg, s.c.). For evaluation of isoniazid effects on morphine reward sensitization, different groups of animals received saline or isoniazid (25, 50 and 75 mg/kg, i.p.) 40 min. before receiving effective doses of morphine (5mg/kg, s.c.).

Results: morphine could induce a significant CPP, but isoniazid failed in the induction of CPP. Pretreatment of isoniazid before morphine on the days of sensation induction, could inhibit sensitization to the rewarding effects of morphine, significantly.
Conclusion: inhibition of sensitization to rewarding effects of morphine showing promising effects of isoniazid for the treatment of morphine addiction.
Keywords: isoniazid; morphine; conditioned place preference; sensitization; mice

P-392

Chronic early life maternal deprivation induced depressive like behavior in young adult male rats

Payam Shahsavar[1,2], Roya Ranjbar[2], Farzaneh Eskandari[2], Soheila Maghami[2], Homeira Zardooz[1,2]

1. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Early life chronic stress can induce psychiatric disorders like depression in adulthood. This long lasting effect might be due to alteration of hypothalamic- pituitary- adrenal (HPA) axis programming, which could be resulted in sustained activation of this system. The subsequent elevation of corticosterone level can affect depressive like behavior. In this regard, the present study investigated the correlation between plasma coricosterone level and depressive like behavior in young adult male rats experienced chronic maternal deprivation during infancy.
Materials and Methods: Male rat offspring divided into 2 groups: stress (STR) and non-stress (non-STR) groups. The animals of the STR group were separated from their mothers during postnatal days (PND) 1 to 21. Blood samples were collected on PND-21, 36 and in young adulthood (53±2 days) to determine plasma corticosterone level. Moreover, in the young adult offspring the depressive like behavior was assessed using forced swim test (FST).
Results: The results showed that plasma corticosterone concentrations were higher in the STR group than the non-STR group on PND-21, 36 and in young adulthood. In addition, the results of FST indicated that the duration of immobility time in STR group was longer than non-STR group.
Conclusion: It seems that chronic early life stress possibly by inducing sustained elevation of plasma corticosterone level caused the incidence of depressive like behavior in young adulthood.
Keywords: Early life stress, Corticosterone, Depressive like behavior

P-393

Pretreatment with crocin along with treadmill exercise ameliorates motor and memory deficits in hemiparkinsonian rats by anti-inflammatory and antioxidant mechanisms

Somayeh Shahidani, Ziba Rajaei, Hojjatallah Alaei

Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

The motor symptoms of Parkinson's disease (PD) are preceded by non-motorized symptoms including memory deficits. Treatment with dopamine replacement medications, only control motor symptoms and does not treatment dyskinesia, non-motor symptoms, and neuroprotection. The purpose of the current study was to examine the neuroprotective potential of crocin and physical exercise in parkinsonan rats. Rats ran on a horizontal treadmill and/or pretreated with crocin at a dose of 100 mg/kg. Then, 16 µg of 6-hydroxydopamine (6-OHDA) was microinjected into left medial forebrain bundle. Crocin treatment and/or exercise continued for 6 weeks. Spatial and aversive memories, rotational behaviour, inflammatory and oxidative stress parameters were assessed at the end of week 6 post surgery. The results showed that pretreatment with crocin alone and in combination with exercise decreased the total number of rotaions as compared with 6-OHDA-lesioned group. Furthermore, treatment of

parkinsonian rats with crocin along with exercise training improved both memories. Biochemical analysis showed that crocin and exercise (alone and in combination) reduced tumor necrosis factor- (TNF) α levels in the striatum. Moreover, treatment with crocin at a dose of 100 mg/kg decreased the lipid peroxidation levels in the hippocampus, while exercise training increased the total thiol concentration. In conclusion, our findings indicated that pretreatment with crocin along with treadmill exercise ameliorated motor and memory deficits induced by 6-OHDA, which is considered to be due to their antioxidant and anti-inflammatory activities. The results suggest that combined therapy with crocin and exercise may be protective for motor and memory deficits in PD patients

Keywords Crocin . Memory . Motor activity . Treadmill exercise . Cytokine . 6-OHDA . Inflammatory biomarkers . Oxidative stress . Parkinson's disease

P-394

The effects of frankincense on depression and anxiety-like behaviors induced by LPS in rats

Seyedeh fatemeh Shahidpoor[1], Seyed Mahmoud Hoseini[2], Fatemeh Zare Mehrjardi[1], Narges Marefati[2]

1. Department of Physiology, School of Medicine Shahid Sadoughi University of Medical Sciences
2. Department of Physiology, Mashhad University of Medical Sciences

Background and Objective: In some types of depression and anxiety disorders the level of inflammatory cytokines increased then leaded to augment the number of WBC.The frankincense is known has anti-inflammatory effects. The effects of frankincense ethyl acetate extract was investigated on lipopolysaccharide- induced depression and anxiety like behavior in rats.

Materials and Methods: 50 male wistar rats were divided into 5 groups: control, LPS group, the groups treated by 50-100 -200 mg/ kg of the extract with LPS (for 6 days). We performed forced swimming test to assessment depression like behavior and elevated plus-maze test and Open field test to evaluation the anxiety disorders. Then, to measure the anti-inflammatory properties of the extract, the rate of WBC were evaluated.

Results: In the open- field test, the total crossing number increased in groups treated with extract also, it has been showed the total distance. LPS decreased significantly the total crossing number and total distance. In forced swimming test, immobility time decreased in extract groups, although this time increased in LPS group. In elevated plus-maze test, LPS diminished the time of spent in open arm whereas this time increased in extract groups. Also, LPS leaded to augment the number of WBC while extract contributed to decrease it.

Conclusion: Our results showed the ethyl acetate extract of frankincense lead to declined symptoms of depression and anxiety disorders by diminished the amount of WBC.

Keywords: frankincense, depression, anxiety, Lipopolysaccharide, WBC

P-395

A new memory impairment model following hippocampal intracerebral hemorrhage

Shima Shirzad[1], Farzaneh Vafaee[1], Asadollah Zarifkar[2]

1. Neuroscience Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Neuroscience, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: Memory impairment is a debilitate disorder affecting the lives of many people worldwide, with no effective treatment so far. There are very few models in which acute and local hippocampal damage can be examined. Therefore, the present study examined a model of memory impairment caused by acute damage following hemorrhagic stroke, and validated it using behavioral and histological tests.

Materials and Methods: In this study, 64 Sprague-Dawley rats were used. Before anesthesia, the animals were placed in the stereotaxy device and 100 µL of autologous blood was slowly injected into left hippocampus. After that, on postoperative days 1, 3, 7, and 14, behavioral tests of neurological deficit score (NDS), locomotor activity,

passive avoidance, and novel object recognition test (NOR) were performed. Finally, perfusion was performed and the brain was removed for histological examinations.
Results: Results indicates that, on days 1 and 3, NDS has a significant decrease in ICH groups compared to sham groups. Nevertheless, no significant difference was observed between groups on the wire hanging test. Passive avoidance memory was significantly reduced in ICH groups, but recognition memory impairment was observed only on postoperative day 14. The volume and number of hippocampal neurons were reduced after surgery, and the damaged area and number of dead-neurons was significantly increased in ICH groups.
Conclusion: Results showed that the slow injection of autologous blood into the hippocampus has caused local damage to this region, thus leading to memory impairment and cell death, without affecting motor, sensory, or other cognitive activities.
Keywords: Intracerebral hemorrhage; passive avoidance Memory; Recognition memory; Hippocampus; Rats

P-396

Evaluation of the alcoholic extract of Portulaca oleracea on modulation of neuropathic and acute pain in rats

Mehdi Sadeghi[1], Afsaneh Vahedi Moghadam[2], Ali Movahed[3]

1. Department of Physiology , Faculty of Medicine , Bushehr University of Medical Sciences , Bushehr , Iran
2. Faculty of Medicine , Bushehr University of Medical Sciences , Bushehr , Iran
3. Department of Biochemistry , Faculty of Medicine , Bushehr University of Medical Sciences , Bushehr , Iran

Background and Objective: Portulaca Oleracea is a medicinal plant with many effects including analgesic and anti-inflammatory properties. This study aimed to investigate the effect of alcoholic extract of Portulaca Olerecea on CCI model of neuropathic pain (Bennet & Xie model) and acute thermal pain induced by Tail Flick.
Materials and Methods: Adult male Wistar rats weighing 200-250 g were used. Sensitivity to mechanical stimuli (mechanical allodynia) and noxious thermal stimuli were evaluated by Von Frey filaments and Tail Flick, respectively. In neuropathic pain studies, animals were randomly assigned to five groups of sham, CCI, two groups subjected to CCI and injected with extract (200 and 400 mg/kg, i.p.) and a group subjected to CCI and injected with normal saline. In these groups, mechanical allodynia was assessed on day 7 after surgery. In acute pain studies, animals were divided to three groups of a group that received normal saline and two groups that received extract (200 and 400 mg/kg, i.p.). In these groups, Tail Flick was measured 30 minutes after normal saline or extract administration.
Results: All of the rats that had experienced CCI, exhibited mechanical allodynia after neuropathy.
Portulaca oleracea could reduce the development of mechanical allodynia after CCI at 200 and 400 mg/kg doses. Thermal acute pain was reduced by 400 mg/kg of the extract.
Conclusion: Our findings indicate that Portulaca Oleracea extract can reduce behavioral symptoms of neuropathic and acute pain.
Keywords: Portulaca oleracea, acute pain, chronic constriction injury (CCI), neuropathic pain

P-397

Ventra tegmental area microinjected-SKF38393 increases regular chow intake in 18 hours food deprived rats

Farzaneh. Saebi Rad[1] , Abbas. Haghparast[2] , Afsaneh. Eliassi [1,3]

1. Department of Physiology, Medical School, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: There are a limited number of central dopaminergic pathways that arise from VTA which are involved in food rewards. Of particular interest for feeding behavior is if VTA D1 dopamine receptors are involved in homeostatic regulation of food intake. Current study was undertaken to investigate the effect of SKF38393 (D1 receptor agonist) on regular chow.
Materials and Methods; Male Wistar rats (220-250 g) were implanted with guide cannula directed to the VTA. Stereotaxic coordinates were, lateral: 1 mm from midline; dorsoventral: 8 mm from skull surface; anteroposterior:

4.8 mm from the bregma. Rats were fed laboratory standard chow and water ad libitum and deprived of food, but not water, for 18 h prior to the execution of the planned studies. After drug injection, the amount of food and crumbs were measured to calculate the amount consumed by the rats in each cage over a 3 h period. Feeding trials normally occurred from Saturday to Wednesday between 9:00 and 12:00 h. All drugs were administered in 0.9% saline.
Results: IntraVTA injection of SKF38393 (0.75, 1.25, 2.5 but not 5 µg) increased feeding in a dose and time-dependent manner. This effect did not affect by SCH23390, 0.005 µg (D1 antagonist). Analysis of the locomotor activity results revealed that VTA microinjection of SKF38393 (2.5 µg) had not effects on locomotor activity.
Conclusion: We suggest that VTA -microinjected SKF38393 increase standard chow. This stimulatory effect is probably mediated through serotonergic neurons but not D1 dopamine receptors.
Keywords: VTA, SKF, D1 receptors

P-398

The effects of policosanol on learning and memory disturbance and oxidative stress in male rats with Alzheimer's disease induced by β-amyloid (1-40)

Samaneh Safari[1'2], Naser Mirazi[1], Alireza komaki[2], Nesa Ahmadi[1'2]

1. Department of Biology, faculty of basic science, Bu-Ali Sina University, Hamedan, Iran.
2. Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran.

Background and Objective: Alzheimer's disease (AD) is a neurodegenerative disorder that recognized with progressive cognitive function failure which determined by accumulation of beta amyloid (Aβ) in extracellular space. Aβ stimulate kinds of active oxygene and causes oxidative stresses and apoptosis. Policosanole (PCO) is a reducing lipids complement has antioxidant and anti inflammatory activity effects. In this study the PCO effects on memory and learning were investigated in AD rats were induced with in AD rats.
Materials and Methods: In this study 60 male Wistar rats were used. The animals were divided in 6 groups (n=10): Control, Sham (Aβ Solvent, intraventricular microinjection), AD (Aβ intraventicular microinjection), Acacia Gum (50mg/kg, 8 weeks gavaged), PCO (50mg/kg, 8 weeks gavaged) and AD with PCO (50mg/kg, 8 weeks gavaged). Standard passive avoidance test and morrise water maze Test were used to evaluate retention and recall evaluation of memory and learning. After behavioral evaluation, serum MDA was evaluation using specified kit. Data were analyzed by SPSS. Statistical significance was set at $p \leq 0.05$.
Results: The results of this study showed that Aβ intraventricular injection caused reduces spatial memory and passive avoidance. PCO causes recovery spatial memory and passive avoidance. In addition, serum lipid peroxidation (MDA level) in AD group was significantly greater versus PCO group.
Conclusion: Our results demonstrate that PCO has neuroprotective effects and can protect of memory with hypo lipidemic and antioxidan activity.
Keywords: Alzheimer's disease, Policosanole, Learning and memory, MDA, Rat

P-399

The effect of hydro-alcoholic extract of fumaria officinalis leaf on pain and seizure by pentylentetrazole-induced mice

Fatemeh Taleahmad[1*], Fatemeh Nabi[1], Mahdi Alizadeh[1], Fariba Ansari[1], Zahra Kiasalari[2], Mohsen Khalili[2]

1. School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective: There are many reports for mutual mechanisms for seizure and pain alleviation. Also with respect to the herbal medicine recommendation in new medicine, in this study we used the extract of an important candidate fumaria officinal for relief of pain and seizure in mice.
Materials and Methods: In two series of experiments 5 groups i.e control, positive control and three doses of extract (200,600 and 800 mg/kg) were conducted to pain and seizure analysis. For assessment the pain formalin(%2.5,50µl) was injected to hind paw, and the licking duration and frequency were measured for a period of 45 min. However,

we used PTZ(100 mg/kg) for induction of the seizure.The initiation time (s) for myoclonus, clonus and the tonus were considered for seizure command.
Result: Our results indicated that the extract in three doses (200,600 and 800 mg/kg) can reduced the formalin acute and chronic pain. Also the start time for seizure behaviors i.e myoclonus, clonus and seizures could elevated markedly in lower doses of the extract (200 and 600 mg/kg)
Conclusion: In addition,treatment of the mice with hydro-alcoholic extract of fumaria officinalis leaf could significantly reduce the pain and increase the initiation time of the seizure.
Keywords: Pain, Seizure, Fumaria officinalis leaf, Mice

P-400

The effect of extraction of Cyperus rotundus rhizome on elevated platform stress-induced memory retrieval impairment in adult male mice

Taheri Darush, Khajehpour Lotfollah, Seyyednejad seyyed Mansour

Departement of Biology, Faculty of Science, Shahid Chamran University of Ahvaz, Ahvaz, Iran

Background and Objective: Stressful conditions have various biological effects on humans and animals, such as memory deficits. Cyperus rotundus rhizome has some biological effects, such as memory improvement. In this study, we evaluated the effect of extraction of Cyperus rotundus rhizome on impairment of memory retrieval induced by elevated platform stress.
Materials and Methods: In this experimental research, 42 adult male mice (6 groups) were used. Memory was assessed by step through instrument, as passive avoidance model, in two phases (training in first day and testing in second day) and Step through latencies was recorded for retrieval evaluation. The animal received extract of Cyperus rotundus rhizome (20, 50mg/kg) by oral gavage for 7 days, before retrieval testing day. Animals were placed on the platform for 15 minutes, to induction of stress, before the test phase.
Results: The results of this study shows that stress (15 min., pretest.), reduced memory retrieval. The oral administration of rhizomes extract of Cyperus rotundus (20, 50 mg/kg, daily), seven days before training, reversed the effect of stress on retrieval. However these doses of Cyperus rotundus alone had no effect on memory retrieval in unstressed animal.
Conclusion: According to the findings of this study, it seems that the rhizomes extract of Cyperus rotundus protects the memory retrieval against the Negative effects of pretest stress induced by elevated platform.
Key words: Cyperus rotundus, Elevated platform, memory retrieval, stress

P-401

Protective effects of vitamin K2 against neurodegeneration

Zahra Tayarani-Najaran

Medical Toxicology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and Objective: Vitamin K (Vit K2) is a fat-soluble vitamin, which is naturally present in two forms: Phylogloquinone (Vit K1) and manaquinon (vit K2). Neuroprotection using compounds with dual functions of anti-apoptotic and antioxidant effects fight against neurodegeneration. Vitamin K2 plays as a cofactor in many biochemical pathways, including sphingolipid synthesis in the nervous system which is involved in many cellular events, including proliferation, differentiation, cellular communication and alteration. The presence of vit K2 has been identified in all tissues of the body, however few studies have evaluated the influence of vit K on behavior and cognition in the nervous system. Materials and Methods: Here we have reviewed also investigated the protective effects of vitamin K2 in in vitro model of Alzheimer and Parkinson's diseases. The protective effects of vitamin K2 against beta-amyloid or 6-OHDA-induced apoptosis in PC12 cells, ROS level, glutathione level, sub G1, and detecting apoptotic protein expression level (Bax, PARP, MAPK, caspase 3) were measured. Results: The results showed that beta-amyloid and 6-OHDA significantly decreased cell viability, glutathione and apoptosis, and

increased ROS, in PC12 cells, while the pretreatment with vitamin K2 significantly decreased the cell death. Conclusion: Generally, the results may present a new insight about the potential protective action of vitamin K2 against the progression of neurodegeneration. Further studies may warrant the use of vitamin K2 as an antioxidant and anti-apoptotic agent in slowing nerve injury in neurodegenerative disease.
Keywords: Alzheimer's disease; beta-amyloid; hydrogen peroxide; vitamin K2; Parkinson's diseases

P-402

Quetiapine reverses paclitaxel-induced neuropathic pain in mice: Role of alpha2- adrenergic receptors

Alireza Abed[1], Mohammad Javad Khoshnoud[2], Mehdi Taghian[3],Mahbubeh Aliasgharzadeh[4], and Azam Mesdaghinia[1]

1. Physiology Research Center, Kashan University of Medical Sciences, Kashan, Iran
2. Department of Toxicology and Pharmacology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
3. Department of Oral and Maxillofacial Surgery, School of Dentistry, Mazandaran University of Medical Science, Sari, Iran
4. School of Pharmacy, International Branch, Shiraz University of Medical Sciences, Shiraz, Iran

Background and Objective:Paclitaxel-induced peripheral neuropathy is a common adverse effect of cancer chemo - therapy. This neuropathy has a profound impact on quality of life and patient's survival. Preventing and treating paclitaxel-induced peripheral neuropathy is a major concern. First- and second-generation antipsychotics have shown analgesic effects both in humans and animals. Quetiapine is a novel atypical antipsychotic with low propensity to induce extrapyramidal or hyperprolactinemia side effects. The present study was designed to investigate the effects of quetiapine on the development and expression of neuropathic pain induced by paclitaxel in mice and the role of α2-adrenoceptors on its antinociception.
Materials and Methods:Paclitaxel (2 mg/kg IP) was injected for five consecutive days which resulted in thermal hyperalgesia and mechanical and cold allodynia.
Results:Early administration of quetiapine from the 1st day until the 5th day (5, 10, and 15 mg/kg PO) did not affect thermal, mechanical, and cold stimuli and could not prevent the development of neuropathic pain. In contrast, when quetiapine (10 and 15 mg/kg PO) administration was started on the 6th day after the first paclitaxel injections, once the model had been established, and given daily until the 10th day, heat hyperalgesia and mechanical and cold allodynia were significantly attenuated. Also, the effect of quetiapine on heat hyperalgesia was reversed by pretreatment with yohimbine, as an alpha-2 adrenergic receptor antagonist.
Conclusion:These results indicate that quetiapine, when administered after nerve injury can reverse the expression of neuropathic pain. Also, we conclude that α2-adrenoceptors participate in the antinociceptive effects of quetiapine.
Keywords: Hyperalgesia, Mice, Neuropathic pain, Paclitaxel, Quetiapine, Yohimbine

P-403

Gallic Acid Nano phytosome Suppresses Excessive Self-Grooming in Autism-Like Rat Models

Hanieh Abbas Alipour [1*], Akbar Hajizadeh Moghaddam[1], ,vahid hasantabar [2]

1. Department of Biology, Faculty of Basic Sciences, University of Mazandaran, Babolsar, Iran.
2. Faculty of chemestry, University of Mazandaran, Babolsar, Iran

Background and Objective: Gallic acid is known as a potent antioxidant active compound of the medicinal plant such as sumac (Rhus coriaria L.). However, low solubility and permeability through the gut wall limited development of gallic acid as a therapeutic agent. Nano-phytosome is one of the lipid based nano-carrier and fast growing attractive way of delivering botanical based nutraceuticals. Autism Spectrum Disorder is associated with a wide range of characteristics including repetitive behaviors and social deficit. This research was therefore aimed the neuroprotective effects of gallic acid nano phytosome on repetitive self-grooming in prenatal valproic acid-induced rat model of autism.
Materials and Methods:Valproic acid (600 mg/kg) was administered intraperitoneally to the pregnant rat on gestational day 12.5. Prenatal valproic acid-exposed rat were divided into 2 groups on postnatal day 21. gallic acid

and its nano phytosome (20 mg/kg) was given to the experimental group while distilled water was given to the control group for 4 weeks.
Results: Utilizing the Grooming test, we found that gallic acid nano phytosome prevented repetitive behaviors in offspring of VPA-treated rats. The data suggested that gallic acid nano phytosome may play a neuroprotective role and ameliorates autistic-like behaviors.
Conclusion:Taken together, the results demonstrate that gallic acid nano phytosome could be a novel and promising therapeutic strategy in autism spectrum disorders.
Keywords: Gallic acid nano phytosome; Valproic acid; grooming behavior; rat

P-404

Evaluating the effect of Naringenin on Perphenazine induced catatonia in rats

Gholamreza Houshmand[1], Amirali Arimi[1], Sara Assadpour[2], Atefeh Arab Firozjae[1], Mitra Mahmoudi[1], Bahar Azadmanesh[1]

1. Department of Pharmacology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
2. Molecular and Cell biology Research Center , Faculty of Medicine , Mazandaran University of Medical Sciences , Sari , Iran.

Background and Objective:Parkinson's disease is the most common progressive neurodegenerative disorder. It characterized by resting vibration,rigidity or increased resistance to passive movements.Naringenin (4',5,7-trihydroxyflavone)flavonoids are edible in fruits and vegetables and have various biological effects, such as neuroprotective effects,anti-inflammatory and antioxidant activity.Considering the studies done on naringenin and the reports on the various protective effects of naringenin in neural systems, we decided to investigate the possible effectiveness of naringenin in reducing muscle tone symptoms.
Materials and Methods: In this study, The rats were divided into 5 groups of 8. First group (Negative control group) received 5 ml/kg normal saline and 30 minutes later, perfenazine received 5 mg / kg via intraperitoneal(IP) injection. The second group (positive control): administration of bromocriptine at a dose of 30 mg / kg IP injection and 30 minutes after IP injection of perfenazine at a dose of 5 mg/kg.Group 3,4,5: Administration of naringenin at a doses of 100,200,400 mg/kg IP and 30 minutes after injection of perfenazine with a dose of 5 mg/kg. Finally, the animals of each group from the point of view of muscle stiffness at 20, 40, 60, 90, 120, 180, 240, minutes after injection of perfenazine were measured by Moruporgo test.
Results:the study showed that Increasing the dose of naringenin to 200 mg/kg resulted in an increase in the effect of naringenin on the prevention of catatonia.Through the effects of naringenin in 200 and 400 mg/kg are nearly identical, the best dose is 200 mg / kg.
Conclusion: naringenin is effective in preventing pseudoparcinsonism disease caused by the use of perfenazine in rats.
Keywords: Parkinson's disease, Naringenin, catatonia, Perphenazine

P-405

Spatial learning paradigm can increase post-stress total time of REM sleep in immobilized rats

Fatemeh Erfani Sharifian[1], Farideh Bahrami[1,2], Zahra Bahari[1,2]

1. Department of Physiology and Medical Physics, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran.
2. Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

Background: Stress can induce sleep disturbance and has been claimed to be one of the triggering factors of emotional-related sleep disorders, including insomnia. It seems that rapid eye movement stage of sleep is the state most altered with stressful conditions. However, there are conflicting studies in this regard due to the differences in the various models of stress. It seems that environmental factors such as learning constitutes profound physiological changes in sleep pattern to restore homeostasis of sleep. Therefore, we examined the interaction of prior stress and learning (spatial memory) on total post-stress REM sleep, NREM sleep and also waking time in rats. Material and methods: The sleep signals recorded for each rat during 2 hours for 3 consecutive days. Immediately after recording of sleep and awakening signals, animal subjected to immobilization stress for 2 hours in each day. Then, after induction of stress, post-stress and post-learning (spatial memory) sleep signals recorded for each animal during 2 hours. Results: Immobilization stress resulted in significant post-stress decrease in total REM sleep time. However, total time of NREM markedly increased following stress. However, learning task result in significantly increase in

post-learning REM time. Moreover, total time of NREM did not change markedly following learning process. Interestingly, learning process significantly decreased total time of awakening as compared with pre-learning condition. Additionally, learning significantly increased post-stress total REM time. However, learning process did not any significant change in the post-stress total time of NREM and awakening. Conclusion: Our data suggested that immobilization stress leads to post-stress decrease in total REM sleep time. However, learning process increased post-stress total REM time. It seems that learning has been able to overcome on inhibitory effects of stress on REM sleep.
Key words: REM Sleep, EEG, Immobilization Stress, Learning, Rat

P-406

Reinstatement of morphine seeking behavior by the forced swim stress and drug-priming: role of orexin receptor within the ventral tegmental area

Ronak Azizbeigi[1], Abbas Haghparast [2]

1. Department of Physiology, Faculty of Veterinary Medicine , Sanandaj Branch, Islamic Azad University, Sanandaj, Iran
2. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences,

Background and Objective: The orexinergic system has an essential role in the induction of reward-related behaviors to several drugs of abuse. Highly relevant to this function, orexin-containing neurons from the lateral hypothalamus project densely to the ventral tegmental area (VTA), implicated in motivation and reward. The present study was designed to determine the effect of administration of TCS-OX2- 29 as a selective orexin-2 receptor (OX2R) antagonist, into the VTA on the drug-priming and Forced-Swim Stress (FSS)-induced reinstatement of morphine.Materials and Methods: Adult male Wistar rats weighing 220-250 g were entered in a conditioned place preference (CPP) paradigm. The CPP was induced by injecting morphine (5mg/kg, S.C for 3 days) and lasted for eight free morphine days, the reinstatement was induced by administration of effective priming dose of morphine (1mg/kg, sc). CPP score and locomotor activity of animals were recorded by Ethovision software. Animals received bilateral microinjection of different doses of TCS-OX2- 29 (0.3, 1, 3 and10 µg/0.3µl/side) and were subsequently tested for reinstatement.
Results: Results indicated that administration of TCS-OX2-29 in the VTA significantly suppressed drug priming-induced reinstatement dose –dependently. Furthermore, intra-VTA administration of TCS-OX2-29 could inhibit effect of FSS on reinstatement of morphine.
Conclusion: Our finding suggested that orexin-2 receptors in the VTA may be involved in stress and drug-priming-induced reinstatement of morphine–seeking behaviors.
Keywords: Reinstatement, Forced Swim Stress, orexin receptor, ventral tegmental area, Conditioned Place Preference

P-407

Central injection of neuropeptide Y modulates sexual behavior in male rats: interaction with GnRH and KNDy secreting neurons

Vahid Azizi[1], Shahrbanoo Oryan[2], Homayuon Khazali[1], Abdolkarim Hosseini[1]

1. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran.
2. Department of Animal Biology, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran.

Background and Objective: Neuropeptide Y (NPY) is regarded as a key regulator of the hypothalamic-pituitary-gonadal (HPG) axis. In addition, kisspeptin (encode by Kiss1 gene), neurokinin B (encode by Tac3 gene) and dynorphin (encode by Pdyn gene) (known as KNDy secreting neurons) are powerful upstream regulators of gonadotropin-releasing hormone (GnRH) neuron in the hypothalamus. The present study investigates the impacts of the intracerebroventricular (ICV) injection of NPY and BIBP3226 (NPY receptor antagonist (NPYRA)) on male sexual behavior.
Materials and Methods: Fifty-six rats were divided into 4 groups intracerebroventricularly received 3µl vehicle, NPY (2.3 nmol), BIBP3226 (7.8 nmol) and BIBP3226 + NPY in order to study the sexual behavior, and the other rats received the same treatments for studying gene expression. In order to see whether NPY signals can be relayed

through the pathway of kisspeptin/neurokinin B/dynorphin, the gene expression of these peptides as well as Gnrh1 gene in the hypothalamus were measured. Data were analyzed using SPSS.
Results: The ICV injection of NPY decreased the latencies and increased the frequencies of sexual parameters of the male rats in a significant way. In contrast, NPYRA antagonized the stimulative effects of NPY. Moreover, data from real-time PCR indicated that injection of NPY significantly increased the gene expression of Gnrh1, Kiss1 and Tac3 and decreased the Pdyn while treatment with NPYRA controlled the modulative impacts of NPY.
Conclusion: NPY can exert its impacts on the sexual behavior of male rats via modulation of the KNDy secreting neurons as an interneural pathway to GnRH neurons.
Keywords: Neuropeptide Y, BIBP3226, Kisspeptin, Neurokinin B, Dynorphin, Sexual behavior

P-408

Carvacrol attenuates cytotoxicity induced by amyloid β25-35 via activating protein kinase C and inhibiting oxidative stress in PC12 Cells

Zahra azizi, Mona Salimi, Samira Choopani, Nasser Naghdi

Department of Physiology and Pharmacology, Pasteur Institute of Iran, Tehran, Iran.

Background and objective: Despite more than a century of intensive research on AD, few effective treatment options have been developed. Nowadays, several medicinal plants and their constituents have been suggested as possible treatments for AD. In this study, the neuroprotective effect of carvacrol against Aβ25-35-induced cytotoxicity was evaluated, and the potential mechanisms were determined. In this regards, we investigated whether carvacrol could inhibit cytotoxicity and oxidative damage caused by Aβ through antioxidant activity and stimulation of protein kinase C (PKC).
Matherials and Methods: PC12 Cells were pretreated with Aβ25-35 for 2 h followed by being incubated with carvacrol for additional 48 h. Cell viability was measured by MTT method. Flurospectrophotometer was employed to observe intracellular reactive oxygen species (ROS) production. PKC activity was analyzed using ELISA.
Results: Our results indicated that, carvacrol could protect PC12 cells against Aβ25-35-induced cytotoxicity. Furthermore, the results demonstrated that, Aβ25-35 induces intracellular ROS production, while carvacrol could reverse this effect. Moreover, carvacrol could elevate PKC activity similar to Bryostatin-1. So, we mainly reported two points: first, carvacrol could reduce ROS levels in Aβ-treated PC12 cells, and second it might act as a PKC activator.
Conclusion: This study provided the evidence regarding the protective effect of carvacrol against Aβ25–35-induced cytotoxicity in PC12 cells. Also, the results suggested that, neuroprotective effects of this compound against Aβ25-35 might be through attenuating oxidative damage and increasing the activity of PKC as a memory-related protein. Thus, carvacrol was found to have therapeutic potential in preventing or modulating AD.
Keywords: Alzheimer's disease (AD), amyloid β (Aβ), carvacrol, reactive oxygen species (ROS), protein kinase C (PKC), PC12 cells

P-409

Selective alterations in purinergic P2X7 receptor expression during methamphetamine-induced addiction and withdrawal syndrome in the hippocampus of male rats

Azizi Hana, Hatami Homeira*, Kholghi Akram, Shima Roshani

Department of Animal Biology, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.

Background and Objective: The ATP-sensitive P2 purinoceptors are implicated in microglia activation. The receptor P2X7 (P2X7R), has been implicated in the pathophysiology of medical conditions of central nervous system. Methamphetamine (METH) exposure is known to promote microglial activation and production of proinflammatory cytokines and chemokines. Since psychostimulants evoked synaptic plasticity and long-term memories in neurons, so the aim of this study was to investigate the alterations of P2X7R during methamphetamine-induced addiction and withdrawal syndrome in the hippocampus of male rats.
Material and Methods: 28 male Wistar rats were randomly assigned into four experimental groups (n=7): Control, Saline, Methamphetamine (10 mg/kg, i.p. for 5 days) and Spontaneous methamphetamine withdrawal syndrome (72 hour later). Hippocampus tissue were assayed for the expression of P2X7R gene using RT- PCR.

Results: Chronic administration of methamphetamine to control group decreased the P2X7R gene expression in comparison to control group ($p<0.001$). In Spontaneous methamphetamine withdrawal syndrome group, the level of P2X7R gene expression did not changed in comparison to control group, but in comparison to methamphetamine group increased and approached to the level of control group.
Conclusion: It is known that P2X7R plays an important role in the underlying mechanism of METH-induced microglial activation. Therefor it seems, the purinergic system may be a new, valuable tool in searching for a new strategy of management of methamphetamine dependence.
Keywords: Purinergic P2X7 receptor, Methamphetamine, Hippocampus

P-410

The conditioned medium of mesenchymal stem cells derived from human embryonic stem cells stimulates angiogenesis after ischemic stroke in rats

Afsaneh Asgari Taei[1], Maryam Farahmandfar[1], Gholamreza Hassanzadeh[2], Leila Dargahi[3], Sanaz Nasoohi[4], Mehdi Kadivar[5]

1. Department of Neuroscience and Addiction Studies, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Anatomy, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
3. Neurobiology research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5. Department of Biochemistry, Pasteur Institute of Iran, Tehran, Iran

Background and Objective: Mesenchymal stem cells (MSCs) therapy shows considerable promise for ischemic stroke. However, various adverse effects and low survival rate of the transplanted cells within the host brain are unsolved obstacles. The paracrine mediated actions have been proposed to explain the beneficial effects of MSC transplantation after ischemia. Here, we examined the effect of conditioned medium (CM) of MSCs derived from human embryonic stem cells on neurological function and angiogenesis marker in a rat model of ischemic stroke.
Materials and Methods: Focal cerebral ischemia was produced by middle cerebral artery occlusion (MCAO) and reperfusion. Injections of the CM or DMEM (5µl) were respectively done into the left lateral ventricle of the treatment and control animals three times at 1, 24 and 48 hours after MCAO. In another set of treatments, injection of CM was performed at a single dose, one hour after MCAO. Behavioral tests were performed on days 1, 3 and 7 after the injury. The mRNA levels of CD31 as a marker of angiogenesis in striatum and cortex was assessed using quantitative PCR at day 7 of experiments.
Results: Ischemic stroke is accompanied with increased levels of CD31 in striatum and cortex. Treatment with CM improved neurological function and more prominent at repeated doses, significantly increased the mRNA levels of angiogenesis marker.
Conclusion: Our results suggest that CM of mesenchymal stem cells improves functional recovery after ischemic stroke and this effect is likely mediated partly through promoting angiogenesis.
Keywords: Mesenchymal stem cells, Conditioned medium, Ischemic stroke, Angiogenesis

P-411

Environmental enrichment treatment restore impaired hippocampal synaptic plasticity induced by prenatal noise stress

Fatemeh Aghighi, Sayyed Alireza Talaei, Mahmoud Salami

Physiology Research Center, Institute for basic sciences, Kashan University of Medical Sciences, Kashan, I.R. Iran.

Background and Objective: Hippocampal synaptic plasticity, known to be sensitive to stress, can be changed by stress, especially prenatal stress. Environmental enrichment which is defined as a combination of “complex inanimate objects and social stimulation" counteracts cognitive deficits induced by early life stress in animals. Whether environmental enrichment in early postnatal periods can cause a recovery from this deficit is unclear.
Materials and Methods: Offspring were divided into four groups: control group (CON), control enriched animals (EE), stressed animals (PS) and stressed animals introduced to enrichment (SE). Prenatal stress was evoked by noise stress for 2 hrs/day during the last week of the pregnancy. After weaning at postnatal day 22, experimental offspring

were given the environmental enrichment or standard housing condition for one month. The field excitatory post-synaptic potentials (fEPSPs) were recorded from the CA1 area of hippocampus for 30 min. Then, for induction of long-term potentiation (LTP), the tetanus was applied to the Schaffer collaterals and the field potentials were pooled for 120 min post-tetanus.
Results: Prenatal noise stress decreased amplitude of the basic responses and impaired LTP of the hippocampal CA1 region compared to the CON group. However, postnatal environmental enrichment significantly improved deficits induced by prenatal noise stress.
Conclusion: Environmental enrichment treatment on early postnatal periods may be one potentially important target for therapeutic interventions to restore the deficit of synaptic plasticity induced by prenatal stress.
Keywords: Prenatal noise stress, Environmental enrichment, Long-term potentiation; Rats

P-412

Pre-/post-training morphine increases rat hippocampal miR33 expression

Behrang Alani[1*], Abolfazl Ardjmand[2], Sadegh Moradi[2]

1. Department of Applied Cell Sciences, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran
2. Physiology Research Center, Institute for Basic Science, Kashan University of Medical Sciences, Kashan, Iran

The importance of non-coding RNA involved in biological processes, such as learning and memory, has become prominent in recent years. Micro RNAs (miRs) represent a class of small regulatory non-coding RNAs that mediate gene silencing by identifying specific sequences in the target messenger RNAs (mRNAs). In addition, morphine administration at different times relative to training or testing has different effects on animals learning and memory. The aim of the current study was to investigate the expression of miR33 following pre-/post-training administration of morphine in the rat. We used qRT-PCR technique to determine the expression of miR33 on hippocampal samples. We used pre-/post-training administration of different doses of morphine (2.5, 5, or 7.5 mg/kg/ip) in an inhibitory avoidance model of memory. The relative expression of miR33 in different morphine-treated groups was compared with the sham and control groups. The comparison of relative expression of miR33 between sham and control groups showed no difference ($p>0.05$). However, the comparison of relative expression of miR33 between the morphine-treated groups and the control showed a significant difference ($p<0.05$).The pre-/post-training administration of different doses of morphine in the rat alters the relative expression of hippocampal miR33.
Keywords: miR33, Learning, Memory, Rat, PCR

P-413

Overexpression of Protein Kinase Mzeta in the hippocampal dentate gyrus maintains long term plasticity against entorhinal amyloidopathy in freely moving rats

Shayan Aliakbari[1], Hamid Gholami Pourbadie[*1], Niloufar amini[2], Mohammad Sayyah[1], Fereshteh Motamedi[3], Naser Naghdi[1].

1. Department of Physiology and Pharmacology, Pasteur Institute of Iran, Tehran, Iran
2. Department of Biotechnology Petrolum and chemical engineering. Sharif university of Iran, Tehran, Iran
3. Neuroscience Research Center, Shahid Beheshti University of Medical Science, Tehran, Iran.

Introduction: Entorhinal cortex (EC) is one of the first cerebral regions affected in the early phase of Alzheimer's disease (AD). Soluble amyloid beta (Aβ) causes aberrant synaptic transmission in AD models. Protein Kinase Mζ (PKMζ) is involved in long lasting synaptic plasticity.

Materials and methods: Aβ 1-42 or vehicle was bilaterally microinjected into the EC of the male Wistar rats and then, two stainless steel electrodes were implanted into the perforant pathway and DG. They were fixed to the skull after obtaining suitable field potential responses in the DG. After one week, 2µl of lentiviral vector was injected into the DG, and one week later, LTP was induced in freely moving animals and the LTP persistence was monitored in 90 min, 24 h and 7 days.
Results: in the control group, DG-LTP exhibited the largest change at early time (90 min) and remained almost stable until 7 days. In the Aβ treated group, it was smaller initially than the control group, and faded within 3 days. However, induction of PKMζ expression in the DG resulted in facilitation of LTP with the greatest change at 24 h, and LTP robustly remained stable until 7 days. This potentiated effect was reversed by zeta inhibitory peptide (ZIP), a specific inhibitor of PKMζ.
Conclusion: PKMζ dependent pathway could be a potential therapeutic target to combat synaptic failure in the early phase of AD.
Keywords: long term potentiation, Alzheimer's disease, protein kinase Mzeta, dentate gyrus, freely moving

P-414

The effect of hydro-alcoholic extract of Mentha pulegium on pain and seizure induced by pentylenetetrazol in male mice

Mahdi Alizadeh[1*],Fatemeh Taleahmad[1],Fatemeh Nabi[1], Fariba Ansari[1],Zahra Kiasalari[2], Mohsen Khalili[2*]

1. School of Medicine, Shahed University, Tehran, Iran
2. Neurophysiology Research Center, Shahed University, Tehran, Iran

Background and Objective: In recent years, the use of medicinal plants has increased instead of chemical drugs due to fewer side effects and more diverse compounds. The aim of this study was to witness the analgesic and anticonvulsant effect of Puneh plant.
Materials and Methods: In this study, we used 40 male mice, and the PTZ test for evaluating the anticonvulsant effects and formalin and tail immersion tests in hot water to determine the anti-nociceptive effect of the plant were used.
Results: Hydro-alcoholic extracts of Pune leaf significantly decreased pain in the acute and chronic phase in the formalin test, which had the most analgesic effect in 800 mg /kg and all doses were effective in acute pain. Also, in the PTZ test, the anticonvulsant effect in doses of 200 and 600 mg /kg was shown. However, In tail immersion test, the acute pain was unaffected
Conclusion: The results of this study indicated that hydro- alcoholic extract of Pune leaf can reduce chronic and acute pain and also seizure onset time.
Key words: pain, seizure, Ant nociceptive, Mentha pulegium, Mice

P-415

Effect of aerobic exercise on tolerance to morphine usage and pain modulation

Safoura Alizade[1], Hojatollah Alaei [2], Mehdi Kargarfard [3]

1. Faculty of Physical Education and Sports Science, University of Isfahan, Isfahan, Iran
2. School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
3. Faculty of Physical Education and Sports Science, University of Isfahan, Isfahan, Iran

Background and Objective: Pain is one of the important processes controlled by various mechanisms in the central nervous system. Morphine applies analgesic effects through binding to opioid receptors.The analgesic effects of exercise are due to the release of endogenous opioids. Therefore, the present study investigated the effect of aerobic exercise on tolerance to morphine usage and pain modulation.
Materials and Methods: In this research Wistar male rats weighting 250 ± 300 were selected and divided into 4 groups: (1) saline group (S), (2) morphine group (M), (3) saline + exercise (S + E), and (4) morphine + exercise

group (M + E). Exercise groups ran on the treadmill apparatus during four weeks. Three doses of morphine (10, 20, 40 mg / kg in 9 days) were injected interpritoneally. The tail-flick and hot-plate tests were used for pain assessment and then the symptoms of addiction were evaluated.
Results: No significant differences (P > 0.05) were observed among the groups with respect to the anti-nociceptive effect in the tail flick test. but, the morphine + exercise exhibited lowered pain sensitivity as evidenced to have reduced morphine use in the hot plate test. Nearly all the signs exhibited significantly fewer occurrences in the morphine + exercise group as compared with the morphine group.
Conclusion: The exercise might be suggested to reduce using of morphine and modulate pain probably through the release of endogenous opioid.
Keywords: Exercise, morphine, tail-flick, hot-plate, pain, rat

P-416

Selegiline induces adipose tissue-derived stem cells into neuron-like cells through MAPK signaling

Maedeh Amalavar[1], Hadi Feizi[1], Mohsen Alipour[1], Alireza Abdanipour[2]

1. Department of Physiology, Faculty of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran.
2. Department of Anatomical Sciences, Faculty of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran.

Background and Objective: Adipose-derived stem cells (ADSCs) are one of the most well-known and accessible sources of stem cells that can be used for the treatment of neurodegenerative diseases. On the other hand, previous studies have suggested that selegiline, as an irreversible inhibitor of monoamine oxidase, affects stem cells' differentiation into neurons. But the real mechanism of this effect is not clear. This study was conducted to investigate the involvement in Phosphatidylinositol-bisphosphate 3-kinase (PI3K) and mitogen-activated protein kinase (MAPK) pathways in ADSCs differentiation to neuron-like cells using selegiline as inducer.
Materials and Methods: ADSCs were isolated for male rats then cultured in DMEM. ADSCs were treated with selegiline (10-7 M) for 24hrs. Real-time PCR for nestin and neurofilament 68 (NF-68) was performed from control (untreated ADSCs), AD-S (ADSCs treated with 10-7M selegiline), PD (ADSCs treated with 10 µM PD98059 as inhibitor of MAPK, then 10-7 M selegiline), LY (ADSCs treated with 10 µM LY294002 as inhibitor of PI3K, then 10-7 M selegiline), CO-inhibition (ADSCs treated with 10 µM LY294002 plus 10 µM PD98059, then 10-7 M selegiline).
Results: Morphologically, ADSCs have been changed into neuron-like cells. Nestin and NF-68 genes have been overexpressed in the selegiline-treated ADSCs. MAPK inhibition by PD98059 significantly down-regulated the selegiline-induced overexpression of nestin and NF-68 ($p<0.05$).
Conclusion: According to the results, selegiline can induce the gene expression of neural stem cell biomarkers in ADSCs through MAPK pathway activating and so differentiating them into neuron-like cells.
Keywords: Selegiline, Adipose-derived stem cells, PI3K, MAPK

P-417

Recovery from stress-induced depression is impaired in aging possibly by altered expression levels of mir-101b, glutamate transporter SLC1A1 (EAAT3), and Rac1 in the prefrontal cortex of rat models

Arshad Ghaffari-Nasab[1,2], Gonja Javani[3], Hamed Abdollahpour Ranjbar[4]

1. Students' Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
2. Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran.
3. Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
4. Department of psychology, Kharazmi University of Tehran, Tehran, Iran

Background and Objective: Brain aging is associated with a decline in synaptic plasticity, which might contribute to impaired recovery from stress-induced depression. MicroRNA 101b (miR-101b) and its target genes, SLC1A1 and Rac1, are thought to contribute to synaptic plasticity. Therefore, in this study, to introduce a mechanism which

might be involved in impaired recovery from depression during aging, we were interested in comparing expression levels of miR101b, SLC1A1, and Rac1 in the prefrontal cortex (PFC) of young and aged animals 6 weeks after the induction of depression.
Materials and Methods: Twenty-four young, and 24 aged rats were classified into 4 groups; control young, depressed young, control aged, and depressed aged. Depression rat models were given ordinary daily care for six weeks as a recovery period. Sucrose preference, forced swim, and open field tests were done to evaluate depressive mood in 6 animals of each group. The brain tissue of rats that did not undergo behavioral tests in each group was dissected, and PFC used for detecting miR-101b, SLC1A1, and Rac1 by qPCR method.
Results: We found that anhedonia in young but not in aged depressed animals recovers after six weeks. Interestingly, miR-101b, SLC1A1, and Rac1 expression levels in PFC of aged depressed models were significantly recorded compared to aged controls.
Conclusion: Our study demonstrated that recovery from depression is deficient in aging which can be partly attributable to altered expression levels of miR-101b, SLC1A1, and Rac1 in PFC.
Keywords: Brain aging, Depression, miR-101b, SLC1A1, Rac1

P-418

The role of nitric oxide in anticonvulsant effect of aqueous extract of Hyssopus officinalis on seizures induced by pentylenetetrazole.

Masoumeh Gholami[1], Mehdi Sadegh[2]

1. Neuroscience Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.
2. Department of Physiology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran.

Background and Objective: We examined the effectiveness of Hyssopus officinalis (hyssop) aqueous extract on pentylenetetrazole (PTZ)-induced acute seizures and the hippocampus iNOS (inducible nitric oxide synthases) gene expression as a potential mediator of the effects.
Materials and Methods: Adult male Wistar rats were used. Tonic-clonic seizures were induced by intraperitoneal (i.p.) injection of PTZ (80 mg/kg) then behavioral profile during 30 min was characterized by stages defined as seizure scores. Hyssop extract were prepared and injected (i.p.) 15 minutes before the seizure induction at three doses 50, 100 and 200 mg/kg. Experimental groups were as below: (1) saline+PTZ (n=5); (2) Hyssop 50mg/kg+PTZ (n=10); (3) Hyssop 100mg/kg +PTZ (n=10); (4) Hyssop 200mg/kg +PTZ (n=8). Two hours after the experimental procedure, all animals were decapitated, brain was removed and right hippocampus was quickly dissected. After total RNA extraction and cDNA synthesis quantitative PCR were used for gene expression of iNOS.
Results: Our results showed significant increase ($p<0.05$) in latency to reach stages 5 and 6 of tonic-clonic seizure at dose 100 mg/kg hyssop extract. In addition, this dose caused significant increase in the gene expression of iNOS in the hippocampus.
Conclusion: It seems a 100mg/kg dose of hyssop extract might have anticonvulsant effects. However, these anticonvulsant effects might not occur through the iNOS gene expression.
Keywords: Anticonvulsive, Epilepsy, Aqueous extract, Nitric oxide, Hyssopus officinalis.

P-419

Effects of carvacrol and physical exercise on motor and memory impairments associated with Parkinson's disease

Ziba Rajaei[1], Leila Hamzehloei[2], Mohammad Ebrahim Rezvani[2]

1. Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Physiology, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Objective: Parkinson's disease (PD), a progressive neurological disorder, presents motor and non-motor impairments. Carvacrol is a naturally occurring phenolic monoterpene that is found in the essential oils of the Lamiaceae family. The present study was undertaken to investigate the effects of carvacrol and treadmill exercise on memory deficit, rotational behavior and oxidative stress biomarkers in a 6-OHDA-lesioned rat model of PD.
Methods: Wistar rats were treated with carvacrol at a dose of 25 mg/kg and/or ran on a treadmill for a week. Then, 6-OHDA was microinjected into medial forebrain bundle and treatments continued for 6 more weeks. Aversive memory, rotational behavior and oxidative stress biomarkers were assessed at the end of week 6.

Results: 6-OHDA-leasioned group showed a significant increase in rotational behavior and a decrease in step-through latency in passive avoidance test as compared with sham group. These behaviors were accompanied by increased lipid peroxidation levels and decreased total thiol concentration in the striatum and/or hippocampus of hemiparkinsonian rats. Moreover, treatment with carvacrol and exercise reduced rotational behavior and improved aversive memory deficit, which was accompanied by decreased lipid peroxidation levels and increased total thiol concentration in the striatum and/or hippocampus.
Conclusion: Treatment with carvacrol and treadmill exercise ameliorated motor and memory deficits by modulating oxidative stress in the striatum and hippocampus of hemiparkinsonian rats. Therefore, combination of carvacrol and treadmill exercise could be effective therapeutic tool for treatment of neurobehavioural deficits in PD patients.
Key words: Carvacrol, Treadmill exercise, Aversive memory, Motor behavior, Oxidative stress, Parkinson's disease.

P-420

Improvement of stress-induced amnesia by probiotic treatment in rats: Implication of GABA-A receptors

Kimia Alizadeh[1], Ameneh Rezayof[1], Hamid Moghimi[2], Sakineh Alijanpour[3]

1. Department of Animal Biology, School of Biology, College of Science, University of Tehran, Tehran, Iran
2. Department of Microbiology, School of Biology, College of Science, University of Tehran, Tehran
3. Department of Biology, Faculty of Science, Gonbad Kavous University, Gonbad Kavous, Iran.

Background and Objective: Brain structure and physiological activities can be modulated by stress signaling pathway and gut microbiota. There is a functional interaction between the gut-brain axis and cognitive functions under stress. Given the impact of stress on memory-related neurotransmitter systems, the aim of the present study was to examine the effect of probiotic treatment on stress-induced amnesia via investigating the role of GABA-A receptors.
Material and Methods: Male Wistar rats were isolated two weeks after birth and were fed with probiotic water (PW; a mixture of Lactobacillus brevis, Lactobacillus plantarum, and Bifidobacterium bifidum) or tap water (TW) for five weeks. Animals bilaterally cannulated in the lateral ventricles with a stereotaxic apparatus on 6th week. On the first day of 8th week, a step-through passive avoidance task was used to evaluate memory formation. Immediately after successful training, acute stress was induced by placing each animal on the elevated platform. 24 hours after training, the animals were tested to measure memory retrieval.
Results: 30 min exposure to acute stress decreased step-through latency in the passive avoidance task in TW animals, indicating stress-induced amnesia. Interestingly, feeding animals with PW for five weeks improved the impairing effect of acute stress on memory formation. Intracerebroventricular injection of muscimol, a GABA-A receptor agonist, inhibited the improving effect of probiotic on stress-induced amnesia but had no effect on stress-induced amnesia in TW animals.
Conclusion: Probiotics can be a good treatment for the impairing effects of acute stress on memory formation, presumably via modulating GABA neurotransmission.
Keywords: Memory; Acute stress; Probiotic water; GABA-A receptors; Rat(s)

P-421

Anti-aging Activities of Ceftriaxone in Mice Treated with D-galactose

Iman Fatemi[1], Elham Hakimizadeh[2], Jalal Hassanshahi[2], Ayat Kaeidi[2], Mohammad Allahtavakoli[2], Ali Shamsizadeh[2], Mohammad Reza Rahmani[2]

1. Research Center of Tropical and Infectious Diseases, Kerman University of Medical Sciences, Kerman, Iran.
2. Physiology-Pharmacology Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

Background and Objective: It has been shown that Ceftriaxone (Cef) has beneficial effects in Alzheimer disease. In the current study, the effect of Cef in a mice model of aging was investigated.

Materials and Methods: Forty male mice were randomly divided into four groups (10 mice in each group) as follows: Control (as healthy normal animals), D-galactose (DG) group (treated with 500 mg/kg/day DG for 6 weeks), and DG + Cef group (treated with DG plus Cef 200 mg/kg/day for 6 weeks). Anxiety, working memory and physical power were evaluated by the Elevated plus-maze (EPM) test, Y maze and swimming exhaustion test, respectively.
Results: Our results showed that Cef (200 mg/kg) decreased anxiety-like behaviors as well as increased in working memory and physical power in aging mice.
Conclusion: Based on our findings, Cef declines neurocognitive dysfunctions in the DG-induced model of aging possibly through its antioxidative properties.
Key words: Aging, Ceftriaxone, D-galactose, Oxidative stress, Mice.

P-422

Effect of cerebrolysin on memory impairment-induced by chronic alcohol consumption in rats: Role of oxidative stress and apoptosis

Fereshteh Farajdokht[1], Javad Mahmoudi[1], Saeed Sadigh-Eteghad[1], Ladan Vaghef[2]

1. Neurosciences Research Center, Tabriz University of medical Sciences, Tabriz, Iran.
2. Department of Psychology, Faculty of Education & Psychology, Azarbaijan Shahid Madani University, Tabriz, Iran.

Background and objective: Acute or chronic alcohol abuse has deleterious effects on the brain function such as cognitive performance. This study investigated the effect of cerebrolysin (CBL), a combination of neurotrophic factors, on the cognitive performance, oxidative stress status, and apoptosis-related proteins in chronic ethanol subjected rats.
Materials and Methods: The animals were divided into 5 groups as follows: Control, Ethanol + NS, Ethanol+ CBL 1, Ethanol + CBL 2.5, and Ethanol + CBL 5. Animals in the control group were administered saline and ethanol groups were received 4 g/kg ethanol for 30 days and then treated with normal saline or three doses of CBL (1, 2.5, and 5 ml/kg) for a month, respectively. Morris water maze (MWM) test was performed to assess spatial memory. The hippocampal lipid peroxidation marker (MDA levels) and enzymatic antioxidant activities of SOD, GPx, and total antioxidant capacity were also evaluated. Western blotting was used to examine the protein expression of apoptotic factors such as Bcl-2, BAX, and cleaved-caspase 9 and 3 in the hippocampus.
Results: The results revealed that CBL treatment improved cognitive performance of alcoholic animals in the MWM. These results were followed by attenuation of MDA levels in the alcoholic rats and enhancement of antioxidant defense in the hippocampus. Moreover, CBL reduced hippocampal Bax/Bcl-2 ratio and cleaved-caspase 9 and 3 levels.
Conclusion: The findings of the present study provide evidence for the promising therapeutic effect of CBL in chronic ethanol consumption through counteracting oxidative stress and apoptosis markers.
Keywords: Ethanol, Memory, Oxidative stress, Apoptosis, Hippocampus

P-423

Effect of Syringic acid on pain, oxidative stress and pentylenetetrazole -induced seizure in male rats

Foroozan S, Farbood Y, Sarkaki A, Mard SA

Department of Physiology, Persian Gulf Physiology Research Center, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Background and Objective: Antioxidant compounds have been extensively investigated as a pharmacological alternatives to prevent epileptogenesis. The objective of the present study was to investigate the effect of Syringic acid on pain, oxidative stress and PTZ-induced seizure in male rats.
Materials and Methods: 48 male Wistar rats (200-250 g) were divided randomly into six groups: Control; PTZ (50 mg/kg, I.P); SA + PTZ (received SA at doses of 25, 50, 100 mg/kg respectively); PHB + PTZ (received Phenobarbital 80 mg/kg). Syringic acid or normal saline were administered 30 minutes before PTZ-convulsion induction. Immediately after PTZ-injection; length of convulsion and racine-convulsion scores were evaluated in thirty minutes. Subsequently, ninety minutes after the seizure, pain were evaluated. Then; rats were anesthetized, brains were removed and the SOD level were measured by ELISA.
Results: In this study, the effect of Syringic acid anticonvulsant on duration of seizure and racine-convulsion scores was observed. In addition, Syringic acid appeared to show a supra-additive effect for analgesia in the tail-flick test.

Biochemical observations showed that the oxidative stress were significantly improved in seizure groups under treatment with SA.
Conclusion: Based on the results obtained in this study Syringic acid can be effective in controlling Pentylenetetrazol-induced seizures. The beneficial effects of SA may be due to its antioxidant properties.
Keywords: Syringic acid, Seizure, Pentylenetetrazol, Oxidative stress, Pain, Rat

P-424

Portulaca oleracea, relieves neuropathic pain following chronic constriction sciatic nerve injury in rat: anti-inflammatory and antioxidant activity

Fatemeh Forouzanfar[1,2*], Hassan Rakhshandeh[3], Hossein Hosseinzadeh[4,5], Mohammad Bagher Khorrami[6], Samira Asgharzade[7,8]

1. Neuroscience Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Department of Neuroscience, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3. Pharmacological Research Center of Medicinal Plants, Mashhad University of Medical Sciences, Mashhad, Iran
4. Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran
5. Pharmacodynamics and Toxicology Department, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
6. Social Security Organization, 17th Shahrivar Hospital, Mashhad, Iran.
7. Cellular and Molecular Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran
8. Department of Molecular Medicine, School of Advanced Technologies, Shahrekord University of Medical Science, Shahrekord, Iran

Background and Objective: Neuropathic pain responds poorly to drug treatments. The present study investigated the therapeutic effect of Portulaca oleracea, in chronic constriction injury (CCI)-induced neuropathic pain in rats.
Materials and Methods: Neuropathic pain was performed by putting four loose ligatures around the sciatic nerve. Acetone drop, von Frey hair, radiant heat tests were done to evaluate cold allodynia, mechanical allodynia and heat hyperalgesia, respectively. The levels of Interleukin-1β (IL1β) and Tumor necrosis factor-alpha (TNFa) as inflammatory markers as well as oxidative stress markers (Malondialdehyde, total thiol content) were measured in the in the L4–L6 segments of the spinal cord.
Results: CCI resulted in the development of heat hyperalgesia, mechanical allodynia and cold allodynia accompanied by an increase in the contents of TNF-α, IL1β, malondialdehyde, with a reduction in total thiol content. Administration of Portulaca oleracea (100 and 200 mg/kg intraperitoneal) for 14 days in CCI rats significantly alleviated pain-related behaviors, oxidative damage and inflammatory cytokines in a dose-dependent manner.
Conclusion: It is suggested that antinociceptive effects of Portulaca oleracea might be due to antioxidant and anti-inflammatory properties.
Keywords: Antinociceptive effect, Portulaca oleracea, Neuropathic pain, Hyperalgesia.

P-425

Menaquinone-4 effects on working memory impairment and anxiety behavior after transient cerebral ischemia/ reperfusion in male wistar rat

Bahram Farhadi-Moghadam[1], Masoud Fereidoni[1, 2]

1. Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
2. Rayan Center for Neuroscience and Behavior, Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran

Background and Objective: Working memory impairment and anxiety behavior could be induced by transient global cerebral ischemia/reperfusion (TGCI) as one model of brain stroke. Menaquinone 4 (MK-4) is an antioxidant and anti-inflammation known as vitamin K2. This investigation questioned the effects of MK-4 on the mentioned cognitive impairments following TGCI.
Materials and Methods:
28 male wistar rats were randomly selected and divided in 4 groups: sham-control,

TGCI, TGCI+DMSO (1% v/v), TGCI+ MK-4. Immediately and also 2 hours after reperfusion, 200mg/kg MK-4 were injected intraperitonially. 7 days later rats were examined using Y maze and also open field apparatus to evaluate working memory sufficiency and the level of anxiety behavior, respectively.
Results: TGCI could reduce spontaneous alternation compared with the sham-control group significantly ($p < 0.01$). But MK-4 increase percentage of spontaneous alternation compare to TGCI and TGCI+ DMSO ($p < 0.05$). Rats in TGCI + DMSO and TGCI groups spent significantly less time in the center zone of open field apparatus compared to sham-control group which can be interpreted as the elevation of anxiety behavior ($p < 0.001$). But the time spent in the center zone was significantly increased in TGCI+MK-4 group compare with injured groups ($p < 0.001$).
Conclusion: Results showed that MK-4 could improve working memory (short-term memory) and also reduced anxiety behavior after TGCI. Probably, antioxidant and anti-inflammatory aspects of MK-4 decrease oxidative stress and neuro-inflammation proceeding factors in the brain which needs more investigations.
Keywords: Transient Global cerebral ischemia/ reperfusion; Menaquinone-4; Y maze, Open field.

P-426

The effect of safranal on prevention of learning and memory deficits following intracerebroventricular injection of colchicine in the rat

Farzane Fereidooni[1], Ensie Azadi Ahmadabadi[1],Shahram Jalalzadeh[1], Zahra Kiasalari[2], Mehrdad Roghani[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
3. Neurophysiology Research Center, Department of Physiology, Shahed University, Tehran, Iran.

Background and Objective: Cognitive decline is associated with Alzheimer's disease that is considered a chronic and progressive syndrome that finally leads to irreversible loss of neurons. In this study, we assessed whether safranal has a beneficial effect on cognitive function following intracerebroventricular injection of colchicine in the rat.
Materials and Methods: 32 male rats were randomly divided into four groups as follows: Sham, lesion (receiving intracerebroventricular colchicine bilaterally at a dose of 15 microg), and two lesion groups receiving oral safranal at doses of 10 or 50 mg/kg in addition to colchicine. Finally, passive avoidance and Y-maze tests were used to assess learning and memory.
Results: The results showed that intracerebroventricular colchicine significantly reduces alternation and step-through latency in behavioral tests and treatment of lesion group with safranal at a dose of 50 mg/kg significantly improves these parameters.
Conclusion: Taken together, safranal could prevent learning and memory deficits following intracerebroventricular injection of colchicine in the rat.
Keywords: Safranal, Colchicine, Cognitive decline

P-427

The effect of nobiletin on inflammatory response, oxidative stress, cholinesterase, and apoptosis in amyloid beta-induced model of Alzheimer's disease in the rat

Reihane Ghasemi Tarei[1], Zahra Kiasalari[2], Marzieh Fakour[1], Maryam Khorasani[1], Sedigheh Keshtkar[1], Mehrdad Roghani[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Department of Physiology, Shahed University, Tehran, Iran.

Background and Objective: Alzheimer's disease (AD) is the most common cause of dementia. Nobiletin as a natural compound from citrus peels possesses anti-dementia activity. In addition, nobiletin could ameliorate oxidative stress and inflammation. Therefore, this study was conducted to assess the effect of nobiletin on hippocampal

inflammatory response, oxidative stress, cholinesterase, and apoptosis in amyloid beta-induced model of AD in the rat.
Materials and Methods: In this study, 32 male Wistar rats were randomly divided into four groups, including: 1. sham, 2. sham+nobiletin, 3. amyloid beta, 4. amyloid beta+ nobiletin. Rats were injected bilaterally with amyloid beta into the CA1 region of the hippocampus through stereotaxic surgery. Nobiletin was administered at a dose of 10 mg/kg daily one hour after surgery for one week via gavage. Then, oxidative stress markers (MDA, ROS, GSH, SOD, Nrf2, catalase), inflammatory factors (NF-κB, TNF, TLR4), apoptosis parameter (DNA fragmentation) and AChE activity were measured in hippocampal homogenate.
Results: Treatment of nobiletin significantly reduced MDA, ROS and increased SOD with no significant change of GSH, catalase and Nrf2. Another beneficial effect of nobiletin was reduction of inflammatory factors. Besides, nobiletin did not significantly change AChE activity and DNA fragmentation.
Conclusion: According to the findings of this study, we can say that treatment with nobiletin reduces inflammation and oxidative stress. However anti-AChE and anti-apoptotic effects of this agent need to be evaluated more.
Keywords: Alzheimer's disease, Nobiletin, Oxidative stress, Inflammation, Cholinesterase, Apoptosis

P-428

The effect of Thymus vulgaris on rotarod motor performance in the pentylenetetrazol kindled rat

Zahra Qods, Vahid Azizi, Farzin Allahyari, Abdolkarim Hosseini

Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran.

Background and Objective: Epilepsy is a common chronic neurodegenerative disorder disease, it can also, affect motor balance. In this study, the medicinal plant Thymus vulgaris, was used to evaluate its effect on motor deficit caused by pentylenetetrazol (PTZ) in the rat.
Materials and Methods: Twenty-four rats were randomly allocated to 4 groups: control negative under treatment with PTZ (sub-threshold dose 35 mg/kg for one month), control positive under treatment with Phenobarbital (PB-30 mg/kg), and two PTZ groups under treatment with T. vulgaris extract (TVE-50, and -100 mg/kg). Standard rotarod test was used to evaluate motor coordination. Data were analyzed using SPSS.
Results: Motor-skill tasks in rotarod test in PTZ group receiving TVE at a dose of 50 and 100 mg/kg was greater than PTZ group. In addition, PB 30 mg/kg significantly attenuates the motor impairments in treated animals.
Conclusion: Our results showed that TVE could prevent epilepsy and elevate motor coordination in the PTZ-kindled rats.
Keywords: Thymus vulgaris, Epilepsy, Rotarod, Motor coordination, Pentylenetetrazol

P-429

Simvastatin exerts antidepressant-like activity in mouse forced swimming test: Role of NO-cGMP-KATP channels pathway and PPAR-gamma receptors

Reza Naserzadeh[1], Niloofar Abad[1], Behnam Ghorbanzadeh[1], Mojtaba Dolatshahi[2], Mohammad Taghi Mansouri[3]

1. Department of Pharmacology, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran
2. Department of Physiology, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran
3. Department of Anesthesiology, Columbia University Medical Center, New York, NY 10032, USA

Background and Objective: The present study aimed to investigate the potential antidepressant-like activity of simvastatin and the possible involvement of NO-cGMP-KATP channels pathway and PPARg using forced swimming test (FST) in mice. In addition, the interaction between simvastatin and fluoxetine as a reference drug was examined.

Materials and Methods: Simvastatin at doses (20, 30, and 40 mg/kg, i.p.) was administrated 30 min before the OFT or FST. To evaluate the involvement of NO-cGMP-KATP channels pathway, mice were pre-treated intraperitoneally with L-arginine (a nitric oxide precursor, 750 mg/kg), L-NAME (a NOS inhibitor, 10 mg/kg), methylene blue (guanylyl cyclase inhibitor, 20 mg/kg), sildenafil (a PDE-5 inhibitor, 5 mg/kg), glibenclamide (ATP-sensitive K+ channel blocker, 1 mg/kg), and diazoxide (K+ channels opener, 10 mg/kg).To clarify the involvement of PPARg receptors, pioglitazone, a PPARg agonist (5 mg/kg, i.p.), and GW9662, a PPARg antagonist (2 mg/kg, i.p.), were pre-treated with simvastatin.
Results: Immobility time was decreased after simvastatin. Administration of L-NAME, methylene blue, glibenclamide and pioglitazone in combination with the sub-effective dose of simvastatin (20 mg/kg) reduced the immobility time in the FST compared to drugs alone, while co-administration of effective doses of simvastatin (30 mg/kg) with L-arginine, sildenafil, diazoxide, and GW9662 prevented the antidepressant-like effect of simvastatin. In addition, simvastatin (20 mg/kg) potentiated the antidepressant-like effect of fluoxetine through the NO pathway. None of the drugs produced any significant alterations in locomotor activity using OFT.
Conclusion: These results demonstrated that NO-cGMP-KATP channels pathway and PPARg receptors may be involved in the antidepressant-like effect of simvastatin.
Keywords: Simvastatin; Anti-depressant-like; NO-cGMP-KATP channels pathway; PPAR? receptors; Potentiation; Mouse forced swimming test.

P-430

Applying nasal airflow reduces mechanical ventilation-induced cognitive impairment

Sepideh Ghazvineh[1], Mohammad Reza Raoufy[1], Javad Mirnajafi-Zadeh[1], Alireza Salimi[2]

1. Department of physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.
2. Chronic Respiratory Disease Research Center (CRDRC), National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Science , Tehran, Iran.

Mechanical ventilation is a life-saving intervention in critically ill patient. However mechanical ventilation may lead to cognitive disorders. There is evidence that olfactory bulb (OB) activity during nasal breathing continuously generates respiration-coupled oscillations in widespread brain regions where contribute to cognitive behaviors. Therefore, we evaluated the effect of applying nasal airflow on short-term memory and the activity of OB, medical prefrontal cortex (mPFC) and hippocampus (HPC) in mechanically ventilated rats.
Materials and Methods: Male Wistar rats were anesthetized by inhalation of isoflurane (4%). Then, animals were intubated with the needle core dragged out and connected to ventilator (RR=65 breath /min, 2CC/pulse). In nasal airflow group, air puffs were pushed into nostril (frequency = 1Hz) during mechanical ventilation. Local field potential signals were recorded from OB, mPFC and HPC during mechanical ventilation. Twenty four after winning, short-term memory was assessed using Y maze test.
Results: Prominent power peak at 1Hz frequency was observed in OB, mPFC and HPC in nasal airflow group compared to controls. Applying nasal airflow increased delta and theta power in OB, but decreased these rhythms in mPFC and HPC. Behavioral study revealed that applying nasal airflow improved short-term memory 24 h after winning.
Conclusion: he present study suggests that applying nasal airflow reduces mechanical ventilation-induced cognitive impairment through by changing the activity of different areas of the brain.
Keywords: Mechanical ventilation; cognitive disorders; Nasal airflow; Olfactory bulb; Medial prefrontal cortex; Hippocampus;

P-431

Intra-CA1 administration of L-arginine and L-NAME reduces the acquisition of nicotine-induced place preference in the rats

Hassan Ghoshooni[1], Cyrus Jalili[2], Yousef Sadeghi[3], Hedayat Sahraei[1]

1. Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, IRAN
2. Department of Anatomy, Faculty of Medicine, Kermanshah University of Medical Sciences
3. Department of Anatomy, Faculty of Medicine, Shahid Beheshti University of Medical Sciences

Previous studies have shown that nitric oxide (NO) have a role in nicotine-induced place preference. In the present study, the effects of intra-CA1 injections of L-arginine and L-NAME on nicotine-induce place preference were studied. Male Wistar rats (220-250 g) received different doses of nicotine (0.4, 1, and 1.5 mg/kg) and place conditioning was evaluated in this animals. L-Arginine and L-NAME were injected intra-CA1 before each nicotine

injection (acquisition) or after the session completed (expression). Our results showed that nicotine can induced place conditioning in dose of 1.5 mg/kg. Moreover, L-arginine (1, 5 and 10 µg/rat) administration into the CA1 hippocampal area augmented both the acquisition and expression of nicotine-induce place preference, whereas L-NAME (1, 5 and 10 µg/rat) into the CA1 area did not change the nicotine effect. These results indicated that nicotine administration resulted in significant place preference. In addition, intra-CA1 L-arginine administration leads to a change in place conditioning induced by nicotine in the rats which may be indicated a role for nitric oxide in these brain area on nicotine-induced positive reinforcement.
Key Words: Nicotine; Nitric oxide; CA1 area; Conditioned Place Preference; Rat.

P-432

Effect of electroconvulsive therapy (ECT) on depressed male rats which were pre-induced with Alzheimer's disease

Faezeh Ghozatlu[1], Banafsheh Bagheri [1], Mohsen Khalili [2], Mehrdad Roghani [2]

1. School of Medicine, Shahed University, Tehran, Iran
2. Neurophysiology Research Center, Shahed University, Tehran, Iran

Background and objective: Because there is a more progression of depression in patients with Alzheimer disease, and regarding to end stage treatment by ECT for depressed ones, we examined the efficacy of ECT in rats with co-morbidity of depression and Alzheimer disease.
Materials and methods: 40 male rats were divided to 1-Control, 2-Alz, 3-Alz+ECT, 4-Alz+Dep, 5-Alz+Dep+ECT. Sporadic Alzheimer disease (SDA) was induced by STZ (3mg/kg, icv) injection in the rats, and after that the animals were depressed by reserpine (0.2 mg/kg, i.p) treatment for 14 days. Finally group 3 and 5 received ECT for 7 days. However, all groups were subjected to depression, anxiety and obsession tests including: open field, sucrose preference, elevated plus maze, forced swimming and marble tests, however, for evaluation of memory, we used Y maze test.
Results: Obtained data by sucrose preference test showed that application of ECT in depression+Alz rats could reduce depression behaviors. Also, the gained results via open field and elevated plus maze were illustrated the marked antagonized activity of ECT in anxiety behaviors in depression rats.
Conclusion: The results of this study showed that ECT could yield the better therapeutic effects in patients with co-morbidity of depression and Alzheimer disease.
Keywords: Depression, Alzheimer, ECT, rats

P-433

Zncl2 attenuates memory and motor activity impairment induced by hypoxia in rat

Zohreh Ghotbeddin*[1], Hossein Najafzadeh varzi[2, 3], Seyed Reza Fatemi Tabatabei[1], Leila Khaledi[1]

1. Department of Physiology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.
2. Department of Pharmacology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
3. Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

Background and Objective: Hypoxia increases the excitability of neurons by changing in synaptic plasticity leads to memory impairment. Zinc as one of the most important trace elements is needed for proper functioning of the nervous system and homeostasis and many studies indicate that zncl2 directly effect on brain function and have

important role in improving memory and motor activity. So, in this work we assessed the effect of zncl2 following hypoxia on passive avoidance memory and motor activity in young rat.
Materials and Methods: In this study, 40 young rats (Wistar) 10-12 years old (18–22 g) maintained at room temperature 23±2. Rats were divided into four experimental groups: sham, zncl2, hypoxia only, submitted to hypoxia followed by zncl2 treatment. For hypoxia induction rats placed in hypoxia container with 7% O2 and 93% N2 for 15 minutes. In zncl2 group, rats received zncl2 (20mg/kg for 21 days) after their lactation period. Finally, passive avoidance memory, balance and motor activity were assessed respectively by shuttle box, rotarod and open field instruments.
Results: A decreased step through latency and increased time spent in dark room was observed in passive avoidance test after hypoxia ($p<0/05$), which could be inhibited by posttreatment with zncl2. Hypoxia also disrupted balance and motor activity in the rotarod and open field test ($p<0/05$), which could be inhibited by treatment with zncl2.
Conclusion: Results of this study indicated that hypoxia impairs passive avoidance learning, balance and motor activity and zncl2 treatment improve these changes.
Keywords: Zncl2, Hypoxia, Memory, Motor activity, Rat

P-434

Role of CB1 cannabinoid receptors in pentylenetetrazole seizure threshold in mice

Mohammad-Mahdi Ghanbari[1], Marzieh Joneidi[1], Jalal Babaie[2], Majid Golkar[2], Mohammad Sayyah[1*]

1. Department of Physiology and Pharmacology, Pasteur Institute of Iran
2. Department of Parasitology, Pasteur Institute of Iran

Introduction: Epilepsy, with more than 1% worldwide prevalence, is the most common neurological disorder after stroke and Alzheimer's disease. Underlying cause of epilepsy is not found in two-thirds of patients. The endogenous cannabinoids (eCBs) are lipid-derived metabolites that are produced ''on-demand'' by postsynaptic cells and released immediately. CBs have both convulsant and anticonvulsant depending on the involved receptor (CB1 or CB2). However, the role of CB1 receptors in seizure activity is not fully determined. We examined involvement of CB1 receptors in pentylenetetrazole (PTZ) seizure threshold in mice.
Method: Mice (n=10 in each group) received the CB1 receptor agonist, ACEA (0/2, 1, 5 µg/mouse), and the CB1 receptor antagonist, AM251 (0.2, 5, and 10 µg/mouse), and endogenous cannabinoid hydrolytic enzyme inhibitors, JZL(1, 5 µg/mouse) by intracerebroventricular (i.c.v.) injection. Three groups were considered as no injection, and solvent groups. After 10 min for AM251
and 15 min for ACEA and JZL, the threshold of clonic seizures induced by PTZ was determined.
Results: ACEA increased seizure threshold in a dose-dependent manner (31% by 1 µg/mouse, and 26% by 5 µg/mouse, $P<0.05$). JZL increased seizure threshold in a dose-dependently (21% by 1 µg/mouse). AM251 decreased seizure threshold dose-dependently (15% by 10 µg/mouse).
Conclusion: The CB1 receptors are able to modulate PTZ seizure threshold and possess proconvulant effect.
Keywords: Seizure threshold, CB1 Cannabinoid receptors, Pentylenetetrazole, Mice

P-435

The side effect of maternal exposure to Nanoparticles on reflexive motor behaviors in mice offspring

Shahin Hassanpour [1*], Azam Ghanbari [2], Samad Alimohammadi [3]

1. Section of Physiology, Department of Basic Science, Faculty of Veterinary Medicine, Science and Research Branch, Islamic Azad University, Tehran, Iran
2. Doctorate student of Veterinary Medicine, Faculty of Veterinary Medicine, Science and Research Branch, Islamic Azad University, Tehran, Iran
3. Section of Physiology, Department of Basic Sciences, Faculty of Veterinary Medicine, Razi University, Kermanshah, Iran

There are growing reports on adverse effects of various compounds during pregnancy on the growth of the central nervous system, embryo and fetus development, thyroid hormones and liver enzymes. It is reveled over exposure of

the pregnant mice these compounds can impress growth pattern as well as central locomotion and motor behaviors in offspring. Based on our recent report, Prenatal exposure to Zinc oxide nanoparticles (1 mg/ml) significantly reduced reflexive motor behaviors. Zinc oxide nanoprticle(100ml) significantly reduced the embolization rate and increased the angle of the hind leg, reduced the time of the rat offspring right standing and reduced the gripping rate. nevertheless, they had no effect on the front leg and the mouse's geotaxis that is due to the effects of mesotaxis during the infant's growth. The silver nanoparticles (16ppm) had no histopathologic effect on the pregnancy and parturition. Moreover, titanium nanoparticles (500mg/kg) decreased serum calcium and zinc levels in both mother and fetus and increased offspring skeleton deformity, body weight and the hair loss. Also, zinc oxide (2.5 mg/kg) resulted in a dramatic decline in long-term memory and latency while the 1 mg/kg of zinc oxide was almost ineffective. These findings revealed maternal over exposure to nanoparticles had adverse effect on reflexive motor behaviors in offspring.

Keywords: Maternal exposure, Nanoparticles, Reflexive motor behavior, Offspring

P-436

Troxerutin exerts neuroprotection against Lipopolysaccharide (LPS) induced oxidative stress and neuroinflammation through targeting SIRT1/SIRT3 signaling pathway

Sedighe Kardgar

This study was conducted to clarify the potential mechanisms of Troxerutin neuroprotection against Lipopolysaccharide (LPS) induced oxidative stress and neuroinflammation through targeting the SIRT1/SIRT3 signaling pathway.

To establish a model, a single dose of LPS (500 mg/kg body weight) was injected to male Wistar rats intraperitoneally. Troxerutin (100 mg/kg body weight) was injected intraperitoneally for 5 days after induction of the model. Cognitive and behavioral evaluations were performed using Y-maze, single-trial passive avoidance, and novel object recognition tests. The expression of inflammatory mediators, SIRT1/SIRT3, and P53 was measured using the ELISA assay. Likewise, the expression levels of SIRT1/SIRT3 and NF-κB were determined using Western blot assay. Brain acetyl-cholinesterase activity was determined by utilizing the method of Ellman. Reactive oxygen species (ROS) was detected using Fluorescent probe 2, 7-dichlorofluorescein diacetate (DCFH-DA). Furthermore, malondialdehyde (MDA) levels were determined.

A single intraperitoneal injection of LPS was led to ROS production, acute neuroinflammation, apoptotic cell death, and inactivation of the SIRT1/SIRT3 signaling pathway. Likewise, ELISA assay demonstrated that post-treatment with Troxerutin considerably suppressed LPS-induced acute neuroinflammation, oxidative stress, apoptosis and subsequently memory impairments by targeting SIRT1/SIRT3 signaling pathway. Western blot assay confirmed ELISA results about SIRT1/SIRT3 and NF-κB proteins.

These results suggest that Troxerutin can be a suitable candidate to treat neuroinflammation caused by neurodegenerative disorders.

Keywords: Lipopolysaccharide; neuroinflammation; oxidative stress; SIRT1; SIRT3; Troxerutin

P-437

Long-term cold water drinking induces dyslipidemia and liver fatty changes

Said Abdul Ghafour Saeedy[1,2], Ahmad Faisal Faiz[1,2], Marjan Nikbakhtzadeh[1], Bagher Minaei Zangi[3], Mansoor Keshavarz[1*]

1. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Paraclinic, School of Medicine, Herat University, Herat, Afghanistan
3. Department of Anatomy, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Nonalcoholic fatty liver disease (NAFLD) is associated with lifestyle-related disorders like obesity, insulin resistance, type 2 diabetes mellitus, hypertension, hyperlipidemia, and metabolic syndrome. In traditional medicine, cold water drinking (as a lifestyle) is said to be obnoxious for internal organs and there are pieces of evidence regarding the role of ingested water temperature on the body organs. In this experimental research, the effect of

long-term cold water (4 oC) drinking on some aspects of liver function and structure and serum lipid indices are evaluated. 24 male Wistar rats, weighing 180 ± 20 g, were randomly divided in 4 groups (n=6) of room temperature and cold-water users. At the end of the care period, a blood sample was taken for assessment of the liver function tests and lipid indices; a tissue sample of the liver was used for histological studies. Liver enzymes, triglycerides, total cholesterol, and high-density lipoprotein cholesterol (HDL-c) were measured using colorimetric AutoAnalyzer; low-density lipoprotein cholesterol (LDL-c) and very low-density lipoprotein cholesterol (VLDL-c) were calculated by the Friedewald equation. Liver tissue structure was evaluated using H&E staining and microscopic examination. Results showed that long-term cold water drinking significantly increased serum levels of triglycerides, VLDL-c and Alkaline phosphatase (ALP); reduced significantly serum levels of LDL-c; and caused no significant alteration in the serum levels of total cholesterol, HDL-c, Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT). Hepatocellular steatosis was significantly increased in intervention groups compared to the control group. We concluded that long-term cold water drinking can cause dyslipidemia and steatosis.
Keywords: Cold water, Liver marker enzymes, Liver structure, Non alcoholic fatty liver disease.

P-438

Long-term drinking of cold water impairs spermatogenesis and testicular structure

Ahmad Faisal Faiz[1,2] , Said Abdul Ghafour Saeedy[1,2] , Keivan Lorian[1], Marjan Nikbakhtzadeh[1], Bagher Minaei Zangi[3], Mansoor Keshavarz[1*]

1. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Paraclinic, School of Medicine, Herat University, Herat, Afghanistan
3. Department of Anatomy, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Background/aims: As a life style, consistency, temperature, rate and amount of the taken food and water vary according to the choice and cultures and have role in health problems. Testis is the organ which can be affected and the incidence of defective spermatogenesis is increasing probably due to environmental and lifestyle related factors. In old medical books are evidences of the role of meal and water temperature as a life style related factors, on body organs functions. Nevertheless, information regarding the influence of meal temperature is very scarce and controversial; only the acute effects of cold meal consumption are studied and no published data is available about the effects of long term drinking of cold water or meal on body organs. In this experimental research, the effect of long term cold water drinking on some aspects of testicular function and structure were evaluated.
Methods: 24 male Wistar rats, weighing 180 ± 20 g, were randomly divided in 4 groups (n=6) of control, 2 m, 3 m and 2 m cold + 1 m room temperature water. At the end of the care period, spermatogram and testes and epididymis histological studies were done.
Results: Long-term cold water drinking significantly decreased sperm count, sperm progressive motility ((25 ± 1.8 %)) and significantly increased non-progressive motile sperm (5.8 ± 0.9 %) and non-motile sperm (69.1 ± 1.8 %), also Sertoli cells and Leydig cells were significantly damaged.
Conclusion: Long-term cold water drinking can destroy testicular structure and impair spermatogenesis.
Keywords: cold water, spermatogenesis, testicular structure, lifestyle.

P-439

Investigating viability of human leukemia/lymphoma cells upon coadministration of umbelliprenin and radiotherapy

Keyhan Ebrahimi[1], Ramin Bagheri[1], Mohammad Reza Keramati[1], Fatemeh B. Rassouli[3*], Houshang Rafatpanah[2], Mehrdad Iranshahi[4]

1. Cancer Molecular Pathology Research Center, Department of Hematology and Blood Bank, Faculty of Medicine, Mashhad University of Medical Sciences, Iran
2. Inflammation and Inflammatory Diseases Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3. Novel Diagnostics and Therapeutics Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran.
4. Department of Pharmacognosy and Biotechnology, Biotechnology Research Center, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: Umbelliprenin (C24H30O3) is a natural sesquiterpene coumarin found in various Ferula species. It has important pharmacological effects such as antibacterial, anti-inflammatory, anti-oxidant and anti-tumor activities. Despite extensive studies on anticancer effects of umbelliprenin in vitro, it is not clear whether coadministartion of umbelliprenin and routine therapeutic modalities could improve their clinical efficacy. Hence, objective of our research was to investigate effects of umbelliprenin and radiotherapy on human leukemia/lymphoma cells.
Methods: In this study, human leukemia/lymphoma cells (MT-2 cell line) were treated with 20 and 40 µg/ml umbelliprenin for 24 h, and then radiotherapy (4 Gy radiation) was applied. After 48 h recovery of cells, their viability was evaluated by resazurin. Meanwhile, cells treated with 0.2% DMSO + 4 Gy radiation were considered as control.
Results and conclusion: Evaluating viability of MT2 cells revealed that upon coadministration of 20 µg/ml umbelliprenin + radiotherapy, 89% of cells were alive. More interestingly, cell viability was calculated as 63% when 40 µg/ml + radiotherapy was applied. Therefore, findings of present study indicated that beside its known anticancer effects, umbelliprenin could improve efficacy of radiotherapy in leukemia/lymphoma cells.
Key word: Umbelliprenin, Radiotherapy, Human leukemia/lymphoma cells.

P-440

Anti-metastatic potential of crocin on triple negative breast cancer in mice model

Laleh Arzi[1], Gholamhossein Riazi[1], Majid Sadeghizadeh[2]

1. Department of Biochemistry Institute of Biochemistry and Biophysics (IBB), University of Tehran, Tehran, Iran.
2. Department of Genetics, School of Biological Sciences, Tarbiat Modares University, Tehran, Iran.

Background and Objective: Due to the highly aggressive nature and short relapse time of triple negative breast cancer (TNBC), it cannot be overcome with any standard-of-care therapy. However, a vast body of evidence has indicated the efficacy of herbal remedies as treatments for cancer. In particular, crocin, the main carotenoid of saffron, has shown anti-proliferative and proapoptotic effects on primary tumors. In this regard our previous research demonstrated the anti-metastatic properties of crocin on breast cancer cell model (4T1). Thus, this study unprecedentedly aimed to investigate the anti-metastatic potency of crocin on a murine model of metastatic TNBC and its effect on the Wnt/β-catenin pathway.
Material and Methods: Tumors were inoculated by injection of 4T1 cells to mice. During the treatment period, the weights and survival rates of the mice and tumor sizes were measured. Histological analysis of the excised tissues was conducted following euthanization. The expression levels of Wnt/β–catenin pathway genes were measured by Real-time PCR.
Results: Measurement of biochemical parameters showed the nontoxicity of crocin. The crocin treated mice possessed more weight, higher survival rates and smaller tumors sizes. Histopathological analysis showed no metastatic lesions in their livers and lungs. Also, downregulation of the expression of Wnt/β-catenin target genes in tumors and lungs was observed compared to the untreated group.
Conclusion: Our data proposes crocin as a propitious complementary anti-metastatic herbal medicine for treatment of TNBC.
Keywords: Crocin, Triple negative breast cancer (TNBC), Anti-metastatic, Mice model, Wnt/β-catenin
(Approval Number: ir.bums.REC.1395.128)

P-441

Effects of morphine on serum reproductive hormone levels and the expression of genes involved in fertility-related pathways in male rats

Marziyeh Ajdary[2,1], Sina Farzan[3], Yasaman Razavi[2], Abbas Haghparast[4]

1. Abadan School of Medical Sciences, Abadan, Iran
2. Cellular and Molecular Research Center, Iran University of Medical Sciences, Tehran, Iran
3. Department of Anesthesiology and critical care, Tehran University of Medical Sciences, Tehran, Iran
4. Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Endogenous opioid peptides are present in different tissues of the male reproductive tract, suggesting that they may be involved in reproductive function. We focused on the effects of morphine on serum reproductive hormone levels and on markers of the involved in fertility-related pathways were evaluated.

Materials and Methods: A total of 30 male Wistar rats were divided into three groups (n = 10) and intraperitoneally administered the following substances for 20 days: two single daily doses of morphine (10 mg/kg; morphine group), saline (healthy saline), intact group. After confirming the morphine dependence of the experimental groups, all the animals were sacrificed and their total testis tissue was extracted and stored at −80 °C until use. Male reproductive parameters (blood serum of testosterone, luteinizing hormone, and follicle-stimulating hormone) and using Q-PCR and western blot, we evaluated mRNA and protein expression of CREM, TBP, CREB1, HDAC1, and FOS involved in fertility-related pathways were analyzed and compared in the testis samples.
Results: The luteinizing hormone and testosterone levels were significantly lower in the morphine-administered group than in the saline and intact groups ($P < 0.05$). Moreover, the expression of all five target genes was downregulated in the morphine group ($P < 0.05$). The proteins expression of all five target proteins was downregulated in the morphine group ($P < 0.05$).
Conclusion: We concluded that morphine could decrease the reproductive parameters in male rats.
Keywords: Addiction, Morphine, Infertility pathway, Testis

P-442

Ultrasensitive determination of metformin in real samples using a Ag FRET based nanosensor

Sina Azarian[1], Gholamreza Dehghan[1], Masoomeh Shaghaghi[2]

1. Department of Biology, Faculty of Natural Science, University of Tabriz, Tabriz, Iran.
2. Department of Chemistry, Payame Noor University, Tehran, Iran.

Background and Objective: Metformin (MET), as an oral antidiabetic and anti-hyperglycemic agent, is widely used to treat type II diabetes mellitus. Because of its increasing consumption, developing a fast, simple and selective method to determine its concentration in biological samples (serum and urine) and pharmaceutical can be one of the main issues. In this study, we used our previous proposed fluorometric and FRET based nanosensor (Tb3+-phen-Ag NPs system) for the sensitive determination of MET in tablets and serum samples.
Materials and Methods: This method is based on the enhancing effect of MET on the emission intensity of Tb3+-phen complex which was quenched by Ag NPs. A good linear relationship between MET concentration and the enhanced emission intensity of Tb3+-phen-Ag NPs was observed in the range of (0.75-3.7) × 10-6 M under the MET conditions.
Results: The limit of detection (LOD) and limit of quantitation (LOQ) were calculated to be 0.43 × 10-6 M and 1.31 × 10-6 M, respectively. This method was applied to determine MET in pharmaceutical dosage form and in spiked serum samples. The obtained recoveries from tablets and treated serum samples were in the range of 82.32-100.13% and 83.13-109.82%, respectively.
Conclusion: According to the obtained results, this method is a very simple, sensitive and free from interference effects that can be used as an effective and a simple method for the direct rapid determination of metformin in biological samples (serum and urine).
Keywords: Metformin; Phenanthroline; Terbium; AgNPs; Spiked serum sample

P-443

Combinatorial effects of ionizing radiation and 7-geranyloxycoumarin on leukemia/lymphoma cells

Ramin Bagheri[1], Keyhan Ebrahimi[1], Mohammad Reza Keramati[1], Houshang Rafatpanah[2*], Fatemeh B. Rassouli[3], Mehrdad Iranshahi[4]

1. Cancer Molecular Pathology Research Center, Department of Hematology and Blood Bank, Faculty of Medicine, Mashhad University of Medical Sciences, Iran
2. Inflammation and Inflammatory Diseases Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
3. Novel Diagnostics and Therapeutics Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran.
4. Department of Pharmacognosy and Biotechnology, Biotechnology Research Center, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Introduction: Use of ionizing radiation is a common therapeutic modality for different kinds of malignancies including leukemia/lymphoma. Adult T cell leukemia/lymphoma (ATLL) is a rare neoplasm of post-thymic lymphocytes with poor prognosis. 7-geranyloxycoumarin is a natural compound with valuable pharmacological activities. In present study, we evaluated combinatorial effects of ionizing radiation and 7-geranyloxycoumarin on viability of ATLL cells.

Methods: MT-2 cells, an ATLL cell line, were pretreated with 5 and 10 µg/ml 7-geranyloxycoumarin for 24 h. Afterwards, cells were exposed to 2 Gy radiation followed by 48 h recovery, and then, cell viability was assessed by alamar blue. To note, untreated cells and cells treated with 0.2% DMSO for 24 h and exposed to same dose of X radiation were considered as controls.
Results and conclusion: Calculation of cell viability indicated that 89% of cells treated with 5 µg/ml 7-geranyloxycoumarin + radiation were alive, while this amount was as 76% for cells treated with 10 µg/ml 7-geranyloxycoumarin + radiation. Therefore, pretreatment of cells with higher concentration of 7-geranyloxycoumarin resulted in more toxicity induced by ionizing radiation. Accordingly, it seems that 7-geranyloxycoumarin could be used in combinatorial treatments against ATLL, although more research is required to define its mechanism of action.
Key word: 7-geranyloxycoumarin, Ionizing radiation, Adult T-cell leukemia/lymphoma, Combinatorial effects

P-444

Application of Nanoparticles in the drug delivery system associated with central nervous system cancer

Mohammad Ali Pahlevan Neshan[1], Arsalan Jalili[2], Nazila Bostanshirin[3]

1. Department of Cellular and Molecular Biology, Faculty of Sciences, Islamic Azad University, Science and Research Branch.
2. Department of Stem Cells and Developmental Biology at Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran
3. Department of Microbiology, School of Medicine, Alborz University of Medical Sciences, Karaj, Iran

Background: The drug delivery system by nanoparticles delivers the drug directly and specifically to the target tissue and reduces the adverse side effects due to the effect of the drug on other tissues. The brain is naturally protected by a blood-brain barrier. This barrier prevents a tumor in the brain from passing through the drug and affecting the corresponding part or restricting the amount of passage. The purpose of this article is to investigate carriers that are able to pass drugs through the blood-brain barrier and discharge the drug in the target tumor.
Method: Relevant English-language literature were searched and retrieved from PubMed search engine (2009_2019). The following keywords were used: "Nanoparticles", “drug delivery”, ”cancer” and “central nervous system”.
Results: Specific targeting of the cell can be done by binding the drug to carriers based on nanoparticles. Various nanostructures including liposomes, polymers, silicon or carbon materials and other nanoparticles as carriers in the drug delivery system have been investigated. Research has shown that fat, protein, and gold are the three main ingredients in the preparation of nanoparticles for the treatment of central nervous system related cancers.
Conclusion: This new type of treatment, especially when it comes to the importance of the dosage of the drug due to its complications, as well as the greater sensitivity of the tissue in question compared to other tissues is important. In addition, blocking the blood-brain barrier from passing medication is one of the major problems in treatment that is largely addressed by these carriers.
Keywords: Nanoparticles, drug delivery, central nervous system, cancer

P-445

In vitro wound healing activity of Scrophularia striata hydroalcoholic extract

Rasool Haddadi[1,2], Pari Tamri [1,2], Fatemeh Javani[3]

1. Department of Pharmacology & Toxicology, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran
2. Medicinal Plants and Natural Products Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
3. Department of Microbiology, Islamic Azad University, Tehran North Branch, Tehran, Iran

Background and objective: Scrophularia striatais is an Iranian medicinal plant and has been used in traditional medicine for the treatment of burns and wounds. This study was performed to investigate the wound healing activity of S. striata hydroalcoholic extract (SSE) in vitro.
Materials and methods: The effects of S. stritat on viability, proliferation and migration of human dermal fibroblast (HDF) and human umbilical vein endothelial cells (HUVECs) were investigated by using MTT and in vitro scratch assay methods, respectively. Furthermore the effect of SSE on angiogenesis was evaluated by using in vitro tube formation assay.
Results: The results of this study showed that SSE had significant proliferative and migratory effects on fibroblast and endothelial cells. In addition, the formation of tube-like structures by HUVECs cultured in MatrigelR was significantly increased in cells treated with SSE compared to control group.

Conclusion: These findings suggest that S. striata promote wound healing by enhancement of fibroblast and endothelial cells proliferation and migration and has potential for the treatment of wounds.
Key words: Scrophularia striata; In vitro wound healing; Angiogenesis; Fibroblast; Endothelial cells

P-446

Application of Monoclonal Anti Bodies Enhances the Cytotoxicity of Natural Killer Cells in Breast Cancer

Arsalan Jalili

Department of Stem Cells and Developmental Biology at Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Introduction: Breast cancer is a major health-care problem worldwide. HER2 overexpression is associated with aggressive disease and decreased survival. Natural killer (NK) cells play a key role in killing of tumor cells. Specified monoclonal antibodies for different tumor cell antigens can enhance the function of NK cells against that targeted tumor. When the antigen-binding fraction of the antibodies bind to the tumor cell and the constant region of the antibody binds to CD16 on the NK cells, NK cells get activated and ADCC is triggered. Due to the prevalence of breast cancer in Iran, we have decided to do a comprehensive study in this area.
Methods: Relevant English-language literature were searched and retrieved from PubMed search engine (2009-2019). The following keywords were used: "Natural Killer Cells", “Monoclonal Anti body” and “Breast Cancer”.
Results: Antibody- dependent NK cell activation results in the release of cytotoxic granules as well as the secretion of pro-inflammatory cytokines such as IFNγ, TNFα, and chemokines. There are many studies showing the enhanced function of NK cells by accompaniment with anti-HER2 mABs (trastuzumab and pertuzumab) in targeted killing of breast cancer cells. HER2-specific antibodies can trigger natural killer (NK) cell-mediated antibody-dependent cellular cytotoxicity and indirectly enhance the development of tumor-specific T cell immunity.
Conclusion: Despite the use of cytokines for expansion and activation of NK cells, using anti-HER2 mABs (trastuzumab and pertuzumab) in therapeutic regimens can enhance the function of natural killer cells in breast cancer patients.
Keywords: Natural Killer Cells, Monoclonal anti body, HER2, Personalized Medicine, Breast Cancer.

P-447

Testosterone and Voluntary Exercise Decrease Apoptosis in the Pancreas of Castrated Diabetic Rats

Leila Chodari[1*], Vajihe Ghornanzadeh[2], Hassan Dariushnejad[3]

1. Department of Physiology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran.
2. Razi Herbal Medicine Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran
3. Department of Medical Biotechnology, Faculty of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

Objective : beta cell death causes reduced insulin secretion and beta cell mass that exacerbate symptoms of type 2 diabetes. Exercise training and testosterone administration increases β-cell mass in animals with diabetes.
Methods: type 2 diabetes was induced by high fat diet and injection of low dose STZ (35mg/kg; ip). After 2 months of treatment with testosterone (2mg/kg/day) or voluntary exercise alone or in combination, pancreas tissue samples were collected and used for apoptosis by tunnel assay and p53 protein measurement by ELISA method. Oral glucose tolerance test (OGTT) was performed on overnight fasted rats.
Results: testosterone and exercise significantly decreased the blood glucose, HbA1c levels, HOMA-IR and increased insulin level and p53 protein expression in treated diabetic and diabetic castrated groups compared to diabetic group. Furthermore, simultaneous treatment of diabetic and diabetic castrated rats with testosterone together voluntary exercise had a synergistic effect on reducing p53 expression, blood glucose, HbA1c levels, HOMA-IR and

subsequently decreasing apoptosis. Conclusion: our results suggest that testosterone and voluntary exercise can reduce pancreatic apoptosis in rats with diabetes and in castrated rats with diabetes. The apoptosis decreasing effect of testosterone and voluntary exercise is associated with the reduced expression of p53 level and blood glucose, HbA1c levels, HOMA-IR and finally increasing insulin levels.
Keywords: testosterone, voluntary exercise, apoptosis, p53, type 2 diabetes, diabetic castrated rats

P-448

In vitro release of Levonorgestrel from reservoir solution core (RSC) rings

Hosseinzade F[1], Tabesh H[1*], Farzaneh F[2]

1. Department of Life Science Engineering, Faculty of New Sciences and Technologies, University of Tehran, Iran
2. Preventative Gynecology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Abnormal Uterine Bleeding (ABU) is one of the most common diseases among women that is treated with progesterone hormones e.g. Levonorgestrel. Vaginal Rings (VRs) are torus-shaped polymeric devices which has been recently developed for sustained and topical active pharmaceutical ingredients delivery. The use of vaginal rings has several advantages, including controlled drug release, single use, possibility of low dose administration, possibility of multi-drug loading, bypassing hepatic first-pass metabolism, non-interference with sexual intercourse.
Materials and Methods: Medical grade silicone fibers were used to fabricate rings, joined together by a poly-lactic acid cap. Three prototypes with loading percentages of 0.1, 0.2 and 0.4 of Levonorgestrel relative to paraffin as Levonorgestrel carrier were designed and fabricated precisely. These VRs were placed in acetate buffer as release medium into shaker incubator at 37 ° C and 80 rpm. For in vitro investigations of drug release samples collected on daily bases for 30 days.
Results: The fabricated VRs revealed the ability for prolonged release of Levonorgestrel over the desired time (3 weeks between each menstrual cycle). After the second day, an almost constant release rate (ca. 100 microgram/day) were achieved until the thirtieth day with negligible fluctuations.
Conclusion: The use of VRs for the prolonged release of Levonorgestrel, especially for the treatment of AUB, would be a good alternative to hormonal tablets minimizing their adverse side effects.
Keywords: Vaginal Rings (VRs), Silicone Elastomer, Levonorgestrel, Prolonged Drug Release, Abnormal Uterine Bleeding (AUB)

P-449

Effect of TAT-Signaling Fusion System Along with GroEL/ES Chaperones Co-expression on Secretory Expression of Somatropin

Mohammad Rabbani

Human Growth Hormone (somatropin) is one of the most widely used recombinant proteins that stimulates growth, cell reproduction and cell regulation in humans. Low protein yields, inclusion body formation, normally caused problems in industrial processes of this protein. To overcome some of these difficulties, the production of somatropin along with two common signal peptides, namely TorA or SufI were assessed in this study, in co-expression with a cytosolic chaperone, GroEL. The target protein and the two signal sequences (TorA and SufI) were synthesized and cloned into an expression plasmid (pET-22) using Ndel and Xhol endonucleases. His-tag was used at the C-terminus of somatropin in order to assist with purification and Western blotting. The expression vector (pGro7) containing chaperone proteins (GroES/EL) and one of the expression vector containing the signal sequence (and the target protein) were co-expressed in BL21 DE3 expression host. IPTG and L-Arabinose were used to induce the target genes. The results showed although some of the expressed proteins were exited from the cytoplasm

to periplasmic space, there were also an accumulation of proteins (probably as inclusion body) inside the cytoplasmic area. Western blot analysis showed that the inclusion of signal sequence in the cassette containing target protein could assist with an excursion of the protein to the periplasmic space and culture media. These findings suggest that TAT promote transportation of the target protein out of the cytoplasm space. This secretory system completes the folding of the protein structure and transfers the mature protein to the periplasmic space.

P-450

Application of microporous scaffolds in continues drug delivery of Clindamycin

Maryam rezaei[1], Hadi Tabesh[1], saeed gholami[1], Behzad Houshmand[2]

1. Faculty of New Sciences and Technologies, Tehran University, Tehran, Iran.
2. Faculty of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Background and Objective: Clindamycin is an antibiotic used for treat mild to moderate cases of a number of bacterial infections, including bone or joint infections, pelvic inflammatory disease and etc. In treatment of bone defects, infections are usually seen during one week post-surgery. Sustained local drug delivery in such cases would be more effectively and efficiently than systemic administration. To bridge this challenge, we design and fabricate a composite scaffold as bone graft which also provides continues release of Clindamycin at the site of bone defect.
Materials and Methods: The proposed composite scaffolds comprise gelatin, β -TCP and zeolite, loaded with Clindamycin with two amount of 0.01 (GTZ-A), 0.001 (GTZ-B) w/w (Clindamycin/scaffold). Then the scaffolds were investigated to determine the release rate of Clindamycin in-vitro in the PBS medium using spectrophotometry technique.
Results: In the drug release test, in the first hour we detected a burst release for both scaffolds about 19 mg and 10 mg Clindamycin for GTZ-A and GTZ-B respectively. GTZ-A could release approximately 3 mg for 5 days however GTZ-B scaffold released about 1mg Clindamycin per day for the same period. Nevertheless, the amount of drug released in this period had an almost decreasing trend, with a very moderate gradient, indicating that the drug could continually release from the scaffold.s
Conclusion: Scaffolds made from gelatin, β -TCP and zeolite loaded with Clindamycin could substitute congenital bone grafts while benefited from continues release of Clindamycin at the site of bone defect.
Keywords: Clindamycin, zeolite, scaffold, infection, bone graft

P-451

Cancer cell migration and invasion research based on gradient microfluidic chip

Laleh Rafiee, Mohamadmahdi Samandari, shaghayegh Haghjooy Javanmard

Applied Physiology Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

Background and Objective: Metastasis is the primary cause of cancer mortality. The mechanism of metastasis has been under vast research and may translate into effective cancer therapies. Due to the complexity, high cost and ethical issues associated with animal models, in vitro models of cancer invasion are more general. However, conventional 2D invasion models lack many essential elements of the tumor microenvironment, like as a 3D ECM. The development of microfluidic systems as in vitro cancer cell migration models, particularly, offers advantages over conventional methods of studying cancer cell migration and invasion.
Material and Methods: The chip was fabricated in polydimethylsiloxane using standard soft lithographic methods. It was autoclaved and all four hydrogel scaffold regions were filled with Matrigel fixed in this scaffold. The metastatic breast cancer cells (MCF7, MDA-231) was cultured in the chip in a 3D tumor model.

Results: We have developed a pump less microfluidic-based culture chip to mimic cancer cell migration and invasion across the basement membrane in the effect of the chemical gradient of multiple factors. By using this chip we showed that MDA-231 cells were more invasive than MCF7 cells.
Conclusion: It is shown that our system can monitor cell migration and invasion in real-time, as compare to Boyden chambers and Transwells. It enables the 3D chemotactic responses of cells cultured in gels and has the ability to control many aspects of the local cellular microenvironments.
Keywords: Microfluidics, Invasion, Migration,3D cell culture

P-452

Investigation of the estrogen effects and determine the role of its classical receptors on liver damage caused by Traumatic brain injury in male rats.

Nader Shahrokhi[1], Sedigheh Amiresmaili[2], Mohammad Khaksari[3]

1. Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.
2. Physiology Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.
3. Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences. Kerman, Iran.

Background and Objective: Previous studies have shown that female sex hormones have a neuroprotective effect after traumatic brain injury (TBI). This study tested the hypothesis that attenuation of TBI-induced liver injury after 17β-estradiol (E2) treatment mediated through the estrogen classic receptors.
Materials and Methods: The animals were randomly divided into six groups: Sham, TBI, TBI + E2, TBI + Vehicle (DMSO) + E2, TBI + ICI + E2, TBI + MPP + E2, TBI +PHTPP + E2 group. E2 (33.3 µg/kg) was administered 30 min after TBI. 1 dose (150 µg/Kg) of each of MPP, PHTPP, (50 µg/Kg) of G15, and (4.0 mg/kg) ICI182780 was injected two times, 24 hr apart, before TBI and estrogen treatment. Liver damage is assessed using hepatocyte function parameters: alkaline phosphatase (ALP) aspartate aminotransferase (AST), alanine aminotransferase (ALT) and histological analysis (e.g., H&E staining) after 24 h from TBI.
Results: The results showed that TBI significantly increased the ALP, ALT, and AST levels. E2 infusion reduced levels of these enzymes compared to TBI. ($P< 0.01$), whereas all the antagonists used reverse this effect of E2.
Conclusion: administration of MPP and PHTPP or ICI inhibited the E2-induced decrease in aminotransferase levels, this may suggest that these effects were mediated via both classical (ERα, ERβ) receptors.
Keywords: Traumatic brain injury, Liver injury, Estradiol, Classic estrogen receptors.

P-453

The effect of carvacrol on hippocampal damage caused by chronic cerebral hypoperfusion

Azadeh Shahrokhi Raeini[1], Fatemeh Zare Mehrjerdi[2], Mohammad Ebrahim Rezvani[2], Fatemeh Safari[1]

1. Student Research Committee,Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Neuro BioMedical Center, Department of physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Background and Objective: The purpose of this study was to investigate of the effect of Carvacrol (CAR) on histological changes in the rats exposed to chronic cerebral hypoperfusion (CCH). Carvacrol is a compound isolated from some plants and herbs, and is specially abundant in oregano. Carvacrol has displayed antimicrobial, antioxidative activities
Materials and Methods: Twenty rats were divided into 4 groups: sham operaed group, chronic cerebral hypoperfusion (CCH) group, CCH+CAR 25 group and CCH+CAR 50 group. In order to create vascular dementia

model, Common carotid arteries were occluded permanently. One day after ischemia, carvacrol was given as gavage for 60 days. Morphological changes of hippocampus were assessed using Nissl staining.
Results: Two months after the complete obstruction of the carotid arteries, a significant decrease in the healthy cell density in the hippocampal CA1 sub region was observed. Carvacrol reduces the damage to the hippocampus in the ischemic rats.
Conclusion: According to the findings, carvacrol can have a protective effect on neuronal damage caused by CCH.
Key words: Rats, Chronic cerebral hypoperfusion, Carvacrol

P-454

Investigation of level of substanceP and CGRP in brain and spinal cord in experimental endometriose in rat and therapetic effect of royal jelly on them

Hossein Shahrokhi, Mahnaz Taherianfard

Department of Basic Sciences, School of Veterinary Science, Shiraz University, Shiraz, Iran.

Introduction: Presence of endometrial gland and stroma in extra uterine places is endometriosis. The aim of present investigation was the effect of royal jelly (RJ) on the CNS; CGRP and substance P concentrations in rat model of endometriosis.
Methods: Thirty-two Sprague Dawley female rats weighting 150-250 gr were used. All rats were randomly assigned to 4 groups as follow: Control, Sham, positive control, treatment. Administration of RJ 200mg/kg was performing orally in treatment group. After 21 days in all groups, spinal cord and brain preparation was done. Assessments of CGRP and substance P levels were done by ELISA test.
Results: According to present data RJ, significantly decrease endometriosis mass size compared to positive control. Brain CGRP was significantly higher in positive control than those other groups; while this factor in spinal cord was significantly lower than those other groups. Both brain and spinal CGRP in treatment group had not significant difference compared to control and sham group. Brain substance P in positive control and treatment groups were significantly lower than those other groups. Substance P in spinal cord had no significant difference relative to all other groups.
Conclusion: According to present study results, RJ can reduce the size of mass in endometriosis. It may be that changes in CGRP and substance P in the brain and spinal cord lead to endometriosis induction; while oral administration of RJ can improve these disorders.
Key words: Endometriosis; CGRP, substance P, royal jelly

P-455

Effect of topical ointment formulation of Urtica dioica extract in the treatment acid burn in mice

Sara Shojaeizad, Siavash Parvardeh, Mohammad Abbas Sheykholeslami , Shiva Ghafghazi

Department of Pharmacology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Acid burn is one of the most severe kinds of burns which may affect patient's quality of life for a long time. The treatment of acid burns is not usually successful and the resulting scar tissues will remain for lifetime. In this study, the effect of topical application of Urtica dioica extract was examined for the treatment of sulfuric acid-induced burn wound in mice.
Materials and methods: Male NMRI mice weighing 30 to 35 g were used in this study. In order to induce burn wound, the animals were first anesthetized and the skin hairs in the back of the neck were removed. Then 20 µl pure sulfuric acid was applied on the skin surface. The animals were randomly divided into 6 groups (n=6) including negative control (without treatment), positive control (phenytoin), vehicle group, and three other groups in which the

topical ointment of Urtica dioica extract were applied once daily for 21 days. The surface area of the wounds was measured on days 3,7,14,21.
Results: Treatment of mice with topical ointment of Urtica dioica extract significantly decreased the surface area of the burn wounds compared to that of control group. The wound healing effect of Urtica dioica extract ointment was significantly better than that of phenytoin ointment as the positive control.
Conclusion: It was ultimately attained that topical ointment of Urtica dioica extract possesses wound healing effect and is capable of treating acid burn as well as improving injured tissues .
Keywords: Wound healing, Acid burn, Mice, Urtica dioica, Ointment

P-456

Medication errors reduction in cancer patients: the role of the clinical pharmacologist

Ali Eishy Oskuyi[1] , Hamdolah Sharifi[2,3] , Rahim Asghari[1]

1. Department of internal medicine, Faculty of Medicine, Urmia University of Medical Sciences, Urmia-Iran.
2. Inpatients Safety research center , Urmia University of Medical Sciences,Urmia , Iran
3. Department of Pharmacology, Pharmacy Faculty, Urmia University of Medical Sciences, Urmia- Iran

Background and Objective: Medication errors occur frequently at any stage of the treatment process, involves the whole medical team, including physicians, pharmacists, and nurses specially in patients with cancer. The main objective of this study is to describe, evaluate and document the prevention of medication errors by clinical pharmacologist consultations in patients with cancer.
Materials and Methods: We assessed the effect of clinical pharmacologist consultation by acceptance of interventions recommended due to dosage, frequency, duration of therapy errors, and drug-drug interactions. All medication errors detected by clinical pharmacologist were reported in the format of medical consultation. A documentation template was designed to collect the patient data (sex, age, diagnosis), written prescriptions and drug-specific recommendations. For the descriptive analysis of medication errors, the data showed as frequency (percentage of errors).
Results: This study included a total of 296 patients with an average age of 48.67±19.76 years of whom 47.30% was female. In total, 936 prescribing errors were detected. The specialist physicians accepted 897 of prescribing errors. The highest frequency of error (47%) was DDIs which were detected in 66.22% of the patients. Improper dose (17.41%), wrong frequency (16.67%) , food-drug interaction (10.26%) had the later frequencies, respectively. Wrong-route administration and wrong-drug indication had the lowest frequencies , respectively (5.13% and 3.53%).
Conclusion: Pharmacological consultation in the hematology-oncology ward revealed many medication errors. The trust of physicians in the views of the clinical pharmacologist led to a large part of these errors being accepted and resolved.
Key words: clinical pharmacologist, medication error, patient safety

P-457

Protective effects of long term testosterone administration on epididymal sperm parameters in experimental varicocele male rats

Anahid Shafie, Behjat seifi, Ghorbangol Ashabi, Mehri Kadkhodaee, Farzaneh Kianian, Keivan Lorian

Department of Physiology, Faculty of Medicine, Tehran University of Medical Science, Tehran, Iran

Background and Objective: Varicocele is one of the most important causes of male infertility characterized by abnormal dilation and tortuosity of the pampiniform plexus veins. Steroidogenesis potent of leydig cells is decreased in varicocele. The present study is designed to evaluate whether testosterone as a steroid agent has protective effects on epididymal sperm and testis parameters in varicocele-induced male rats.
Methods and Materials: Adult male rats were randomly assigned to 3 groups: varicocele, sham, and testosterone. In the varicocele group, the left renal vein was partially ligated. In the sham group, partially ligation of the left renal vein was not performed. In the testosterone group, five weeks after the induction of varicocele, 400µg/kg

testosterone was given subcutaneously for four weeks. The left caudal epididymis was used to assess sperm motility and viability. Testis tissue samples also resected to determine indices of weight and volume.
Results: Varicocele caused significant decreases in the progressive motile sperm and viability compared with sham group. Administration of testosterone significantly increased the progressive motile sperm and viability in varicocele rats compared with varicocele group. However, there were no significant differences in the weight and volume of testis among groups.
Conclusion: This study suggested that long term testosterone administration improved sperm parameters in varicocele male rats. Therefore, testosterone appears to be useful for the treatment of varicocele-induced male infertility.
Keywords: Varicocele; Testosterone; Progressive motile sperm; Viability

P-458

Investigation the effects of Iranian snake, Naja naja oxiana venom on the level of blood glucose of experimental diabetic rats

Shiva Shahdadi, Farshid Hamidi, Behrooz Fathi

Department of Basic Sciences, School of veterinary medicine, Ferdowsi University of Mashhad, Mashhad-Iran

Background and Objective: Diabetes is a chronic disease that occurs as a result of impaired insulin production and function which in turn lead to increase level of blood glucose and many complications. Snake venom is a complex mixture of pharmacologically active compounds. In this study, the effect of Iranian snake, Naja naja oxiana venom on level of blood glucose of diabetic male rats was investigated.
Materials and Methods: The combination of nicotinamide (NA) (230 mg/kg) and streptozotocin (STZ) (65 mg/kg) was used to induce type two diabetes (T2D), and STZ (55 mg/kg) alone was used to induce type one diabetes (T1D). After induction of (T2D) in 24 male rats, they were divided into 3 groups: one as control and two other groups received the venom at 0.2 and 0.4 mg/kg. After induction of (T1D) in 16 male rats, one as control and other group received the venom at 0.2 mg/kg. A group of 8 rats received the venom at 0.2 mg/kg for 7 days and then received STZ at 55 mg/kg. Blood glucose level was measured with glucometer and intraperitoneal route (IP) has been used for all injections.
Results: The Naja naja oxiana venom significantly reduced the blood glucose in both types (I & II) diabetic rats. The venom has not any effect on level of blood glucose of healthy rats and also unable to prevent the STZ action.
Conclusion: The results showed that Naja naja oxiana venom has anti-diabetes effect and can be a potential treatment for diabetes.
Keywords: Diabetes, Naja naja oxiana, Venom, Streptozotocin, Nicotinamide

P-459

The effect of ghrelin intrahippocampal injection on avoid memory in rat

Vahideh sahraiian, Homayoun Khazali*

College of Biological Sciences, Shahid Beheshti University, Tehran, Iran

Introduction: Today, memory impairment in neurodegenerative diseases Like Alzheimer, is one of the major dilemmas. Ghrelin is a peptide hormone that is synthesized by hypothalamus, pituitary, and some other tissues. This hormone may affect learning and especially motion memory in the hippocampus. The aim of this study is investigating of the effects of ghrelin intrahippocampal injection on avoid memory. 36 male rats were divided into 6 groups, including control, saline, ghrelin (0.3, 1.5 or 3 nmol) and citicoline. All groups were trained in the shuttle box test for 3 times to each rat. Results: the result showed that dosage 3 nmol of ghrelin significantly can be improved avoid memory in competition to citicholine ($P<0.0001$). Conclusion: It seems that ghrelin could be used to treat memory disorders such as Alzheimer's disease.
Keywords: Ghrelin, shuttle box performance test, avoid memory, Alzheimer's disease

P-460

The effects of Sitagliptin on the serum and ovarian inflammatory mediators of rats with polycystic ovary syndrome

Azadeh Safaeian

Background and objectives: The utilization of the drugs that improve metabolic syndrome and insulin resistance has clinical significance in control of PCOS and this syndrome is associated with related to low grade local and systemic inflammatory states, we designed this study to evaluate the effects sitagliptin, as an inhibitor of DPP-4, on inflammatory biomarkers in the ovary of PCOS rats.
Materials and Methods: After induction of PCOS by single injection of estradiol valerate at dose of 4 mg/rat, rats were divided into 4 groups including the normal, Control, PCOS + sitagliptin 25 and PCOS + sitagliptin 50. control group received daily administration of vehicle and treatment groups that received siagliptin at a dose of 25 or 50 mg/kg (P.O.) for 30 days. Thereafter, animal ovaries were removed for analysis of the gene expression. To evaluate the mRNA expression of the inflammatory mediators interleukin 1 (IL-1) and transforming growth factor β (TGF-β) after total RNA extraction, cDNA synthesized and Real time-PCR was performed. The serum levels of CRP were also determined.
Results: Induction of PCOS significantly led to increases mRNA expressions of IL-1 and TGF-β in the ovaries in compared to normal group. Treatment with sitagliptin significantly reduced the elevated mRNA expressions of IL-1 and TGF-β in the ovary.
Conclusion: Generally, the results of this study showed that sitagliptin can ameliorate the signs of polycystic ovary syndrome. In addition, the results indicate that part of the improvement effects of sitagliptin can be mediated by reducing ovarian inflammatory markers.
Key words: PCOS, Sitagliptin, Inflammatory, Rat

P-461

Behavioral effect of yettrium oxide nanoparticle on spatial memory imporovement in cholestatic male wistar rats

Sima Samadi[1], Shahrbano oryan[1], Delaram Eslimi Esfahani[1], Akram Eidi[2], Adel Salari Esker[1,*]

1. Department of Animal Science, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran
3. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran

Background and purpose: Cholestasis is defined as a decrease in bile flow, due to impaired secretion by hepatocytes or to obstruction of bile flow through intra-or extrahepatic bile ducts. Bile duct ligation (BDL) is shown to induce cholestasis-related liver function impairments, as well as consequent cognitive dysfunctions (i.e. impaired learning and memory formation). Several studies have shown the anti-oxidant and anti-apoptotic effects of Yettrium oxide nanoparticle. The aim of this study was to investigate the effect of yettrium oxide nanoparticles on spatial memory improvement in cholestasis male wistar rats.

Method: In this study, 42 male rats weighing 200-250 g were used. They were divided into four groups: control, sham group (underwent laparotomy without bile duct ligation), BDL, and the BDL rats received yttrium oxide. We used shuttle box for learning and memory assessment.
Findings: The results showed that yttrium oxide nanoparticle can improve learning and spatial memory in cholestasis male rats by increasing time spending in the chamber of shuttle box test.
Conclusion: This data suggest that antioxidant and anti-apoptotic properties of yttrium oxide nanoparticle can significantly alter learning improvement and spatial memory.
Key words: Cholestasis, Bile duct ligation, Spatial memory, yttrium oxide

P-462

The nephron-protective role comparison between saline, mannitol, ringer and saline-furosemide hydration process in cisplatin induced nephrotoxicity in male rats

Alireza Samimiat[1], Bahar Mazaheri[1], Farzaneh Ashrafi[2], Ardeshir Talebi[3], Mehdi Nematbakhsh[1,4,5]

1. Water and Electrolytes Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Internal Medicine, Hematology/Oncology Division, Isfahan University of Medical Sciences, Isfahan, Iran
4. Department of Clinical Pathology, Isfahan University of Medical Sciences, Isfahan, Iran
5. Department of Physiology, Isfahan University of Medical Sciences, Isfahan, Iran

Background: Cisplatin (CP) is known as a first choice treatment for solid tumors, however nephrotoxicity has remained as the most important side effect. In order to avoid CP induced nephrotoxicity, hydration is suggested. The main objective of the study is to consider different hydration protocols during CP therapy.
Materials and Methods: 42 Wistar male rats in 7 groups of experiments were treated with saline alone, CP alone and CP with one of the protocols of hydrations including: saline, mannitol, dextrose, saline & furosemide, saline & mannitol. One week later, the serum levels of blood urea nitrogen (BUN) and creatinine (Cr) were measured. The clearance of Cr (ClCr) and the kidney tissue levels of malondialdehyde (MDA) also was determined. The tissue staining was applied to find the tissue damage, and the damages were scored to report kidney tissue damage score (KTDS).
Result :The result indicates that the survival time of rats treated with CP accompanied with mannitol or furosemide supplementations reduced significantly ($P<0.05$). The serum level of BUN and Cr in the groups treated with mannitol and dextrose increased significantly when compared with control group ($P<0.05$). CP administration itself decreased the ClCr significantly compared to non-CP treated group ($P<0.05$). The kidney tissue levels of MDA were decreased in all CP treated groups significantly ($P<0.05$). The pathology findings revealed a higher KTDS in the groups hydrated with mannitol, dextrose or saline-furosemide.
Conclusion: It seems all of the supplementations don't have a considerable protective effect; however, normal saline has lowest harmful effect.
Keywords: Hydration, Mannitol, Furosemide, Nephrotoxicity, Cisplatin, Rats

P-463

Biological therapies, effective medical disciplines for patients with nonsmall cell lung carcinoma

Saba Talebian[1], Fatemeh B. Rassouli[1,2*]

1. Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
2. Novel Diagnostics and Therapeutics Research Group, Institute of Biotechnology, Ferdowsi University

Introduction: Lung cancer is a common malignancy worldwide with high incidence and mortality rate. Based on pathological characteristics, vast majority of patients (around 80%) are diagnosed with nonsmall cell lung carcinoma (NSCLC). Better understanding of NSCLC biology has led to development of novel therapeutic modalities with promising clinical outcomes. Herein, we focused on currently available biological therapies for NSCLC, with emphasis on antiangiogenics and anti-EGFR antibodies.

Methods: Number of recent review articles included key words nonsmall cell lung carcinoma, biological therapy, monoclonal antibody, angiogenesis and EGF receptor were extracted in databases PubMed, Web of Science and Scopus.
Results and Conclusion: Among monoclonal antibodies that target angiogenesis in NSCLC, bevacizumab, ramucirumab and nintedanib improve survival rate of patients when used in combination with chemotherapy drugs such as paclitaxel. In addition, cetuximab and necitumumab, which target the extracellular domain of EGFR, combined with routine toxic agents including cisplatin and gemcitabine lengthen survival of NSCLC patients. In conclusion, biological therapies have improved treatment results in a substantial proportion of NSCLC patients, however, combinatorial disciplines instead of sequential treatments result in more effective and promising outcomes.
Keywords: Nonsmall cell lung carcinoma, Biological therapy, Monoclonal antibody, Antiangiogenics, EGFR

P-464

The protective effect of coadministration of Melatonin and Atorvastatin on semen parameters in male rats

Ehsan Aali[1,2], Yazdan Naderi[1], Arezoo Bajelan1, Mehdi Ghaebi[1]

1. Department of Pharmacology, School of Medicine, Qazvin University of Medical
2. Cellular and Molecular Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

Background: Antioxidant agents are known to improve male semen parameters. Melatonin and Atorvastatin are considered as two major antioxidant agents. In this study, the effects of co-administration of these two agents on male semen parameters have been investigated.
Materials and methods: male Wistar rats were studied in separate 5 groups. The normal control, oligospermic and treatment groups. Oligospermic and treatment groups received single dose of busulfan (10 mg/kg) to induce testicular tissue damage and oligospermia. The treatment groups received Atorvastatin (100 mg/kg, ip), Melatonin (1mg/kg, ip), and co-administration of Melatonin and Atorvastatin (same dose, ip) for 8 weeks. At the end of study, animals were scarified and posterior epididymis was isolated and incubated in 1ml HTF solution at temperature of 37 ° C and 5% humidity for 30 minutes. Semen parameters including sperm count, motility and viability were evaluated.
Results: The percentage of live sperms in the control, oligospermic, melatonin received group, atorvastatin received group and Melatonin-atorvastatin received group was 72%, 23%, 45% , 24.3% , 59.6% respectively. The percentage of sperm progressive movement in animals was respectively 64%, 18.1%, 39.3%, 36.4%, 49.4%. The total sperm count was respectively 634,243,480,470, 563.
Discussion: In this study it has been observed that Melatonin had a significant positive effect on all three semen parameters , and Atorvastatin had a positive effect especially on motility and also on sperm count but did not affect sperm viability. Co-administration of melatonin and atorvastatin, showed notable improvement of semen parameters even more than using each agent separately.

P-465

Methotrexate through pro-inflammatory cytokines reductions could ameliorate sepsis Complications in LPS-induced mice.

Yaser.Jafari Khataylou[1],Azita Alijamaat[2]

1. Assistant professor of immunology, Department of Pathobiology, Faculty of veterinary medicine, University of Tabriz,Tabriz,Iran.
2. Veterinary student at University of Tabriz,Tabriz, Iran.

Background and Objectives: Sepsis is a life-threatening factor which causes many people to die and the percentage of mortality increases with age . Sepsis could be caused by various bacteria and the inflammation is an important immune response against these pathogens one of the most important mediators of inflammation is the secretion of

pro- inflammatory cytokines such as IL-1 and IL-6. These cytokines could be harmful to body tissues when they are not regulated properly, which is one of the most important causes of body damage and Methotrexate could be effective as a pro- inflammatory cytokines reducing drug.
Materials and Methods: mice were divided into 3groups,randomly .Group A consisted of mice that were received normal saline .Group B included mice that were received LPS intraperitoneally (0/75 mg/animal). Group C contained mice which received Methotrexate (37.5 mg / kg, i.p) 1 and 6 hours after LPS administration followed by blood was collected from the tail vein of mice and the cytokines (IL-1 & IL-6) were measured in serum samples by Commercially available enzyme-linked immunosorbent assay (ELISA) kits.
Results: Our data showed that serum cytokines levels in treated LPS-induced mice was lower significantly ($p<0.05$) in compared to LPS-induced mice and in LPS-induced mice was higher significantly ($p<0.05$) in compared to control group.
Conclusion: Methotrexate is effective to reducing pro-inflammatory cytokines productions and due to its effect it could be used as a suitable strategy to treat septic shock.
Keywords: Methotrexate, LPS, sepsis , cytokine , mice

P-466

The study of treadmill exercise on the cardiac injury and behavioral deficits induced by methadone maintenance treatment and brain BDNF changes in behavioral sensitization phenomenon in morphine withdrawn rats

Maryam Alizadeh[1, 2, 3*], Mahdi Zahedi-Khorasani[1, 2], Hossein Miladi-Gorji[1, 2]

1. Laboratory of Animal Addiction Models, Research Center of Physiology, Semnan University of Medical Sciences, Semnan, Iran.
2. Department of Physiology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran
3. Student Research Committee, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran.

Introduction: Dependency to opioids is neuropsychological disease and healthy problem in the world and MMT is the common accepted cure that is currently used for reduction of it's adverse effects. But addicted people that are

under methadone maintenance treatment still have a continued vulnerability to relapse and they are at increased risk for many physical, psychological and heart disorders. Hence, the existence of effective intervention in this therapy is nessecery. One of the best interventions is exercise and therefore this study was designed to examine the effect of mild treadmill exercise on the behavioral, locomotor sensitivity and heart problems in morphine withdrawn rats receiving MMT.
Methods: In this study 340 male wistar rats used in three section as behavioral (16 group), locomotor sensitization (16 group) and heart ischemia (16 group). The rats were chronically depended with bi-daily doses (10 mg/kg, SC, at 12 h intervals) of morphine for 14 days. After that, the animals received methadone maintenance treatment for 30 days (1mg/kg/day in first two days, 2 mg/kg/day in secend two days and 3 mg/kg/day for the rest of period), contemporary this animals were forced to run on a motorized treadmill for 30 days (5 days in a week in 30 minutes) during morphine withdrawal. Then, rats were studied for the behavioral tests as naloxone-precipitated withdrawal signs, anxiety like behavior with EPM, depressive like behavior with SPT and the craving to morphine consumption in morphine preference model. Similarly, locomotor sensitization and ventral pallidum-ventral tegmental area BDNF measurment examined.
In heart studies, induction of ischaemia were did by isoproterenol (85 mg/kg, SC for two days) and 24 hours after second injection of isoproterenol, animals were anesthesied by sodium thiopental and then, hemodynamic indices (dp/dtmax, dp/dtmin, SBP, DBP, MABP, HR, LVSP and LVEDP), biochemical (cTI), stress oxidative (GPx, SOD, MDA) and histopathology (edema, inflamation and necrosis) were examined.
Results: Our results showed mild treadmill exercise decreased naloxone-precipitated withdrawal signs, the anxiety/depressive-like behaviors and the voluntary morphine consumption in morphine withdrawn rats receiving MMT, but had no effect on behavioral sensitization and VP-VTA BDNF levels that previously induced by morphine dependency and then modulated with MMT. In heart studies, chronic treatment of methadone in non-ischemic non-dependent group, significantly increased all of the hemodynamic factors and decreased LVEDP, also significantly increased MDA and decreased GPx and SOD, Furthermore, histopathological indices worsen in this group, but this effects modulated by morphine in non-ischemic dependent groups. All of heart indices worsen in ischemic non-dependent groups and this harm effects modulated by protective effects of morphine that previously induced in dependency period and exercise and methadone didn't affect this results in morphine withdrawn rats receiving chronin methadone and exersice.
Conclusion: Mild treadmill exersice decreased the severity of physical dependence, anxiety/depressive-like behaviors and the voluntary morphine consumption in morphine withdrawn rats receiving MMT, although it doesn't affect behavior sensitization and VTA-VP BDNF level. Therefore, mild exercise propram recommend in addicts receiving MMT. But, chronic misusage of methadone increase heart damage in rats without previous history of chronic morphine use, hence the use of chronic methadone must be cautiously.
Keywords: Morphine, Methadone Maintenance Treatment, Withdrawal sign, Anxiety, Depression, Relapse, Locomotor Sensitization, BDNF and Heart Ischemia

P-467

The effect of oral administration of hydroalcoholic extract of quercus, crisium vulgare and falcaria vulgaris on preventing gastric ulcer induced by ethanol on antioxidant parameters in rats

Abolfazl Farahi, Javad Sajedianfard, Said Nazifi, Ali Mohammad Basatinya

Department of Basic Sciences, School of Veterinary Science, Shiraz University, Shiraz, Iran.

Background and Objective: gastric ulcers, are open sores that develop on the lining of the stomach due to the failure of the gastric defenses against the deleterious factors. Nowadays, treating gastric ulcer with herbal medicines has been a major success. In this study, the effect of hydroalcoholic extracts of these plants on antioxidant parameters in gastric ulcers induced by ethanol was investigated.
Materials and Methods: 30 male rats were randomly allocated into 6 groups: Control group (intact animals), Sham group (distilled water was gavaged for 14 days. Negative control group (omeprazole was administered at for 14 days (20 mg/kg)). Experimental groups (hydroalcoholic extracts were gavaged for 14 days (500 mg/kg)). gastric ulcer

was induced by ethanol gavage 1 ml/200 g/kg; Then antioxidant parameters were measured by using Elisa. Data were analyzed by using SPSS.
Results: Administration of ethanol to rats of sham group resulted in severe lesions in stomach, while mucosal lesions in negative control group as well as groups treated with ethanolic extract of plants, which used, (especially quercus) were very mild with regard to ulcer area and number. Significant differences were observed in serum levels of antioxidant parameters in groups of rats.
Conclusion: In conclusion, hydroalcoholic extracts of Considerable plants has a gastroprotective effect against ethanol-induced gastric ulcer in rats.
Keywords: Quercus, Cirsium vulgare, Falcaria vulgaris, Gastric ulcer, Rat, Antioxidant

P-468

Comparison between the Effects of Hydroalcoholic Extract of Dill and Statins on Lipid Profile

Zahra Forouzandeh* , M ahmoud Rafieian, Mahbubeh Setorki

1. Postgraduate of Animal Physiology, Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran
2. Professor of Pharmacology, Medical Plants Research Center, Shahrkord University of Medical Sciences, Shahrekord, Iran
3. Assistant Professor of Physiology, Department of Biology, Izeh Branch, Islamic Azad University, Izeh, Iran

Background and objective: A transient increase of blood concentration of lipids after meal is able to increase the risk of atherogenesis. This study aimed to determine the effects of Anethum graveolens L. (dill) consumption on atherosclerosis and hepatic risk factors.
Material and Methods: In an experimental study, 32 male New Zealand rabbits were randomly allocated to four groups toreceive normal diet, a diet containing 1% cholesterol, a diet containing 1% cholesterol plus 200 mg/kg dillpowder, and a diet containing 10 mg/kg lovastatin. Risk factors of atherosclerosis including glucose, totalcholesterol (TC), triglyceride (TG), apolipoprotein B (ApoB), alanine aminotransferase (ALT), aspartateaminotransferase (AST), low density lipoprotein cholesterol (LDL-C), nitrite, nitrate, fibrinogen, and factorVII were measured and compared between different groups.
Results: Consumption of dill caused a significant reduction in glucose compared to thehypercholesterolemic diet group. Dill powder significantly decreased LDL-C, TC, AST, ALT, andfibrinogen. No significant differences were found between dill group and hypercholesterolemic diet group inApoB, factor VII, nitrite, and nitrate.
Conclusion: According to our findings, postprandial consumption of dill may have beneficial effects onatherosclerosis and hepatic risk factors.
Keywords: Aneth olens, Atherosclerosis, Dill, Lipid profile

P-469

The effect of nobiletin on behavioral function in plus elevated and forced swim tests in amyloid beta-induced model of Alzheimer's disease in the rat

Marzieh Fakour[1], Zahra Kiasalari[2], Reihane Ghasemi[1], Maryam Khorasani[1], Sedigheh Keshtkar[1], Mehrdad Roghani[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Department of Physiology, Shahed University, Tehran, Iran.

Background and Objective: Alzheimer's disease (AD) is the most common form of dementia that is considered a chronic and progressive syndrome, that leads to the irreversible loss of neurons, particularly in the cortex and

hippocampus. In this study we considered whether nobiletin has any effect on behavioral function in plus elevated and forced swim tests in amyloid beta-induced model of Alzheimer's disease in the rat.
Materials and Methods: 32 male rats were randomly divided into four groups as follows: group A (Sham), group B (sham+nobiletin), which were administrated nobiletin (10 mg/kg) daily one hour after surgery for one week via gavage, group C (Aβ): which amyloid β1-40 (2 nanomol/2 µl) was injected into hippocampal region (CA1) bilaterally, and group D (Aβ + nobiletin), which were administrated nobiletin (10 mg/kg). Furthermore, two behavioral tests including elevated plus maze and forced swimming tests were used to assess animal performance.
Results: The results showed that group C has a significant increase regarding anxiety, Moreover, Aβ group which was treated with nobiletin exhibited significant reduction of the aforementioned parameters. Meanwhile, no significant changes were observed in nobiletin-treated sham group.
Conclusion: Taken together, these findings suggest that nobiletin could reduce anxiety in amyloid beta-induced model of AD in the rat with no significant effect on depression.
Keywords: Alzheimer's disease, Amyloid beta, anxiety and depression, Nobiletin, Elevated plus maze, Forced swimming test

P-470

Evaluation of antiviral properties of Yarrow alcoholic extract in ovo inoculation of Newcastle disease virus

Javad Rezanejad[1], Adel Feizi[2]

1. College of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
2. Assistant Professor, Department of Clinical Sciences, Tabriz Branch, Islamic Azad University, Tabriz, Iran

Yellow Yarrow (Achillea biebersteinii) is a kind of plants belonging to the Astraceae family which found in Europe, Turkey, Iran and Central Asia. In addition to its traditional application, this plant is remarkable due to its extract characteristics in modern medicine and various industries. The aim of this study was to evaluate the antiviral properties of alcoholic extract of yarrow on Newcastle disease virus.
Material and methods: for this purpose, the plant extract was prepared at 200 and 400 mg/ml dilutions and inoculated with virus (500µl of extract plus 500 µl of each virus dilution) into 9-day-old fertilized egg by Allantois fluid injection method. The eggs were kept at 350c and after 7 days, the EID50 virus and virus + extract composition were calculated by REED and MUNCH method.
Results: results showed that yellow yarrow extract at 200 and 400mg/ml dosage decreased the potency of the virus 50 and 100 times compared to the virus group respectively.
Conclusion: in this study, since at the beginning, the extract were adjacent to the virus and then injected into the eggs; it is likely that the plants antiviral properties may be influenced on the structure or ligands of the virus, so that it prevented the virus binding to the cell. It may also affect the process of virus replication within the cell. Due to the antiviral properties of yellow yarrow, this plant can be used for various industries, especially pharmaceuticals.
Key word: Achillea biebersteinii, Newcastle, egg

P-471

Morphine affects TLR 4-MyD 88-NF-κB Signal Transduction Pathway of breast cancer cell line

Shaghayegh Haghjooy-Javanmard[1], Ahmad Ghasemi[1], Bahareh Zarrin[1], Ismail Laher[2], Golnaz Vaseghi[3*]

1. Applied Physiology Research Center and Department of Physiology, Cardiovascular Research Institute, Isfahan University of Medical sciences, Isfahan, Iran
2. Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, BC, Canada
3. Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical sciences, Isfahan, Iran

Background and Objective: The TLR4 gene promotes migration in adenocarcinoma cells. We investigated the effect of morphine on TLR 4-MyD 88-NF-κB expression and migration.
Materials and Methods:The migration of estrogen receptor-positive (MCF7) breast cancer cells was evaluated after 24 and 48 hours incubation with morphine, with the Boyden chamber method. Morphine effects on TLR 4-MyD 88-NF-κB mRNA expression was determined by quantitative Real-Time polymerase chain reaction, Interleukin 1 beta concentration was studied by ELISA.

Results: Morphine at the dose of 50 µM increased expression of the mentioned genes. Migration of cell line was increased. No changes were observed in interleukin 1 beta concentration.
Conclusion:We showed that Morphine can influence the TLR 4 expression and its migration in the breast cancer cell, which may depend on time and concentration.
Keywords MCF7 breast cancer. TLR 4-MyD88-NF-κB, Morphine

P-472

Search for and evaluation of pharmacodynamic and pharmacokinetic parameters of selective blocker of TRPA1 ion channels

Evgeniya A. Beskhmelnitsyna[1], Mikhail V. Pokrovskii[1], Dmitriy V. Kravchenko[2], Alexandr L. Kulikov[1], Tatyana V. Avtina[1], Darya V. Rozhnova[1], Vladimir I. Yakushev[1], Mikhail A. Martynov[1]

1. Belgorod State National Research University, Belgorod, Russia
2. Chemical Diversity Research Institute of the Corporate Group of ChemRar High-Tech Center, Khimki, Russia

Introduction. According to the literature, almost 30 million people daily take analgesics from the group of non-opioid analgesics, but in more than half of them 4-6 hours after taking the medication, the severity of pain is unchanged.
Objective. to search for the most active molecules potential selective inhibitors of the TRPA1 ion channel with further investigation of their pharmacodynamic effects, toxicological safety, pharmacokinetic parameters and organ distribution, as well as to assess their impact on the psychoemotional state, general locomotor activity levels and anxiety in laboratory animals.
Materials and methods. According to the results of in vitro tests, the most active molecule under code ZC02-0012 was selected from the pool of candidates. Further its analgesic activity was evaluated using an acetic acid-induced writhing test and a hot plate test; its anti-inflammatory activity was studied in the acute exudative paw edema model; in the open field and elevated plus-maze tests the influence of ZC02-0012 on the general locomotor activity levels and the anxiety of the laboratory animals was studied. The pharmacokinetic parameters and organ distribution of the substance ZC02-0012 were studied using a HPLC with ultraviolet absorption method.
Results and discussion. According to the results of in vitro tests, it was found that IC50 of ZC02-0012 was 91.3 nmol. The preclinical studies showed that ZC02-0012 possessed pronounced analgesic and anti-inflammatory activities and absence of the influence on the behavior and anxiety of the laboratory animals. Absolute bioavailability of ZC02-0012 in rabbits was 47%, while ZC02-0012 was intensely distributed into organs and tissues. The highest content of ZC02-0012 is typical of liver, kidneys and lungs, the lowest – for muscle tissue. Most of the substance is undergone rapid biotransformation and excreted as metabolites.
Keywords: TRPA1 ion channel antagonists, ZC02-0012, NSAIDs

P-473

N-acetyl cysteine and estrogen treatment can improve ovarian function after cryopreserved ovary transplantation

Fatemeh Ebrahimi, Meysam Nasiri, Saeed Zavareh, Taghi Lashgarbluki

School of Biology, Damghan University, Damghan, Iran

Objectives: Ischemia/Reperfusion shock and delay in angiogenesis are important issues after ovarian transplantation. In this study, we aimed to investigate the effects of N-acetylcysteine (a potent antioxidant) and estrogen on ischemia damage and angiogenesis after ovarian transplantation.
Materials and Methods: Mice (age 6-8 weeks) were divided into following groups: Group 1: fresh ovarian tissue transplantation; Group 2: cryopreserved/warmed tissue transplantation; Group 3: cryopreserved/warmed ovarian transplantation + NAC; Group 4: cryopreserved/warmed ovarian transplantation + estrogen; Group 5: cryopreserved/warmed ovarian transplantation + NAC and estrogen. To further analysis grafts were extracted on days 2 and 7 after transplantation.
Results: Our results showed that, enzymatic activity of SOD and GPX at day 2 and also total antioxidant capacity (TAC) at day 7 post-transplantation were significantly decreased in group 2 compared to group 1. NAC and estrogen

treatments alone and their combination, could dramatically improve TAC levels but there was no effects on the SOD and GPX activity. Histological analysis also revealed that, cryopreservation reduced the number of primordial and primary follicles at day 2 and day 7 but it increased the number of preantral and antral follicles at day 7. NAC significantly improved the number of all four follicular phases at days 2 and 7. Estrogen administration also increased the antral follicular count. Our results also showed significant angiogenesis after treatment with NAC and estrogen alone and in combination.
Conclusion: Single dose NAC at day2 and estrogen at day7 post transplantation, could improve ovarian oxidative damage, de novo folliculogenesis, follicular development and angiogenesis after transplantation.
Key words: Ischemia/reperfusion, Hypoxia, Angiogenesis

P-474

Evaluation and comparison of protective effects of Curcumin and vitamin E against acrylamide induced oxidative stress and cytotoxicity

Sanam Ashrafi[1], Mehdi Evazalipour[2], Zahra Hesari[3], Ehsan Zamani[1*]

1. Department of Pharmacology and Toxicology, School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran.
2. Department of Pharmaceutical Biotechnology, School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran.
3. Department of Pharmaceutics, School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran

Background and Objective :Acrylamide, a neurotoxic, genetic, and carcinogenic agent, is one of the compounds produced at high temperatures during the preparation of carbohydrate-rich foods. Acrylamide-induced cytotoxicity is associated with oxidative stress. Curcumin is a natural potent antioxidants found in turmeric, which can suppress the formation of ROS and reduce lipid peroxidation. In this study, the cytotoxicity and oxidative toxicity of acrylamide were evaluated in Hu02E fibroblast cells. Furthermore, the protective effect of Curcumin was compared with vitamin E as a known antioxidant.
Method: In this in vitro study, Fibroblast Cell line (Hu02) was treated in groups as follows: control (receiving normal saline), acrylamide (5mM), acrylamide + curcumin (2.5 µM), acrylamide + curcumin + vitamin E (10 µM) and acrylamide + vitamin E. After 24 hours, cell viability, lipid peroxidation and glutathione oxidation were evaluated in treatment cells.
Result: The results showed that acrylamide significantly reduce cell viability. On the other hand, increased lipid peroxidation and glutathione oxidation were observed. It was interesting that curcumin significantly increased cell viability and protected the cells against oxidative damage as well as vitamin E.
Conclusion: In this study, we proved that acrylamide can decrease cell viability by inducing of oxidative stress. Furthermore, we showed that curcumin have a huge antioxidant properties similar to vitamin E that led to increasing of cell survival exposed with acrylamide. Therefore, the use of the natural antioxidant such as curcumin seems to be useful in preventing of acrylamide's toxic effects in preparing of high carbohydrate foods.
Keywords: Acrylamide, Curcumin, Oxidative stress, Cell viability, Hu02 fibroblast cells.

P-475

Effect of Thioflavin-T on the levels of Leptin, Adiponectin, Insulin and histological examination of the liver on male NMRI with high fat diet

Nafiseh Amaniekhtesar

Introduction: Obesity, a public health problem of the first order for industrialized and non-industrialized countries dramatically cause a reduction in overall life expectancy. Obesity is considered to be a major risk factor for chronic diseases such as CHD and hypertension, type 2 diabetes, and some types of cancer. Effect of Thioflavin-T was evaluated on body weight and blood glucose, insulin, insulin resistance, leptin, adiponectin and liver histological in male NMRI mice with high fat diet.
Materials and methods:The mice were randomly divided into five groups: The normal group,sham group,Experimental group 1:mice were given Thioflavin-T 5 mg/kg, Experimental group 2: Thioflavin-T 10 mg/kg, Experimental group 3: Thioflavin-T 15 mg/kg via intragastric gavage for 4weeks.

Results: In this study the amount of body weight of experimental groups was significantly reduced in comparison with Sham group. The amount of leptin, insulin and blood glucose of the experimental groups compared to Sham group showed a significant decrease. Serum adiponectin levels in the experimental groups compared to the sham group was increased. administration of thioflavin-T in different doses, causes finding polymorphonuclear cells in liver of the experimental groups, which the amount of these cells was more in the experimental group3.
Conclusion: It could be suggested that Thioflavin-T may be potentially effective candidates in obesity treatment and diabetes.
Keywords: obesity, Thioflavin-T, leptin, adiponectin

P-476

Phytochemical analysis and protective effects of date palm pollen extract in gentamicin induced nephrotoxicity

Neda Omidian, Houshang Najafi, Zeynb Mohamadi Yarijani

Medical Biology Research Center, Kermanshah University of Medical, Sciences, Kermanshah, Iran

Background and objective: Date palm pollen (DPP), the male reproductive dust of palm flowers, has been reported to possess potential profits in the treatment of different diseases from ancient times. The current study aimed to bioassay the phytochemical analysis of hydroalcoholic extract of Iranian date palm pollen and its effects on gentamicin (GM) induced nephrotoxicity in rat.
Materials and methods: Crude extract of DPP was phytochemically evaluated to determine the presence of alkaloids, flavonoids, phenols, saponins, terpenoids, sterols, tannins, anthraquinones, anthocyanins, coumarins and musilage according to standard methods. Thirty five male Wistar rats were divided into five groups (n=7) as control, sham, gentamicin, gentamicin+DPP (200 mg/kg), and gentamicin+DPP (400 mg/kg). The gentamicin group received vehicle during the experiment, and GM was injected from the third day (100 mg/kg, i.p). But the gentamicin+DPP groups received intraperitoneal hydroalcoholic DPP extract, 200 or 400 mg/kg, respectively, for 9 days and GM (100 mg/kg) from the third day. Renal function was evaluated through measurement of creatinine and urea-nitrogen in plasma.
Results: Phytochemical analysis showed that the hydroalcoholic extract of DPP mainly contain flavonoids (4+), triterpenoids (4+), sterols (3+), and alkaloids (2+). In vivo study demonstrated that GM resulted in significant increases in the plasma creatinine and urea-nitrogen; which following the administration of DPP decreased to their values in sham group, dose dependently.
Conclusions: Hydroalcoholic extract of DPP mainly contain flavonoids, triterpenoids, sterols, and alkaloids. DPP extract has protective effects against gentamicin induced renal functional disturbances.
Keywords: Date palm pollen, Gentamicin, Nephrotoxicity.

P-477

Improved spatial long-term memory, behavioral outcomes, and neuroprotective effect after progesterone administration in rat with traumatic brain injury: role of progesterone classic receptors

Ladan Amirkhosravi[1], Mohammad Khaksari[2], Vahid Sheibani[3], Nader Shahrokhi[1], Mohammad navid Ebrahimi[4]

1. Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Neuroscience Research Center, Institute of Neuropharmacology and Physiology Department, Kerman University of Medical Sciences, Kerman, Iran

3. Neuroscience Research Center, Kerman University of Medical Sciences, Kerman, Iran

4. Physiology Research Center, Institute of Neuropharmacology and Physiology Department, Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: In the present study, the role of classic progesterone receptors in mediating the neuroprotective effects of progesterone on inhibition of brain edema, damages of blood brain barrier and long-term behavioral disorders were investigated.
Materials and Methods: Ovarectomized female rats received progesterone or vehicle injection intraperitoneally 30 min after traumatic brain injury (TBI). They also received an injection of RU486, classical progesterone receptor antagonist 90 min before the progesterone. The brain water (BWC) and Evans blue (EB) contents were measured at 24 h and 5 h after brain injury, respectively. Intracranial pressure (ICP) and cerebral perfusion pressure (CPP) and beam walk task (BW) were measured before TBI and at different times after TBI. Locomotor activity, anxiety-like behavior and spatial memory were evaluated in the previous days and days 3, 7, 14, and 21 after trauma.
Results: Progesterone prevented the increase of BWC and EB after TBI, and this effect was inhibited by RU486. The RU486 inhibited decremental effect of progesterone on ICP as well as increasing effect of progesterone on CPP at different times after TBI. Also, the increase in traversal time and reduction in vestibulomotor score in the BW task were improved by progesterone, and RU486 inhibited this effect. TBI induced motor, cognitive and anxiety-like disorders, which lasted for 3 weeks post TBI, but progesterone prevented these cognitive and behavioral abnormalities. Similar to the above parameters, RU486 opposed this progesterone effect.
Conclusion: Our study suggested that, the classic progesterone receptors have neuroprotective effects after TBI and also prevent long-term behavioral and cognitive deficits after TBI.
Key word: progesterone classic receptors, neuroprotection, behavioral outcome, memory, traumatic brain injury,

P-478

The evaluation of VEGF and HIF-1α genes polymorphisms and multiple sclerosis susceptibility

Arian Amirkhosravi[1], Mohsen Saravani[2,3], Mohsen Rokni[4], Mehrzad Mehrabani[5,6] Sanaz Faramarz[7,11], Iman Fatemi [8], Mojdeh Esmaeili Tarzi [9], Mohammad Hadi Nematollahi [10,11*]

1. Food, Drug, Cosmetic Safety Research Center, Kerman University of Medical Sciences, Kerman, Iran
2. Department of Clinical Biochemistry, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
3. Cellular and Molecular Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
4. Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
5. Herbal and Traditional Medicines Research Center, Kerman University of Medical Sciences, Kerman, Iran
6. Department of Traditional Medicine, School of Persian Medicine, Kerman University of Medical Sciences, Tehran, Iran

7. Kerman Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
8. Research Center of Tropical and Infectious Diseases, Kerman University of Medical Sciences, Kerman, Iran
9. Physiology Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
10. Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran
11. Department of Clinical Biochemistry, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran

Background: Multiple sclerosis (MS) is an autoimmune disease that leads to myelin sheets destruction. Hypoxia-inducible factor 1 (HIF-1) has several roles in cells like inducing inflammation and angiogenesis. Recently, several lines of evidence have indicated the role of hypoxia response and HIF-1 signaling pathway in the autoimmune disease like MS. The aims of present study were to evaluate the effects of HIF-1α genes polymorphisms and VEGF (as a major target gene of HIF-1α) gene polymorphism on MS susceptibility.
Materials and Methods: The 150 MS patients and 150 healthy age and gender-matched people as a control group participated in the study. The PCR-RFLP method was used for genotyping.
Results: Our results showed that the AA genotype of VEGF rs699947 polymorphism was significantly higher in the control group than the case group (P=0.004). Also, we showed the significant between VEGF rs699947 polymorphism and MS in recessive inheritance model (P=0.005). Regarding the VEGF rs699947 polymorphism allelic distribution, the A allele frequency was significantly higher in the control group than the case group (39% vs 28.7, respectively, P=0.009) and 0.63 fold decreased the MS susceptibility (OR=0.63, 95%CI=0.44- 0.88). There was no significant difference between the two groups in HIF-1α rs11549465 genotypic distribution. The HIF-1α C111A polymorphism was non-polymorphic in our study population except in case group that 9 subjects carried the CA genotype.
Conclusion: Taken to gather, we showed a significant association between VEGF rs60047 polymorphism and MS susceptibility. However, our results didn't show a significant association between MS and HIF-1α polymorphisms.
Keywords: VEGF, HIF-1α, gene polymorphism, multiple sclerosis

P-479

Impact of acute psychological stresses and CRH administration into PVN and CeA nuclei on food intake and serum leptin level in adult male rats

Mina Sadat Izadi, Maryam Radahmadi, Maedeh Ghasemi, Atefeh Rayatpour

Department of Physiology, School of Medicine, Isfahan University of Medical Science, Isfahan, Iran.

Background and Objective: Corticotrophin-releasing hormone (CRH) is one of the either pivotal neuropeptides in stress conditions or considerable regulatory factors in energy homeostasis. The paraventricular nucleus (PVN) and central amygdala (CeA), as two prominent nuclei on feeding behavior, have CRH receptors. This study investigated the effects of CRH administration into PVN and CeA nuclei on food intake and serum leptin level under acute both social and isolation stresses.

Materials and Methods: Sixty-six male rats were divided into control, social (SS) and isolation stress (IS), sham PVN/CeA, CRH treated PVN/CeA (2µg/kg), SS/IS-CRH-PVN and SS/IS-CRH-CeA groups. Rats were under stresses for 24 hours. The food intake was measured after 16–18h of food deprivation.
Results: The food intakes were significantly declined in the CRH-PVN group compared to the control, SS, and IS groups ($P<0.01$, $P<0.05$, and $P<0.05$, respectively). Food intake in the SS-CRH-PVN group significantly ($P<0.01$) increased relative to the CRH-PVN group. Otherwise, food intake significantly ($P<0.05$) decreased in the CRH-CeA group compared to the control group. Also, the serum leptin levels were increased in the IS ($P<0.05$), CRH-PVN ($P<0.01$), and IS-CRH-PVN ($P<0.01$) groups compared to the control group. While, serum leptin level was significantly ($P<0.05$) lower in the SS-CRH-PVN group than in the CRH-PVN group.
Conclusion: Both PVN and CeA nuclei regulate food intake by different mechanisms. Finally, the PVN seems to be more effective on regulating of food intake behavior and more sensitive to changes of leptin level than CeA.
Key words: stress, CRH, PVN, CeA, Food intake, leptin.

P-480

The efficiency of magnetic Nanoparticles functionalized by gallic acid in crossing the Blood-Brain barrier in Listeriosis Infection in rats

Mehrdad Azarmi[1], Hadi Maleki[1], Nader Nikkam[1], Hassan Malekinejad[2]

1. Faculty of Life Sciences & Biotechnology, University of Shahid Beheshti, Tehran, Iran.
2. Department of pharmacology and toxicology, Faculty of Pharmacy, Urmia University of Medical sciences, Tehran, Iran.

Background and Objective: Biocompatibility, size and external conductibility make the magnetic nanoparticles (MNPs) fascinating substances for drug delivery purposes. We aimed to functionalize MNPs with gallic acid and use them as guidable drug carriers to treat CNS listeriosis in rats.
Materials and Methods: MNPs were prepared by the sonochemical method and functionalized by gallic acid. The physicochemical characteristics of NPs were evaluated by TEM, DLS, ZP, FTIR, XRD, and VSM techniques. Gallic acid release rate was assessed by dialysis bag method. Oral gavage was used for inoculation of rats. CNS infection was approved by detection of the listeriolysin O (hly) gene in brain parenchyma. The MNPs ability in crossing the BBB was evaluated by Perl's Prussian blue staining and confirmed by ICP-OES spectrometry. The RT-qPCR was used to evaluate the efficacy of gallic acid and suitability of the delivery system.
Results: Characterization tests revealed superparamagnetic iron oxide NPs functionalized by gallic acid with an average size of 17 nm, zeta potential of -37 and crystal size of 7 nm. The release assay showed a reducing rate over time. CNS infection was approved by visualizing of the 164 bp amplicon in agarose gel. Perl's staining showed the success of MNPs in crossing the BBB and was confirmed by ICP-OES. The RT-qPCR showed elimination of L. monocytogenes in rats treated by the functionalized MNPs.
Conclusion: The functionalized MNPs were prosperous with the aid of external magnetic field in crossing the BBB and curing listeriosis.
Keywords: Magnetic Nanoparticle, Drug delivery, Blood-Brain barrier

P-481

The protective effect of melatonin on benzo(α)pyrene-induced neurotoxicity in mice

Samira Barangi, Soghra Mehri, Gholamreza Karimi, Ehsan Zamiri

Department of pharmacodynamics and toxicology, School of pharmacy, Mashhad University of Medical Science, Mashhad, Iran

Background: Benzo (a)pyrene [B(a)P] is a polycyclic aromatic hydrocarbon which is considered as a widespread pollutant. In the B (a) P metabolic pathway, the generation of highly reactive compound and oxygen free radicals cause to oxidative damage of macromolecules, tissue destruction, apoptosis and cell death in vital organs such as brain, heart and liver.
Melatonin, a circadian hormone secreted by the pineal gland, exerts various biological activities such as anti-oxidation and anti-apoptosis, suggesting that melatonin has neuroprotective effect against different brain injury. In addition, it is proposed that the administration of melatonin influences the autophagy pathway which is known as one of the critical cellular homeostatic mechanisms.

Objective: Present study aimed to evaluate the protective effect of melatonin on B (a)P-induced neurotoxicity through its effect on the autophagy and apoptotic pathway.
Materials and Methods: Forty Male BALB/c mice divided into four groups and treated for 28 days; 1)the control group was received B(a) P and melatonin solvent by oral gavage and intraperitoneally (i.p.), respectively, 2)B(a)P (75 mg/kg, oral gavage), 3)melatonin (20 mg/kg, i.p.) and 4)B(a)P + melatonin group. Malondialdehyde (MDA) and reduced glutathione (GSH) contents were determined in brain. Western blot was conducted for the expression of LC3 II/I, Beclin1, Caspase-3, Bcl2 and Sirt1.
Results: Mice treated with B (a)P showed a marked increase in MDA and reduce GSH which inverse by melatonin administration. Additionally, western blot analysis indicated significant changes in autophagy and apoptosis pathways proteins by concurrently administration of B(a)P and melatonin.
Conclusion: These findings suggest that melatonin attenuates B(a)P-induced brain injury through Sirt1-autophagy pathway regulation.
Keywords: Benzo (α)pyrene, Melatonin, Neurotoxicity, Apoptosis, Autophagy, Sirtuin1

P-482

Safety assessment of a new strain of native Iranian Lactobacillus pentosus (IBRC=11143) in male Wistar rats

Saba Bahrehvar[1], Shiva Khezri[1], Amir Abbas Barzegari[2], Vahid nejati[1]

1. Department of biology, Faculty of science, Urmia University, Urmia,
2. Department of Biology, Faculty of Basic Science, University of Maragheh, Maragheh, East Azerbaijan Province, IR Iran

Background and Objective: It is believed that the consumption of an adequate amount of live lactic acid bacteria (as probiotics) may improve the health of their host. Many strains of lactic acid bacteria are generally considered to be safe. However, recent studies have shown that some strains of these bacteria may have adverse effects. Thus, the purpose of this study was to investigate the safety of a new strain of native Iranian Lactobacillus pentosus (IBRC=11143) in male Wistar rats.
Materials and Methods: The toxicity of the strain of Lactobacillus pentosus was evaluated in a 28-days sub-chronic toxicity study. Three groups of rats (n=6) received saline or 1 × 10 8 and 1 × 10 9CFU/rat of this stain through gavage once a day for 28 consecutive days. On day 29, under systemic anesthesia, blood, serum and tissue samples of liver and kidney were obtained for analyzing different blood, serum, and tissue factors. Data analyzed with SPSS software.
Results: Analysis of tissue sections showed no significant alteration in the liver and kidney. However, a significant rise in ALP level was observed in rat serum. Some blood parameters (Lymphocyte, RBC, and HCT) also showed significant elevations in the groups that received the bacteria.
Conclusion: The results indicate the toxic effects of Lactobacillus pentosus (11143) on rats. Therefore, this lactobacillus strain may not be a good choice as probiotic
Keywords: Lactobacillus pentosus; Toxicity; Rat

P-483

Synthesis of 1,4- dihydropyridines from benzalldehyde and 2-chloro benzaldehyde, 4-methylbenzaldehyde, 5-bromo, 2-hydroxybenzaldehyde and cinnamaldehyde using diethyl ammonium nitrate ionic liquid catalyst and iron magnetic nanoparticles and their medical usage in medicine

Shahin Papi[1], Mehdi Forozesh[2], Hamidreza Nazifi[3], Abdollrazzagh Barzagar[4], Foroutan Salehinejad[5]

1. Ph.D. in chemistry from Arak Azad University, Teacher of Payame Noor University
2. Tehran, Deputy of development and Forensic medical equipment of the country
3. Khorram Abad, Director of Forensic Medicine of Lorestan Province
4. Tehran, Deputy of Forensic Medicine Organization of the country
5. Khorram abad, Pharmacologist

Dihydropyridines have numerous medical and pharmaceutical applications. Dihydropyridines derivatives are the strongest group of compounds known for calcium cation uptake. By absorbing calcium, these compounds reduce the entry of calcium into the cell and thereby lower blood pressure. They are used in treatment of brain diseases and tumors, as well as in the production of various drugs. In this new method, for the dihydropyridine derivatives synthesis, we used ferric oxide magnetic catalyst to increase the efficiency and speed of reaction and reduce the impurities from materials. The reaction method is as mentioned: the reaction of ammonium acetate, aromatic aldehyde and ethyl acetoacetate, in the presence of iron oxide magnetic nanoparticle catalyst, in solvent conditions with solvents or without them, through reverse distillation was performed and studied in terms of impurities existence and reaction speed. Using computational software and optimizing reaction conditions in terms of temperature, catalyst, time and type of material used and changing the structure of output products, we found that the 1,4 dihydropyridines compounds have antioxidant properties useful for preventing autoimmune diseases.
Firstly, the ionic liquid catalyst of diethyl ammonium nitrate was obtained from the reaction of dimethylamines and nitric acid. This ionic liquid was then used in presence of aldehydes and ammonium acetate and beta-decarbonyl compounds under solvent conditions. Then, by creating a suitable environment for a multi-component reaction, a variety of products with high efficiency can be prepared from 4-1 dihydropyridine derivatives in short time. The composition of these products is specified by FT-IR spectra.

P-484

Investigating the effect of Busulfan on Leydig cell maturation in testicular tissue of male wistar rats

Sajad Talkhabi, Shahrbano oryan, Hanieh Jalali, Delaram Eslimi Esfahani, Adel Salari Esker

Department of Animal Science, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran

Background and Objective: The use of anticancer drugs have adverse effect on cells and body organs, including the reproductive system .So efforts to recognize the effects of these drugs have been increased in recent years. The destructive effects of Busulfan through alkalizing properties in the spermatogenesis process are well known. Leydig cells in testicular tissue are responsible for producing testosterone .The aim of this study was to investigate the effect of Busulfan on testicular tissue leydig cell maturation .
Materials and Methods: Twelve Immature male Wistar rats were randomly divided into two groups. The first is the control and experimental group received intraperitoneal injection of Busulfan at 28 days of age with a dose of 20 mg/kg. The left testis of the animals was removed on the 54th day after birth to histological examination. After tissue sectioning and staining with hematoxylin and eosin, the cells were counted and the data were analyzed by statistical software.
Results: The Leydig cells in the experimental group showed a significant decrease compared to the control group.
Conclusion: Busulfan prevents DNA replication by alkylation of DNA. As a result, the mitosis process is not performed and the number of Leydig cells decreases. And because Leydig cells play a role in producing testosterone and fertility، reducing the number of these cells can play a role in reducing fertility.
Key words: Busulfan, testis, Leydig cells, Cancer

P-485

The effects of chronic Pistacia vera seed oil treatment on working memory and spatial learning and memory

Mahsa Hassanipour[1*], Mohammad Pak-Hashemi[1], Mohammadreza Mohammadinasab[1], Iman Fatemi[2]

1. Physiology-Pharmacology Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran; Department of Physiology and Pharmacology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.
2. Research Center of Tropical and Infectious Diseases, Kerman University of Medical Sciences, Kerman, Iran.

Background and Objective: Pistacia vera, a member of Anacardiaceae family, is an important herbal medicine in Iran. Pistacia contains different active pharmaceutical substances with antioxidants and anti-inflammatory functions. Studies showed that Pistacia species have neuroprotective properties on central nervous system disorders but the effects of pistachio oil have not yet been reported on the cognitive performance. In this study we investigated the nootropic effects of pistachio oil on male Wistar rats.

Materials and Methods: Twenty-one male Wistar rats (200-250 g) were used in this study. The animals randomly assigned to three groups: Control, treatment groups with pistachio oil (1 ml/kg, oral) and pistachio oil (4 ml/kg, oral). All treatments were performed for 21 consecutive days. Then, cognition was evaluated by Morris water maze (MWM) and the Y-maze continuous alternation task (Y-CAT). Pistachio from Akbari species with genetic code: M30, was obtained from Rafsanjan region of Iran and cold extraction method was used for oil extracting.
Results: Data revealed that chronic treatment with both doses of pistachio oil improved working memory in Y-CAT (all $P<0.05$) but failed to play significant effects on spatial learning and memory in MWM.
Conclusion: These results suggested that pistachio oil could enhance the working memory and may be a candidate for improving the cognition after clarification of possible mechanisms.
Keywords: Pistacia vera, Working memory, Spatial learning and memory, Rat

P-486

Survey of Protective Effects of Vitamin E and cerium Oxide Nanoparticles on Chlorpyrifos-Induced Oxidative Stress on the Liver enzymes

Mohammad Reza Khaksar[1], Abedin Saghafipour[2]

1. Department of Occupational Health, Faculty of health, Qom University of Medical Sciences, Qom, Iran
2. Department of Public Health, Faculty of health, Qom University of Medical Sciences, Qom, Iran

Background and Objective: The liver is exposed to many of the oxidizing agents for chronically and inevitably such as Chlorpyrifos (CPF), and the reduction in the harmful effects of these agents is considered in the physiological performance of the liver. so this study was designed to evaluate the protective effects of Vitamin E and cerium Oxide Nanoparticles on liver enzymes facing oxidative stress factors such as CPF as separately and combine together.
Materials and Methods: Male Wistar rats were randomly divided in eight groups, includes groups that were received normal saline intraperitoneal injection, CPF at a dose of 7.5 mg/kg via gavage., Vitamin E at a dose of 150 mg/kg via gavage, cerium oxide nanoparticles (NPs) 35 mg/kg by intraperitoneal injection, CPF and vitamin E simultaneously, CPF and cerium oxide NPs simultaneously and CPF, vitamin E and cerium oxide NPs simultaneously once a day for 4 weeks. Then, at the end of the treatment, the levels of liver enzymes, including alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) were compared between these groups.
Results: After analyzing the data, results showed that the activity of all enzymes in CPF group increased significantly and groups which were treated by vitamin E and CeO2 NPs along with CPF showed reduction in the levels of these enzymes.
Conclusion: Based on our results, the organophosphate CPF has toxic effects on the liver enzymes and interestingly the administration of vitamin E and CeO2 NPs causes protective effects against CPF.
Keywords: Chlorpyrifos, Vitamin E, CeO2 nanoparticles, Aspartate aminotransferases, Alanine transaminases, Alkaline phosphatase, Lactate dehydrogenase, Liver

P-487

Anticancer properties of fruits mentioned in the Holy Quran

Layasadat khorsandi[1, 2], Maryam Shirani[3]

1. Cellular and Molecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2. Department of Anatomical Sciences, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
3. Toxicology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Background and objective: About 18 fruits and plants are mentioned in the Holy Quran. In the Holy Quran, some fruits such as grapes, pomegranates, figs, and olives have received particular attention probably due to their high nutritional value. Holy Quran mentioned consuming fruits several times. In this article, anticancer properties of the Quran's fruits were studied.
Materials and methods: In this study, some scientific databases such as Scopus, Google Scholar, PubMed, and Science Direct was used. Also, Holy Quran and books about traditional medicine and medicinal plants were studied.
Results: Resveratrol (a polyphenol derived from grapes) is involved in the prevention of cancer by changing the cell division cycle, apoptosis, inflammation, and metastasis pathways. Pomegranate has anti-mutagenic, antioxidant and

anti-inflammatory agents, such as flavonoids, ellagic acid, tannins, and gallic acid, which prevent the growth of cancer cells. God has sworn to fig in the Quran. According to studies, fresh fig juice has an anti-cancer effect. Olives 6 times are cited in the Holy Quran. Olive oil plays an important role in preventing and improving cancer due to phenolic and unsaturated fatty acids.
Conclusion: The findings of this study indicate that religious teachings on the use of Quranic fruits are based on scientific logic that are intended to increase the health and longevity of humans. It is recommended to add these fruits to the daily diet.
Key Words: Holy Quran, cancer, grapes, pomegranates, figs, olives

P-488

Evaluation the effect of Combination of Gundelia tournefortii, Echinops percicusl and Althaea officinaalis extracts on Wound Healing in lab Rabbit

Mohammad Darvishpour[1],Reihaneh Hoveida[1*],Mohammad Hejazi[2]

1. Department of Biology, Doroud Branch,Islamic Azad University, Lorestan, Iran
2. Department of Animal Science, Khorramabad Branch,Islamic Azad Univercity,Lorestan,Iran

Background and objective: in the different cultures, the herbal plants have been used as a medicine source. Using them is common in the most traditional medical methods to heal wounds. This plan aims to survey and compare the combinations of the extract of some plants including Gundelia Tounefortii, Echinops Percicusl, and Altaea Oficinaalis on the wound recovery of the laboratory rabbits.
Material and method: the extract of Gundelia Tounefortii, Echinops Percicusl, and Altaea Oficinaalis were provided and mixed. Then, sixe male New Zealandian rabbits were bought and randomly divided into three test, control, and sham groups. Next, on the each side of the animals' spine, some 2× 2cm wounds were made. For the test group, the above combination, and for the sham group, Zinc Oxide cream were used; and nothing was given to the control group. The wound surface was measured on the 7th, 14th, and 21st days and the wounds were taken on the 21st day to be studied pathologically.
Results: analysis of statistics indicate that compared to control group, in test group Netrophils are less ($p< 0.001$), Macrophages are less($P<0.01$), blood veins are less ($P<0.05$), fibroblasts are more ($P<0.001$), and epidrom thinkness ($p<0.001$) increased; and there are a meaningful difference among all factors.
Conclusion: we conclude combination of the above-mentioned extract is significantly effective on the wound recovery and can be used instead of the chemical medicine.
Keywords: Gundelia Tounefortii, Echinops Percicusl, Altaea Oficinaalis, extract, wound

P-489

Assessment of follicular development of immature mouse ovarian tissue encapsulated in sodium alginate grafted under the kidney capsule: An Experimental study

Maryam Dehghan[1], Mojdeh Salehnia[2], Shirin Shahbazi[3]

1. PhD student of Anatomy, Department of Anatomy, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Professor of Histology and Embryology, Department of Anatomy, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
3. Department of Genetics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran

Background and Objective:This study aimed to evaluate the developmental rate of ovarian follicles and the incidence of cell death in grafted immature mouse ovarian tissue encapsulated and non-capsulated in sodium alginate
Materials and Methods:Female(NMRI)mice (n=50)were divided into 3 groups as follows: Group A: the right ovary was removed and encapsulated in sodium alginate then transplanted under kidney capsule, Group B: the right ovary

was removed and without encapsulation transplanted under kidney capsule, in both transplanted groups the left ovary was intact. Group C: control group, the both ovaries were intact. After transplantation, in the first and fourth estrous cycles at proestrus phase. The morphology of the grafted ovaries, and the percentage of normal follicles was evaluated using hematoxylin and eosin staining.The incidence of apoptosis cell death was evaluated by anti-BAX Immunohistochemical staining
Results:At first and fourth estrous cycle, almost 99.5% of follicles had normal morphology and no significant difference was observed between the groups.The follicular development and growth rate in the two grafted groups, was significantly higher than the control group, moreover these rates were higher in capsulated group than non-capsulated once ($p<0.05$).In spite of the presence of some BAX positive cells in the preantral and antral follicles there was no remarkable reaction for BAX antibody in the primordial and primary follicles in studied groups
Conclusion: Despite the high developmental rat and premature ovarian reserve depletion in grafted groups that can affect the longevity of transplanted tissue, while sodium alginate has a positive effect on the follicular development in grafted tissue
Keywords: Ovarian tissue, Transplantation, Sodium alginate, Follicular development, Cell death

P-490

Investigation the effects of honey and nitroglycerin on wound healing in male rats

Alireza Raji-amirhasani[1], Mohammad Khaksari hadad[2], Mehdi Ahmadinejad[3], Ehsan Mirkamandar[4]

1. Ph.D student of medical physiology, Physiology and Pharmacology Department, Kerman Medical School, Kerman University of Medical Sciences, Kerman, Iran.
2. Endocrinology Research Center and Department of Physiology and Pharmacology, School of Medicine, Kerman University of Medical Sciences, Kerman , Iran
3. Dept. of Intensive Care Unit, Kerman University of Medical Sciences, Kerman, Iran.
4. Physiology and Pharmacology Department, Kerman Medical School, Kerman University of Medical Sciences, Kerman, Iran.

Background and Objective: Drugs and many traditional medicine compounds have long been used to accelerate the wound healing process. We investigated the effect of honey and nitroglycerin on wound healing.
Materials and Methods: Animals were randomly divided into 4 groups: control group (CTL): In this group, no medication intervention was performed after the wounding. Phenytoin group: in this group after creating wound, Animals were dressed with Phenytoin cream daily. Honey group: Animals were dressed with honey ointment every day after wounding. Nitroglycerin group: Animals were dressed with Nitroglycerin ointment every day after wounding. The ulcer surface was measured on days 1,4,8,12,16 and on the last day, when the ulcer was completely improved, and at these times, a sample was removed from healing wound for histological examination.
Results: The results showed that there was a significant difference in the recovery process in honey and Nitroglycerin groups compared to control and phenytoin groups. Histological results in honey and nitroglycerin groups also showed an improvement in inflammation and epithelial formation but were not statistically significant.
Conclusion: It seems that honey and nitroglycerin accelerate the wound healing. However, more studies are needed to investigate the effects of these drugs and the Synergistic effects of them on the wound healing.
Keywords: Skin ulcers, Honey, Nitroglycerin, Phenytoin , Skin wound

P-491

The effects of electromagnetic field and N-acetyl cysteine on ovarian function after ovary transplantation in mice

Khadijeh Rasaiefar, Maryam Hajighasem Kashani, Saeed Zavareh, Meysam Nasiri

School of Biology, Damghan University, Damghan, Iran

Introduction: One major problem in survival of the ovarian implants is vascular failure, which leads to tissue ischemia. In this study, the effects of N-acetyl cysteine (NAC) and electromagnetic field on the improvement of ovary transplantation were examined.
Materials and Methods: mice (6-8 weeks) were randomly divided into five groups. (Group 1) Fresh ovarian tissue transplantation; (Group 2): Cryopreserved ovary transplantation; (Group 3) Cryopreserved ovary transplantation + NAC; (Group 4) Cryopreserved ovary transplantation + electromagnetic field (EMF) of 1.2 mT and 15 Hz frequency twice a day for 4 hours, two days after transplantation; (Group 5) Cryopreserved ovary transplantation + NAC and EMF. The mice were sacrificed at days 2 and 7 post-transplantation.
Results: There were significant decrease in SOD and GPX enzymatic activity, at day 2 and total antioxidant capacity (TAC) levels at day 7 post-transplantation, in group 2 compared to group 1. NAC could improve TAC levels. Also, EMF treatment alone and in combination with NAC, could decrease MDA levels. Histological analysis revealed

that, cryopreservation reduced the number of primordial and primary follicles at day 2 and day 7 but it increased the number of preantral and antral follicles at day 7 post-transplantation. NAC and EMF each alone significantly improved the number of four follicular phases at day 7. Our results also showed significant angiogenesis after treatment with NAC and EMF each alone.
Conclusion: Single dose NAC at day2 and EMF at day7 post transplantation, could improve ovarian oxidative damage, de novo folliculogenesis, follicular development and angiogenesis.
Keywords: Electromagnetic field, N-acetylcysteine, Antioxidant, Ovary transplantation

P-492

The Prevalence and Predictors of Overweight and Obesity and their five-year incidence in a General Population: A Community-based Study in Southeastern Iran (KERCADR Study, Phase 2)

Hamid Najafipour[1], Mehdi Bagheri[2*], Shadan Saberi[3], Mitra Shadkam Farokhi[4], Raheleh Amirzadeh[1], Farzaneh Rostamzadeh[5]

1. Professor of Physiology, Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Assistant Professor of Cardiology, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
3. Assistant Professor of Physiology, Gastroenterology and Hepatology Research Center, Institute of Basic and Clinical Physiology Sciences Kerman University of Medical Sciences, Kerman, Iran
4. Researcher, Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
5. Assistant Professor of Physiology, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

Objective(s): The aim of study was to assess age- and sex-standardized prevalence of overweight (OW), obesity (OB), and central obesity (COB) and their five-year incidence and associated variables in an adult population in Iran.
Methods: In a randomized cluster household survey (2014-2018), 10,000 adult individuals aged 15-80 years were enrolled in the study, among which 2818 persons were participants of phase1 (2009-2011) in Kerman, southeastern of Iran. OW was defined as BMI of 25-29.9 kg/m2, OB as BMI ≥30 kg/m2, and COB as waist circumference >88cm for women and >102cm for men.
Results: The overall prevalence of OW-OB-COB was 35.8% (37% men, 35% women), 22.3% (16% men, 26.3% women), and 31.1% (15.6% men, 41.2% women), respectively. The prevalence of OW/OB increased by age (AOR=2.8 for 25-34 years to 7.4 for 45-54 years vs 15-24 years). Female gender (AOR=1.4), higher education (AOR=1.7), and low physical activity (LPA) (AOR=1.3), smoking (AOR=0.55) and opium use (AOR=0.79), were the most significant predictors. The overall prevalence of OW and OB increased from 33.3% to 35.8% and from 15.4% to 22.3%, respectively, during the 5-year period between phases 1 and 2. The 5-year incidence of OW-OB-COB was 2.4, 1.9, and 2.3 per hundred population/year, respectively.
Conclusion: OW and OB affected almost 60% and COB 31% of the adult population, indicating high prevalence of these abnormalities. Middle aged, female gender and LPA caused higher incidence rate of OW/OB. Appropriate interventions and strategies with focus on higher risk population are needed to reduce cardiovascular risk consequences.
Keywords: Body mass index, Overweight, Obesity, Central obesity, Risk factors, Incidence, Iran

P-493

The effects of swimming exercise and Nepeta menthoides on depression like behavior induced by reserpine

Faezeh Rezaei [1], Maryam Malekian [1], Mohsen Khalili [2], Batool Rahmati [2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran
2. Neurophysiology Research Center, Shahed University, Tehran,Iran

Background and Objective: Physical activity has long been associated with mental health. Nepeta menthoides is a native Iranian herb recently acknowledged for its anti-depressant properties. This study attempts to determine the effects of swimming exercise and Nepeta menthoides on reserpine induced depression in rats.
Materials and Methods: Male rats (n=80) were assigned to 8 groups: 1-Saline, 2-Reserpine (0.2 mg/kg, i.p for 14 days) 3-Swimmig Exercise(30 min swimming sessions 5 days a week) 4-Nepeta (200 mg/kg), 5-Reserpine+Nepeta, 6-Reserpine+Swimming exercise, 7-Reserpine+Nepeta+Swimming exercise, 8-Reserpine+Fluoxetine, Finally, the behavioral tests including sucrose preference, elevated plus maze and open field were performed.

Results: Obtained data showed that depressed rats which were treated with Nepeta+ Exercise expressed higher preference for sucrose relative to other groups. However, if combined Nepeta+Exercise could not significantly antagonize the effect of reserpine on motor activity and time spent in the open arms of elevated plus maze, but mentioned items showed notable improvements in the Nepeta group.
Conclusion: Combined treatment with Nepeta+exercise was able to alleviate anhedonia in depressed rats. Nevertheless, anxiety behaviors were not significantly affected by the mentioned treatment.
Keywords: Depression, Reserpine, Swimming Exercise, Nepeta menthoides

P-494

Probiotic treatment improves the impaired spatial cognitive performance and restores synaptic plasticity in an animal model of Alzheimer's disease

Rezaei Asl Z[1], Sepehri GR[1] and Salami M[2]

1. Department of Physiology, School of Medicine, Kerman University of Medical Sciences, Kerman, I. R. Iran
2. Physiology Research Center, Kashan University of Medical Sciences, Kashan, I. R. Iran.

Background and objective: Studies demonstrate a close link between gut microbiota and brain function, and evidence indicating that damage to gut flora lead to degrees of brain dysfunction is increasing. Especially neurodegenerative diseases such Alzheimer's disease (AD) are very sensitive to modifications of the gut microbiome. Accordingly, supporting the gut microbiota has been considered as a possible strategy for AD treatment. In this study, behavioral and electrophysiological aspects of brain function were evaluated in an animal model of AD (Alz group) stablished by intracerebroventricular injection of β-amyloid peptide.
Materials and Methods: Fifty rats were randomly divided into five groups: The control (Con) rats received the vehicle and the Sham group was subjected to the surgical procedure as the Alz animals. Two groups of Alz and Con were also pretreated with a mixture of probiotics for 8 weeks. Spatial learning and memory was assessed in Morris water maze. Also, to evaluate basic synaptic transmission and long term potentiation (LTP), field excitatory postsynaptic potentials (fEPSPs) were recorded in the CA1 area of hippocampus. The change in anti-oxidant/oxidant factors was assessed via measuring the plasma level of total anti-oxidant capacity (TAC) and molondealdehyde (MDA). Brain staining was done to confirm β-amyloid accumulation. Fecal bacteria quantification was accomplished to find how the probiotic supplement affected the gut microbiota.
Results: Our study demonstrated that while the β-amyloid administration weakens maze learning in the Alz animals the probiotic treatment highly improved the spatial navigation. Electrophysiological experiments showed that the β-amyloid injection had no effect on normal synaptic transmission. LTP was substantially suppressed in the Alz rats. The probiotic treatment significantly restored LTP in the Alz group and further enhanced it in the Pro+Con group. The intervention also showed a favorable effect on balance of the anti-oxidant/oxidant biomarkers in Alz animals.
Conclusions: This study provides the first proof on positive effect of probiotics on synaptic plasticity in an animal model of AD.
Key words: Alzheimer's disease, LTP, Probiotics

P-495

Effects of prenatal exposure to chrysotile asbestos on hippocampal cell proliferation, astrogliosis and long-term behavioral changes in adult male rat offspring.

Ehsan Raeis-Abdollahi

Background and Objective: Prenatal development is a critical period of life that many environmental pollutants have been suggested to influence fetal growth. Nevertheless, there are still a few investigations into the prenatal exposure to chrysotile and its neurodevelopmental and behavioral outcome in offspring.
Materials and Methods: In this study, twenty-eight pregnant Wistar rats were divided into four groups and received intraperitoneal injections of normal saline, chrysotile, ascorbic acid and the combination of chrysotile and ascorbic acid on gestational days 11, 14 and 17. The maternal serum levels of malondialdehyde (MDA) and prooxidant-antioxidant balance (PAB) and hippocampal MDA content in adult male offspring were measured. At postnatal day 60-62, anxiety-like and depression-like behaviors were examined. Thereafter, the quantitative analysis of Ki-67, NeuN and GFAP positive cells in the hippocampal dentate gyrus (DG) were studied.

Results: Prenatal exposure to chrysotile increased the maternal serum level of MDA and PAB as well as hippocampal MDA content in adult male offspring, also increased the depression- and anxiety-like behaviors of adult male offspring and decreased the hippocampal Ki-67+, NeuN+ and GFAP+ cells in the DG. However, co-administration of ascorbic acid and chrysotile decreased hippocampal lipid peroxidation and increased the Ki-67+, NeuN+ and GFAP+ cells in the DG.
Conclusion: Oxidative stress induced by prenatal exposure to chrysotile, lead to the decrease of the hippocampal cell proliferation and neuronal differentiation as well as astrogliosis of adult male offspring that exhibit more depression- and anxiety-like behaviors in adulthood and ascorbic acid attenuated these changes.
Keywords: prenatal exposure; chrysotile asbestos; Oxidative stress; hippocampal neuronal differentiation and astrogliosis; anxiety and depression; developmental reprogramming.

P-496

The protective effect of troxerutin on plasma level of testosterone and total Leydig cells in type 1 diabetic rats

Zohreh Zavvari Oskuye[1], Rana Keyhanmanesh[2*], Fariba Mirzaei Bavil[2], Keyvan Mehri[1], Gholamreza Hamidian[3]

1. Department of Physiology, Tabriz University of Medical Sciences, Tabriz, Iran.
2. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
3. Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.

Background and Objective: Diabetes can gradually cause damage to the function and structure of male gonads. Our previous studies showed that troxerutin has a suitable anti-hyperglycemic effect. This study was conducted to investigate the effect of troxerutin on function and total number of Leydig cells in type 1 diabetic adult male rats.
Materials and Methods: Fifty adult male Wistar rats randomly divided into 5 groups including control, troxerutin, diabetes, diabetes+troxerutin and diabetes+insulin. Diabetes was induced by 55 mg/kg streptozotocin. Diabetes+insulin group received 4-6 U/day insulin NPH. Troxerutin and diabetes+troxerutin groups received 150 mg/kg troxerutin via oral gavage for 4 weeks. At the end of experiment, animals were anaesthetized and plasma samples were taken for measurement of testosterone by ELISA. Testes were fixed in formalin, processed by standard paraffin embedding and tissue sections were stained by H&E. Total numbers of Leydig cells were estimated by optical fractionator and stereo-investigator software. One-way ANOVA and Tukey's post-hoc were performed for data analysis.
Results: The results showed that diabetes reduced plasma level of testosterone and total Leydig cells significantly compared to control groups. It was indicated that troxerutin and insulin increased plasma level of testosterone and Leydig cells number significantly compared to diabetic group. However total number of Leydig cells in troxerutin and insulin treated groups was significantly lesser that control but testosterone level had not significant diffrences with control group.
Conclusion: This study revealed that troxrutin treatment can be considered as a suitable protective strategy for increasing of fertility in diabetic males.
Keywords: Troxerutin, Diabetes, Testosterone, Leydig cells, Testis

P-497

Protective effects of tannic acid administration on sepsis-induced male infertility in rats

Fatemeh Pourmirzaei, Behjat Seifi*, Mina Ranjbaran, Mehri Kadkhodaee, Farzaneh Kianian, Keivan Lorian

Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Background and objective: Sepsis is a medical emergency which is considered to be one of the most common causes of male infertility. Tannic acid is shown to have protective effects on different organs. This study was designed to investigate the protective effects of tannic acid on sperm motility in male rats after sepsis.
Methods and Materials: Adult male rats were randomly divided into 3 groups: Sham, Sepsis, and Tannic acid. Sham animals were subjected to anesthesia and surgery without cecal ligation and puncture. In the Sepsis group, the cecum is carefully isolated and then ligated just below the ileocecal valve and punctured twice with a 25-gauge needle. The abdominal cavity is then closed in two layers, followed by fluid resuscitation. In the Tannic acid group;

animals were received tannic acid (20 mg/kg, i.p.) 6, 12 and 18 hr after the surgery. Thirty hours after sepsis induction, the left caudal epididymis was used to evaluate the sperm motility.
Results: Sepsis caused significant decrease in the sperm motility. Administration of tannic acid significantly increased the sperm motility in septic rats.
Conclusion: This study suggests that tannic acid administration improves the sperm motility in septic rats. This treatment may be a promising strategy for protection against sepsis-induced male infertility in clinical practice.
Keywords: Sepsis; Tannic acid; Sperm motility

P-498

Effect of dipeptide Noopept on spinal neuron apoptosis and pain behavioral responses during persistent peripheral inflammation

Mona Taghizadeh[1,2], Jalal Zaringhalam[1,2]

1. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and objectives: inflammation actively can cause neuronal apoptosis. Therefore, it can be considerate as a basic mechanism of various diseases. In other hand, increasing reports indicate a complex scenario of interaction between spinal neuron apoptosis and pain behavioral responses such as Thermal hyperalgesia. In view of ongoing debate about the different side effects of analgesic drugs, it is crucial to assess new options such as dipeptide Noopept.
Materials and Methods: Thermal hyperalgesia assessed by means of Radiant heat apparatus at 0, 7, 21 days of study after Persistent inflammation induction by CFA. dipeptide Noopept was administered during the 21 days of study. Apoptotic cells detected by TUNEL technique.
Results: Our finding indicated that following CFA model, hyperalgesia and spinal neuron apoptosis increased at first week after injection and decreased at the third week of study. Our results also suggested that daily administration of dipeptide Noopept during 21 days of study caused significant decrease in hyperalgesia and spinal neurons apoptosis.
Conclusion: these results suggest that during CFA induced inflammatory pain model, thermal hyperalgesia increased due to increment of spinal neuron apoptosis. And also, administration of dipeptide Noopept can cause significant reduction in spinal neuron apoptosis and consequently hyperalgesia in acute and chronic phases of inflammatory pain which required further investigations.
Key words: Inflammation, Spinal neuron apoptosis, Thermal hyperalgesia, dipeptide Noopept

P-499

Atorvastatin reduces depressive-like behavior through inhibiting nitric oxide pathway in ovariectomized mice

Samane Jahanabadi, Pegah Safshekan

Department of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Background and Objective: Atorvastatin has been associated with reduced depressive-like behavior in mice and nitric oxide plays a major role in the pathogenesis of depression. This study was conducted to evaluate the antidepressant-like effects of atorvastatin in ovariectomized (OVX) mice and the possible role of NO pathway. To this end, bilateral ovariectomy was performed in female mice and different doses of atorvastatin were injected alone or in combination with non-specific NO synthase inhibitor (L-NAME) or an NO precursor (L-arginine).
Materials and Methods: The duration of immobility was recorded in the forced swimming test (FST) and Tail Suspension Test (TST) to measure the depressive behavior and also open field test was assessed. Hippocampal levels of NO were determined in all groups. OVX mice showed significantly prolonged immobility time in

comparison with the sham group seven days after the procedure. Atorvastatin (0.1 and 1 mg/kg, p.o.), when injected 1 h prior to behavioral tests, exerted antidepressant-like effects in OVX mice.
Results: Administration of L-NAME (10 mg/kg) with a sub-effective dose of atorvastatin (0.01 mg/kg) showed antidepressant-like effect in OVX mice, but the NO precursor L-arginine (750 mg/kg), suppressed the anti-immobility effect of atorvastatin (0.1 and 1 mg/kg). None of the treatments altered the locomotor behavior in OFT. Also, hippocampal nitrite level was significantly lower in atorvastatin-treated mice compared with control group. Also, co-administration of L-arginine with atorvastatin caused a significant increase in hippocampal nitrite levels.
Conclusion: The present findings suggest that suppression of the NO synthase/NO pathway may be involved in the antidepressant-like effects of atorvastatin in OVX mice.
Keywords: Atorvastatin, nitric oxide, ovariectomy

P-500

The effect of application of logbook practical physiology in the learning of medical and pharmacy students Ramsar Campus, Mazandaran University of Medical Sciences in 1997

Fatemeh hossein zadeh[1], Ali Siahposht-Khachaki [2*]

1. Ph.D. Student of Higher Education Management in Kharazmi University of Tehran, Ramsar Campus.
2. Department of Physiology, Mazandaran University of Medical Sciences, Sari, Iran

Introduction: The log book is a tool for recording the number of learning experiences, documentation of learning stages, and evaluating the quality of practical laboratory training during a course. A guide to learning in the basic sciences, if accompanied by a log book, provides an opportunity for more interaction between the students, the basic science laboratory environment is considered as a good tool for increasing learning in the field of basic sciences. Therefore, this study aimed to investigate the effect of log book physiology application on the learning of medical and medical students in the basic sciences.
Material and Methods: This is an experimental study that was conducted on 100 undergraduate students in pharmacy and medicine. First, a Delphi study, designed and developed a logbook guideline for physiology, was developed. Then, students were randomly divided into experimental and control groups. The control group was trained on a regular basis and the experimental group in the department of physiology lab using logbook. Students' learning in cognitive and skill domain was studied in both groups. Data were analyzed using descriptive statistics (frequency distribution, mean and standard deviation) and inferential statistics (independent t test for comparing mean scores in two groups) using Prism software. Normality of data was confirmed by Kolmogorov-Smirnov test.
Findings: 60% of students believed that the use of blogs was essential in physiological laboratory unit. The mean scores of students in practical physiology in two cognitive and skill areas were higher in the experimental group than in the control group and this difference was statistically significant ($P < 0.05$).
Conclusion: Based on the findings of this study, we concluded that due to the increase in students' score in the field of skills and knowledge in the practical physiology lab, the use of clinical learning guidance increases the learning outcomes in the cognitive and skill domain.
Keywords: Log book, learning, medical students, skill, cognitive

P-501

Neurocognitive manifestation of ovariectomized mice attenuated by hydroalcholic extract of pistachio

Elham Hakimizadeh1, Iman Fatemi[2], Jalal Hassanshahi[1,3], Ayat Kaeidi[1,3], Mohammad Allahtavakoli[1,3], Ali Shamsizadeh[1,3], Ali Roohbakhsh[4], Mohammad Reza Rahmani[1,3]

1. Physiology-Pharmacology Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.
2. Research Center of Tropical and Infectious Diseases, Kerman University of Medical Sciences, Kerman, Iran.
3. Department of Physiology and Pharmacology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.
4. Pharmaceutical Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and Objective: Menopause is associated with depression as well as emotional and memory disorders. Based on the anti-inflammatory and antioxidant effects of pistachio, its effect on depression, cognitive function, anxiety and physical power in ovariectomized mice was investigated.
Materials and Methods: In the current study, fifty female mice were used.Animals were aliquoted into five groups: Control, Ovariectomy (OVX), Ovariectomy + DMSO, Ovariectomy +10 mg/kg pistachio extract and Ovariectomy +100 mg/kg pistachio extract. Pistachio extract used orally in ovariectomized mice for two month.Anxiety, depression, working memory and physical power were evaluated by the Elevated plus-maze (EPM) test, Forced swimming test (FST), Y maze and swimming exhaustion test, respectively.
Results: The results showed that extract of pistachio (more potentially at the dose of 100 mg/kg) decreased anxiety-like behaviors and depression as well as increased in working memory and physical power in ovariectomized mice.
Conclusion: The findings of the current investigation suggest that pistachio extract could be
used as a potential strategy for the attenuation of Ovariectomy -related manifestation.
Key words: Menopause, Ovariectomy, Mice

P-502

The analgesic activity of newly synthesized imidazopyridine compounds as cyclooxygenase inhibitors

Fatemeh Khademabbasi Ardakani

Background and objective: The non-steroid anti-inflammatory drugs (NSAIDs) are considered as an important class of medicines that are used for the treatment of inflammation, pain and fever that act through inhibition of cyclooxygenase enzymes and prevention of prostaglandin synthesis. The imidazopyridine compounds possess various pharmacological activities such as anti-inflammatory, analgesic, anticandidial, antiviral, and anticancer effects. In this study, the analgesic effects of eight new imidazopyridine derivatives was evaluated using formalin test in rats.
Materials and methods: Male wistar rats were used in this study. Drug solutions were prepared in appropriate concentration using dimethylsulfoxide (DMSO) and were administered by intraperitoneal injection at the dose of 40 mg/kg and the volume of 0.5 ml/kg. The control group received DMSO 0.5 ml/kg. One group received celecoxib (40 mg/kg, i.p.) as standard analgesic treatment. Formalin test was done 30 min after drug or vehicle (in control group) administration by subcutaneous injection of formalin solution (5%, 40µl) in rats hind paw. Immediately after formalin injection, rats were transferred to a clear Plexiglas observation box and the pain related behaviors were scored for 60 min according to method described by Dubuisson and Dennis.
Results: The results showed a significant decrease in the AUC of pain score in groups treated with S4, S5, S6, S7 and S8 compared with the control group. Our results suggests that methoxy derivatives of imidazopyridine show more analgesic activity in inflammatory pain compared with methyl derivatives.
Keywords: imidazopyridine compounds; cyclooxygenase, analgesic, formalin test, rat

P-503

Implementation of Interprofessional Education (IPE) in improvement of learning and professional competency in postgraduate students

Majid Khazaei[1], Hossein Karimi Mooneghi[2], Amir Avan[3], Seyed mahdi HasanianMehr[4]

1. Department of Physiology, Mashhad University of Medical Sciences, mashhad, Iran
2. Department of Medical Education, Mashhad University of Medical Sciences, mashhad, Iran
3. Department of Genetic, Mashhad University of Medical Sciences, mashhad, Iran

4. Department of Biochemistry, Mashhad University of Medical Sciences, mashhad, Iran

Background and Objective: Changing form professional education to interprofessional education is one of the new methods in health science education. The aim of this study was to evaluate improvement of learning and professional competency in postgraduate students through designing and implementation of interprofessional education (IPE).
Materials and Methods: This method was started from 1st semester of 2016. First, the Readiness for Interprofessional Learning Scale (RIPLS) questionaire was completed by 80 postgraduate students. Then, IPE method was implemented through lecture/group discussion and practical/laboratory workshops with attendance of students/staffs from different desciplines. For evaluation of implementation, we used Interdesciplinary Education Perception Scale (IPES).
Results: Score of RIPLS questionaire in four domains including team work and collaboration, negative professional identity, positive professional identity and roles and responsibilities were more than average. In IEPS questionaire, before and after implementation, score for four fields including "competency and authonomy" was 33.55±0.5 vs. 38.84±4.5; "Perceived needs for cooperation": 7.50±1.97 vs. 9.07±2.32; "Perception of actual cooperation": 18.20±5.39 vs. 24.53±2.60 and "Understanding others value": 11.20±3.11 vs. 14.84±1.67, respectively and the most improvement was observed in filed of "Perception of actual cooperation".
Conclusion: Using education strategy based on IPE will improve health and responsibility of health system.
Keywords: Postgraduate students, Education, Learning, Interprofessional education

P-504

Educational puzzle for understanding thyroid gland physiology

Fariba Mirzaei Bavil[1], Rafigheh Ghiyasi[1], Hamed Ebrahimzadeh Leylabadlo[2], Milad Mohammadzadeh[1]

1. Department of Physiology, Faculty of medicine, Tabriz University of Medical Sciences, Tabriz, Iran.
2. Department of Bacteriology and Virology, Faculty of medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Since some important topics in physiology require deep and long-term learning, the use of new and innovative methods, such as teaching a puzzle solving method, can be helpful.
Materials and Methods: This study was conducted among medical (n = 150), dentistry (n = 72) and pharmacy students (n = 140) in thyroid gland physiology lesson. Each class was randomly divided into two groups: traditional (lecture and simple teaching) and puzzle (puzzle-solving teaching). In both groups, for performing of pretest and posttest, an image of synthesis and secretion of thyroid hormones was given to students with 8 missing with 16 words, before and after teaching. Then, in both groups, the results of the pertest and posttest were compared to each other separately. Also, the posttest results of the puzzle groups were compared across all three Fields as well as between girls (75%) and boys (25%).
Results: The results showed that there were no significant difference between pretest and posttest in the traditional groups. But in the puzzle groups, this difference was significant ($p<0.05$). Comparing post test results, girls showed a higher score than boys ($p<0.05$). Compare interdisciplinary showed that there was no significant difference between dental and medical students, but the increase was significant too in pharmacy students ($p<0.05$).
Conclusion: Applying creative teaching methods such as solving puzzles can have an important role in promoting education, learning and encourage the students to be creative and innovative.
Keywords: Education, puzzle, physiology

P-505

The effectiveness of game-based pharmacology training on learning outcomes in nursing students

Khadijeh Moradbeygi

Introduction: The inadequate pharmacology knowledge of nursing students will be associated with the risk of medication errors.This research is about to determine the effectiveness of game-based pharmacology training on the learning outcomes in nursing students of Abadan Faculty of Medical Sciences.
Methods: This quasi-experimental interventional study was carried out on third-semester students using census method in 2017-2018. The intervention included clinical game-based pharmacology training during an internship

(including 10 sessions, with each session lasting for 5 hours). The first to third sessions included pharmacology theoretical classes, the fourth to ninth sessions, included playing games, theoretical classes, and clinical work, and the tenth session included a station review program and a competitive pharmaceutical data pool program. The pharmacology learning outcomes assessment questionnaire was completed before and after the intervention by the students, and the data analyzed using the paired t-test.
Findings: A total of 77 students (42 females and 35 males) attended the study until the end of it. The mean age of students was 21 ± 2 years. The total average of students was 15.5 ± 2.8 and their mean pharmacology score was 14.7 ± 3.4. According to pharmacology learning outcomes assessment questionnaire, the mean pretest and post-test scores were 11.2 ± 2.5 and 16.4 ± 3.1. Conclusion: This educational method has been able to increase students' level of learning and concentration and increase their interest and can thus be used as a suitable method for developing their thinking and analytical power.
Key Words: Education, Pharmacology, Game, Nursing

P-506

Beneficial Effects of Tamoxifen and Raloxifene or their Combination with Estrogen on Cardiovascular Indices in Postmenopausal Diabetic Animals

Mohammad Navid Ebrahimi, Mohammad Khaksari

Department of Physiology and Pharmacology, Faculty of Medicine, Kerman University of Medical Sciences, Kerman, Iran.

Background and Objective: The risk of cardiovascular disease caused by diabetes in women is more pronounced in menopause than premenopausal women, which indicates the role of sex steroids as a protective factor. we studied the effects of tamoxifen, raloxifene and 17 β-estradiol on cardiovascular indices in ovariectomized diabetic rats.
Materials and Methods: Female Wistar rats were divided into 11 groups: sham-control, diabetes, diabetes +OVX, oil, oil+ vehicle, tamoxifen, raloxifene, estrogen, tamoxifen+ estrogen and raloxifene+ estrogen. Bilateral ovariectomy (OVX) was performed to create a menopause model. Type 2 diabetes was induced by a high-fat diet and a low dose of streptozotocin. Cardiovascular indices including atherogenic index, cardiovascular risk index 1 and 2, heart weight index, and blood pressure were measured.
Results: An increase of 55% in blood glucose levels was exacerbated in OVX rats, and both tamoxifen and raloxifene produced a significant reduction in blood glucose. Although this decrease were less than the decrease induced by estrogen. The combination of tamoxifen or raloxifene with estrogen exacerbated their effect. The atherogeic index like glucose in the, diabetes +OVX group increased, and with the use of all three drugs this increase was prevented. Although this index was only greater in the tamoxifen + estrogen group compared with the tamoxifen group. Increased cardiovascular risk factors for diabetes and ovariectomy were reduced by all drug groups, individually or in combination. All treatment groups prevented the rise in blood pressure caused by diabetes and ovariectomy.
Conclusion: The results of this study indicate that single use of tamoxifen or raloxifene or their combination with estrogen can have a beneficial cardiovascular effect in animals with menopause model, and the effects of alone consumption and combination they were not different. The determination of mechanism of these drugs is suggested in future studies.
Keywords: Diabetes, ovariectomy, Tamoxifen, Raloxifene, Estrogen

P-507

The effect of testosterone enanthate on Liver tissue in adult male rats

Fereshte Ebrahimian

Testosterone-enanthate is highly used by athletes for body building, because of its metabolic effects, many researches have shown that the high concentration of this component in the plasma may effects natural activity of endocrine glands and function of different organs especially liver.
In this study the effect of high dose of T.E. on liver function in strain rats has been considered. 50 adult male rats were divided in to 5 groups (n=10) as follow.

A. Gonadectomized rats which received TE (5mg/100g B.W.) intraperitoneally weekly, up to 9 weeks.
B. Control group (gonadectomized) received TE
C. Gonadectomized group received equal volume of the solvent (olive oil)
D. Control group (non-gonadectomized) received solvent.
E. Control group without any injection or surgery

After 63 days, liver tissue samples were collected from all groups, and serial sections were prepared for H&E staining. The central vein, interlobular connective tissue, hepatocyte sinusoid were studied for histomorphology.
The results show a significant difference ($p<0.05$) in diameter of above structures in group A in comparison with the control group. The results also express that T.E. can cause diameter increase of central vein, interlobular connective tissue, hepatocyte & sinusoid which is can be the reason of the liver dysfunction and congestion.

P-508

Relationship between adipokines and cardio vascular disease risk factors with Normal-Weight Obesity Syndrome in women

Mohammad Allivand, Javad Sajedianfard, Saeedeh Ahmadi Jokani

Department of Basic Science, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.

Background and objective: Adipose tissue is an endocrine and paracrine organ producing and secreting various active cytokines and biologic mediators. The new syndrome normal-weight obesity (NOW) has identified, characterized by a normal body weight and BMI but a high fat mass (>30%). The present study was to determine relationship between adipocytokines and selected lipid indexes associated with increased cardio vascular disease (CVD) risk with Normal-Weight Obesity Syndrome in women.
Materials and Methods: Anthropometric variables of 40 women 20-40 years of ages from nutrition clinics was analyzed. The groups were 1: 20 women with a normal weight and a BMI<25 (nonobese control group); 2: 20 NWO women with a normal weight, a BMI<25, and a %FM >30% who all of them were in generally good health. Plasma concentration of chemerin and adipocytokines were measured in duplicate by using the multiplex sandwich ELIZA and selected lipid indexes were measured through standard enzymatic colorimetric techniques.
Results: Plasma concentration of chemerin, IL-1α, IL-1β, IL-6, TNF-α, TG, LDL and total cholesterol in the NWO women were significantly greater than control group ($p<0.05$), but no significant differences in HDL were found between the NWO and control groups. Correlation analysis revealed strong associations between adipocytokines, lipid profile (except HDL) and body fat percentage.
Conclusion: It's indicates that are relationship between adipocytokines and selected lipid indexes associated with increased CVD risk with Normal-Weight Obesity Syndrome and also BF% in women. So, we suggest that body fat percentage seems to be a greater potential predictor of CVD than BMI.
Keywords: Adipokines, Chemerin, Fat mass, Normal-weight obesity, Body mass index

P-509

Effect of topical nitrite administration on excisional wound healing in type 2 diabetic male rats

Afzali H[1], Norouzirad R[2], Khaksari M1, Ghasemi A*[2]

1. Department of Physiology and Pharmacology, Afzali Pour Medical Faculty, Kerman University of Medical Sciences, Kerman, Iran.
2. Endocrine Physiology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Background and Objective: Nitric oxide (NO) deficiency in diabetes leads to delayed wound healing. This study aims at determining effects of acidified nitrite cream on wound healing in type 2 diabetic rats. Materials and

Methods: Wistar rats were divided into 6 groups: Control, control+cream-base, control+acidified nitrite cream, diabetes, diabetes+cream-base, and diabetes+acidified nitrite cream. Type 2 diabetes was induced using a high-fat diet followed by a low-dose of streptozotocin (35 mg/kg, I.P.). A full-thickness excisional skin wound was made on the back of rats using 8-mm punch biopsy. Creams were applied once daily for 28 consecutive days and wounds were photographed for macroscopic changes. Rats were sacrificed on days 1, 3, 7, 14, 21 and 28 after wounding and serum concentrations of glucose, lipid profiles, and NO metabolites (i.e. nitrate+nitrite, or NOx) were measured. Results: Wound healing was delayed in diabetic rats compared with controls. In diabetic rats treated with acidified nitrite cream compared to non-treated ones, the percent of initial wound size in the skin was 43% smaller on day 7. Acidified nitrite cream also accelerated healing of the wound in the treated control rats. Serum NOx levels significantly increased at the end of the study in treated diabetic rats. Serum glucose and lipid profile were not affected by acidified nitrite cream. Conclusion: Topical administration of acidified nitrite cream on excisional skin wound improves wound healing in type 2 diabetic rats, probably by increasing the level of NO.
Keywords: Acidified nitrite cream; Diabetic wound; Nitric oxide; Type 2 diabetes.

P-510

The effect of Myricitrin and Vitamin E on insulin resistance, lipid profiles and hepatic enzymes in aging mice induced by D-galactose.

Akram Ahangarpour[1], Mina Omidi[2], Layasadat Khorsandi[3], Fatemeh Ramezani Ali Akbari[2]

1. Department of Physiology, Physiology Research Center, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
1. Department of Physiology, Student Research Committee, Ahvaz Jundishapur University of Medical Science, Ahvaz, IranPhone:
2. Department of Anatomical Sciences, School of Medicine, Cell & Molecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Background and objective: D-galactose, at high concentrations, increases oxidative stress, causing structural and functional changes similar to the aging process. Aging is a risk factor for liver disease, including insulin resistance. This study was performed to evaluate the effect of myricitrin and Vitamin E on liver and pancreatic parameters.
Materials and methods: 72 female adult mice were divided into six groups randomly: 1. control, 2. D-galactose 500 mg/kg/d subcutaneously injected (45 days), 3-5. D-galactose+5, 10 and 20 mg/kg/d Myricitrin, 6. D-galactose+100 mg/kg/d vitamin E by gavage (the last 28 days). This study was measurement metabolic indexes, beta cell function, lipid profile and hepatic enzymes.
Results: Diabetes group had a significant increase in alkaline phosphatase, Myricitrin and Vitamin E were improved this factor. Diabetes group is associated with a significant increase in glutamic oxaloacetic transaminase that Myricitrin and Vitamin E were reduced this toxicity. Myricitrin at 10 mg/kg was more effective than other doses. Vitamin E had toxic effect on SGPT and increased this factor. Myricitrin in 5mg/kg had a better effect on glutamic pyruvic transaminase. Myricitrin and Vitamin E were reduced LDL in the diabetic group. Myricitrin effectively improves changes blood glucose, insulin secretion, HOMA-IR and HOMA-β impaired by D-galactose.
Conclusion: Present data disclosed that myricitrin at low doses has antidiabetic and hepatoprotective effects on liver and pancreatic in aging caused by D-galactose.
Keywords: D-galactose, Aging, Myricitrin, Liver

P-511

Study of Self-Renewal Genes of OCT4, SOX2 and NANOG in Pancreatic Cancer

Golzar Amiri[1], Vahideh Assadollahi[2],Masoud Alasvand[3]

1. Student Research committee, Kurdistan University of Medical Sciences, Sanandaj, Iran
2. Cellular and Molecular Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran
3. Department of Medical Physiology and Pharmacology, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

Background & Objectives: Genes are involved in the control of stem cell self-renewal as a new class of molecular markers of cancer. In this study, the expression of Oct4, Nanog and Sox2 in cell lines MIA Paca-2, PA-TU-8902 and AsPC-1 and pancreatic cancer tissue were examined.
Materials and Methods: In this experimental study, cell lines, MIA Paca-2, PA-TU-8902 and AsPC-1, were cultu ed in DMEM and RPMI- containing FBS 10% in a 37°C incubator containing Co2 5% and humidity 90%. Samples of tumor and non-cancer pancreatic tumor were purchased Iran tumor bank. Extraction of RNA and synthesis of cDNA was performed. Expression levels of Oct4, Nanog and Sox2 were determined using Real-time PCR. The protein expression levels of target genes in the cell lines were studied by flow cytometry and immunocytochemistry.
Results: The expression rate of Oct4, Nanog and Sox2 is more in the cancer cell lines than those in the control (normal tissue) samples. The protein expression levels of target genes in the cell lines were confirmed by flow cytometry and immunocytochemistry.
Conclusions: The genes are involved in stem cell self-renewal as a new class of molecular mrkers of cancer that detected in the pancreatic cell lines. Maybe, these genes play important role in the uncontrolled proliferation of cancer cells.
Keywords: Pancreatic,Nanog,Tumor

P-512

Investigation of rs4986938 G/A Polymorphism in ERβ Gene and its Relationship with Breast Cancer Susceptibility in West of Mazandaran Province, Iran

Ehsan teymori rad[1], Ebrhim Vosoughi[1,2], Shahrbanoo Keihanian[3], Nematollah Ahangar[4*]

1. Student Research Committee, Ramsar Campus, Mazandaran University of Medical Sciences, Ramsar, Iran
2. Azerbaijan National Academy of Sciences, Genetic Resources Institute, Baku, Azerbaijan
3. Department of Internal Medicine, Faculty of Medicine, Islamic Azad University, Tonekabon Branch, Tonekabon, Iran
4. Department of Pharmacology, Faculty of Medicine, Guilan University of Medical Sciences, Rasht, Iran

Background and Objective: Estrogen hormone is a physiological regulator of breast tissue proliferation and changes in its signaling pathways, including the alpha-estrogen receptor, occurs during breast cancer and its progression. Single-nucleotide polymorphisms (SNPs) in genes can lead to differences in cancer susceptibility and response to treatment in different populations. In the present study, we investigated rs4986938 G/A single-nucleotide polymorphism in ERβ gene in breast cancer patients and healthy population in west of Mazandaran province, Iran.
Materials and Methods: A case-control study was performed in 91 healthy women without family history of breast cancer and 71 women with breast cancer admitted to oncology department in Ramsar Imam Sajjad Hospital between April and September 2018. Peripheral blood (3 ml) was taken from the subjects and stored at -20°C. The PCR-RFLP method was used to determine the distribution of rs4986938 polymorphism.
Results: The incidence of breast cancer in individuals with homozygous AA genotype was significantly higher ($P<0.001$) compared to those with GA and wild GG. Moreover, individuals with A allel are at significantly higher and increased risk for breast cancer (OR =8.83, 95%CI = 5.158 - 15.131, P= 0.001).
Conclusion: To the best of our knowledge, this study for the first time suggested that A allele of rs4986938 G/A polymorphism might be a leading allele that cause increased breast cancer susceptibility in west of Mazandaran province.
Keywords: breast cancer, estrogen receptor beta, Iran, Mazandaran, polymorphism

P-513

Protective effect of Myricitrin on nephropathy of aging model induced by D-galactose in female mice

Vahid Radmehr[1], Akram Ahangarpour[2], Layasadat Khorsandi[3], Mina Omidi[1]

1. Department of Physiology, Student Research Committee, Ahvaz Jundishapur University of Medical Science, Ahvaz, Iran. Email:
2. Department of Physiology, Physiology Research Center, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
3. Department of Anatomical Sciences, School of Medicine, Cell & Molecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. Email: layasadat@yahoo.com

Background and aim: Aging is a biological process that leads to oxidative stress in cells and tissues. D-galactose (D-gal) induces aging and plays a role in the pathogenesis of aging. The aim of the present study was to evaluate the effect of Myricitrin as a plant derived antioxidant on blood urea nitrogen (BUN), creatinine (Cr) and, kidney histology of a female mouse model of D-gal induced aging.
Methods: Seventy-two female adult mice were randomly divided into five groups: Control, D-gal at 500 mg/kg/d for 45 days, D-gal + Myricitrin treated groups (these groups received Myricitrin at 5, 10, and 20 mg/kg/d orally for 28 days started at the beginning of the third weeks of experiment). The mice were subcutaneously injected with D-gal (500 mg/kg/d for 45 days). The antioxidant indices, plasma BUN and creatinine levels, kidney histological changes were evaluated.
Results: plasma Albumin, BUN and Cr levels was significantly changed in the D-gal animals in comparison to control group. Myricitrin was improved these factors. Histological changes such as nuclear pyknosis, proximal cell swelling, infiltration of inflammatory cells, tubular dilatation and, vasodilatation were observed in both D-gal. Further, glomerulus diameter was decreased in them. Administration of Myricitrin could attenuate the histological alterations.
Conclusion: Myricitrin may have beneficial effects on aging and aging related kidney disease.
Key words: Aging, D-galactose, Kidney, Myricitrin

P-514

Effect of Hydroalcoholic Extract of Artemisia turanica on Biochemical Parameters in Streptozotocin-Induced Diabetic Rats.

Hassan Bagheri yazdi[1], gholamhassan vaezi[2], Mousa-AL-Reza Hadjzadeh[3], Sara Hosseinian[3]

1. Department of Biology, Farhangian University, Mashhad, Iran
2. Department of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran
3. Department of Physiology, school of Medicine, Mashhad University of Medical Sciences, Mashhad,Iran

Background and Objective: Medicinal herbs are used for treatment of diabetes and its complications. Different species of Artemisia have different healing properties. In this research, the effects of hydro-alcoholic extract of Artemisia turanica (AT) on some biochemical parameters were studied in diabetic rats
Materials and Methods: In this study, 40 male rats were divided into five groups: control, diabetic, and diabetic rats treated with two doses of AT (35 and 140 mg/kg) and metformin (300 mg/kg). Experimental diabetes was induced by a single-dose (60 mg/kg, intraperitoneally (ip)) injection of streptozotocin (STZ). Metformin and AT extract were orally administrated 3 days after STZ injection for 4 weeks. At the end of the study, blood samples were taken from the heart of the rats and the levels of glucose, triglyceride and HbA1c were measured by biochemical methods.
Results: In diabetic group, serum glucose concentration, as well as, serum levels of triglyceride and HbA1c were significantly higher than control group. Administration of metformin and AT extract at dose of 35 mg/kg significantly decreased serum levels of triglyceride and HbA1c when compared to diabetic group.
Conclusion: These findings suggested that AT extract has a therapeutic effect on hyperlipidemia in streptozotocin-induced diabetic rats.
Key word: Diabetes mellitus, Artemisia turanica, HbA1C, Triglyceride

P-515

Menstrual cycle effects on voice characteristics in Iranian women

Seyed Abolfazl Tohidast[1], Faezeh Toozandeh Jani[2], Banafshe Mansuri[1]

1. Assistant Professor, Neuromascular Rehabilitation Research Center, Semnan University of Medical Sciences, Semnan, Iran.
2. Undergraduate Student of Speech Therapy ,Student Research Committee, Semnan University of Medical Sciences, Semnan, Iran.

Background and Objective: Women are subjected to the influence of two major sex hormones including estrogens and progesterone. These hormones target mainly the genital tract. However, they have also been found to affect mucosa, muscles, bone, and other body organs, including the larynx. Hormonal changes in msntrual cycle can affect

the women voice. Therefore, the aim of this study was to investigate the effect of mensturation on voice characteristics of the Iranian women.
Materials and Methods: Eighty five women with a mean age of 20.96±2.05 years participated in this cross-sectional study. The voice of the 20 women who were on the menstrual cycle and 65 women who were not (control group) were recorded producing the vowel /a/. Acoustic voice analyses were performed with PRAAT software on these recordings including F0, jitter, shimmer, and harmonic-tonoise ratio (HNR). Data were analyzed using SPSS.
Results: Data Analysis showd that the F0, jitter, and shimmer was higher in women who were in menstrual cyacle than women who were not. The HNR was lower in women who were on menstrual cyacle. However, none of these differences were not significant (P>0.05).
Conclusion: The present study showed that menstrual cycle can cause negative influences on the voice characteristics in Iranian women, although these influences were not statistically significat. It seems that more studies with larger sample size are needed to make a proper and accurate comment in this regard.
Keywords: Hormonal changes, Mensturation, Voice, Acoustic Parameters.

P-516

The effects of combined vitamin D and estrogen on traumatic brain injury in male rats

Zahra Soltani[1], Nazanin Sabet[2]

1. Endocrinology and Metabolism Research Center, Kerman University of Medical Sciences, Kerman, Iran.
2. Department of Physiology, Afzalipoor Faculty of Medicine, Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: In our previous studies, the role of sex hormones in reduction of brain edema after diffuse traumatic brain injury has been confirmed. This study compared neuroprotective effects of 17β-stradiol and vitamin D, only or with each other.
Material and Methods: Rats were divided into 8 groups as follow: Sham, sham-Treatment, TBI, Vehicle, Vehicle+Vehicle, TBI+E2, TBI+Vitamin D, TBI+E2-Vitamin D. Brain injury was induced by Marmarou's method. E2 and Vitamin D was injected 1 and 12 hours after TBI. Brain edema (via brain water content), blood-brain barrier permeability (BBB) (via extravascular evans blue dye) were measured 24 hours after TBI. The neurological outcome(V.C.S) were assessed -1, ,4,24 hours after TBI.
Results: Brain water content and Evans blue dye content were less in E2 , Vit D, E2+Vit D treated groups comparison to vehicle and TBI groups. V.C.S was increased significantly after trauma, at 4 hours after traumatic brain injury in E2, Vit D and E2+VitD comparison to vehicle and TBI groups.
Conclusion: This study show neuroprotective effects of E2 and Vit D and E2+Vit D. The results suggest that E2 and Vit D probably have neuroprotective function following traumatic brain injury.
Keywords: traumatic brain injury, Vitamin D, 17β-stradiol

P-517

The impact of Noise and Vibration exposure on urine catecholamine metabolites of male subjects

Mohammad Javad Jafari[1], Ameneh Jari[2], Fariba Khodagholi[3], Soheila Khodakarim[4]

1. Associate Professor, PhD in Vital Statistics, School of Public Health and safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Master of Science in Occupational Health Engineering, School of Public Health and safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Associate Professor, PhD in Biochemistry, Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

4. Full Professor, PhD in Occupational Health Engineering, School of Public Health and safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Noise and vibration exposure are important risk factors at many work places which may impact on blood pressure, cardiovascular system and catecholamine level. The aim of this study was to investigate the effect of independent and combined exposure to noise and whole body vibration on blood pressure and heart rate as well as catecholamine metabolites including in male subjects.
Materials and Methods: This experimental study was conducted on 30 male students. Each subject was randomly exposed to 3 levels of noise and 3 levels of whole body vibration both independently and in a combined exposure condition. Before and after each exposure, blood pressure and heart rate were measured and urine samples were collected. Metanephrine and normetanephrine levels were determined using the ELISA method. Calibrated instrumentation and dedicated measurement kits were applied for this purpose. Repeated measures regression with a GEE approach was used for statistical analysis.
Results: Results showed that exposure to whole body vibrations at 2.45 m/s2 causes a significant drop in systolic blood pressure (p=0.003). Also, combined exposure to noise and vibration leads to a significant increase in heart rate (P=0.04). Other exposure conditions had no significant impact on studied physiological parameters(P>0.05).
Conclusion: The secretion of stress hormones due to different noise exposures does not follow any particular trend. Urine catecholamine metabolites cannot be recommended as biomarkers for short term exposure to noise and whole body vibration.
keywords: Metanephrine, Normetanephrine, Noise, Whole Body Vibrations, Heart Rate, Blood Pressure

P-518

Study of the effect of saffron and fluoxetine on depression and endocrine profiles in adult men and women

Javid Z, Jelodar G.A, Sahraeian A

Hormones and neurotransmitters share common pathways and receptor in the brain which are linked to mood, particularly through the hypothalamic-pituitary-gonadal axis. It has been hypothesized that women express episodes depression associated with reproductive events (i.e., premenstrual, postpartum, menopausal transition). Saffron traditionally has been used as a coloring or flavoring agent, as well as an herbal medicine. Moreover, previous studies have introduced crocine as an antioxidant, anticancer, anti-inflammatory, antinociceptive, antidepressant, and antianxiety agent . In this study alteration of endocrine profile in depression and following treatment with saffron in both men and women was evaluated. 28 men and weman (aged 20-55 years)who have assigned as moderate to severe depressed patients by psychologist following filing of Beck form were selected and were randomly divided into two groups. One group (experimental) was treated with fluoxetine and saffron (30 mg daily) and the other group (control) received placebo and Fluoxetine. Before treatment and 28 days after treatment in the fasting state, about 6-5 mm blood patients were obtained. Blood sample of women were collected on the third day of their menstrual cycle. Levels of testosterone, estrogen, progesterone, DHEA, FSH, LH, cortisol and prolactin were measured by ELISA method. The results did not show significant difference in the measured hormones neither in men nor in women of the experimental group compares to the control group. Beck questionnaire value showed lower level in both experimental and control groups compare to the before treatment, which is good sign for treatment of depression. It can be concluded that although saffron and fluoxetine improve depression condition in both sex they did not altered endocrine profile.

P-519

Berberin impact the cognitive and brain electrical activity complications in thioacetamide- induced hepatin encephalopathy in rats.

Sarkaki A[1], Hajipour S[2], Farbood Y[2], Rashno M[3], Dianat M[2], Nesari A[2]

1. National Institute for Medical Research Development,, Department of Physiology, Physiology Research Center, Medicine Faculty, Ahvaz Jundishapur University of Medical Sciences, Ahvaz-Iran.
2. Physiology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz-Iran.
3. Department of Immunology, Cellular & Mollecular Research Center, Medicine Faculty, Ahvaz Jundishapur University of Medical

Sciences, Ahvaz-Iran

Background and Objective. Hepatic encephalopathy (HE) is a neurological disorder in patients with liver disease. It is characterized by cognitive and motor deficits, shortened attention, sleep disturbances that finally may lead to coma and death. Thioacetamide (TAA) is a hepatotoxin which is able to induce hepatic failure (HF) followed by HE. Berberine (BBR) is an isoquinoline alkaloid, extracted from many plants with neuroprotective, antiapoptotic, antiinflammatory and anti-oxidative properties. The aim of this study was to evaluate the effects of BBR on spatial memory, hippocampal long-term potentiation (LTP) in rats with HE.
Materials & Methods: Male Wistar rats (200 ± 20 g) used into 6 groups; 1) Sham; 2) HE; received TAA (200 mg/kg) once every two days for consecutive 14 days. 3- 5) HE rats received BBR (10, 30, 60 mg/kg, i.p.) for 7 days after HE induction. 6) received NMDA receptors antagonist MK-801 before TAA. Spatial memory test and hippocampal LTP recording were done. RM-two-way ANOVA and Tukey's post hoc test and $p < 0.05$ for least difference used for data analysis.
Results. HF could impair cognitive and hippocampal LTP significantly ($p<0.01$) known as HE. Treatment of HE rats with BBR, significantly reverse memory and LTP dose dependently ($p < 0.01$). Blocked of NMDA receptors showed no involvement of these receptors in HE induction by TTA.
Conclusion: Our results suggest that BBR could act against HE-induction may by its free radical scavenging activity and it may act as a therapeutic agent for liver cirrhosis and HE.
Keywords. Hepatic encephalopathy; Thioacetamide; Berberine; Spatial memory; Long-Term Potentiation.

P-520

The evaluation of the Nicotine effect of on the H.P.A axis in male rats4

Negar RahimiMonjez

This study aims to analyze the effects of Nicotine on animals. This analysis is based on sever Smoking and the enhealment of the Nicotines Poisons gas. These effects (none Volunteer organic functions, brain stimuli, heart beat increases, Analgesia) are determined by the central nerve system. In this research intraperitoneal (IP) Injection of Nicotine on HPA axis in male rats were Studied. The animals were divided in to control, experimental and sham groups. The experimental and sham groups were injected with Nicotine and Saline for five days at times between 6:30 to 7:0. After sampling ACTH and cotrticosterone were measured. The finding indicated that Nicotine increase the A.P.A axis activity, Nicotine implements it's effect through (glutamate, 5-HT, dopamine and norepinephrine). Which then regulates C.R.H release and consequently the increase of ACTH and corticostrone secretion

P-521

The roles of autophagy in the formation and differentiation of pancreatic beta cells

Lyasadat Khorsandi, Fatemeh Rezaee Tazangi

Cellular and Molecular Research Center, Jundishapour University of Medical Sciences, Ahvaz, Iran.

Background and Objective: Autophagy deficiency cascade potentially results in the deterioration of whole body energy metabolism and the development of metabolic disorders including diabetes mellitus. Autophagy is a highly conserved process that controls the turnover of organelles and proteins within cells and contributes to the balance of

cellular components. This is essential to the this review summarized the roles of autophagy in differentiation and function of beta cells.
Method: PubMed was searched for articles that presented the function of autophagy in the differentiation of pancreatic beta cells between 1990 and 2015 using the following terms :
Autophagy, diabetes and beta cells in the title/abstract.
Results: Physiological studies showed that deficiency in autophagy causes intercellular accumulation of excess fat, aggregated proteins, and dysfunctional organelles; such autophagy deficiency cascade potentially results in the deterioration of whole body energy metabolism and the development of metabolic disorders including diabetes mellitus. This process provides cells with energy and essential compounds under unfavorable environmental conditions such as oxidative stress and hyperglycemia, which are both observed in diabetes. beta cell mass and pancreatic insulin content were reduced because of increased apoptosis and decreased proliferation of beta cells.
Conclusion: These results suggest that autophagy is necessary to maintain structure, mass and function of pancreatic beta cells, and its impairment causes insulin deficiency and hyperglycemia because of abnormal turnover and function of cellular organelles.
Key words: autophagy, diabetes, beta-cells, insulin resistance, cellular organelles.

P-522

Anti-apoptotic and anti-inflammatory effects of Stachys schtschegleevii methanolic extract in the Liver of type 2 diabetic rats

Gholamreza Hamidian, Reza Rezaie, Ali Esmaeili

Department of Basic sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.

Background and Objective: Diabetes mellitus is a common methabolic disorder of endocrine system which can gradually cause damage to liver function. Our previous studies showed that Stachys schtschegleevii (SS) has anti-diabetic and antioxidant effects. This study was conducted to investigate the effect of SS on histopathological changes, apoptotic index and interleukin-6 (IL-6) level of liver in diabetic rats.
Materials and Methods: Thirty adult male Wistar rats were divided into 5 groups including: control, diabetic, and diabetic treated by 100, 200 and 300 mg/kg methanolic extract of SS for 40 consecutive days by oral gavage. Type 2 diabetes was induced by high-fat diet and low dose of streptozotocin (35 mg/kg). At the end of experiments, animals were uthenized and a part of their liver was fixed in 10% formalin for histological analysis. Apoptotic index wer determined by TUNEL immunohistochemical technique and IL-6 level in liver homogenates was measured by ELISA. ANOVA test and Tukey's post hoc were performed for data analysis by SPSS.
Results: Results showed that diabetes caused sever damage to liver histological structure and increased significantly apoptotic index and IL-6 level in liver compared to control. It was also indicated that SS improved histological structure of liver in diabetic rats and decreased significantly apoptotic index and IL-6 in a dose dependent manner compared to diabetic group.
Conclusion: SS restrains diabetes side effects in liver and is a suitable hepatoprotective. Therefore it can be considered as a therapeutic strategy for improvement of structure and function of liver in diabetic patients.
Keywords: Stachys schtschegleevii, Diabetes, Liver, apoptosis, Interleukin-6

P-523

Environmental exposure to bisphenol A and toxicity of reproductive system

Zohreh Zare[1], Moslem Mohammadi[2], Noorollah Rezaei[3]

1. Assistant Professor, Department of Anatomical Sciences, Molecular and Cell Biology Research Center, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
2. Associate Professor, Department of Physiology, Molecular and Cell Biology Research Center, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
3. Associate Professor, Department of Anatomical Sciences, Molecular and Cell Biology Research Center, School of Medicine, Mazandaran

University of Medical Sciences, Sari, Iran.

Bisphenol A (BPA) is an endocrine disrupting chemical widely used in the manufacture of polycarbonate plastic and epoxy resin to produce a multitude of consumer products, food and drink containers, and medical devices. BPA can migrate into environment and it has been detected in the saliva, blood, urine, and food. Several types of bisphenols, including BPB, BFF, and BPS, are planned to be used as BPA alternatives. However, these analogs may exert similar adverse effects on the physiologic functions. BPA is a reproductive toxicant at a level below the lowest observed adverse effect level (50 mg/kg) as well as a level below the proposed safe level (4 μg/kg). In females, BPA affects ovary, embryo development, formation of mammary gland, and gamete quality for successful in vivo and in vitro fertilization. Furthermore, it can transfer across the placenta and decrease fetal health. BPA can damage testes, spermatogenesis, and sperm quality in males. The exact mechanisms of the toxic effects of BPA and its analogs in reproduction are not fully understood. It is demonstrated that BPA induces oxidative stress and exerts epigenetic effects in the reproductive system. Treatment with BPA increased apoptotic-related factors (Bax and caspases-3 and 9) and decreased expression of anti-apoptotic Bcl-2. BPA can also disrupt the balance of hormones, including testosterone, LH, and FSH, and hormone synthesis-related factors. Taken together, BPA and its analogs can induce reproductive toxicity through various cell signaling pathways.
Keywords: endocrine, bisphenol A, reproduction, toxicity, damage

P-524

Effects of Hypericum Scabrum extract on hippocampal synaptic plasticity in rats fed a long-term high-fat diet

Ghazaleh Omidi, Arezoo Rezvani-Kamran, Ahmad Ganji, Alireza Komaki

Department of Physiology & Neurophysiology Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

Background and Objective: High-fat diet (HFD) can cause deficits in neural function, oxidative stress and decline hippocampal neurogenesis. Hypericum scabrum extract contains compounds to treat neurological diseases. The aim of this study was to investigate the neuroprotective effects of the H. scabrum extract on hippocampal synaptic plasticity in rats that were fed a HFD.
Material and methods: Male Wistar rats randomly divided to six groups (n= 9 per group) as follows and treated for 90 days: (1) Control group (2) Extract 100 mg/kg group (3) Extract 300 mg/kg group (4) HFD group, fed a HFD; (5) HFD+Ext100 group; (6) HFD+Ext300 group. The population spike (PS) amplitude and slope of excitatory post synaptic potentials (EPSPs) were measured in dentate gyrus (DG) area in response to the stimulation applied to the perforant path (PP).
Result: Our results showed that in HFD group vs Control $p<0.001$, HFD+Ext100 compared with HFD $p<0.01$ and HFD significantly decreased the hippocampal PS amplitude compared with HFD+Ext 300 $p<0.001$. There was a significant difference between control and HFD+Ext300 $p<0.05$.
Conclusion: The results of the present study suggest that H. scabrum extract can prevent cognitive impairment caused by the consumption of a HFD. These effects are may be due to the strong antioxidant properties of the extract and its ability to scavenge free radicals.
Keywords: Hypericum Scabrum, Coenzyme Q10, Long-term potentiation, Hippocampus, high-fat diet

P-525

Effect of long-term nitrate administration on protein levels of nitric oxide-producing enzymes in liver, adipose tissue, and skeletal muscle in type 2 diabetic male rats

Majid Shokri[1], Hassan faridnouri[1], Vajiheh Khorasani[2], Sajad jeddi[2], Asghar Ghasemi[2*]

1. School of Biology, Damghan University, Damghan, Iran
2. Endocrine Physiology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Type 2 diabetes is associated with decreased nitric oxide (NO) bioavailability. This study aims at determining effects of nitrate administration on NO synthases (NOS) enzymes in epididymal

adipose tissue, liver, and skeletal muscle in diabetic rats. Materials and Methods: Rats were divided into 4 groups: control, control+nitrate, diabetes, and diabetes+nitrate. Type 2 diabetes was induced using a high-fat diet followed by a low-dose of streptozotocin (30 mg/kg, intraperitoneally). Sodium nitrate (100 mg/L in drinking water) was administered for 6 months. Serum glucose and insulin as well as protein levels of inducible (iNOS), neuronal (nNOS) and endothelial NOS (eNOS) in tissues were measured after 6 months. Results: Before intervention, serum glucose (203±46 vs. 110±24 mg/dL) and insulin (191.4±40.8 vs. 67.0±21.7 pmol/L) were higher in diabetic rats. At the end of the study, serum glucose and insulin levels in nitrate-treated diabetic rats compared to non-treated ones were lower by 15% and 32%, respectively. Compared to controls, diabetic rats had significantly higher levels of iNOS (208% and 24%, in liver and adipose tissue, respectively) and lower levels of eNOS (31% and 59%, in liver and soleus muscle, respectively) and nNOS (70% in soleus muscle). Nitrate administration in diabetic rats restored increased iNOS and decreased eNOS and nNOS levels to their near normal values. Conclusion: Beneficial metabolic effects of long-term nitrate administration in type 2 diabetic rats is partly due to decreased iNOS as well as increased eNOS and nNOS levels in adipose tissue, liver, and skeletal muscle.
Keywords: Nitric oxide; Nitric oxide synthase; Nitrate; Rat; Type 2 diabetes

P-526

The effect of adulthood psychological stress on number or area of Langerhans islets and pancreatic glut2 levels in rats exposed to early life stress

Forouzan Sadeghimahalli[1], Homeira Zardooz [2], Mina Salimi [2]

1. Department of physiology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
2. Neurophysiology Research Center and Department of Physiology, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Background and aim: Early-life events maybe impair the development of pancreas and induce the defect in metabolic responses to stress in adulthood. So, we studied the effect of early-life stress on number or area of Langerhans islets and pancreatic glut2 levels in response to psychological stress in adult rats.
Material and Methods: Male Wistar rats were divided into 4 groups: Control (no stress), Early-STR (with foot-shock via communication box at 2 weeks of age), adult-STR (with psychological stress at 8-10 weeks of age), Early+adult-STR (with foot-shock stress at 2 weeks and psychological stress at 8-10 weeks of age).Stress was induced for 5 consecutive days (2 times/day) at two levels of age. At the end, following anesthesia, adult rats were decapitated and dissected to remove pancreas to measure of number or area of islets and glut2 levels via western blot.
Results: Early stress in Early-STR group reduced significantly glut2 levels as compared to Control group ($P<0.001$) while in STR-group it was enhanced as compared to control group. In Early+adult-STR group the glut2 significantly was increased as compared to Early-STR group ($P<0.05$) and decreased as compared to STR-group ($P<0.001$) and control group ($P<0.01$). Number of islets in Early+adult-STR group significantly was higher than the other groups ($P<0.01$).While in this group area of islets did not show significant changes at the same of group.
Conclusion: We conclude, early life stress maybe predispose organism to metabolic disorders such as impaired glucose homeostasis later in life. These defects in response to adult stress can heighten.
Keywords: early life stress, GLUT2, psychological stress, Langerhans islets.

P-527

Effect of hypothyroidism protein levels of nitric oxide-producing enzymes in cardiovascular system in male rats

Roghaieh Samadi, Sajad Jeddi, Asghar Ghasemi*

Endocrine Physiology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background objective: Thyroid hormones play important roles in normal functions of cardiovascular system and liver and hypothyroidism causes cardiovascular diseases and hepatic dysfunction. Thyroid hormones affect nitric oxide (NO) system and the aim of this study is to investigate the effect of hypothyroidism on protein levels of three isoforms of NO synthase, including endothelial NOS (eNOS), inducible NOS (iNOS), and neuronal NOS (nNOS) in aorta, and heart tissues.

Material and methods: Sixteen male Wistar rats were divided into the hypothyroid and the control groups. Hypothyroidism was induced by administration of 500mg/L propylthiouracil (PTU) via the drinking water for a period of 21 days. Nitric oxide metabolites (i.e. nitrate+nitrite or NOx) concentrations in serum as well as iNOS, eNOS, and nNOS protein levels in aorta and heart tissues were measured at day 21. Results: Hypothyroid rats had lower serum NOx levels serum compared with controls (31.0±3.7 vs. 54.9±2.6 µmol/L, $p<0.001$). Compared with controls, hypothyroid rats had significantly lower levels of iNOS in the aorta (34%), and heart (27.4%). In addition, hypothyroidism decreased the protein levels of nNOS in the aorta (14.8%), and increased it in the heart (45.5%). Protein levels of eNOS were comparable between hypothyroid and controls rats in both tissues. Conclusion: Hypothyroidism decreased protein levels of inducible isoform of NOS in cardiovascular system while in case of neural isoform of NOS increased it in heart and decreased it in aorta. These changes may contribute on increased cardiovascular mortality in hypothyroidism.
Keywords: Hypothyroidism; Nitric oxide synthase (NOS); Rat.

P-528

The Effect of Fennel on Lipid Profile of Streptozotocin-induced Diabetes Rats

Zahra Samadi Noshahr[1*], Mahnaz Allahyari[1], Abolfazl Khajavi Rad[1, 2]

1. Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Objective: The aim of the present study was to evaluate the beneficial effect of fennel hydro-alcoholic extract on lipid profile of STZ-Induced diabetic male rats.
Methods: 32 male albino Wistar rats weighing 250±30 g were randomly divided in to 4 groups (n=8) including 1- control, 2- diabetic, 3 and 4- diabetic rats treated with Fennel (200 and 400 mg/kg body wt. respectively), for 6 wks. Diabetes was induced by a single dose of STZ (60 mg/kg i.p). At the end of the study, animals were fasted then euthanized and blood was collected from the heart.
Results: STZ induced diabetic rats depicted the increased TC, TG, LDL-c, diminished level of HDL-c ($P<0.001$). Oral administration of Fennel extract at a dose of 200 and 400 mg/kg b.w daily for 42 days results in a momentous decrease significantly ($p< 0.05$ and $p<0.001$ respectively) the levels of TC, TG, and LDL-c. While it increases the level of HDL-c to a significant ($p<0.01$) level.
Conclusion: The current study suggested that the treatment with Fennel exhibited beneficial effects on lipid profile in STZ- induced diabetes in male rats and could be considered for further evaluation in drug development.
Key words: diabetic rats, Fennel, lipid profile, Streptozotocin

P-529

The impact of oral adminstration of the walnut leaf (Juglans regia L.) extracts and the activity and distribution of aldose reductase in diabetic rat testis

Abbasi Z, Jelodar GA

Background: Strong relationship between increased aldose reductase (AR) activity and the risk of chronic complications of diabetes have been shown. Important flavonoids in the walnut leaf have several physiological properties including antioxidant, anti-bacterial, anti-viral, anti-inflammatory, anti-mutagenic, anti-cancer and activation or inactivation of certain enzymes. Objective: This study aimed to investigate the impact of oral

administration of different doses of cyclohexane and ethanol extracts of walnut leaf on distribution and activity of AR in testis of diabetic rat.
Materials and Methods: Fifty- six adult male Sprague-Dawley rats were randomly divided into seven groups as follow: control and diabetic control (received vehicle), treatment control 1 &2 (received 250 mg/kg body weight (BW) of cyclohexane and ethanol extracts respectively), treatment 1 (received 250 mg/kg cyclohexane extract), and treatment 2 & 3 (received 150 and 250 mg/kg ethanol extract respectively). Diabetes was induced by single intraperitoneal injection of streptozotocin (60 mg/kg BW). Extracts of walnut leaf and vehicle were administrated by gavage for 30 days. The Elisa kit was used to measure activity and concentration of the AR. Distribution of AR in testis investigated by immunohistochemistry technique.
Results: Both cyclohexane and ethanol extracts of walnut leaf, caused a significant reduction in the activity of AR in the testis and improved the distribution of this enzyme in sertoli cell of treated diabetic groups compared to control groups.
Conclusion: Oral administration of cyclohexane and ethanolic extracts of walnut leaf can improve fertility disorders in diabetics by decreasing the activity and distribution of AR in the testis.
Keywords: Aldose Reductase, Diabetes mellitus, testis, Walnut leaf

P-530

Antioxidant effect of the methanol extract of soybean seeds (Glycine max L.Merr.) on oxidative stress in in rats with Esteradiol Valerate - induced Polycystic Ovary Syndrome

Sanaz Alivandi Farkhad, Abdolkarim Hosseini, Parisa Darabi

Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran.

Background and Objective: Polycystic ovary syndrome (PCOS) is a heterogeneous disorder characterized by hyperandrogenism, oligoovulation/anovulation, the presence of polycystic ovaries and/or abnormal oxidative stress (OS). It has been reported that isoflavones (genistein and daidzein) in soybean seeds have antioxidant activities. This research aimed to determine the effect of the methanol extract of soybean on the histological structure and oxidative stress in the PCOS rats.
Materials and Methods: To induce PCOS, 32 female vistar rats, weighing 170-180 g received single dose injection of Estradiol Valerate (IM, 4 mg/kg). Control group receive no injection. After 60 days the animals divided to control, PCOs and PCOs treated that were given soybean extract (50 mg/kg of body weight, 100 mg/kg of body weight) for 21 days. After three weeks, the ovaries of all groups were removed, and following preparation of ovarian homogenates, oxidative stress (total antioxidant capacity (TAC) and total oxidant status (TOS)) was evaluation using commercial ELISA kit following the manufacturer's protocol (ZellBio GmbH, Germany) Data were analyzed using SPSS.
Results: The soybean extract treatment significantly improved PCOS symptoms, in a dose-dependent manner, as compared with PCOS group. Soybean extract treatment also improved ovarian total oxidative/antioxidative status as compared with PCOS
Conclusion: Soybean treatments may provide therapeutic effects by reducing the consequences of experimental PCOS owing to the antioxidant properties of its components, including isoflavones.
Keywords: Genistein, Polycystic ovary, Oxidative stress, Soybean

P-531

Administration of Ziziphus Jujuba during neonatal and juvenile growth period improved liver oxidative damage of propylthiouracil-induced hypothyroid rats

Vajiheh Alikhani

Background and Objective: The objective of this study was to investigate the effects of Ziziphus Jujuba (Z. jujuba) extract administration during neonatal and juvenile growth period on liver oxidative damage of propylthiouracil (PTU)- induced hypothyroid rats.
Materials and Methods: The pregnant rats were kept in separate cages. After delivery, the mothers and their offspring were randomly divided into five groups and treated: (1) control; (2) PTU, 0.005% in their drinking water; (3-5) PTU-plus 100, 150 or 200 mg/ kg Z. jujuba extract. After lactation period, the offspring continued to receive the same experimental treatment for the first 8-weeks of their life. Ten offspring of each group were randomly selected, the liver tissues were removed.
Results: Malondialdehyde (MDA) concentration was increased while; thiol, superoxide dismutase (SOD) and catalase (CAT) concentrations were decreased in the liver tissues of PTU treated rats. Treatment with 150 and 200 mg/ kg decreased MDA while, increased thiol concentrations in the liver tissues compared to PTU group. Treatment with 200 mg/kg Z. jujuba increased CAT and SOD concentrations in the liver tissues compared with PTU group.
Conclusion: The results of this study demonstrated that administration of Z. jujuba extract during neonatal and juvenile growth period has an improving effect on hepatotoxicity in PTU- induced hypothyroid rats.
Key words: Ziziphus Jujuba, Propylthiouracil, Hypothyroidism, Liver function tests

P-532

N-acetylsysteine increases mortality rate at aluminum phosphide poisoning rats

Khadijeh Farrokhfall*

Medical Toxicology and Drug Abuse Research Center(MTDRC), Birjand University of Medical Sciences, Birjand, Iran

Introduction: Aluminum phosphide (ALP) is a household insecticide known as rice pill and is the most common form of suicide in Iran. Oxidative stress is its important mechanism and serum glucose level as a major prognostic factor in its poisoning. The purpose of this study was to evaluate the effect of NAC on carbohydrate metabolism in ALP exposed rats. Materials and Methods: A study was performed on 40 rats including; control, poisoned groups ALP (6 mg / kg, orally), control and poisoned treated with NAC (100 mg / kg in IV in 4 doses of 30 minutes followed by 2, 4 And 6 hours after ALP or normal saline gavage). The next day, blood samples were taken to measure plasma glucose, MDA, glutathione and insulin levels. Finally the pancreas was isolated and digested for insulin secretion. Results: ALP reduced serum glucose and insulin. This effect was much more pronounced in NAC treatment poison rats. In fact mortality in the ALP group was somewhat 40% and NAC evoked a further increase to 70%. Isles insulin secretion at poison rats was apparently reduced and NAC injection had no effect on the insulin release. NAC consumption inhibited glutathione enzyme activity with a further reduction in oxidative stress at poison rats. Discussion and Conclusion: NAC increased the mortality rate despite improving the oxidative status and glucose metabolism. However all dead animals had severe hypoglycemic (37.12 ± 6.17). The effect supports our ideas that sever hypoglycemic effect of NAC counteracting with its antioxidants properties.
Key words: aluminum phosphide, N-acetylsysteine, metabolism, rat

P-533

Evaluation of serum CMPF level in pre-diabetes patients compared to normal people

Shohreh Fardipour

Hormozgan University of Medical Sciences, Medical School.

Background and Objective: Diabetes, the proper term for diabetes mellitus (DM), is a major epidemic of this century that occurs worldwide (1). Pre-diabetes mellitus (PDM) is defined as an abnormal glucose status. According to the WHO classification, pre-diabetes includes deficiency in fasting glucose (IFG), glomerular tolerance test (IGT), and compound labeled (IGT + IFG) (2, 3). Considering that the number of people suffering from Pre-diabetes is rising considerably and by 2040 the world will reach 482 million; the total cost of diabetics in 2017 is estimated at $ 327 billion. Due to the side effects of the disease and the cost of treatment, the screening of people at the Pre-diabetes stage is very important (4). In this study, we examined the relationship between CMPF and glucose.
Materials and Methods: In this study, 44 healthy subjects and 44 pre-diabetic patients were selected. The Serum levels of FBS, BUN, Cr, lipid profiles, liver enzymes, HbA1c, BMI, age and CMPF were measured in Pre-diabetes patients compared to normal people, and compared the relationship between these parameters in two groups.
Results: In this study, there was a significant relationship between age, BMI, FBS, Ch, TG, HDL, LDL, ALP and HbA1c in pre-diabetic patients compared to normal subjects ($P<0.01$).In addition to, the findings of the study showed that there was a significant difference between the serum levels of CMPF in Pre-diabetes patients compared to normal people
Conclusion: Considering the significant correlation between serum CMPF levels in pre-diabetes individuals compared to normal individuals, this parameter can be suitable biomarkers for diagnosis of pre-diabetes, but more research is needed with more sample size and wider geographical areas.
Keywords: Diabetes Mellitus, pre-diabetes, CMPF, HbA1C, FBS

P-534

Effect of crocin combined with voluntary exercise on TNF-α and IL-6 of HFD/STZ induced type 2 diabetic rats

Vajihe Ghorbanzadeh[1], Hassan Dariushejad[2], Leila Chodari[3], Mustafa Mohammadi[4]

1. Razi Herbal Medicines Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran
2. Department of biotechnology, Lorestan University of Medical Sciences, Khorramabad, Iran
3. Department of medical physiology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran
4. Drug Applied Research Center of Tabriz University of Medical Sciences, Tabriz, Iran

Background and Objective: due to key role of inflammation in pathogenesis of type 2 diabetes mellitus, aim of this study was evaluating the influence of crocin together with voluntary exercise in high-fat diet-induced diabetic rats.
Materials and Methods: twenty-eight male wistar rats divided into four groups: Diabetes (rats consume high fat diet for 4 weeks and were injected with low dose STZ(35mg/kg)), Diabetes-crocin (diabetic rats received crocin (50mg/kg oral) for 8 weeks, Diabetes-exercise (diabetic rats performed voluntary exercise for 8 weeks), Diabetes-crocin-exercise (diabetic rats received crocin combined voluntary exercise for 8 weeks). At the end of training, rats were anestatized and blood samples were collected and used for evaluation of IL-6, TNF-α analysis. Results: our results showed significantly increase in TNF-α and IL-6 in diabetic rats, which these parameters significantly decreased by induction of voluntary exercise and crocin. In Diabetes-crocin-exercise group, the levels of IL-6 and TNF-α decreased as compared with Diabetes-crocin and Diabetes-exercise. Conclusion: The results of this study showed that voluntary exercise with crocin improves inflammation and inflammatory mediators in type 2 diabetes and prevents diabetes-induced damage.
Key words: crocin, voluntary exercise, dibetes, IL-6, TNF-α

P-535

Contribution of nitric oxide synthases in impaired cardiac function in male rats with transient congenital hypothyroidism

Mahboubeh Ghanbari, Sajad jeddi, Reza Norouzirad, Asghar Ghasemi*

Endocrine Physiology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objectives: Thyroid deficiency during pregnancy is a common endocrine disorder that can cause transient congenital hypothyroidism (TCH) in offspring. Cardiovascular disorders related to TCH are present at birth and continued during adulthood. Decreased cardiac output, lower number of endothelial cells, and decreased serum nitric oxide metabolites (i.e. nitrate+nitrite or NOx) have been shown in adult offspring born with TCH. Thyroid hormone regulates level and activity nitric oxide (NO) synthases (NOS) and these enzymes have direct effect on cardiac function; the aim of this study is therefore to evaluate the involvement of NOS isoforms in cardiac function attenuation of offspring rats with TCH. Material and methods: TCH was induced by adding 0.025% 6-propyl-2-thiouracil in drinking water of female rats throughout their pregnancy, while controls consumed tap water. During adulthood, cardiac function parameters of male offspring rats were measured and protein levels of NOS isoforms [i.e. neuronal NOS (nNOS), inducible NOS (iNOS) and endothelial NOS (eNOS)] were measured in left ventricular. Results: Cardiac function parameters were significantly lower in offspring with TCH compared to controls; TCH rats had also higher level of iNOS (6.12±0. vs. 4.78±0.27 ng/mg protein; P=0.008) and nNOS (4.87±0.28 vs. 3.55±0.23 ng/mg protein; P=0.003) compared to control while there was no differences in eNOS concentration between two groups. Conclusion: Results of this study showed that impaired cardiac function in rats with TCH is at least in part due to the increased iNOS and nNOS levels in the heart.
Keywords: Transient congenital hypothyroidism; Cardiac function; NOS isoforms, Male rat

P-536

Vitamin C supplementation by preserving the survival of pancreatic beta cells through a miRNA- related signaling pathway ameliorate metabolic disorder in type 2 diabetes

Rafighe Ghiasi [1,2], Mohammad Reza Alipour [1,2]

1. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
2. Department of Physiology, Tabriz Faculty of Medical Science Tabriz University of Medical Sciences, Tabriz- Iran

Type 2 diabetes is a major global health burden; however, its pathogenesis remains largely unknown. MicroRNA expression and theirs downstream genes have recently been reported to be altered in diabetes. As miR- 34a Sirtuin1, have key roles in apoptosis and survival of pancreatic beta cells , this study aimed to evaluate the effects of vitamin C on β- cells apoptosis , their survival and pancreatic expression levels of miR-34a and sirtuin1, and metabolic parameters in type 2 diabetes.
Methods: Twenty-eight male Wistar rats were randomly divided into four groups: control (Con), Vitamin C (Vit), diabetes (Dia) and diabetic vitamin C (Dia- Vit) (n = 7). Type 2 diabetes induced by the combination of high-fat diet (HFD), 4 weeks) and streptozotocin (35 mg/kg. ip). After induction of diabetes, the rats received vitamin C (200 mg/kg via gavage, 5daye/weekly) for 12 weeks. At the end of the intervention, blood and samples of the pancreas were prepared for measurement of metabolic parameters and histological study.
Results: This study indicated a significant reduction in pancreatic expression levels of Sirtuin1, serum levels of HDL, quantitative insulin sensitivity check index (QUICKI), and a significant increase in pancreatic expression levels of miR-34a, β-cells apoptosis and serum levels of LDL in diabetic rats. Vitamin C resulted in a significant improvement in sirtuin1, miR-34a expression, QUICKI, and metabolic parameters. In addition, histological findings indicated a considerable improvement in β-cells apoptosis and their survival.
Conclusions: This study suggested that miRNA-related signaling pathway maybe a promising therapeutic target for diabetic complications.
Keywords: Diabetes, Vitamin C, Sirtuins1 (SIRT1), miR-34a, Insulin Resistance

P-537

High-fat feeding before, during and after pregnancy affects HPA axis activity in rats

Roxana Karbaschi[1,2], Homeira Zardooz[1,3], Rezvan Arian[3,4]

1. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Faculty of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

3. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

4. Department of Dentistry, Shahid Beheshti University of Medical Sciences, Iran.

Background and Objective: High-fat consumption is common in modern societies and become one of the main threats to public health that not only threatens the health of mothers and pregnancy process, but also can increase the offspring's susceptibility to different disorders. Given that a diet rich in fat can act as a stressor and alter the pituitary-adrenal axis (HPA) activity and adversely affect offspring health, this study was conducted to examine the effect of high-fat feeding during pre-pregnancy, pregnancy and lactation on HPA axis activity and adrenal gland weight in female Wistar rats.
Materials and Methods: Animals were randomly divided into control (C) and high-fat (HF) groups and fed with either a normal diet (2 g% soybean oil, 4.75% Kcal as fat) or a HF diet (35 g% cow butter, 58.2% Kcal as fat) during pre-pregnancy (4 weeks), pregnancy and lactation. Blood sampling was performed in fasting state, at the end of lactation in both groups to measure plasma corticosterone concentrations. Then the animals were decapitated and the adrenal gland tissue was removed and weighted.
Results: In high-fat fed rats, plasma corticosterone level and adrenal gland weight were significantly higher than the controls.
Conclusion: It seems that high-fat feeding during prepregnancy- pregnancy- lactation periods may act as a stressor and stimulate the HPA axis, therefore the subsequent elevation of plasma corticosterone concentration could adversely affect the growth and development of offspring.
Keywords: high-fat feeding, pituitary-pituitary-adrenal axis, corticosterone

P-538

Platelet rich plasma (PRP) improve impaired glucose hemostasis, disrupted insulin secretion and pancreatic oxidative stress in streptozotocin-induced diabetic rat

Narges Karbalaei[1,2], Marzieh Zarin[2], Sara keshtgar [2], Marzieh Nemati[2]

1. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences., Shiraz, Iran, Iran

2. Department of Physiology, Faculty of Medicine, Shiraz University of Medical Sciences, Shiraz

Background and Objective: The therapeutic effect of platelet-rich plasma (PRP) was considered as a biological treatment in various medicine fields. Our study aims to investigate the effects of PRP on impaired glucose homeostasis, disrupted islet insulin secretion and pancreatic oxidative status in STZ- induced diabetic rats.
Materials and Methods: Sixty-four Sprague–Dawley male, in the weight range of 250–280 g were randomized to four groups including control, diabetic, PRP and diabetic-PRP and each group divided into two subgroups. The rats received the PRP (0.5 ml/kg, SC injection) twice weekly for 4 weeks. intraperitoneal glucose tolerance test were done and plasma glucose and insulin levels were measured. At the end of experiment, insulin content and release of isolated islets and pancreatic oxidative stress markers were assayed.
Results: Compared with the control group, the plasma glucose and MDA levels in diabetic group were significantly high and plasma insulin level and pancreatic antioxidant activity of superoxide dismutase (SOD) and catalase were low. In the diabetic isolated islets, insulin secretion and content were decreased. PRP treatment could significantly reduce plasma glucose and increase plasma insulin in both control and diabetic rats. PRP therapy reduce MDA levels and enhance antioxidant enzyme activity, islet insulin secretion and content in pancreas of diabetic rat.
Conclusion: These findings show that PRP as a rich source of growth factors can improve the secretory impairment of pancreatic islet in STZ-diabetic rats probably by decreasing oxidative stress in pancreas and regulating of plasma insulin and glucose levels.
Key Words: PRP; Diabetic rat; islet insulin secretion, oxidative stress

P-539

Effects of IMODTM on oxidative stress and histological alterationsin the heart of diabetic male rats

Ahad Karimzadeh, Arshad Ghaffari-nasab, Gonja Javani

Department of Physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

Background and Objective: Stress oxidative is one of the main outcomes in diabetic tissues. Cardiac complication is a major medical problem of diabetic mellitus and can affect life quality of diabetic patients. So identify strategies

that can be effective in the treatment of this problem is very important. One of these strategies includes the use of herbal compounds or drugs. In this regard the positive effects of IMODTM observed in some tissues, which is likely to be effective in reducing cardiac complications of diabetes. Therefore, in this study, we examined the effect of intraperitoneal injection of this drug on oxidative stress and antioxidant activity in the heart tissue and serum of diabetic rats.
Materials and Methods: Forty adult male Wistar rats (250-300 g) were divided randomly in 4 groups: 1) control, 2) IMOD (20 mg/kg/day, ip), 3) diabetes, 4) diabetes+IMOD. For inducing diabetes, streptozotocin (STZ, 60mg/kg, ip, single dose) was injected. IMOD treatment was done for eight weeks. At the end of the intervention, heart tissues were removed and used to study of oxidative stress, antioxidant defense, and histological changes.
Results: Diabetes leads to increased lipid per oxidation, oxidative stress markers (MDA, LDH), tissue damage, and also reduces the antioxidant defense (GPX, SOD, CAT, TAC) in the heart tissue. IMOD therapy reduces oxidative stress and antioxidant defense in diabetes-IMOD compared to diabetic control group.IMOD also improves the pathological changes in the diabetic hearts.
Conclusion: it is concluded that IMOD therapy can reduce cardiac complications of diabetes and pathologically improves tissue injuries.
Key words: diabetes, IMOD, oxidative stress, antioxidant defense, lipid profile

P-540

L-arginine low dose can elevate menopausal estrogen

Fatemeh Lakzaei[1], Manizheh Karami[2*],Mohammadreza Jalali Nadoushan[3]

1. Ph.D student, Dept of Biology, School of Basic Sciences, Shahed University

2. Associate Professor,Dept of Biology, School of Basic Sciences, Shahed University

3- Professor, Dept of Pathology, School of Medicine, Shahed University

Background and Objective: Menopause in women always has consequences like infertility, hot flashes, sleep disorders, and so on. In menopause, the ovaries are cystic, the estrogen hormone decreases and the LH increases. Studies have also shown that nitric oxide (NO) level in postmenopausal women is reduced due to decreased estrogen level. In this study, L-arginine, which has already been shown to have anti-aging effects, is used to elevate the estrogen level.
Materials and Methods: Elder Wistar rats with menopausal polycystic ovaries, which was identified by Pap smear to be in the diestrus phase, were randomly classified into control and L-arginine groups. The control received saline (1 mL/kg) for three consecutive days intraperitoneally. The experimental group received L-arginine identified doses (5, 25, and 50 mg/kg, i.p.) for three consecutive days. At the end, anesthesia was performed and the blood was collected and the estrogen level was measured. Ovaries were biometrically were examined, and were fixed in the formalin. They were stained by H&E and the ovarian cysts were counted microscopically. The data were analyzed by the ANOVA.
Results: The control group has statistically a meaningful number of cysts with low level estrogen. L-Arginine low doses of (5 and 25 mg/kg) showed to reduce the cyst and increased the estrogen level.
Conclusion: L-arginine can increase estrogen levels in menopausal rats and also reduce the number of cysts in the ovary, so, L-arginine can be candidate to be used to improve menopausal symptoms.
Key Words: L-arginine, Low dose, Ovarian cyst, Menopausal, Estrogen

P-541

Diabetes Induced by Methylglyoxal and Endoplasmic Reticulum Stress Stop by Gallic Acid and L-glutamine In Male Mice

Akram Ahangarpour[1], Shahnaz Mojadami[2], Seed Ali Mard[1], Layasadat Khorsandi[3]

1. Department of Physiology, Physiology Research Center, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

2. Department of Physiology, Student Research Committee, Ahvaz Jundishapur University of Medical Science, Ahvaz, Iran.

3. Department of Anatomical Sciences, School of Medicine, Cell & Molecular Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Background and objective: Hyperglycemia and insulin resistance are hallmarks of non-insulin dependent diabetes, increases Methylglyoxal (MGO) and lead to endoplasmic reticulum stress (ERS) in β-cells. Purpose of this study was to stop diabetic damages in pancreas and evaluate the effect of gallic acid (GA) and L-glutamine (GLU) on pancreatic parameters and Endoplasmic Reticulum Stress (ERS).

Materials and methods: 60 male mice were induced diabetes by MGO orally for 28 days consecutive, then they divided into following treatment groups:(1) Normal control received saline, (2) Diabetic control received MGO 600 mg/kg, (3) Diabetic treated with GA 30 mg/kg, (4) Diabetic treated with GLU 500 mg/kg, (5) Diabetic treated with GA and GLU, (6) Diabetic treated with Metformin 150 mg/kg for 7 days.This study was measurement metabolic indexes, beta cell function and hepatic enzymes.
Results: GA and GLU were reduced ERS in the diabetic group and effectively improve blood glucose, insulin secretion, HOMA-IR and HOMA-β impaired by MGO. Present data disclosed that GA and GLU have antidiabetic and hepatoprotective effects on liver and pancreatic in Diabetes group.
Conclusion: At the end of study we found treatment with Gallic Acid and L-glutamine can stop damages of diabetes in pancreas and liver.
Keywords: Methylglyoxal, Endoplasmic Reticulum Stress, Gallic Acid, L-glutamine, Mice

P-542

Hepatoprotective effect of Descorainia sophia ethanolic extract on antioxidant enzymes activity against carbon tetrachloride induced damage in Wistar rats

Mahboubeh Mahlouji[1], Akram Eidi[1], Pejman Mortazavi [2], Shahrbanoo Oryan[3]

1. Department of Biology, Faculty of Basic Science, Science and Research Branch, Islamic Azad University,Tehran, Iran.
2. Department of Pathology, Faculty of Veterinary Medicine, Science and Research Branch, Islamic Azad University, Tehran, Iran.
3. Faculty of Biological Science, Kharazmi University, Tehran, Iran.

Background and Objective: Various studies have shown the antiinflammatory and antioxidant effects of Descorainia sophia. The purpose of this study was to evaluate the ability of hepatoprotective Descorainia sophia ethanolic extract in liver damage induced by carbon tetrachloride in male Wistar rats.
Materials and Methods: In this experimental study, 60 male Wistar rats were randomly divided into 10 groups of 6. The groups was included: normal control, intoxified control (intraperitoneally injection 0.5 ml/kg of carbon tetrachloride), normal experimental (Descorainia sophia ethanolic extract at doses of 10, 50, 100 and 200 mg/kg , intragastrically), intoxified experimental (intraperitoneally injection 0.5 ml/kg of carbon tetrachloride and Descorainia sophia ethanolic extract at doses of 10, 50, 100 and 200 mg/kg, intragastrically). After 28 days, the levels of antioxidant enzymes superoxide dismutase, catalase, glutathione peroxidase in liver homogenate were evaluated using specified kits. Data were analyzed using one-way ANOVA and Tukey test. The criterion was significant ($p<0.05$).
Results: Our results showed that administration of carbon tetrachloride significantly decreased the levels of antioxidant enzymes in the intoxified control group as toward to normal control ($p<0.001$). Administration of Descorainia sophia ethanolic extract significantly increased the levels of antioxidant enzymes in the liver of intoxified experimental groups in comparison with intoxified control group ($p<0.05$).
Conclusion: Descorainia sophia is likely to have liver protection through its flavonoids, which can scavenge free radicals and reduce the carbon tetrachloride-induced oxidative stress, improve the levels of antioxidant enzymes.
Keywords: Carbon tetrachloride, Liver toxication, Descorainia sophia, Hepatoprotection, Rat.

P-543

The Effect of Estradiol Against Tributyltin Toxicity in Rat Pancreatic Islets

Faezeh Ghaemmaleki[1], Sara Mostafalou[1], Maryam Baeeri[2], Mona Navaee[2], Mohammad Abdollahi[2], Perham Mohammadi[3]

1. Department of Pharmacology and Toxicology, School of Pharmacy, Ardabil University of Medical Sciences
2. Toxicology and Diseases Group, The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences, Tehran, Iran
3. Department of Physiology and Pharmacology, School of Medicine, Ardabil University of Medical Sciences

Introduction: Tributyltin is known as an endocrine disruptor and has been reported to interfere with estrogen receptors exerting its toxic effects through disrupting related endocrine pathways. It is known as an “obesogen” and was reported to disrupt glucose homeostasis leading to diabetes. This study was designed to assess the effects of tributyltin and estradiol on rat pancreatic islets.

Methods: Pancreatic islets of male rat were isolated, grouped (10 islets in each group) and cultured in RPMI 1640 for 24 hours at 37° C. After calculating EC50 of tributyltin and estradiol by using MTT assay, islets were treated with estradiol and tributyltin for 24 hours. Then viability and level of reactive oxygen species (ROS), Insulin secretion and apoptosis were measured.
Results: Tributyltin decreased cellular viability of islets along with an increase in the ROS formation, while estradiol increased viability and decreased ROS when added to both control group and tributyltin treated group. Tributyltin also increased insulin secretion and induced apoptosis, while estradiol caused a decrease in insulin secretion and apoptosis.
Conclusion: Our results indicate that estradiol can protect islets of the pancreas by inhibiting apoptosis and decreasing ROS as well as insulin secretion. It can be concluded that function of estrogen receptors in the pancreas particularly β-cells might be an important target for pharmacological and toxicological modifications in order to discover new aspects of pathophysiology and therapeutic strategies for diabetes.
Keywords: Islets of Langerhans, Estrogen receptors, Estradiol, Tributyltin

P-544

Effect of high dose of testosterone enanthate on the blood cells and RBC index in male rats

Sahar Mohamadi Vala

The androgen hormones & their derivatives are widely used for the treatment of androgen deficiency disease previous studies show that these hormones had various effect on different body organs including blood tissues.
This studies 50 male adult rats were divided in to 5 groups of
A- Control
B- Sham operated rats receiving TE
C- Gonadectomized rats receiving TE groups
D- Sham , operated rats receiving same volume of vehicle
E- Gonadectomized rats receiving same volume of vehicle after 63 days of experimental period the blood samples were collected from the heart & blood cells were counted by coulter counter.
The results show that the number of RBC, RBC index, (MCV, MCH, MCHC), hemoglobin & platelet were not significantly changes after TE treatment in gonadectomized rats. However, the number of WBC was significantly decreased in gonadectomized rats treated with TE.
This result in can be concluded that the TE probably interfere the WBC synthesis pathway through the effect on bone marrow.

P-545

Effect of Capparis Spinosa Alcoholic Extract on the Isolated Rat Pancreatic Islets

Mohsen Azad[1], Shahab Bohlooli[1], Perham Mohammadi[2], Sara Mostafalou[1]

1. Department of Pharmacology and Toxicology, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran.
2. Department of Physiology and Pharmacology, School of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran.

Objective: From ancient time, plants were used to cure human diseases. Capparis spinosa L. belongs to the Capparaceae family and was reported to have some biological activities such as cytotoxic, anti-inflammatory, antimutagenic, antioxidant and anti-diabetic effect. It has very active chemical groups such as alkaloids, phenolic, flavonoids, tannins, and many other minerals. Phenol compounds have antioxidant activity and can scavenge free radicals so that plants containing these compounds have promissing effects for human health. Moreover, flower bud

pickles of C.spinosa are traditionally used as a food supplement for treatment of diabetes. The aim of this study was to evaluate the effect of C.spinosa alcoholic extract on cellular viability and oxidative stress in rat pancreatic islets.
Material and Method: In this experimental set up, the male rats were anesthetized and their pancreas were removed, then the islets of Langerhans were isolated and incubated in vitro for 24 hours. The islets were incubated with plant extract for 24 hours after which cellular viability and production of reactive oxygen species were measured.
Results: The C.spinosa bud alcoholic extract markedly increased survival of the islet cells. This effect increased by increasing the doses of extract and greatest effects were observed in 103 and 104 µgmL-1 ($p < 0.001$). Also, at mentioned concentrations, ROS production was reduced up to 37% ($p < 0.01$) and 72 % ($p < 0.001$) of control, respectively.
Conclusion: Based on these results, we suggest that C.spinosa can be a promising candidate for prophylaxis and treatment in therapeutic strategies of diabetes.
Keywords: Capparis Spinosa L, Diabetes, Extract, Islets, Oxidative stress, Viability

P-546

The effects of tropisetron on liver injury in streptozotocin-induced diabetic rats

Shiva Gholizadeh[1],Roya Naderi [2,3*],Nima Mahmodian[3]

1. Department of Biochemistry, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran
2. Nephrology and Kidney Transplant Research Center, Urmia University of Medical Sciences, Urmia, Iran
3. Department of Physiology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

Objectives: This study aimed to evaluate the effect of tropisetron on liver injury induced by diabetes. Methods: Thirty five male Wistar rats were assigned to five groups (n=7): control (C), tropisetron (T), diabetic (D), diabetic + tropisetron (D+T), and diabetic + glibenclamide (D+G). Diabetic rats were treated with tropisetron (3 mg/kg body weight/day) or glibenclamide (1 mg/kg/day) for two weeks. Results: Liver from diabetic rats exhibited a significant increase in alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), cholesterol (Chol), triglycerides (TG), low-density lipoprotein (LDL), and atherogenic index, and a significant decrease in liver glycogen, serum albumin, and high-density lipoprotein. Treatment with tropisetron significantly abrogated diabetes-induced perturbation in these parameters. These effects were equipotent with glibenclamide, suggesting that tropisetron treatment is associated with a hepatoprotective effect against diabetic injury. Conclusion: The results of this study manifested the significance of using tropisetron as a promising remedial agent to improve diabetic complications.
Keywords: Diabetes, tropisetron, glibenclamide, lipid profile, liver

P-547

PIH improves pancreatic islet function and survival in vitro and in vivo

Marzieh Nemati[1], Narges Karbalaei[1,2]

1. Department of Physiology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
2. Histomorphometry and Stereology Research Center, Shiraz University of Medical Sciences., Shiraz, Iran

Background: Pancreatic islet transplantation is suggested as an effective treatment option in diabetes but as a standard therapy it has some challenges. A major limitation is the lack of accessible quantities of viable and functional islets for transplantation due to multiple factors including loss of vasculature, hypoxia and environment destruction. This destruction is caused during islet isolation through impairment islet extracellular matrix so, removal of this trophic support leads to reduce islets survival. Reconstruction of islet microenvironment may be a

good solution for this problem. According to this, we investigate the effects of pancreatic homogenate islet (PIH) on islet microenvironment reconstruction and consequently on the survival and function of the islets.
Method: pancreatic islets were isolated from Sprague-Dawley rats and divieded into two groups. Viability, insulin content and insulin releasing of cultured islets were evaluated. In vivo experiments, Islets were inserted into sub capsular kidney space of diabetic rats with or without PIH. Transplantation outcomes were evaluated by plasma glucose, insulin levels, glucose tolerance tests, and PDX1 and insulin gene expression.
Results: Viability and insulin release in PIH-treated was significantly higher than that in control group. After transplantation of islets, PIH recipient rats showed significant decreases in fasting and non fasting blood glucose concentration and their response to glucose challenge was improved.
Conclusion: islet treatment with PIH can be successfully increase transplant outcome may be through the effect of PIH on improvement of cell matrix interaction which has beneficial effects on the islets survival and function and transplantation outcome

P-548

Normobaric oxygen therapy improves glucose metabolism in obese male rats

Reza Norouzirad[1,2], Pedro González-Muniesa[3], Mahboubeh Ghanbari[1], Sajad Jeddi[1], Asghar Ghasemil[*]

1. Endocrine Physiology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Dezful University of Medical Sciences, Dezful, Iran
3. University of Navarra, Department of Nutrition, Food Science and Physiology, School of Pharmacy and Nutrition, Pamplona, Spain

Background and Objective: Obesity is associated with chronic hypoxia. Tissue hypoxia contributes to adipose tissue dysfunction, development of insulin resistance, and glucose intolerance. In this study, we hypothesized that long-term treatment with hyperoxia improves glucose metabolism in obese male rats. Materials and Methods: Male Wistar rats (n=24) weighing 190-210g, were randomly divided into four groups (n=6): control (C), control+hyperoxia (C-O2), obesity (O), and obesity+hyperoxia (O-O2). Obesity was induced using high-fat diet (~58% of calories from fat) for 9 weeks until the end of the study. C-O2 and O-O2 groups were exposed to 95% oxygen for 2 h/day, all days except Fridays, for 5 weeks; rats in C and O groups were kept in normobaric normoxia condition. Body weight (every 3 days), fasting serum glucose (every 2 weeks), insulin, lactate and glucose tolerance (at the end of the study) were measured. Insulin sensitivity/resistance indices were calculated at the end of the study. Results: In untreated obese rats, weight gain and serum levels of glucose, insulin, and lactate were higher than controls. At the end of the study, hyperoxia decreased body weight (AUC 10543±243 vs. 9185±192, P<0.0001), serum glucose (AUC 5079±79 vs. 4140±140, P<0.0001), insulin (275.2±42.4 vs. 184.4±28.0 pmol/L, P=0.0395), and lactate (AUC 1792±41.0 vs. 1386±59.0, P<0.0001) concentrations in obese rats. Moreover, hyperoxia increased glucose tolerance and insulin sensitivity in obese rats. Conclusion: Hyperoxia has beneficial metabolic effects on glucose metabolism in obese rats; this effect is at least in part due to weight loss, improved glucose tolerance, and improved insulin sensitivity.
Keywords: Glucose metabolism; Hyperoxia; Insulin resistance; Obesity; Oxygen; Weight loss

P-549

The effect of exenatide, a glucagon like peptide 1, on anthropometric indices (body weight, WHR, ovary weight) in rats with poly cystic ovarian syndrome

Asma vatankhah[1], Mohammad Ebrahim Rezvani[2] , Mahin Izadi[2] , Sima Vatankhah[1]

1. Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, Iran
2. Department of Physiology, School of Medicine, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran

Background: Polycystic ovary syndrome (PCOS) is a complex endocrine and metabolic disorder associated with ovulatory dysfunction. The level of anthropometric indices (body weight, WHR, ovary weight) is low in women

with PCOS that have been attributed to obesity which is common among these women. The aim of this study was to investigate the effects of exenatide on the anthropometric indices (body weight, WHR, ovary weight) in PCOS rats.
Materials and methods: Twenty eight normal cyclicity female wistar rats weighting 175-200 g were used in this study. PCOS was induced through the injection of 4 mg estradiol valerate per rat. PCOS rats were treated by the different doses of exenatide (50, 100 mg/kg).
Results: The result of study showed that the weight gain was no significantly different among the experimental groups. Exenatide significantly reduced ovarian weight and WHR in doses of 50 and 100 mg/kg ($p<0.05$).
Conclusion: exenatide, a glucagon like peptide, had the useful effects on diabetes mellitus and metabolic syndrome with reduced body weight, ovarian weight and WHR in PCOS rats. We conclude that exenatide can improve metabolic indices and type 2 diabete in PCOS rats.
Keywords: polycystic ovarian syndrome, exenatide, body weight, WHR, ovary weight, metabolic syndrome, diabetes mellitus.

P-550

The expression of SIRT1, inflammatory proteins, and tissue injury in pancreas of ovariectomized diabetic rat: Beneficial effect of swimming exercise

Hadi Yousefi[1], Parisa Habibi[2], Nasser Ahmadiasl[3], Alireza Alihemmati[4]

1. Khoy university of medical sciences, Khoy, Iran
2. Department of physiology, Faculty of Medicine, Hamedan University of Medical Sciences, Hamedan, Iran
3. Department of physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
4. Department of Histology & Embryology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: The postmenopausal years are related with an increasing in fasting blood glucose, insulin content and subsequently increasing in proinflammatory cytokines. This study designed to evaluate effect of swimming exercise on pancreas of ovariectomized diabetic rat.
Materials and Methods: Female Rats were divided into, sham and bilateral ovariectomized (OVX) groups. OVX was rerandomized into three groups control (OVX), OVX+diabetic (OVX.D) OVX.D+exercise (OVX.D.E). After surgical recovery, high fat diet (HFD) together with single dose of streptozotocin (30 mg/kg; IP) used to induction of diabetes. Swimming exercise (1 hr/day) performed for 8 weeks coincident with beginning of HFD regime. At the end of 8 weeks, pancreas tissue was removed and Western blotting analysis was performed on homogenates of pancreatic tissue and, Hematoxylin-Eosin staining was used to histopathological assessment.
Results: Swimming exercise decreased inflammation and tissue injury, and this decline was seems to be correlated with the expression of SIRT1. Increasing SIRT1 by exercise accompanied with reduces of NF-kB and IL-1β expression, and prevents tissue injury. OVX.D significantly increased Nf-kB and IL-1β expression, and decreased SIRT1 compared to sham group ($P<0.05$). Significant reduction of Nf-kB and IL-1β, and increasing of SIRT1 was observed during swimming exercise ($P<0.05$).
Conclusion: Swimming exercise eliminates the inflammation of contracting diabetes in postmenopausal state and support the potential preventing effect of exercise in pancreatic injury after menopause.
Keywords: Diabetes, Ovariectomy, Nf-kB, IL-1B, SIRT1, Swimming exercise

P-551

Remote limb ischemic preconditioning accelerates recovery of renal function following ischemia-reperfusion injury: the possible role of lactate as a mediator

Zahra Akbari[1], Hossein Fatemikia[1], Zeynab karimi[2], Kaveh Tanha[3], Mohammad Reza Farzaneh[4], Majid Asadi[3], Khalil Pourkhalili[1]

1. Department of Physiology, Faculty of Medicine, Bushehr University of Medical Sciences, Iran.
2. Nephro-Urology Research Center, Shiraz University of Medical Sciences, Iran.
3. Persian Gulf Nuclear Medicine Research Center, Bushehr University of Medical Sciences, Iran.
4. Department of Pathology, Faculty of Medicine, Bushehr University of Medical Sciences, Iran.

Background and Objective: Despite numerous studies showing protective effects of remote ischemic preconditioning (RIPC), the exact nature of the circulating mediators which carries the preconditioning signal from the remote site to the target organ have not been identified yet. Here we aimed to determine if RIPC alone increase lactate production in the circulation; and if exogenous administration of lactate could induce renal protection against ischemia reperfusion (IR) injury.
Materials and methods: Twenty-eight male Sprague Dawley rats were randomly divided into four groups: Sham (laparotomy without ischemia and reperfusion), IR group (Laparotomy with 45 min bilateral renal ischemia and 24 h reperfusion), RIPC+IR group (three cycles of RIPC cycles applied to the both hind limbs before laparotomy and then 45 min bilateral kidney ischemia and 24 h reperfusion) and Lactate+IR (750 mg/kg Sodium L-lactate before renal IR). Kidney function was assessed by quantitative evaluation of 99mTc-DMSA renal scan using a dual-head small-animal SPECT imaging system. Serum and urine sodium (Na+), potassium (K+), creatinine (Cr) and blood urea nitrogen (BUN) was measured and glomerular filtration rate (GFR) was estimated by creatinine clearance.
Results: Application of RIPC markedly increased lactate level in preconditioned limbs and significantly improved 99mTc-DMSA renal uptake, decreased serum K+, Cr and BUN levels and increased creatinine clearance as an index of glomerular filtration rate (GFR). Administration of lactate increased 99mTc-DMSA renal uptake and improved renal function parameters.
Conclusions: The results of this study indicate that lactate can be considered as a possible signal in the mediation of RIPC effects.
Keywords: Remote Ischemic Preconditioning, Renal Ischemia-reperfusion, Lactate

P-552

The Effect of Plantago Major on Kidney Function in Adriamycin Induced Nephrotoxicity

Mahnaz Allahyari[*1], Zahra Samadi Noshahr[1], Zohreh Naji Ebrahimi Yazd[1], Sara hosseinian[1, 2], Samira Shahraki[1], Abolfazl Khajavi Rad[1,2]

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Objective: Nephrotoxicity is one of the important side effects of Adriamycin (ADR) in treating various cancers Plantago Major (P.M) is one of the plants that traditionally used for the treatment of many diseases and has various biological activities such as antioxidant, anti-inflammatory and immunomodulatorys actions.This study aimed to evaluate the protective effects of P.M against ADR-induced nephrotoxicity in rats.
Method: 40 male Wistar rats were randomly divided into 4 groups: 1-control 2-ADR (5 mg/kg, IV) 3- P.M (600mg/kg) + ADR 4- P.M (1200mg/kg) + ADR. The study period was 35 days. Animals were orally treated with P.M hydro-alcoholic extracts 70% for 6 days. Then ADR is administered intravenously on day 7 and extract continued for 28 days. Serum and urine samples were collected on days 0, 14, 21 and 28 and concentrations of urea, creatinine, urine output, urea clearance, and glomerular filtration were determined.
Results: ADR injection caused significant changes were in clearance urea, glomerular filtration rate compared with control group ($p<0.05$). Consumption of extract P.M with two doses of 600 and 1200 improved significantly urea clearance and glomerular filtration rate($p<0.01$).
Conclusion: The results of present study showed that the hydro-alcoholic extracts of P.M improve kidney function, in ADR-induced nephrotoxicity, possibly via their antioxidant properties. However, future studies are required to determine the exact mechanisms involved in P.M effects on ADR induced kidney toxicity.
Keywords: kidney function, Adriamycin, Plantago Major

P-553

The renoprotective effects of naringin and trimetazidine through inhibition of apoptosis and downregulation of micoRNA-10a in renal ischemia/reperfusion injury model

Negin Amini, Mohammad Badavi, Alireza Sarkaki, Mahin Dianat, Seyyed Ali Mard, Akram Ahangarpour

The Persian Gulf Physiology Research Center and Department of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Background and Objective: Renal ischemia/reperfusion (I/R) injury is a common cause of acute kidney injury. The production of free radicals and reactive oxygen species are considered as important factors contributing to I/R injury. Naringin (NAR) as an antioxidant has the properties of free radicals' scavengers. Trimetazidine is an anti-

ischemic drug and can protect mitochondria. The primary purpose of this study was to evaluate the renoprotective effects of NAR and TMZ on microRNA-10a, and apoptosis factors expression in renal I/R injury.
Materials and Methods: Forty rats Sprague-Dawley were divided into five groups randomly: Sham, IR injury, (TMZ, 5 mg/kg, intravenously, before reperfusion), (NAR pretreatment, 100 mg/kg, intraperitoneally, before ischemia), and TMZ plus NAR. To induction of I/R injury in all groups except sham, the kidney pedicles was clamped for 45 minutes, followed by 4h of reperfusion. Real-time PCR was used to determine the genes expression. $p<0.05$ was considered significant.
Results: I/R injury significantly increased the mRNA expression of Bax and caspase-3 ($p<0.001$, $p<0.01$), decreased the Bcl-2 mRNA expression ($p<0.01$), and the plasma level of miR-10a significantly elevated ($p<0.05$) compared to the sham group. Pretreatment with NAR, TMZ, and co-administration significantly decreased the plasma level of microRNA-10a ($p<0.05$, $p<0.05$, and $p<0.01$, respectively), caspase-3 ($p<0.001$), and BAX mRNA expression ($p<0.01$), but increased the Bcl-2 mRNA expression in the kidney tissue ($p<0.05$).
Conclusion: The results showed that the NAR, TMZ, or co-administration had renoprotective effects through preventing apoptosis, or reducing the plasma level of miR-10a.
Keywords: Naringin, trimetazidine, microRNA-10a, anti-apoptosis, renal ischemia/reperfusion injury

P-554

Effect of gender difference on brain and kidney tissue alteration after different reperfusion times from renal ischemia – reperfusion in rats

Fakhri Armin[1], Aghdas Dehghani[1],Fariba Azarkish[2], Ali Atashabparvar[3]

1. Department Of Physiology, School Of Medicine, Hormozgan University Of Medical Sciences, Bandar Abbas, Iran.
2. Molecular Medicine Research Center, Hormozgan Health Institute, Hormozgan University Of Medical Sciences, Bandar Abbas, Iran.
3. Department Of Pathology, Faculty Of Medicine, Hormozgan University Of Medical Sciences, Bandar Abbas, Iran.

Background And Objective: Renal ischemia-reperfusion (RIR) injury is leading to acute kidney injury and initiates an inflammatory responses that may cause systemic inflammation and induce impairment of remote organs such as brain. There isn't enough evidence that the impact of gender on renal IRI induced- brain injury. So, we evaluated the effect of sexual dimorphism on brain tissue alterations 3,24,48 h after bilateral renal ischemia in rats.
Material and Methods:80 wistar rats (8group) include two main groups (40 male and 40 female) .Each of them were divided in four subgroups including: 1- control (sham- operated).2- renal ischemia(RI)+3h (IR by 3 hours reperfusion), 3-RI +24h (IR by 24h reperfusion), 4-RI+48h(IR by 48h reperfusion). Sham groups are exposed to surgery without ischemia process. Ischemic groups underwent 45min bilateral renal ischemia. After reperfusion time, blood samples were obtained for the renal function measurements. The kidney and brain removed and was fixed in 10% formalin solution for pathological assessment.
Results: The serum levels of BUN, Cr and kidney tissue damage increased in both gender and peaked at the 24h post ischemia. The total brain tissue damage and gliosis increased from 3h after ischemia and necrosis elevated from 24h post ischemia in both gender, but in male more than female. Brain vascular congestion increased at 3h after ischemia and then decreased.
Conclusions: RIR induced brain tissue damage in male more than female rats.
Keywords: Renal ischemia‑reperfusion, Acute kidney injury, Remote organ

P-555

Protective effect of Rheum turkestanicum against gentamicin-induced nephrotoxicity

Mohammad Taher Boroushaki[1], Samaneh Boroumand-Noughabi[2], Azar Hoseini[3]

1. Department of Pharmacology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Pathology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Pharmacological Research Center of Medicinal Plants, Mashhad University of Medical Sciences, Mashhad, Iran
Background and Objective(s): Gentamicin belongs to the family of aminoglycoside antibiotics and is a preferred drug in developing countries because of its low cost, availability, and potent effects against bacterial. However, gentamicin can induce nephrotoxicity. In this research, hydroalcoholic extract of Rheum turkestanicum was used

against gentamicin- induced nephrotoxicity and its effect against gentamicin-induced nephrotoxicity in rats has been investigated.
Materials and Methods: The rats were placed into one of these groups: saline group, gentamicin group that received gentamicin 80 mg/kg/day for six days, and two treatment groups that received R. turkestanicum intraperitoneally at doses of 100 and 200 mg/kg body weight, respectively, 1 hr before gentamicin injections. Urine samples were collected at 24 hr to measure glucose and protein concentration. Blood samples were collected to determine serum urea and creatinine. One kidney was homogenized to measure malondialdehyde and thiol, and the other kidney was kept for pathological studies.
Results: Gentamicin increased the level of urinary glucose and protein, and increased malondialdehyde while it decreased thiol in kidney tissue, and increased the concentration of urea and creatinine in the serum. Histopathological pathology revealed renal damage following gentamicin usage; however, the extract was able to improve gentamicin toxicity.
Conclusion: R. turkestanicum has positive effects in the attenuation of gentamicin-induced nephrotoxicity.
Keywords: Rheum turkestanicum, Gentamicin, Reactive oxygen species, Malondialdehyde,
Oxidative stress

P-556

The Reno-Protective Role of Angiotensin 1-7 in Cisplatin Induced Nephrotoxicity

Zahra Pezeshki[1,3], Farzaneh Karimi[1,3], Sayyedehnikta Kassaei[1], Samira Choopani[1,3], Ardeshir Talebi[1,2], Mehdi Nematbakhsh[1,3,4]

1. Water and Electrolytes Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Clinical Pathology, Isfahan University of Medical Sciences, Isfahan, Iran
3. Department of Physiology, Isfahan University of Medical Sciences, Isfahan, Iran
4. IsfahanMN Institute of Basic and Applied Sciences Research, Isfahan, Iran

Background: Nephrotoxicty; is one of the most important limitation of CP therapy. CP-induced nephrotoxicity is gender dependent. It was hypothesized that Ang1-7 could protect the kidney against CP-induced nephrotoxicity. So this study was designed to determine the protective role of angiotensin 1-7 (Ang1-7) against CP induced nephrotoxicity in male and female rats.
Methods & Materials: 35 male (331±7.4 g) and female (196.5±5.9 g) Wistar rats in 6 groups were used in this study. The male rats received saline as vehicle (Group 1, n=7), single dose of CP (7.5 mg/kg) (Group 2, n=5), or single dose of CP plus daily injection of Ang1-7 (30µg/kg/day.ip) (group 3, n=7). The female rats in groups 4, 5 or 6 (n= 5, 5, 6) were treated as groups 1-3. One week later, the blood samples were obtained and the animals were sacrificed.
Results: The increased kidney tissue damage, kidney weight, and the serum levels of BUN and Cr induced by CP was attenuated significantly by Ang1-7 ($P<0.05$) in male rats. However, the protective role of Ang1-7 against CP induced nephrotoxicity was not detected in female rats.
Conclusion: Ang1-7 may act as suitable supplement to attenuate CP induced nephrotoxicity in male rats possibly due to its effect on kidney circulation.
Key words: Cisplatin; Angiotensin 1-7; Nephrotoxicity; Gender

P-557

Cisplatin Alters Sodium Excretion and Renal Clearance in Rats: Gender and Drug Dose Related

Sima Jilanchi

Background: Nephrotoxicity is one of the side effects of cisplatin (CP) therapy which is gender related. CP disturbs renal function through glomerular filtration rate and electrolytes transport disturbances. This study was designed to compare some markers related to renal function in two protocols of CP treatment in rats.
Materials and Methods: Male and female rats were subjected to receive single (treat 1; 7.5 mg/kg) and continues doses (treat 2; 3 mg/kg/day for 5 days) of CP, and the measurements were compared with control animals.

Results: The serum level of blood urea nitrogen (BUN) and creatinine (Cr), and Cr-clearance, kidney tissue damage score, kidney weight, body weight change, and Na excretion was altered significantly ($P < 0.05$) in animals treated with continuous dose of CP (treat 2), while alteration of BUN and Cr was gender related. The kidney levels of malondialdehyde and nitrite were significantly different between male and female in two protocols of treatments.
Conclusion: Renal function after CP therapy alters in rats' gender dependently, and it is related to protocol of treatment.
Keywords: Cisplatin, gender, rats, renal function

P-558

Cyclosporine-A induced nephrotoxicity in male and female rats: Is zinc a suitable protective supplement?

Samira Choopani[1], Sayyedehnikta Kasaei[1], Ardeshir Talebi[1,2], Mojgan Mortazavi[3], Yousef Gheisari[4], Mohammad Matinfar[3], Mehdi Nematbakhsh[1,5,6]

1. Water and Electrolytes Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Clinical Pathology, Isfahan University of Medical Sciences, Isfahan, Iran
3. Isfahan Kidney diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
4. Department of Genetics and Molecular Biology, Isfahan University of Medical Sciences, Isfahan, Iran
5. Department of Physiology, Isfahan University of Medical Sciences, Isfahan, Iran
6. Isfahan MN Institute of Basic and Applied Sciences Research, Isfahan, Iran

Background and Objective: Cyclosporine (CYC) is an immunosuppressant drug used widely in kidney transplant patient. The major side effect of CYC is nephrotoxicity. In this study, three different doses of CYC alone or accompanied with zinc (Zn) supplement were administrated in male and female rats to determine the kidney tissue damages and functions.
Materials and Methods: Male and female rats were treated with 10, 50 or 100 mg/kg/day of CYC alone or accompanied with 10 mg /kg/day of Zn sulfate for 10 days. The parameters related to renal function were determined and the kidney tissues were subjected to histological evaluation.
Results: All male and female animals were treated with high dose CYC (100 mg/kg/day) alone or accompanied with Zn supplement during the experiment. The data obtained for the serum levels of creatinine (Cr) and blood urea nitrogen/Cr ratio, clearance of Cr, kidney weight (KW), sodium (Na) filtration rate, Na excretion rate and Na excretion fraction (%) in surviving animals suggest a role of gender in the variation of these factors. The kidney tissue damage score (KTDS) was increased as the dosage of CYC was elevated, and the Zn supplement attenuated the KTDS in animals treated with low dose CYC (10 mg/kg/day).
Conclusion: The CYC-induced nephrotoxicity may be gender-related, and the 10 mg/kg dose of Zn sulphate as a supplement may possibly prevent the induced nephrotoxicity in males due to its antioxidant effects.
Keywords: Cyclosporine, Gender, Nephrotoxicity, Renal function, Zinc

P-559

Nephroprotection of Long-term exercise is mediated through H2S in 5/6 nephrectomized rats

Abdollah Sajedizadeh, Mahdi Hajiaghaei, Mehri Kadkhodaei, Behjat Seifi*, Mina Ranjbaran

Physiology Department, Tehran University of Medical Sciences, Tehran, Iran

Background and Objective: Physical exercise is shown to have protective effects on chronic kidney disease (CKD). CKD is associated with a reduction in renal hydrogen sulfide (H2S) concentration. In this study we evaluated the role of PAG (H2S synthesis inhibitor) in the protective effects of physical exercise in male rats.
Materials and Methods: Twenty four male Wistar rats (250–300 g) were assigned into 4 groups: 1) Sham 2) CKD 3) Exercise 4) PAG. In the Sham group, anesthesia and surgery were performed without removal of the kidney mass.

To induce CKD, 4 days after removing upper and lower one-third parts of the left kidney, total right nephrectomy was performed. Three weeks after induction of CKD, exercise was performed. In PAG group, animals were received PAG (i.p., twice a week) for 8 weeks in addition to CKD and exercise. In 3 animals of each group, telemetry transmitter for continuous arterial blood pressure recording was inserted in the aorta at the same time of total nephrectomy. At the end of the twelfth week, blood samples were collected to measure renal functional (levels of plasma urea and creatinine) and inflammatory indices (TNF-α and IL-6).
Results: Eight weeks exercise significantly improved serum creatinine, BUN, inflammation, and hypertension compared to the CKD group. PAG administration significantly abolished all beneficial effects of long term exercise.
Conclusion: The results suggests that regular exercise ameliorates renal damage, inflammation and hypertension in 5/6 nephrectomized rats. The protective effects of long-term physical exercise may be mediated by H2S.
Keywords: Chronic kidney disease; Physical exercise; PAG

P-560

Evaluation of Rheum turkestanicum in Hexachlorobutadien-Induced Renal Toxicity

Azar Hosseini[1], Sahar Fanoudi[1], Arezoo Rajabian[1], Samaneh Boroumand[2,3], Azita Aghaee[1] and * Mohammad Taher Boroushaki[4]

1. Pharmacological Research Center of Medicinal Plants, Mashhad University of Medical Sciences, Mashhad, Iran,
2. Department of Pathology, Faculty of Medicine, Mashhad university of Medical Sciences
3. Deparment of Hematology and blood banking, Faculty of Medicine, Mashhad university of Medical Sciences
4. Department of Pharmacology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran,

Background Hexachlorobutadien is nephrotoxic agent in rodents. The mechanism of toxicity includes generation of free radicals, depletion of thiol groups and production of toxic metabolites. Antioxidant compounds may reduce HCBD-nephrotoxicity. In this research we investigated the effect of Rheum turkeatanicum extract against HCBD-toxicity. Materials&Methods The animals were divided to four groups which were including control (saline, 1mL/kg), HCBD (100 mg/kg) and treatment groups which received extract at doses 100 and 200 mg/kg. The extract were administered as intraperitoneally (i.p.) 1h before HCBD injection (i.p.). The animals were anesthetized by ether, 24h after HCBD administration. Results The results showed elevation of serum creatinine, serum urea, urinary protein, urinary glucose, malondialdehyde levels in kidney and reduction of thiol in kidney by HCBD. The histopathological studies showed that there was apoptosis and necrosis in HCBD treated groups. Administration of R.turkestanicum reduced HCBD toxicity. The extract reduced hitopathological changes in kidney. Conclusion It may be concluded that the nephroprotective effect of extract may be due to different mechanisms such as antioxidant activity or by decreasing the toxic metabolites of HCBD or inhibition of enzymes which are involved in the bioactivation of HCBD such as glutathione-S-transferase (GST) or cysteine-S-conjugate β-lyase.
Key words: Rheum turkestanicum, Hexachlorobutadien, Renal toxicity, Oxidative stress, Malondialdehide

P-561

Thymoquinone ameliorates kidney fibrosis in a rat model of unilateral ureteral obstruction

Sara Hosseinian[1,2], Abolfazl Khajavi Rad[1,2], Samira Shahraki[1], Zahra Samadi Noshahr[1], Somayyeh Mahzari[1], Mahnaz Allahyari[1]

1. Department of physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Neurogenic inflammation research center, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and Objective: Unilateral ureteral obstruction (UUO) causes severe renal tubule-interstitial fibrosis. Because of many pharmacologic properties of thymoquinone (TQ), in this study, the effects of TQ against kidney fibrosis were investigated in rats with UUO.

Materials and methods: Thirty male Wistar rats were divided into three groups: Sham operated, UUO, and the animals with UUO treated with TQ. The expression of Collagen IV and transforming growth factor (TGF)-β1 were meausured by immunohistochemistry. Renal interstitial fibrosis was assessed by Masson's trichrome staining.
Results: UUO markedly increased renal expression of TGF-β1 and collagen IV and induced interstitial fibrosis. TQ significantly downregulated the expression of these fibrotic markers and interstitial fibrosis.
Conclusion: TQ could be regarded as a potent therapeutic agent for treatment of UUO-induced kidney fibrosis.
Keywords: Unilateral Ureteral Obstruction, Thymoquinone, Fibrosis.

P-562

Stem Cell Therapy Ameliorate Ischemia-Reperfusion of Kidney After 24 h Reperfusion

Leila Hafazeh[1], Saeed Changizi-Ashtiyani[2], Faezeh Ghasemi[3], Houshang Najafi[4], Saeed Babaei[5], Farshid HaghverdiF[6]

1. Ms.c Student. Department of Physiology, Arak University of Medical Sciences, Arak, Iran
2. Department of Physiology, Arak University of Medical Sciences, Arak, Iran.
3. Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran.
4. Medical Biology Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran.
5. Department of Anatomy, School of Medicine, Arak University of Medical Sciences, Arak. Iran
6. Department of Internal Medicine, School of Medicine, Arak University of Medical Sciences, Arak. Iran.

Introduction.The mortality rate in patients with acute kidney injury (AKI) is high. The aim of this study was to evaluate the efficacy of Adipose-derived- mesenchymal stem cells (AD-MSC) in renal ischemia-reperfusion (I/R) model in rats.
Materials and Methods.In this study, 28 male Wistar rats were studied in 4 groups: Control, Sham, I/R24 +PBS, I/R24 + AD-MSC. Induced renal I/R was performed by blocking the renal arteries for 45 min and then 24 h for reperfusion. Measurement of urine volume and osmolarity, as well as measurement of plasma creatinine (Crp), blood urea nitrogen (BUN) parameters and calculation of creatinine clearance (CCr), absolute sodium excretion (UNaV◦), fraction exertion of sodium (FENa), absolute potassium excretion UKV◦) and fractionexertion of potassium (FEK). The right kidney was removed to measure the malondialdehyde (MDA) and ferric reducing antioxidant power (FRAP) and the left kidney to study the tissue.
Results. I/R caused a significant increase of Crp, BUN, UNaV◦, FENa, FEK, MDA level and tissue damage and decreased CCr, urinal osmolality, and FRAP level. Following AD-MSC treatment, the levels of FENa, Crp, FEK, MDA and tissue damage decreased significantly and, urinary osmolality increased significantlyin the I/R24+ AD-MSC group compared to the I/R24 +PBS group. While FRAP values were significantly increased ($p<0.001$).
Conclusion. Treatment with AD-MSC reduced tissue damage and oxidative stress, increased antioxidant activity, and improved kidney function after 45 min of ischemia and 24 h reperfusion.
Keywords: Adipose-derived- mesenchymal stem cells, Ischemia-reperfusion, Oxidative stress, Acute kidney injury

P-563

The impact of different time of renal ischemia- reperfusion on lung histological change in male and female rats.

Aghdas Dehgahni, Fariba Azarkish, Ali Atashparvar

School of Medicine, Hormozgan University, Bandar Abbas, Iran.

Background and Objective: progression to Lung dysfunction following renal ischemia-reperfusion (RIR) is the important target of RIR induced-remote injury.Evidences indicated that the severity of kidney and lung injury with IRI can be affected by gender. We investigate gender differences in IRI induced- lung injury in different reperfusion time.

Method and Materials: 80 Male and Female rats were assigned into 8 groups: Group1 and 2: (male and female Shame groups respectively). Group3 and 4(male and female- 3hr reperfusion groups, respectively), Group5 and 6(male and female-24hr reperfusion groups, respectively), Group7 and 8 (male and female- ISC48hr groups, respectively). Rats exposed to renal ischemia for 45 min and 3, 24 and 48 hr reperfusion time. After reperfusion, blood samples were obtained for measuring the serum level of blood urea nitrogen (BUN), creatinine (Cr), nitrite, and malondialdehyde (MDA).The kidneys and lung tissues were removed for MDA and nitrite measurements and evaluate the histological changes.
Results: the rise in Cr and BUN reached the peak at 24 h reperfusion in both gender. Renal IR in female lead to significant increase in serum nitrite at 3h reperfusion. In male rats, MDA increased in 3 h reperfusion group but not in females. Kidney and brain tissue damage enhanced reperfusion time dependently in both gender.
Conclusion: Renal IRI caused kidney and lung dysfunction specific at 24h post ischemia. Considering gender difference, female gender may be more sensitive to NO system compared with males. Male exhibit more rapid IRI injury than females.
Keywords: renal ischemia-reperfusion, Lung, Gender difference

P-564

Comparison of systemic and centrally erythropoietin administration on kidney protection during severe hemorrhagic shock in rats

Mina Ranjbaran, Mehri. Kadkhodaee, Behjat Seifi*

Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Background and objective: In this study, we compared the beneficial effects of peripheral and central erythropoietin (EPO) administration on renal functional, oxidative, inflammatory and apoptotic parameters during hemorrhagic shock (HS) in rats.
Materials and Methods: Animals were divided into four groups. 1) Sham rats were subjected to stereotaxic surgery and cannulation of femoral artery and vein. 2) Prior to induction of hemorrhage in HS group, animals were subjected to stereotaxic surgery in lateral ventricle. HS was induced by removing 50% of total blood volume and then animals were resuscitated and scarified at the end of the post-resuscitation period. 3) EPO-systemic group, 300 IU/kg erythropoietin was administered over 10 min before resuscitation into the femoral vein and 4) EPO-central group, 2 IU erythropoietin was administered before resuscitation into the left lateral ventricle. At the end of the procedures, urine samples were stored and kidney tissue samples were harvested for ex-vivo measurements.
Results: EPO administration significantly improved kidney functional indices (urinary NAG-Cr ratio, and NGAL concentration) compared to the HS group. EPO also reduced the oxidative stress indices and significantly prevented the rises in renal tissues TNF-α and IL-6 mRNA expression and cleaved caspase 3 protein level compared to the HS group.
Conclusion: The protective effects of EPO-central appeared in the dose of 2 IU/5 µl while for systemic administration the dose of 300 IU/kg was effective which is approximately 50 times of centrally administration. It seems that centrally administered EPO is associated with more favorable outcomes than systemic treatment.
Key words: Erythropoietin; Hemorrhagic shock; Oxidative stress; Inflammation; Intraventricular infusion

P-565

Study the role of gender in the effect of sodium hydrogen sulfide on renal damage induced by ischemia reperfusion injury in rats

Shadan Saberi[1], Majid Askaripour[2], Hamid Najafipour[3]

1. Assistant Professor of Physiology, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Ph.D student of Physiology, Department of Physiology and Pharmacology, Kerman University of Medical Sciences, Kerman, Iran
3. Professor of Physiology, Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

Background and objective: Renal ischemic reperfusion (RIR) is a well-established model to study acute kidney injury.Different responses were seen in physiopathological conditions between two sexes the same in renal disease. Hydrogen sulfide (H2S), The third known gasotransmitter, has several biologic activities.This research aimed to clarify the role of gender in the effect of H2S donor,sodium hydrogen sulfide (NaHS), on renal damage induced by IR.
Material and methods: 84 male and female Wistar rats were randomly divided into control, sham, control+NaHS (100µm/kg ip), sham+NaHS, IR, and IR+NaHS groups.To induce ischemia, renal pedicles were clamped for 45 min, followed by 24 h reperfusion. The blood and 24-h urine samples were stored at -70 ºC until processed. Serum levels of BUN and Cr (SBUN,SCr),the urine level of albumin, urine flow,and clearance of creatinine as GFR were measured.
Result: Ischemia increased SBUN and SCr in both genders.NaHS administration does not affect serum and urine parameters in control and sham groups that represented its safety.NaHS increased albuminuria induced by IR non significantly in females,but this increase wasn't seen in males. Urine flow was increased by IR compared with the sham group in females ($p<0.001$),while this increase was insignificant in males($p=0.07$).NaHS vanished the difference was seen in females significantly but didn't have any effect on males.GFR was reduced by IR in both genders and NaHS decreased it more in both sexes.
Conclusion: NaHS affected females more than males in ischemic condition, although it wasn't protective.
Keywords: renal ischemia reperfusion, NaHS, gender, renal damage, GFR, albuminuria

P-566

The effect /of angiotensin1-7 and losartan on renal ischemic/ reperfusion injury in male rats

Tahereh safari

Department of Physiology, Zahedan University of Medical Sciences, Zahedan, Iran

Background and Objective: Ischemia/reperfusion (I/R) is a major cause of acute kidney injury. Several studies have shown that renin angiotensin system (RAS) and AT1 activation are involved in various forms of kidney diseases. Likewise, angiotensin 1-7 and losartan could possibly protect the kidney against I/R damage. Therefore, we investigate renal injury, administering the drugs before and after I/R.
Materials and Methods: Fifty-four male Wistar rats were randomly assigned to five groups as follows. 1- sham-operated (sham), 2- saline group, 3- losartan group that received 10mg/kg ip , 4- Ang1-7group that were treated with Ang1-7, 50µg/kg/ip 5- Ang 1-7+ losartan simultaneously. Groups 2-5 consist of two subgroups receiving the medication before or after ischemia. After I/R and taking blood samples, level of blood urea nitrogen (BUN), creatinine (Cr), nitrite, malondialdehyde (MDA), lactate dehydrogenase(LDH)and total antioxidant capacity (TAC) were measured in serum. Likewise, nitrite, MDA and TAC were measured in the homogenized kidney tissue.
Results: After the induction of I/R, the BUN, Cr, LDH and kidney tissue damage score (KTDS) have increased. The administration of Ang1-7 alone or simultaneously with losartan has decreased the levels of above factors. Also, kidney MDA and nitrate level have significantly increased($P<0.05$). The administration of losartan and Ang1-7 separately or simultaneously reduced renal damage significantly($P<0.05$).
Conclusion: According to the results of this study, it can be claimed that the effect of losartan in the presence of Mas receptor is statistically significant and kidney damage dramatically decreases.
Key words: Ischemia/reperfusion, Angiotensin 1-7, losartan, renal damage

P-567

Evaluating the effect of chronic Ethanol consumption on alteration of glomerular filtration barrier proteins genes expression and matrix metalloproteinases 2 and 9 activity in the kidney of male rats

Mahrokh Samadi[1], Alireza Shirpoor [2]

1. Department of Physiology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran
2. Department of Physiology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

Background and objective: Chronic ethanol ingestion is associated with functional alteration and structural damage in the kidneys, but the precise molecular underlying is not well known. The aim of this study was to investigate the

effect of chronic ethanol exposure on nephrin, podocin genes expression and matrix metalloproteinases 2 and 9 activity in the kidney of rats.
Materials and Methods: Sixteen male Wistar rats with an initial body weight of 220±10 gr were divided into the following two groups: 1- control, 2- ethanol. rats in the ethanol group received ethanol with a dose of 4.5 g/kg body weight (Merck KGaA, Darmstadt, Germany) saluted in tap water (20% w/v) intragastrically by gavage once a day, for six weeks. For quantification of nephrin and podocin mRNA expression, we applied real-time RT- PCR, and activity of matrix metalloproteinases 2 and 9 in rat kidney assayed by Elisa.
Results: 42 days administration of ethanol significantly decreased the nephrin and podocin mRNA expression compared to the control group ($p < 0.05$), also the results revealed a ignificant increase in matrix Metalloproteinases 2 and 9 activity in the ethanol group, compared to that in the control group.
Conclusion: These findings indicate that ethanol-induced kidney abnormalities may in part be associated with the decrease of nephrin, podocin genes expression and increase of matrix metalloproteinases 2 and 9 activity as a molecular mediator.
Keywords: Ethanol, Kidney, nephrin, podocin, MMP2, MMP9, Rat

P-568

Dextrose Hydration May Promote Cisplatin-induced Nephrotoxicity in Rats:Gender-related Difference

Farzaneh Karimi[1], Sayyedehnikta Kassaei[1], Azar Baradaran[1,2], Farzaneh Ashrafi[1], Ardeshir Talebi[1,2], Zahra Lak[1], Mehdi Nematbakhsh[1,3,4]

1. Water and Electrolytes Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Clinical Pathology, Isfahan University of Medical Sciences, Isfahan, Iran
3. Department of Physiology, Isfahan University of Medical Sciences, Isfahan, Iran
4. IsfahanMN Institute of Basic and Applied Sciences Research, Isfahan, Iran

Background and Objective: Cisplatin (CP) as an anticancer drug may affect the plasma glucose level while diabetic subjects are protected against CP-induced nephrotoxicity. In the current study, the role of dextrose hydration during CP therapy on CP-induced nephrotoxicity was evaluated.
Materials and Methods: Sixty-nine male and female rats into 12 groups were subjected to hydrate (15 mL/kg) with vehicle or different doses of dextrose (2%, 10% and 20%) before and after CP (7.5 mg/kg) administration, and one week later the biochemical and kidney function markers, and histology finding were determined.
Results: All the animals co-treated with CP and dextrose 20% were expired during one week of experiment. Administration of CP alone increased kidney damage (kidney tissue damage score, KTDS) and kidney weight (KW). It also elevated the blood urea nitrogen (BUN) and BUN-creatineine ratio (BUN/Cr) levels in the serum. In addition, CP decreased body weight and creatinine (Cr) clearance (CLCr) significantly in both male and female rats ($p<0.05$), however dextrose (2% and 10%) did not alter the mentioned parameters in male, but dextrose 10% supplement increased the serum levels of BUN, Cr and BUN/Cr ratio, KW and KTDS significantly in female rats ($p<0.05$).
Conclusion: Our data not only did not support the nephro-protective role of dextrose hydration during CP therapy but also indicated that dextrose hydration during CP therapy act as risk factor to promote CP induced nephrotoxicity in female rats. Prohibition of high carbohydrate (glucose) diet during CP therapy is recommended.
Keywords: cisplatin, nephrotoxicity, dextrose, rat, gender

P-569

Eugenol effects on metabolic-syndrome renal damages

Fatemeh Kourkinejad Gharaei[1], Tahereh Safari[2], Mohammad Reza Shahraki[2], Halimeh Lakzaei[1], Mehdi Jahantigh[3], Abasali Niazi[3]

1. Student Research Committee, Zahedan University of Medical Sciences, Zahedan, Iran
2. Department of Physiology, Zahedan University of Medical Sciences, Zahedan, Iran
3. Department of Pathology, Zahedan University of Medical Sciences, Zahedan, Iran

Background & Objective: Metabolic syndrome caused due to insulin resistance. Chronic kidney disease caused by metabolic syndrome. Eugenol is an antioxidant component in cloves oil.Eugenol effects against oxidative stress and nephrotoxicity have been showed. This study was designed to demonstrate effects of eugenol on metabolic syndrome induced nephrotoxicity.
Materials and methods: 35 Male Wistar rats were chosen randomly divided in five groups including: 1) tap water; 2) water with fructose10%; 3) water with fructose10% plus sweet almond oil (i.p.); 4) water with fructose10% plus eugenol 50mg/kg/day (i.p.); 5) water with fructose10% plus eugenol 100mg/kg/day (i.p.). The above rats consumed water for 60 days, and at the beginning of day 31st, injection started for duration of 30 days. Assessment of serum, urine and homogenized kidney parameters were done at the end of the study.
Results: Treatment with eugenol at doses of 50 and 100 resulted in a significant reduction in the level of serum BUN and Cr($P<0.05$). The kidney level of MDA increased in fructose group and treatment with a dose of 50 eugenol decreasing its level ($P<0.05$). The amount of proteinuria increased in fructose group compared ($P<0.001$). It is noteworthy that treatment with eugenol did not affect the level of this factor with any of the used doses.
Conclusion: Our results also indicate improved renal functioning and decrease in lipid peroxidation, although eugenol doses used in this study did not reduce proteinuria. This finding may be related to the applied doses and or their duration.
Keywords: Eugenol, insulin resistance syndrome, kidney injury

P-570

Induction of acute kidney injury in rats by low dose glycerol

Negin Givechian, Mehri Kadkhodaee, Ghorbangol Ashabi, Behjat Seifi, Farzaneh Kianian, Arash Abdi

Department of Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Background and objective: Glycerol injection in rats is a commonly used method to induce acute kidney injury (AKI). The injection leads to rhabdomyolysis, with the release of the intracellular muscle content to the extracellular compartment and eventual induction of AKI. Since high dose of glycerol causes abnormality in other organs, in this study, we aimed to evaluate the effects of lower doses of glycerol compared to the suggested effective dose (10 mg/kg) usually used in articles.
Materials and methods: Rats were divided into three groups: Control without intervention; Low dose glycerol injection with a dose of 5 mg/kg (G5), High dose glycerol injection with a dose of 10 mg/kg (G10). Twenty-four hours after intramuscular injection of glycerol in hind limbs, rats were anesthetized with ketamine and xylazine. Serum urea (BUN) and creatinine levels were measured to assess renal function. Data were analyzed using SPSS.
Results: Both BUN and creatinine levels were significantly elevated in G5 and G10 groups compared to the control group ($P<0.05$).
Conclusion: Our results showed that half of the commonly suggested glycerol dose in literature could significantly induce acute kidney injury with almost the same results. More studies are underway to confirm the results.
Keywords: Acute kidney injury, Glycerol, Rhabdomyolysis, BUN, Creatinine

P-571

The effect of estrogen on renin-angiotensin system receptors (Mas, At1) in kidney damage induced by ischemia / reperfusion in ovariectomized female rats

Halimeh Lakzaei, Tahereh Saferi

Department of Physiology, Zahedan University of Medical Sciences, Zahedan, Iran

Background and Objective: I/R is one of the side effects of kidney transplantation. The role of sex hormones in renal injury is the subject of many studies. This study attempts to interfere with the effect of these hormones on the RAS.

Materials and Methods: Forty-eight female Wistar rats were ovariectomized and a week later they were divided into three groups. The control group received Sesame oil on a weekly basis for 4 weeks, Groups 2 and 3 were first ovariectomized and then received estradiol and sesame oil for four weeks respectively. The treatments for all groups include yours, Ang-1-7, and the combination of these two. 72 h after reperfusion were measurements, serum levels of BUN, Cr and serum and kidney levels MDA and kidney tissue damage score (KTDS). Results: BUN, creatinine, and KTDS were increased after induction of I/R. On the other hand, the treatments used included losartan, Ang1-7 and their combination in the absence of estradiol reduced the amount of these items. ($P<0.05$). The increase in MDA after ischemia was reduced by the treatment used in the absence of estradiol ($P<0.05$). Conclusion: Our results showed that estradiol not only did not improve renal function. While blocking the AT1 receptor by losartan, angiotensin 1-7 and administration of the two together in the absence of estradiol had a better effect on kidney damage. But estradiol also plays a role in preventing kidney damage as an antioxidant.
Keywords: Estrogen, ischemia reperfusion, renin-angiotensin system, angiotensin 1-7

P-572

Effect of Sesame Oil Against Kidney Damage in Doxorubicin-Induced Nephrotic Rat

Somayyeh Mahzari[1], Abolfazl Khajavi Rad[1,2], Sara Hosseinian[1,2], Samira Shahraki[1], Zahra Samadi Noshahr[1], Mahnaz Allahyari[1]

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Background and Objective: Doxorubicin (DOX) is an important anti-cancer drug which can cause renal toxicity. Because of potent anti-infammatory and antioxidant properties of sesae oil (SO), the aim of the current study was to investigate the effect of SO against doxorubicin (DOX)-induced kidney tissue damage in rat.
Materials and methods: In this study two doses of SO (3 and 6 ml/kg) were administrated orally for 6 consecutive weeks and DOX (5 mg/kg) was intravenously injected on the 4th day of the experiment. At the end of the study, animals were anaesthetized with ether and left kidneys were quickly removed. Histopathological changes were evaluated with hematoxylin and eosin staining.
Results: Renal tissue sections from the control group showed normal architecture. DOX administration caused marked tubular and glomerular degeneration, intratubular hyaline cast formation, tubular dilatation and inflammatory cells infiltration. However, treatment of DOX-treated rats with SO significantly improved renal histopathological features compared to the DOX group.
Conclusion: The current study suggests that SO is able to improve kidney tissue damage in DOX-induced nephrotic the rats.
Key words: Doxorubicin, Sesame Oil, Nephropathy, Pathology.

P-573

P-coumaric acid pretreatment attenuate cisplatin induced renal and hepatic functional disturbances, oxidative stress and tissue damages

Zeynab Mohamadi Yarijani, Houshang Najafi

Medical Biology Research Center, Kermanshah University of Medical, Sciences, Kermanshah, Iran

Background and objective: The aim of this study was to investigate the effect of p-coumaric acid against functional disturbances, oxidative stress and tissue damages induced by cisplatin in kidney and liver.

Materials and methods: Male Wistar rats were divided into three groups (n=7): Control group that administered 20% ethanol by gavage for seven consecutive days; Cisplatin group, which received single dose of cisplatin (8mg/kg) intraperitoneally (ip) on the fifth day; and p-coumaric acid + cisplatin group, received single dose of cisplatin (8mg/kg) and p-coumaric acid (100mg/kg) was administered by gavage in 20% ethanol for seven consecutive days. The concentration of plasma creatinine, urea-nitrogen, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were evaluated for renal and hepatic function assess. Also, oxidative stress was evaluated through measuring malondialdehyde (MDA) and ferric reducing/antioxidant power (FRAP) levels, and histopathologic injuries were assessed using H & E stained sections.
Results: Administration of cisplatin resulted in significant increases in the plasma creatinine, urea-nitrogen, ALT, AST, and ALP and tissue damages and MDA level in the kidney and liver and a decrease in FRAP level in the kidney tissue. Administration of p-coumaric acid led to improvement in the function of kidney and liver, reduction of oxidative stress and also a decrease in tissue injuries.
Conclution: p-coumaric acid has protective effects against functional disturbances, oxidative stress and tissue damages induced by cisplatin.
Keywords: P-coumaric acid, ALT, AST, ALP, MDA, FRAP

P-574

Non-protective effect of alcohol in cisplatin induced nephrotoxicity rat model

Fatemeh Moslemi[1], Farzaneh Ashrafi[1,2], Bahar Mazaheri[1,3],Fatemeh Emami[1,4,5]

1. Water & Electrolytes Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Internal Medicine, Oncology-Hematology Section, Isfahan University of Medical Sciences, Isfahan, Iran
3. Department of Clinical Pathology, Isfahan University of Medical Sciences, Isfahan, Iran
4. Department of Physiology, Isfahan University of Medical Sciences, Isfahan, Iran
5. IsfahanMN Institute of Basic & Applied Sciences Research, Isfahan, Iran

Background: Alcohol consumption unfortunately, is more common throughout the world. There are some controversial documents about moderate alcohol consumption and chronic kidney disease (CKD). Despite the prohibition of alcohol in our culture, the prevalence of cancers and the side effects of anticancer drugs; cisplatin (CP) have made some people to suggest alcohol consumption in preventing the side effects of anticancer drugs during cancer therapy. This study was designed to investigate the role of alcohol consumption in CP induced nephrotoxicity.
Materials and Methods: 35 male and female Wistar rats were randomly into 3 experimental groups of alcohol (ethanol, ALC), CP and ALC+CP. ALC was gavaged (3 g/kg) daily for a week. CP was injected as single dose (7.5 mg/kg, i.p) at the first day of experiment and 1 hour after ALC administration.
At the end of 7th day, all the animals were placed in metabolic cage and urine samples were collected for 4 hours. Finally, biomedical and histological parameters were performed.
Results: During the experiment, a total of eight animals were expired, and 27 were remained for sacrificed day (8th day). The survival time for the groups of ALC, CP and ALC+CP groups were 7.75±0.18, 7.5±0.42 and 7.45± 0.39 days with no significant difference between the groups (P = 0.98). The serum level of blood urea nitrogen (BUN), creatinine (Cr) and kidney tissue damage score (KTDS) increased in group that received CP with ALC.
Conclusion: The results indicated that alcohol did not perform a protective effect against CP induced nephrotoxicity.
Keywords: alcohol, cisplatin, nephrotoxicity, female and male rats

P-575

Zinc and ischemia preconditioning in renal ischemia/reperfusion

Bahar Mazaheri[1*], Fatemeh Emamil[*], Fatemeh Moslemil[*], Ardeshir Talebi[1,2], Mehdi Nematbakhsh[1,3,4]

1. Water and Electrolytes Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Clinical Pathology, Isfahan University of Medical Sciences, Isfahan, Iran
3. Department of Physiology, Isfahan University of Medical Sciences, Isfahan, Iran
4. IsfahanMN Institute of Basic and Applied Sciences Research, Isfahan, Iran

Background: Renal ischemia/reperfusion (RIR) is a cause of kidney dysfunction during/after renal transplantation in clinic. The aim of this study was to investigate the effect of preconditioning ischemia (IPC) and zinc (Zn) supplementation on renal RIR.
Methods: 60 unilateral nephrectomies male and female Wistar rats were divided into 5 groups. Groups 1: Rats as sham-operated group were subjected to surgical procedure without RIR. Groups 2 (Isch): Rats were undergoing left kidney ischemia for 30 min followed by 48 hr reperfusion. Group 3 (Zn+Isch): Rats were treated as group 2 but they received Zn sulphate (30 mg/kg) 1 hr before induction of left kidney ischemia. Group 4 (PC+Isch): Rats were treated as group 2 but they underwent 1 min of IPC followed by 3 min reperfusion repeated for 3 times before induction of main ischemia. Group 5 (Zn+Isch+PC): Rats were subjected to receive both Zn sulphate and IPC before induction of left kidney main ischemia. Urine samples were collected in the last 6 hr of reperfusion, and biochemical and histology measurements were performed.
Results: The serum level of creatinine (Cr), normalized kidney weight (KW) and kidney tissue damage score (KTDS) increased by RIR significantly ($P<0.05$). These parameters were attenuated by Zn ($P<0.05$). However, IPC or co-treatment of Zn and IPC did not improved the biochemical and histology markers altered by RIR.
Conclusion: Zn supplement performed a protective role against RIR while such protective effect was not observed by IPC alone or by co-treatment of Zn and IPC.
Keywords: Renal ischemia/reperfusion; Zinc

P-576

Learning and memory performance and synaptic plasticity in CA1 hippocampal neurons following acute kidney injury and estradiol replacement in ovariectomized rats

Maryam Malek, Fatemeh Sharifi, Parham Reisi

Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

Background and Objective: Neurological complication may occur in patients with acute or chronic renal failure; however, in patients with acute renal failure, the signs and symptoms are usually more pronounced and progress rapidly. Oxidative stress and nitric oxide in the hippocampus following kidney injury may be involved in cognitive impairment in patients with uremia. Although many women still continue taking hormone therapy for menopausal symptom relief, there are also some controversies about the efficacy of exogenous sex hormones especially estrogen therapy alone in postmenopausal women with kidney injury.
Materials and Methods: Herein, for the first time to the best of our knowledge, we characterized spatial memory and short/long term synaptic plasticity at the CA1 synapse of uremic ovariectomized rat model of menopause with estradiol replacement alone.
Results: While estradiol replacement in ovariectomized rats without uremia promotes synaptic plasticity, it has impairing effect on spatial memory through hippocampal oxidative stress under uremic conditions with no change on synaptic plasticity. It seems that exogenous estradiol potentiated the deleterious effects of AKI with increasing hippocampal oxidative stress.
Conclusion: However, estrogen may have some positive effects on cognitive function in healthy subjects, but its efficacy in menopause subjects under uremic states such as renal transplantation patients needs to be further investigated in terms of dosage and duration.
Keywords: Synaptic plasticity, hippocampus, learning and memory, acute kidney injury, estradiol replacement, ovariectomized rats

P-577

Effect of troxerutin on expression of miRNA192, TGF-β and SIP1 levels of kidney tissue in type 1 diabetic male rats

Rana Keyhanmanesh, Gholamreza hamidian, Zohreh Zavari, Farzad Bahari, Milad Mohammadzadeh, Monireh Seyfollahzadeh, Fariba Mirzaei Bavil.

Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Nephropathy is one of the most important complications of diabetes. The increase of TGF-β and miRNA192 levels in diabetic conditions, by suppressing SIP1, increases the level of collagen in the kidney. So, we inspected the effect of troxerutin on cellular processes of nephropathy, from the aspect of the miRNA and its related pathways.
Materials and methods: fifty male wistar rats (200-250 g) were randomly divided into 5 groups (n=10): control, control under treatment with troxerutine (150 mg/Kg/day/PO). Diabetic (induced by STZ 55 mg/kg, IP, single dose). Diabetic+ Insulin, under treatment with insulin, (4-6 units/day, NPH). Diabetic+Troxerutin (150 mg/Kg/day/PO) for 4 weeks. At the end, the kidney tissue of all animals were extracted for the measurement of miRNA192, SIP1 and TGF-β. Proteins and miRNA were measured by ELISA and RT-PCR respectively.
Results: Diabetes caused a meaningful increase in TGF-β and micRNA192 levels, but troxerutin and insulin decreased them ($p<0.05$). On the other hand, diabetes considerably decreased SIP1 levels but troxerutin increased it ($p<0.05$). There was no significant difference between insulin and troxerutin.
Conclusion: Diabetes can provoke nephropathy by increasing collagen levels and accumulation of extracellular matrix by the means of increasing the amount of TGF-β and subsequently increasing miRNA192 and inhibiting SIP1. But troxerutin has a reverse effect on this process, and it can probably prevent diabetic nephropathy by increasing SIP1 levels.
Keywords: Diabetes, Troxerutin, miRNA192, TGF-β, SIP1

P-578

Maternal ethanol exposure during pregnancy and lactation impairs the kidney of male offspring through alteration of podocyte proteins genes expression, Matrix Metalloproteins (MMPs) and inflammatory stress: a 3- month follow-up

Farideh Nezami majd[1,2] , Alireza shirpoor[1,2]

1. Nephrology and kidney Transplant Research Center, Urmia University of Medical Sciences, Urmia, Iran
2. Department of Physiology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran.

Background and Objective: Ethanol exposure during pregnancy is associated with the malformation and dysfunction of the kidney in the offspring. However, the precise underlying molecular mediators involved in ethanol-induced kidney abnormalities are not well known. This study examined the effect of prenatal and postnatal ethanol exposure on the offspring's kidneys structural, functional and molecular alterations both on postnatal (PN) day 21 and 90.
Materials and Methods: Pregnant wistar rats on Gestation Day (GD)7 were divided into two groups, control and ethanol groups. Rats in the ethanol group received ethanol from GD7 throughout lactation.
Results: The results revealed a significant alteration in mRNA expression of nephrin, podocin, and vascular endothelial growth factor receptors (VEGFR), as well as MMPs amounts in kidneys of the offspring. Cystatin C level, the ratio of cystatin C/serum creatinine, serum creatinine showed a significant increase but urine creatinine and GFR showed a significant decrease in the offspring from ethanol group compared to those in the control group. Histopathological changes such as fibrosis, kidney cells proliferation, leukocytes infiltration, and vacuolization have also been seen in the kidney of the offspring after 21 and 90 days from birth.
Conclusion: Taken together, these results provide evidence as to pre and early postnatal ethanol exposure renalotoxicity is in part associated with alteration of nephrin, podocin and VEGFRs genes expression, as well as MMPs activity changes. Furthermore, in the current study it was found that these molecular alterations were triggered by inflammatory reactions manifested by fibrosis, proliferation, and PMN infiltration.
Keywords: pregnancy; Ethanol; kidney; nephrin; Matrix Metalloproteins; Cystatin C

P-579

Bilateral renal denervation prevents induction of hypertension by long-term feeding moderately high-fat diet in obesity-prone rats

Seyed Mostafa Shid Moosavi, Somayeh Nazari

Department of Physiology, Shiraz University of Medical Sciences, Shiraz, Iran

Background and objective: It has been suggested that renal sympathetic overactivity contributes to obesity-induced hypertension. It was aimed to reveal the effect of bilateral renal denervation (BRD) in development of hypertension by moderately high-fat (MHF) diet.
Materials and methods: Male Sprague-Dawley rats (initial weights, 200-220 g) were fed either normal low-fat (LF group, n=12) or MHF diet (32% kcal as fat) for 10 weeks. Rats received MHF diverged into obesity-prone (OP) and obesity-resistant (OR) that were clearly distinguishable from 4th week. Thereafter, half of the OP and OR rats were subjected to BRD and, hence, 4 groups of OP, OP/BRD, OR and OR/BRD were formed (n=12). Body weight (BW) and systolic pressure (PS) were measured weekly, and tail-blood was taken every other week for analyzing lipid profile.
Results: There were similar progressive increases of BW during 10 weeks in the LF, OR and OR/BRD groups, but the OP and OP/BRD groups had statistically larger BW from week 2 ($P<0.05$) and >50g at the final week ($P<0.001$). From weeks 4-6, plasma cholesterol and LDL in the OP and OP/BRD groups but triglycerides in all groups fed MHF became higher than those of the LF group ($P<0.05$-0.001), whereas plasma HDL did not differ in all groups. Importantly, PS was elevated only in the OP group that it became statistically higher from 5thweek ($P<0.01$) and reached to 138.1±1.9 versus 123.6±0.8 mmHg of the LF group at final week ($P<0.001$).
Conclusion: The renal sympathetic activity plays an important role in pathogenesis of obesity-induced hypertension.
Keywords: Obesity, Blood pressure, Sympathetic nervous system, Diet, Kidney

P-580

The effect of estrogen on renal ischemic-reperfusion-induced kidney injury in ovariectomized rats

Samin Nahavandi[1], Aghdas Dehghani[2], Saeedeh Ahmadi[2]

1. Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
2. Department of Physiology, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Background and objective: Renal ischemia reperfusion (RIR) injury is a pathological process that leading to acute kidney injury (AKI). Effects of sexual hormones especially estrogen on RIR is inevitable. Based on this evidence, the purpose of this study is to assess the influence of estrogen on renal injury caused by RIR in female rats after ovarectomy.
Material and method: 40 female wistar rats were ovarectomized and classified into 4groups including sham group without receiving estradiol valerat (OVX Sham), sham group receiving estradiol valerat (OVE Sham), ischemia group receiving estradiol valerat (OVE Ischemia) and ischemia group without estradiol valerat treatment (OVX Ischemia). Bilateral ischemia was performed for 45minutes in all groups except sham group. Before creating ischemia model, OVE group was received intramuscular injection of 500µg/kg estradiol valerat for 2 weeks. Then, after 24 hours of reperfusion, blood samples of heart were collected for serum analysis and right kidney was separated for pathological experiment. Also, left kidney was homogenated to evaluate tissue Malondialdehyde (MDA) and Nitric oxide (NO).
Results: Estrogen administration lead to enhancement of NO serum concentration in Ischemia group compared to sham group. Serum level of BUN and Creatinine increased significantly in both OVE and OVX Ischemia groups but the serum level of MDA exhibited no difference in none of the groups.
Conclusion: The injury of Ischemia reperfusion in the presence and absence of estrogen is inevitable. Estrogen as a sexual female hormone could affect NO system and performs its role on female sex during ischemia through this route.
Keywords: Ischemia reperfusion, Renal ischemic-reperfusion, Acute kidney injury, Estrogen

P-581

The effect of zinc sulfate on miR-122, miR-34a, antioxidants, biochemical and histopathological parameters following hepatic ischemia/reperfusion injury in rats

Ghaidafeh Akbari[1], Seyyed Ali Mard[2], Mahin Dianat[3], Esrafil Mansouri[4]

1. Yasuj University of Medical Sciences, Yasuj, Iran.
2. Physiology Research Center (PRC), Research Center for Infectious Diseases of Digestive System, Dept. of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
3. Physiology Research Center (PRC), Dept. of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

4. Cellular and molecular research center, Department of Anatomic sciences, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Background and Objective: Liver ischemia-reperfusion (I/R) injury is a situation which occurs in conditions including pringle maneuver, and liver transplantation. The regulatory effect of zinc sulfate (ZnSO4) on several liver disorders well-known, but its effects on microRNAS (miR-122 and miR-34a) have not been evaluated. The goals of this study were to identify the protective effects of ZnSO4 on I/R-induced liver injury in rats.
Materials and Methods: Thirty two male Wistar rats randomly assigned into the four groups (8 each group): Sham, I/R, ZnSO4 pretreatment, and ZnSO4+I/R groups. In sham, and ZnSO4 pretreatment groups, animals received normal saline (N/S, 2 ml/ kg), and ZnSO4 (5 mg/ kg) for 7 consecutive days, intraperitoneally (ip), then only laparotomy was performed. In I/R, and ZnSO4+I/R groups, N/S and ZnSO4, respectively, were given with the same dose, time, and route, before induction of ischemia for 45 min followed by reperfusion for 60 min. Blood sample was taken for biochemical, and microRNAs analysis, tissue specimens also were obtained for measurements of antioxidant activities, and histopathological evaluations.
Results: Our results showed that ZnSO4 pretreatment ameliorated histopathological changes decreased the increased serum levels of liver enzymes, miR-122, and miR-34a, and enhanced the decreased activity of antioxidant enzymes following hepatic I/R injury.
Conclusion: The present study indicated that ZnSO4 had potential hepatoprotective action against I/R-induced injury. Therefore, it has been suggested that, it can be administered as an anti-miR before elective hepatic surgeries for prevention of this complication.
Keywords: Zinc sulfate, Ischemia/reperfusion, Liver, MiR-122, MiR-34a, Rat

P-582

Cannabinoids reduced human colorectal cancer cell proliferation and migration through CB2 receptors

Alenabi A[1], Alizadeh A[1], Malekinejad H[2*]

1. Department of Pharmacology & toxicology, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran
2. Department of Pharmacology & Toxicology, School of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran

Background and Aims: Cannabinoids as the active components of Cannabis sativa have been used traditionally to reduce the pain. Recently, many research groups demonstrated that cannabinoids are strong anti-cancer substances. This study was aimed to show any potential anti-cancer property of CB2 agonist GW833972A on human colorectal cancer cells.
Methods: In this study very firstly concentration- and time-dependency assays by using MTT colorimetric test as a cytotoxicity assay were performed. The cytotoxicity assays were followed by testing the potency of given cannabinoid in the reduction of cancer cell migration. All experiments were performed both in the presence or absence of CB2 antagonist SR144528 to highlight the molecular pathway.
Results: Our results showed that CB2 agonist reduced cell viability of HT-29 cells in a clear concentration- and time-dependent fashion. We found that CB2 agonist at 50 □M reduced 60% of cell viability when compared to non-treated cells. Treatment with CB2 agonist for 48 h resulted in substantial reduction of cell viability. The cell migration assay confirmed our cytotoxicity test results as CB2 agonist prevented from migration of HT-29 cells. The results also were in line with cytotoxicity test in terms of concentration-and time-dependency. Using CB2 antagonist reversed the results in both used endpoints.
Conclusion: Our results suggest that CB2 agonists could be considered as anti-cancer agents. To confirm these findings further studies are warranted to highlight mechanism of cytotoxicity and further phase II and III clinical studies.
Key Words: Colorectal cancer, CB2 receptors, Cytotoxicity, Cell migration

P-583

The effects of alpha7 nicotinic acetylcholine receptors gene suppression on nicotine-induced apoptosis and cell cycle arrest of human hepatoma HepG2 cells

Khalil Hajiasgharzadeh[1], Mohammad Hossein Somi[2], Ahad Mokhtarzadeh[1], Dariush Shanehbandi[1], Behzad Baradaran[1*]

1. Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
2. Liver and Gastrointestinal Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Nicotine-induced cytotoxic effects have been reported in several studies, but the underlying mechanisms remain elusive. Among different subtypes of nicotinic receptors, the alpha7 nicotinic acetylcholine receptor (α7nAChR) is one of the main nicotinic receptors that functionally expressed by a variety of human normal and cancer cells such as liver cells. The aim of this study was to investigate the influences of nicotine on cellular proliferative and apoptotic activities and tried to determine the involvement of α7nAChR in these functions.
Materials and Methods: Human hepatoma HepG2 cells were used to investigate the effects of treatments with nicotine and specific siRNA targeting α7nAChR expression. The MTT assay, DAPI staining assay, and flow cytometry assay were applied to measure the cell viability, apoptosis and cell cycle progression of the cells, respectively. In addition, the changes in the mRNA level of the genes were assessed by qRT-PCR.
Results: Compared to control groups, the cells treated with nicotine exhibited significant dose-dependent decreases in cell viability (log IC50 = -5.12±0.15). Furthermore, nicotine caused apoptosis and cell cycle arrest, especially at G2/M Phase. The qRT-PCR revealed that nicotine increased the mRNA levels of α7nAChR as well as caspase-3 and suppressed the expression of cyclin B1. Treatment with α7-siRNA abolished these effects of nicotine.
Conclusion: These experiments determined that upregulation of α7nAChR by nicotine inhibits HepG2 cells proliferation and induces their apoptosis. These effects blocked by treatment with α7-siRNA, which indicates the involvement of α7nAChR pathways in these processes.
Keywords: Alpha7 nicotinic acetylcholine receptor; Small interfering RNA; Nicotine; HepG2; Apoptosis

P-584

The effect of low-fructose diet on serum adiponectin and TNFα levels and some parameters of non-alcoholic fatty liver disease due to high fat diet in the Sprague-Dawley rat

Babak Hassankhan[1], Parichehreh Yaghmaei[1], Kazem Parivar[1], Azadeh Ebrahim-Habibi[2]

1. Department of Biology, Faculty of Basic Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran.
2. Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Background and Objective: Excessive dietary fructose consumption may be a risk factor for the development of Non-alcoholic fatty liver disease (NAFLD). High fructose diet can promote lipogenesis, oxidative stress and insulin resistance. Although fructose produces deleterious metabolic effects, fructose-1-phosphate as a metabolite of it, increases activity of glucokinase as an enzyme that plays a key role in the control of glucose homeostasis. In this study, a low-fructose diet was used to evaluate its effect on serum adiponectin and TNFα levels and some parameters of NAFLD due to high fat diet in the Sprague-Dawley rats.
Materials and Methods: Male rats were divided into normal control group, high fat diet group and fructose group (n=8). The high fat control group was orally treated with the high fat emulsion diet (HFD) and fructose group orally treated with the HFD plus fructose (1g/kg) once per day via gavage for six weeks.
Results: After six weeks, in fructose group receiving fructose at a dose of (1 g/kg), serum adiponectin level increased and serum TNFα level decreased. In addition, serum glucose, insulin, insulin resistance and serum lipid profile significantly decreased and PGC-1α gene expression in adipose tissue of fructose group significantly increased compared to the high fat control group (P<0/05).
Conclusion: Our results showed that a low-fructose diet could prevent hypoadiponectinemia, TNFα activation and insulin resistance that they are features of nonalcoholic steatohepatitis (NASH). These data also indicate that the low-fructose diet might provide a beneficial treatment for insulin resistance and NAFLD.
Keywords: Non-alcoholic fatty liver disease, Adiponectin, TNFα, Fructose, Low-fructose diet , Insulin resistance.

P-585

The protective effect of acetyl-L-carnitine in carbon tetrachloride-induced model of acute liver injury in the mouse

Vahid Khodashenas[1], Amir Rostami[2], Atieh Mousavi [3] , Mehrdad Roghani[4]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
2. School of Medicine, Shahed University, Tehran, Iran.
3. Department of Anatomical Sciences, Iran university of medical Sciences, Tehran, Iran.
4. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective: Acute liver injury (ALI) is a common complication following virus infection and use of anti-pyretic drugs. For induction of experimental ALI, carbon tetrachloride (CCl4) is sometimes used. Acetyl-L-carnitine (ALC) has shown protective effect in some bodily tissues. This study was conducted to evaluate its protective effect in CCl4 model of ALI in the mouse.
Materials and Methods: Male mice (NMRI strain) were randomly divided into 4 equal-sized groups, i.e. control, CCl4, and CCl4 groups pretreated with ALC at doses of 50 or 200 mg/kg. For induction of ALI, CCl4 (10 ml/kg, i.p.) were injected. After 24 h, mice were anesthetized and measurement of liver biomarkers including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) was performed in addition to liver determination of some oxidative stress parameters.
Results: Our findings showed that ALC at a dose of 200 mg/kg, but not at a dose of 50 mg/kg, significantly reduces serum ALT and AST and lowers oxidative-stress-related parameters including malondialdehyde (MDA) and estimated level of reactive oxygen species (ROS) in CCl4 model of ALI.
Conclusion: It is concluded that ALC could alleviate CCl4-induced ALI, partly through mitigation of oxidative stress.
Keywords: Acute liver injury, Carbon tetrachloride, Acetyl-L-carnitine, Oxidative stress

P-586

Dapsone reduced acetic acid-induced inflammatory response in rat colon tissue through inhibition of NF-kB signaling pathway

Asma Rashki[1,2], Amir Rashidian[1,2], Alireza Abdollahi[3], Nazgol-Sadat Haddadi[1,2], Mohsen Chamanara[2,4],Faiza Mumtaz[1,2], Ahmad Reza Dehpour[1,2*]

1. Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
3. Department of Pathology, Imam Hospital, Tehran University of Medical Sciences, Tehran, Iran
4. Department of Pharmacology, School of Medicine, Aja University of Medical Sciences, Tehran, Iran

Background and Objective The purpose of this study is to examine the protective effects of Dapsone on inflammation of intestinal tissue via the inhibition of NF-kB pathway in acetic acid-induced colitis in rats.
Materials and Methods Acute colitis was produced by intra-rectal instillation of 2 mL of 4% acetic acid diluted in normal saline. Then, two hours after induced of colitis, DMSO as vehicle, dexamethasone and dapsone were given to the animals intraperitoneally (i.p.) and continued for 5 following days. Evaluation of macroscopic and microscopic damages was done. Myeloid peroxidase enzyme (MPO) activity was measured by biochemical technique. Moreover, tumor necrosis factor-α (TNF-α) activity was identified by ELIZA and the expression level of pNF-kB protein was evaluated by immunohistochemistry (IHC).
Results Dexamethasone and dapsone decreased the macroscopic and microscopic damages compared with acetic acid group ($p<0.001$). Additionally, these agents decreased the activity of MPO ($p<0.001$), TNF-α ($p<0.001$) and the expression level of p-NF-kB ($p<0.001$) in rat colon tissue compared with acetic acid group.
Conclusion It is proposed that the anti-inflammatory activity of dapsone on acetic acid-induced colitis in rats may include the inhibition of NF-kB pathway
Keywords: Dapsone, Ulcerative colitis, Acetic acid, NF-kB

P-587

Effects of single and double therapy with 17-AAG, Capecitabine and Irinotecan on proliferation and oxidative stress status of HT-29 colorectal carcinoma cells

Shima Zeynali-Moghaddam[1,3], Fatemeh Kheradmand[2], Hassan Malekinejad[3]

1. Department of Clinical Biochemistry, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran
2. Department of Clinical Biochemistry, Cellular Molecular and Solid Tumor Research Center, Urmia University of Medical Sciences, Urmia, Iran
3. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Urmia University of Medical sciences, Urmia, Iran

Background and Objectives: There are various treatment regimens for colorectal cancer treatment including chemotherapy, radiation and surgery. Already great improvements in cancer chemotherapy have been occurred, however in some cases treatments are inadequate and require novel drug regimens. In this study we investigated the

effects of single and double therapy with 17-AAG, Capecitabine and Irinotecan on proliferation and oxidative stress status of HT-29 colorectal carcinoma cells.
Materials and Methods: HT-29 cells were seeded for 24 h and then were treated either by individual compound or double combination for 24 h. To measure the cell viability, the WST-1 colorimetric assay was performed. At the same time the MDA content and total antioxidant capacity as biomarkers for oxidative stress and NO content as an index of nitrosative stress were assessed.
Results: A synergistic interaction was observed in viability test of all double treatment groups. The results of NO determination revealed that only Cap single treatment reduced the NO generation. The highest MDA concentration was found in supernatant of cells, which exposed to IR. Total antioxidant capacity in exposed cells to all compounds either in single or combination treatments, was declined significantly ($p \leq 0.05$). The 17-AAG treatment showed the highest potency in the reduction of TAC.
Conclusion: Our findings indicate that although the combination therapy resulted in remarkable cytotoxicity, the oxidative stress biomarkers however showed the highest potency of compounds when they were used in single form, suggesting another pathway of cytotoxicity in combination therapy regimen.
Keywords: Colorectal cancer, 17-AAG, Combination therapy, Oxidative stress.

P-588

Evaluation of the therapeutic potential effect of Fas receptor gene Knockdown in experimental model of Non-Alcoholic Steatohepatitis

Feryal Savari[1], Seyyed Ali Mard[2], Mohammad Badavi[1], Annahita Rezaie[3], Mohammad Kazem Gharib-Naseri[1]

1. Physiology Research Center (PRC), Dept. of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
2. Persian Gulf's Physiology Research Center (PRC), Research Center for Infectious Diseases of Digestive System [Alimentary Tract Research Center], Dept. of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
3. Department of Pathobiology, School of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.

Background and Objective: Stimulation of Fas death receptor is introduced as a major cause of nonalcoholic steatohepatitis (NASH) progression through suppression of cell viability. Therefore, the blocking of death pathways is hypothesized to be express new approaches to NASH therapy. For this purpose, current experiment applied synthetic small interference RNA (SiRNA) to trigger Fas death receptor and to show its potential therapeutic role in designed NASH model.
Materials and Methods: Male mice were placed on a western diet (WD) for 8 weeks and exposed to cigarette smoke during the last 4 weeks of feeding to induce NASH model. In the next step, Fas SiRNA was injected to mice aiming to examine specific Fas gene silencing, after 8 weeks. As a control, mice received scrambled SiRNA. Reversible possibility of disease was examined by 3 weeks of recovery.
Results: Analysis of data is accompanied with the significant histopathological changes (steatosis, ballooning and inflammation, increased lipid profile and hepatic enzyme activities (AST, ALT, ALP) plus TBARS as well as decreased antioxidants levels in NASH model. Upon Fas-SiRNA injection, almost all measured parameters of NASH such as overexpression of Fas receptor, caspase3, NF-kB genes and marked increase of hepatic TNF-α were significantly restored and were remained nearly unchanged following recovery liking as scrambled groups.
Conclusion: The suppression of Fas receptor signaling subsequent RNAi therapy may represent an applicable strategy to decline hepatocyte damages and so NASH progression in mice.
Key words: NASH; western diet; cigarette smoke; SiRNA; Fas receptor; apoptosis, inflammation

P-589

Gastroprotective Effect of Zingerone on Ethanol-Induced Gastric Ulcers in Rats

Neda Sistani Karampour [1], Ardeshir Arzi [1,] Anahita Rezaie [2] , Marzieh Pashmforoosh [3] and Fatemeh Kordi [3]

1. Department of Pharmacology, Jundishapur University of Medical Sciences, Ahvaz 6135715794, Iran;
2. Department of Pathobiology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz,
3. Department of Pharmacology, Jundishapur University of Medical Sciences, Ahvaz 6135715794, Iran;

Background and objectives: Zingerone is an ingredient of ginger (Zingiber officinale) withdifferent pharmacological activities. Several studies have investigated the effect of zingerone on various gastrointestinal

diseases, including irritable bowel syndrome and diarrhea. This study is aimed to evaluate the effect of zingerone on ethanol-induced gastric ulcers in rats.
Materials andMethods:Gastric ulcers were induced by ethanol (96%, 5 mL/kg, po) in male wistar rats and zingerone (50, 100, and 200 mg/kg) was administrated orally. Normal saline and ranitidine were used as negative and positive control, respectively. In this study, the number and length of ulcers, and malondialdehyde (MDA) and nitric oxide (NO) levels in stomach tissues were determined.
Results: The findings showed that the mean number and length of gastric ulcers were significantly lower in zingerone-received groups than ethanol group ($P < 0.05$). The level of malondialdehyde was decreased in the stomach of zingerone groups ($P < 0.05$) compared to the ethanol group. In addition, zingerone treatment prevented the decrease of nitric oxide level by ethanol in the stomach tissue.
Conclusions: The present study showed that zingerone has a protective effect on the ethanol-induced gastric ulcer, which may be due to its free radical scavenging activity.
Keywords: gastric ulcer; zingerone; ethanol; malondialdehyde; nitric oxide; rat

P-590

Expression of MT1 receptor in patients with gastric adenocarcinoma and its relationship with clinicopathological features

Ramin Ataee[1,4],Nafiseh Nasri Nasrabadi[1,2],Farshid Sargazi[1], Seyedeh Habibeh Mirmajidi[3]

1. Pharmaceutical sciences research center, Mazandaran University of medical sciences, Sari. Iran
2. Pharmaceutical Sciences Research Centre, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Department of Medical Biotechnology, School of Advanced Medical Sciences and Technology, Shiraz University of Medical Sciences, Shiraz Iran
4. Thalassemia research center, Hemoglobinopathy Institute ,Mazandaran University of medical sciences, Sari Iran

Gastric cancer accounts 8% of the total cancer cases leading to 10% of total cancer deaths worldwide. Recently, it has been well documented some anti-cancer roles of melatonin in some malignancies as breast and colon cancer; as well as some its protective roles in the GI tract that have been known as free radical scavenger, antimitogenic and apoptotic properties. According to the anti-cancer effects of melatonin, wide distribution of this neurohormone in GI tract and some proposed physiologic and pharmacologic roles for this neurohormone, this study initially scheduled to determine the expression of melatonin receptor MT1 in tissue samples of adenocarcinoma cancer patients. A total of 10 gastric adenocarcinoma patients and 10 normal individuals were examined for MT1 gene expression by real-time PCR. Additionally, for screening of different alleles of MT1 in our samples, the SSCP-PCR procedure was developed. Our results have shown interestingly high expression for MT1 receptor in cancer and marginal cancer groups comparing with normal group. Our findings also have shown that a remarkable association between MT1 receptor mRNA levels and grade in individuals over age 50. PCR-SSCP analysis results showed a variation between individuals which may be effective on their gene expression patterns. According to our knowledge, for the first time this study evaluated the expression of MT1 receptor gene in gastric adenocarcinoma. Moreover, these results show the defending role of melatonin in the GI system.
Key words: Melatonin, Gastric adenocarcinoma, MT1 receptor, Gene expression, polymorphism.

P-591

Butyrate and deoxynivalenol: challenges and beneficial effects for intestinal barrier

Arash Alizadeh[1], Saskia Braber[2], Johanna Fink-Gremmels[3]

1. Division of Pharmacology and Toxicology, Department of Basic Science, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.
2. Division of Pharmacology, Faculty of Science, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, The Netherlands
3. Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands

Background and objective: The aim of this study was to evaluate the potential beneficial effects of Butyrate as a microbial fermentation product against mycotoxin deoxynivalenol (DON) induced adverse effects on intestinal epithelial cells. DON as a frequently encountered contaminant in grain and related byproducts is an important risk

factor for intestinal barrier integrity. The intestinal tract as the largest interface between host and external world is of major importance for nutrient utilization and health. Impairment of intestinal integrity is accompanied by increased risk that hazardous substances flux inside body and exert different inflammatory and allergic reactions.
Materials and methods: Utilizing an in vitro model with human intestinal epithelial cell-line (Caco-2), the effect of butyrate on intestinal integrity, cell viability and inflammatory reactions was measured in a trans well system via transepithelial electrical resistance (TEER) and Lucifer yellow paracellular transport as well as IL-8 release into apical and basolateral compartment.
Results: Obtained results showed that butyrate could not prevent or moderate the DON-induced alterations on intestinal barrier integrity and IL-8 production. Moreover, butyrate exacerbates the alterations and damages on epithelial cells 24h post DON exposure.
Conclusion: Taken together, these findings support previous findings that DON has the potency to induce adverse effects on intestinal epithelial barrier integrity. Butyrate could not show a protective effect against these specific DON-induced barrier damages in the in vitro model applied, but may exert a positive effect on the microbiome and pH balance in the large intestine under in vivo conditions.
Keywords: Butyrate, Deoxynivalenol, Caco-2 cells, TEER, IL-8

P-592

The modulation effects of Shilajit on serum levels of cytokines and adipokines in rats with the non-alcoholic fatty liver disease

Baran Ghezelbash[1], Nader Shahrokhi [2], Mohammad Khaksari [3], Gholamreza Asadikaram[3]

1. Afzalipour School of Medicine, Kerman University of Medical Sciences, Kerman, Iran.
2. Physiology Research Center, Kerman University of Medical Sciences, Kerman, Iran.
3. Endocrinology, and Metabolism Research Center, Kerman University of Medical Sciences, Kerman, Iran.

Background/Objectives: The non-alcoholic fatty liver disease is a common cause of chronic liver disease which associated with obesity and diabetes and has a worldwide outbreak. The aim of this study is to evaluate the effect of Shilajit, as medicine of Ayurveda, on the serum changes in cytokines and adipokines caused by NAFLD.
Methods: Thirty- five Wistar male rats (160 ± 20g) after establish fatty liver models by feeding a high- fat diet (HFD, 12 weeks), were randomly divided into five groups (n=7 rats/each group); Control (standard diet), Veh (HFD + vehicle), high dose Shilajit (HFD + 250 mg/kg/day), low dose Shilajit (HFD + 150 mg/kg/day), pioglitazone (HFD + 10 mg/kg/day). The serum levels of IL-1β, IL-6, TNF- α, IL-10, adiponectin, and resistin were measured after the two-weeks of intervention.
Results: The results showed that in the Veh group the serum levels of IL-1β, IL-6, TNF-α, and resistin ($p<0.05$) significantly increased, while IL-10 and adiponectin levels decreased ($p<0.01$) in comparison to the control group. However, treatments with high and low doses of Shilajit as well as pioglitazone significantly decreased IL-1β, TNF-α, and resistin ($p<0.01$), while increased IL-10 and adiponectin ($p<0.01$) in comparison to Veh group.
Conclusion: The study showed that Shilajit by modulating the serum levels of cytokines, adipokines, and can improve NAFLD.
Keywords: NAFLD, Shilajit, HFD, adipokines, cytokines, glucose, insulin

P-593

Therapeutic effects of Tumor Necrosis Factor-α (TNF-α) on Gastric cancer in the in-vitro model

Mohammad Hosein Gheini

Shahed University , Medical Faculty, Department of Anatomy & Pathology

Introduction: Gastric cancer is the most common lethal malignancy in the iranian men and the second one in the world. Although Helicobacter pylori is believed to be the major etiological factor in the cancer of stomach, the host immune response to H. pylori have important role in the pathogenesis of malignancy. This study has been designed to determine the effects of TNF-α on the proliferation of malignant epithelial cells.
Material & Methods: The human gastric carcinoma cell line (AGS) were cultured in the presence of increased concentrations of TNF-α. Proliferation of the cells was evaluated by bromodeoxyuridine (BrdU) test, based on BrdU

usage for DNA synthesis; and total viable cell numbers by MMT assay. Results was analyzed by one-way analysis of variance and t-test. P<0.05 was considered significant.
Results: TNF-α decreased DNA synthesis and cell number of AGS cells in culture (P<0.01). This effect is dose-dependent up to the concentration of 10ng/mL, and there is no difference in upper concentrations.
Conclusions: TNF-α suppresses the proliferation of malignant gastric epithelial cells. It seems that signals via tyrosine kinase activity are essential in this effect. Since the overall effects of proliferation rate and apoptosis lead to total viable cell number, other factors, such as gastrin and interferon-gamma might also contribute to this effect.

P-594

Chronic psychological stress and non-alcoholic fatty liver disease

Elham Karimi-Sales[1, 2], Elnaz Nakhjiri[1, 2]

Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Department of Physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and Objective: Non-alcoholic fatty liver disease (NAFLD), one of the most common chronic liver diseases worldwide, includes a broad range of liver complications ranging from simple fatty liver to non-alcoholic steatohepatitis (NASH), liver fibrosis, and more severe liver problems including liver cirrhosis and hepatocellular carcinoma. Previous studies showed that chronic stress could change blood glucose level, carbohydrate metabolism, and hepatic lipid synthesis.
Methods: PubMed, Scopus, and Cochrane Library databases were searched to find articles assessing the relationship between psychosocial stress and NAFLD. A narrative review of these articles was conducted.
Conclusion: There is an association between psychological distress and chronic liver disease mortality. Furthermore, a positive link between psychological stress and NAFLD has been suggested. In this regard, job-related stress increased the risk of NAFLD among Chinese police officers. Similarly, chronic stress elevated hepatic cholesterol and triglyceride contents and also diminished visceral fat mass and food consumption in mice. In this case, chronic stress could induce steatosis and NASH through stimulating visceral adipose lipolysis and consequently increasing liver free fatty acid input and also by stimulating inflammatory cytokines secretion. On the other hand, it has been suggested that in normal dietary conditions chronic psychosocial stress led to hepatic inflammation and oxidative stress but did not cause hepatocellular injury. Interestingly, this type of stress had a protective effect on hepatocellular injury in NASH-inducing high-fat diet-fed animals. Therefore, further studies are needed to clarify the effects of stress on NAFLD/NASH development and progression.
Key words: Psychological stress, Non-alcoholic fatty liver disease, Non-alcoholic steatohepatitis

P-595

In all 3,4-methylenedioxymethamphetamine (MDMA) decrease regional blood flow and induce necrosis in the rat liver

Ravieh Golchoobian[1], Fatemeh Nabavizadeh[2], Mehrdad Roghani[3], Alireza Foroumadi[4]

1. Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
2. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
3. Neurophysiology Research Center, Shahed University, Tehran, Iran
4. Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran

Background & objectives: MDMA (3,4-methylenedioxymethamphetamine, ecstasy) is often abused by youth as a recreational drug. MDMA abuse is a growing problem in different parts of the world. An important adverse consequence of the drug consumption is hepatotoxicity of different intensities. However, the underlying mechanism of this toxicity has not completely understood.
Material and Methods: In this study, we investigated possible types of cell death as underling mechanisms of MDMA hepatotoxicity in rat.
Results: MDMA could transiently increase serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) followed by tissue necrosis. However, it could significantly decrease liver tumor necrosis factor- (TNF-α) and liver blood flow in MDMA received animals. Unexpectedly, in MDMA treated rats, Bax, Bcl-xl, Bcl-2, Fas, Fas ligand (FasL), caspase 8, cytochrome c and caspase 3 gene expression and DNA fragmentation were nearly unchanged.
Conclusions: In all, MDMA could transiently increase serum transaminases, decrease regional blood flow and induce tissue necrosis of liver. MDMA hepatotoxicity seems to be mediated via tissue necrosis rather than apoptotic and inflammatory pathways.
Keywords: Hepatotoxicity, 3,4-methylenedioxymethamphetamine, Apoptosis, Necrosis

P-596

Study Of Diosgenin On Acute Liver Failure Induced By LPS/D-Gal In Male C57 BL/6 Mice

Seyed Mahdi Mohamadi Zarch, Tourandokht Balouchnejadmojarad, Davoud Nourabadi, Ali Mohammad Khanizadeh, Mehrdad Roughani

Background: Acute liver failure (ALF) is a fatal clinical syndrome, which leads to a rapid loss of normal liver function. Diosgenin is a natural steroidal sapogenin found in various plant families. Various studies have shown that Diosgenin have therapeutic or preventive effect in various diseases such as cancer, cardiovascular disorders, type 2 diabetes, neurodegenerative disorders. In this study, we evaluated effects of diosgenin on mice model of ALF.
Method and materials: Animal model of ALF was induced by intraperitoneal injection of lipopolysaccharide (LPS) /D-galactoseamine (D-Gal). The male C57BL/6 mice were randomly divided into 3 groups: control group, LPS/D-Gal group and LPS/D-Gal + diosgenin group (50 mg/kg). Mice in the LPS/D-Gal group received a combination of LPS (50 µg/kg) and D-Gal (400 mg/kg) intraperitoneally. LPS/D-Gal + diosgenin group received orally diosgenin 24 hours and 1 hour before receiving LPS/D-Gal. markers of liver injury including ALT, AST and ALP were measured by auto analyzer in blood samples and levels of IL-1β, IL-6, TLR4, TNF-α and NF- κB were measured in hepatic tissue by using Elisa method.
Results: administration of diosgenin could greatly reduce serum levels of ALT, AST and ALP ($P < 0.001$). Hepatic levels of IL-1β ($P < 0.01$), IL-6 ($P < 0.01$), TLR4 ($P < 0.001$), TNF-α ($P < 0.01$), NF- κB ($P < 0.001$) decreased significantly in comparison with the LPS/D-Gal group.
Conclusion: Diosgenin led to reduction of liver injury indices and inflammatory proteins, so, probably diosgenin has hepatoprotecive effects against ALF via reducing inflammation.

P-597

An imidazoline receptor1 (IR1) agonist alleviated the ER stress induced genes expression in the mice liver

Azam Moslehi, Tahereh Komeilli-Movahed

Cellular and Molecular Research Center, Qom University of Medical Sciences, Qom, Iran

Background and Objective: Endoplasmic reticulum (ER) stress is been known as a condition of unfolded or misfolded proteins accumulation in the ER lumen. ER stress is induced under pharmacologic stimuli, dietary demands, viral infections and oxidative stress circumstances and is closely associated with several chronic diseases such as obesity, atherosclerosis, type 2 diabetes and fatty liver. ER stress induces glucose-regulated protein 78 (GRP78) and activating transcription factor 6 (ATF6) genes, as two important sensors in the ER lumen, and effects

on the expression of lipid metabolism related genes. It has also been reported that allantoin activates imidazoline I receptor and decreases inflammation and apoptosis. Recent studies have shown that allantoin alleviates the obesity, hyperlipidemia and hyperglycemia. We evaluated allantoin effects on MCD diet induced ER stress in the mice liver.
Materials and Methods: To do so, mice received saline and allantoin as the control groups. ER stress induced by the methionine-choline deficient (MCD) diet and in the MCD- allantoin group, mice received MCD diet with daily injections of allantoin. Real-time RT-PCR was done for GRP78, ATF6, sterol regulator element binding proteins 1c (SREBP1c), fatty acid synthase (FAS) and peroxisome proliferator-activated receptor alpha (PPARα).
Results: MCD diet induced ER stress and increased GRP78 and ATF6. Also, expressions of SREBP1, PPARα and FAS increased, as lipid metabolism related genes. However, treatment with allantoin decreased gene expression of them.
Conclusion: This study indicated that allantoin could attenuate ER stress and improved lipid metabolism related genes.
Keywords: Allantoin, ER stress, GRP78, Liver, SREBP1

P-598

Complex interactions of heavy metals and Metallothioneins in colorectal cancer: a review of experimental and clinical evidences

Fatemeh Maghool, Mohammad Hassan Emami

Poursina Hakim Digestive Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Background and Objective: Metallothioneins (MTs) are a family of small cysteine-rich proteins involved in many (patho) physiological processes. Emerging evidence shows that MT plays a crucial role in cell differentiation, proliferation, and apoptosis as well as participating in the homeostasis of some metals involved in tumor growth and progression. Several mechanisms have been proposed to explain how interaction of metals such as Zn and Cu and Metallothioneins may lead to carcinogenesis and prevention. The objective of this review is to provide a summary of the most consistently reported interactions of metals and MTs in colon carcinogenesis and prevention.
Material and Method: The more recently published studies (2000–2019) searched in MEDLINE, EMBASE and Cochrane Library between 2009 and 2019 for articles that examined involvement of metals and Metallothioneins in colorectal cancer.
Results: In both animal model of colon cancer (DMH‑treated rats) and colorectal tumors in human, MT mRNA gene expression was down regulated in colonic precancerous and cancerous tissue.
Possible mechanisms by which MT may protect against colon carcinogenesis include detoxification and homeostating of metals (reduction of metal uptake, sequestration of metal, and enhanced export out of cells), and protection against DNA damage, and oxidative stress as an antioxidant. However, the availability of some metals is required for both MT gene expression and protein degradation, so reinducing MT expression by metal supplementation might represent a novel strategy to improve responses to therapeutic agents.
Conclusion: A number of interactions between different divalent metals and MTs are suggested in colon carcinogenesis and prevention, but the findings need well-characterized experimental and clinical trials before conclusions regarding the precise underlying mechanisms can be reached and utilized for colon cancer prevention and/or treatment.
Keywords: Metallothioneins, heavy metals, colorectal cancer, carcinogenesis

P-599

Protective effects of metadoxine and montelukast against acetaminophen-induced liver injury in mice

Mohsen Minaiyan, Parvin Mazraati

1. Department of Pharmacology and Pharmaceutical Sciences Research center, Isfahan School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran
2. Isfahan School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Background and objective: Acetaminophen is a widely used OTC drug which at high doses might cause liver damage and even death. The hepato-protective effects of metadoxine and montelukast have been demonstrated in some models of liver injuries but in the present study their beneficial effects on acetaminophen-induced hepatotoxicity was evaluated.
Materials and methods: Male mice were randomly divided to 7 groups as following: normal (normal saline 10ml/kg), negative control (acetaminophen 650 mg/kg), metadoxine (200, 400 mg/kg), montelukast (50, 100 mg/kg), and N-acetyl cysteine (NAC, 300 mg/kg). Hepatotoxicity was induced by oral acetaminophen (650mg/kg) and treatments were carried out 2 h later. Twenty four later the animals were sacrificed and serum levels of AST,

ALT, ALP and total bilirubin as well as liver tissue histopathology and contents of GSH and MDA were analyzed in treatment groups.
Results: Acetaminophen alone increased serum activities of ALT, AST, ALP in addition to liver damage exhibited by centrilobular necrosis, fatty changes and sinusoidal congestion in comparison to normal group. NAC, montelukast and metadoxine caused significant decline in hepatic transaminase levels as well as dip in MDA and replenishment in GSH reservoir in acetaminophen treated groups. Total bilirubin concentration was elevated by acetaminophen showed a slight decrease in response to treatments. The liver of treatment groups showed significant improvement in histopathology parameters assessment.
Conclusion: It is concluded that metadoxine and montelukast could protect against acute liver toxicity due to acetaminophen and their effects could be attributed to restoration of intracellular redox homeostasis, anti-inflammatory and anti-apoptotic properties.
Key words: Hepatotoxicity, Metadoxine, Montelukast, Acetaminophen, Mice

P-600

CDK9 has a crucial role in cardiac differentiation by modulating of DNA methylation profile in myomiRs promoter.

Leila Abkhooie[1,2], Vahideh Tarhriz[2], Mohammad Saeid Hejazi[1,2,3], Mostafa Moradi Sarabi[4], and Hossein Ghanbarian[5]

1. Department of Molecular Medicine, Faculty of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
2. Molecular Medicine Research Center, Biomedicine institute, Tabriz University of Medical Sciences, Tabriz, Iran
3. Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran
4. Department of Biochemistry and Genetics, Lorestan University of Medical Sciences, School of Medicine, Khorramabad, 381251698 Iran
5. Cellular and Molecular Biology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Cdk9 is a catalytic core of the positive transcription elongation factor b (P-TEFb) has a critical role regulation of Myocardial microRNAs (MyomiRs). In this research, we investigated the role of CDK9 in the methylation of three important myomiRs including miR (1, 133 and 206) during different developmental stages.
Materials and Methods: For overexpression of CDK9, the PCEP4/CDK9 plasmid was transfected to C2C12 cells. Transfected and control C2C12 cells were differentiated and the profile of DNA methylation mRNA expression of miR 1, 133 and 206 was evaluated in transfected and control C2C12 cells by bisulfite sequencing.
Results: Our results of methylation analysis indicate that although it was not observed significant increase in methylation of myomiRs (miR-1,133 and miR-206) in the early stage of differentiation however, overexpression of CDK9 cause to increase methylation of miR-1 and miR-206 promotors in the late stage of differentiation. Moreover, we didn't observe hypermethylation in the miR-133 promoter during the differentiation. This finding showed that overexpression of CDK9 can interact on expression of myoniRs profiles by DNA methylation of their promoters.
Conclusion: In this study, we showed that although the expression of CDK9 enhances the cardiac differentiation in early stage of differentiation, however the overexpression of CDK9 cause to change mRNA expression patterns of myomiRs during the late stage of differentiation. This change inhibits the differentiation by DNA methylation of myomiRs promoters.
Keywords: DNA methylation, CDK9, myomiRs, cardiac differentiation.

P-601

Effect of triplet therapy with stem cells plus triiodothyronine plus exercise on brain damage in a middle-aged rodent model of stroke

Kobra Akhoundzadeh[1,2,3], Abedin Vakili [2]

1. Department of Nursing, School of Nursing & Midwifery, Qom University of Medical Sciences, Qom, Iran.
2. Physiology Research Center, Semnan University of Medical Sciences, Semnan, Iran.
3. Nervous System Stems Cells Research Center, Department of Anatomical Sciences, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran.

Background and Objective: Our previous study showed that Stem cell therapy plus thyroid hormone (T3) and exercise could improve stroke injury in young mice. Aim of this study is to assess whether combination bone marrow stromal cells (BMSCs) with thyroid hormone (TH) and exercise (EX) can diminish stroke damage in middle-aged mice.
Materials and Methods: Middle Cerebral Artery occlusion (MCAO) was induced for 45 minutes and reperfusion was allowed for 7 days in albino mice. Bone marrow stromal cells (1×105) were injected intracerebroventricularly 24h after ischemia. Mild exercise and T3 injection (20 µg/kg/daily S.C) were started 24h after MCAO and continued

for 6 days. Animals were randomly divided into seven groups: sham, PBS (as control), BMSCs, TH, EX, BMSCs+TH, BMSCs+Ex and BMSCs+TH+Ex. Infarct size, neurological function, and apoptosis (Tunnel- positive cells) were evaluated at 7th day after MCAO.
Results: Combination of stem cell transplantation along with exercise and thyroid hormone did not significantly reduced the number of TUNEL-positive cells, infarct size and neurological deficit 7 days after ischemia in middle-aged mice (P>0.05).
Conclusion: Although our previous study showed that post-stroke treatment BMSCs with exercise and thyroid hormone improved stroke injury in young mice, the result of present study reveals this combination therapy is not effective in middle aged mice. Therefore these findings emphasize that age is an important determinant in response to stroke treatment.
Key words: Cerebral ischemia, Bone marrow stromal cells, Thyroid hormone, Exercise, Apoptosis, Middle-aged

P-602

Mesenchymal stem cell-derived endometrium promote neurogenesis and motor function recovery in a mouse model of Parkinson's disease

Saeid Bagheri-Mohammadi[1,2*], Rasoul Ghasemi[1], Mahdi Noureddini[2, 3], Behrang Alani[3]

1. Department of physiology and neurophysiology research center, School of Medicine, student research committee, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of physiology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran
3. Department of Applied Cell Sciences, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, I.R. Iran

BACKGROUND: Parkinson's disease (PD) is a neurodegenerative disease caused by the loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc). The ground-breaking developments in stem cell research in the last decade have revived the interest for intracerebral cell transplantation as a therapeutically approach for PD. The experimental research with intranasal administration of stem cells in PD mouse model can work and in some cases induce major, long-lasting improvement. This research was done for evaluating effect of intranasal delivery of HEDSCs in mouse model of PD.
METHODS: In the present study, the intranasal route was used for administration of human endometrium-derived stem cells (HEDSCs)-GFP labeled in a mouse model of PD in three doses (104, 5×104 and 105 cells µl-1). During 120 days after stem cell administration, behavioral tests including rotational behavior test, rotarod test, and open field test were examined. In addition, immunohistochemistry was used to assay, GFP, human neural Nestin, and tyrosine hydroxylase (TH) markers in the fixed brain tissue at the SNpc.
RESULTS: The result showed intranasal delivery of HEDSCs can enhanced behavioral parameters compared with control group significantly. The data from immunohistochemistry revealed that the GFP and also Nestin as a differential neuronal biomarker was expressed in SNpc. Beside, TH as a dopaminergic neuron marker significantly increased after HEDSCs therapy in an optimized dose 5×104 cells µl-1.
CONCLUSIONS: Our data suggest that intranasal administration of HEDSCs improve the PD symptoms in the mouse model of PD dose-dependent manner as a noninvasive method.
KEYWORDS: Parkinson's disease, Endometrial stem cells, Intranasal delivery, Dopaminergic neurons, Neurogenesis

P-603

leukemia inhibitory factor (LIF) over expression protect adipocyte derived mesenchymal stem cells against oxidative and serum deprivation strress in vitro

Mohammad Reza Tabandeh*, Kamran Kavousi Nejhad

Department of Biochemeistry and Molecular Biology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran

Background and Objective: The leukemia inhibitory factor (LIF) is a pleotrophic factor, whose effects have been shown on the pluripotency and survival of rodent stem cells. Despite the results on the beneficial effects of LIF on stem cells, the role of LIF over-expression on protection of ATDMSc during oxidative and serum deprivation stress is unknown.
Materials and Methods: In this study, ADMSCs cells were isolated from adipose tissue of male C57BL/6 mice and characterized phenotypicaly by determination of expression of stemnes factors and surface markers. LIF was over expressed by transfection of ADMSCs using the pIRES2-EGFP vector. ATDMSc with LIF over expression was

exposed to 0.5 mM H2O2 for 1h (oxidative stress) or cultured in medium containing 2% FBS for 24 h (serum deprivation). MTT and trypan blue staining were used to indentify the viability of cells under stress conditions.
Results: The results showed that reduction in survival rate in ATDMSc cells with higher expression of LIF was significantly higher than non-transfected cells under oxidative stress. Decreased survival rate in ATDMSc cells with higher expression of LIF (65.12 ± 5.33) was significantly higher than non-transfected cells (42.57 ± 6.78) under serum deprivation.
Conclusion: our results showed that the resitance to oxidative stress and serum dprivation in ATDMSc cells increases when they expose to higher level of LIF. This finding may be one of the mechanisms of LIF in maintaining the survival and pluripotency of stem cells in in vitro conditions.
Keywords: adipocyte derived mesenchymal stem cells, oxidative stress, serum deprivation, Leukemia inhibitory factor.

P-604

In vivo cytokinesis blocked micronucleus assay with cytochalasin B in the Balb/c mouse Bone Marrow stem cells

Romina Javaheri[1*], Masoud Saleh-Moghadam[1]

1. Doctor of Veterinary medicine student, Faculty of Veterinary medicine,Ferdowsi University of Mashhad, Iran
2. Assistant professor,Graduate Department of Biochemistry, Faculty of Science, Payame Noor University of Mashhad, Iran

Objective: Cytochalasin B is presently being used as a cytokinesis inhibitor in the cell divisions to treat some types of cancer.And the in vivo micronucleus assay is routinely performed to detect clastogenic and other chromosomal damage as a result of test samples being exposed to toxic substances.
Materials and Methods.Balb/c male mice (25-30 gr) are divided into 2 groups:control and experimental.The control group received distilled water whereas experimental groups were injected into abdominal cavity with cytochalasin B (1, 2, 3 and 5 mg/kg BW). After 24 hours, sacrificed after being anesthetized by chloroform. Both femora were dissected, and bone marrow cells were flushed out with 1 mL PBS and pipetted several times. The cell suspension was centrifuged at 1,000 rpm for 5 min, the supernatant was withdrawn, and the cell pellet was resuspended and placed on a clean glass slide.
Results .This research seeks to determine the appropriate dosage of cytochalasin B to inhibit cytoplasm divisions. 1, 2, 3, and 5 mg/kg.bw of the medicine was used per kilogram of mice weight and the result was evaluated 24 hours after the treatment. The micronuclei assay was used to detect binuclei pronormoblast (stem cells).Statistical analysis was performed with Anova and Tukey using SPSS for windows.$P < 0.001$ was considered statistically significant.
Conclusion.In this study ,the results indicate the highest frequency of the binuclei pronormoblast (stopped in cytokinesis) when a 3mg/kg.bw dosage was taken for each kilogram of mice.
Keywords: Stem cells, pronormoblast, cytochalasin B, cytokinesis, micronucleus test

P-605

The effect of Cytochalasin B and TIO2 Nanoparticles in the Balb/c mouse Bone Marrow stem cells in vivo

Rahele Javaheri [1], Masoud Saleh-Moghadam [2]

1. ph.D student of comparative Histology, Faculty of Veterinary medicine,Ferdowsi University of Mashhad, Iran
2. Assistant professor,Graduate Department of Biochemistry, Faculty of Science, Payame Noor University of Mashhad, Iran

Objective:Cytochalasin B is presently being used as a cytokinesis inhibitor in the cell divisions to treat some types of cancer.And the in vivo micronucleus assay is routinely performed to detect clastogenic and other chromosomal damage as a result of test samples being exposed to toxic substances. TiO2 nanoparticles can cause negative health effects, such as respiratory tract cancer in rats. However, the mechanisms involved in TiO2-induced genotoxicity and carcinogenicity have not been clearly defined and are poorly studied in vivo.
Materials and Methods:Balb/c male mice (25-30 gr) are divided into 2 groups:control and experimental.The control group received distilled water whereas experimental groups were injected into abdominal cavity with cytochalasin B (1, 2, 3 and 5 mg/kg BW) .And In present work , mice groups were injected with nanoparticle anatase TiO2 (

100, 500, 1000 mg/kg BW), then the cytotoxic effect of TiO2 nanoparticles on mice bone marrow (pronormoblast cells) was investigated.After 24 hours, sacrificed after being anesthetized by chloroform. Both femora were dissected, and bone marrow cells were flushed out with 1 mL PBS and pipetted several times. The cell suspension was centrifuged at 1,000 rpm for 5 min, the supernatant was withdrawn, and the cell pellet was resuspended and placed on a clean glass slide.
Results :This research seeks to determine the appropriate dosage of cytochalasin B and TiO2 nanoparticles to inhibit cytoplasm divisions. 1, 2, 3, and 5 mg/kg.bw of the medicine and 100,500,1000 mg/kg TiO2 was used per kilogram of mice weight and the result was evaluated 24 hours after the treatment. The micronuclei assay was used to detect binuclei pronormoblast (stem cells).Statistical analysis was performed with Anova and Tukey using SPSS for windows.$P < 0.001$ was considered statistically significant.
Conclusion.In this study ,the results indicate the highest frequency of the binuclei pronormoblast (stopped in cytokinesis) when a 3 mg/kg.bw dosage of cytochalasin B and 100 mg/kg.bw dosage of TiO2 nanoparticles was taken for each kilogram of mice.
Keywords: stem cells, pronormoblast, cytochalasin B,TiO2 nanoparticles ,cytokinesis, micronucleus test

P-606

Differentiation of Rat bone marrow Mesenchymal stem cells with different ages into cardiomyocyte after treatment with neonatal rat cardiac extract

Fatemeh Halvaeipoor, Fatemeh Jamalzadeh, Fatemeh Safari, Fariba Akhondzadeh, Mansour Esmailidehaj

Department of Physiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Background and objective: one of the most accessible sources of stem cells for cell therapy is bone marrow stem cells. cellular extracts from variety of cell types, such as the heart, also acts as a stimulant to differentiate bone marrow stem cells into the cells of the same type of tissue. Since the age of the ability to differentiate adult stem cells decreases, we are trying to answer the question of how the infant's heart tissue extract whit increases the age of the adult stem cell, as it affects the differentiation of these cells.
Materials and Methods: MSCs (aged 7, 30 and 60 days) were placed in differentiation medium (3-day-old rat heart extract (Ex) in different doses, in presence and absence of Aza) for 24 hours. Finally, Expression of desmin gene in these groups was evaluated using Real Time RT-PCR technique on the days 18 and 27.
Results: The 7 and 30-day MSCs, induced by Aza, had a significant increase in the expression of Desmin in comparison to the control group. Among the groups that were exposed to the Aza + Ex induction medium, the expression of desmin in 7-day cells in all doses of the extract and 30- and 60-day cells was increased only in Aza + 50. In addition, in 60-day-old cells, Aza and extract alone could not lead to maximum induction .
Conclusion: These result reveal that at as the age of the BMSC is lower, the heart extract has a greater effect on the differentiation of these cells into cardiomyocytes.
Keywords: Bone marrow mesenchymal stem cell; Rat; Heart extract; Aging; Desmin

P-607

Sox2 mediated trans-differentiation of melanocytes toward neural progenitor cells, an approaches for application in neurodegenerative disorders

Samaneh Dehghan, Ghazale Shahbazi, Naser Aghdami, Mohammad Javan

Introduction: Transdifferentiation of somatic cells into neural progenitor cells (NPCs) by defined factors holds great promise for cell therapies to apply in neurodegenerative diseases. Here we aimed to introduce a new approache for transdifferentiating human melanocytes to NPCs by forced expression of Sox2 transcription factor. Generation of these cells has considerably enhanced cell therapy for treatment of neurodegenerative disorders. To evaluate the possibility of transdifferentiation of isolated human melanocytes toward NPCs by Sox2 transcription factor; melanocyte was transfected by Sox2 expressing lentiviral vector, then incubated in neural induction and neural expansion media. The expression of NPCs markers was been investigated by Real time PCR and immunofluorescence in different time point both in vitro and in vivo. Additionally, the efficacy of these newly generated cells for myelin repair assessed in an experimental model of demyelination by cuprizone. Luxol fast blue

(LFB) and fluoroMyelin staining were performed to examine demyelination level in corpus callosum.We showed that a single transcription factor, Sox2, was sufficient for transdifferentiation of human melanocytes into multipotent NPCs. In vitro, Sox2- induced NPCs exhibited morphological and molecular properties that were similar to control NPCs. In addition, the induced NPCs were able to form neurospheres with efficiency comparable with control NPCs and expressed NPC markers. The converted cells were capable of surviving and attaining oligodendrocyte lineage phenotypes after transplantation into demyelinated corpus callosum of mouseOur results suggest a new approach for establishing human NPCs through Sox2-driven conversion of melanocytes which are readily available for sampling in patients with relevant deasises.

Keywords: Melanocyte; Transdifferentiation; Neural progenitor cells; Sox2 transcription factor; Myelin repair; Cuprizone

P-608

Human endometrial stromal cells protect against cisplatin-induced acute kidney injury by inhibiting cellular apoptosis

Hadis Zeinali[1], Mahnaz Azarnia[1], Peyman Keyhanvar[2], Reza Moghadasali[3], Somayeh Ebrahimi Barough[4]

1. Faculty of Biological Sciences, Kharazmi University, Tehran, Iran
2. Stem Cell And Regenerative Medicine Institute (SCARM), Tabriz University of Medical Sciences, Tabriz, Iran
3. Department of Stem Cells and Developmental Biology at the Cell Sciences Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran.
4. Department of Tissue Engineering, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

Background and Objective: Acute kidney injury (AKI) is a significant global public health problem. Current therapies for AKI mainly include supportive care and renal replacement therapy. Despite these therapies, the five-year mortality rate for patients with AKI remains >50%. Studies have investigated the feasibility, safety, and efficacy of mesenchymal stem cells (MSC)-based therapies for kidney disease. Human MSCs are isolated from diverse tissues, including endometrium. Apoptotic cell death is a prominent and characteristic feature of AKI induced by cisplatin. In this study, we investigated effect of human endometrial stromal cells on cisplatin-induced apoptosis in AKI.

Materials and Methods: 24 rats were randomly allocated to 4 groups: control, model (5 mg/kg cisplatin, IP), PBS (200 µl PBS 3h after cisplatin, IV), cell (1×106 endometrial stromal cells/200 µl PBS 3h after cisplatin, IV). After 5 days, We dissected animals and fixed kidneys. Apoptosis was determined by a TUNEL kit (Roche, Germany). Data were analyzed using imagej software and SPSS.

Results: The number of TUNEL-positive cells markedly increased in model and PBS groups compared with the control group. Cell therapy significantly reduced the number of TUNEL-positive cells in cell group as compared with model and PBS groups.

Conclusion: Our results showed that injection of human endometrial stromal cells decrease cell apoptosis, therefore they may improve AKI.

Keywords: human endometrial stromal cells, cisplatin, acute kidney injury, apoptosis

P-609

Study the correlation between the mesenchymal bone marrow stem cells features and postoperation outcomes of patients with severe left ventricular dysfunction candidated for off-pump coronary bypass surgery

Zakieh Sadat Sheikhalishahi

Introduction: heart failure happens as a result of reducing differentiation and function of cardiomyocyte, that related to stem cell as a non differentiation cell that have ability to differentiate to other cell such as cardiomyocyte. Ageing process have adverse effect on stem cells in all tissue like Hart.

According to researches stromal cell of heart lose their differentiation potential just after birth and MSC migrate from bone marrow to damaged the tissue. In this research we trying to find that are the quality and quantity of MSC related with outcomes of patients with severe left ventricular dysfunction candidate for CABG.
Material and methods: in this research MSC from sternum bone marrow extracted during CABG and transfered in cell culture medium. the stem cells counted in dayes4,7and 14 by using tipan-blue coloured and then doubling time calculated. The patients document outcomes are assessed with their MSC doubling time.
Results: the assessment of relation between MSC doubling time as the speed index with patients follow-up has shown that there is no meaningful relation between doubling time and the patient follow-up.
Conclusion: based on the finding of this study a clear relationship between the rate of proliferation of MSC, age and improvement of tissue damage not seen. so this lack of communication can be related to the role of paracrine secretion of the MSC. Therefore the role of MSCs in secretion of autoimmune Factors and the reduction inflammatoy and immune response in tissue repair is strengthened.

P-610

Conditioned Medium Derived from Hypoxic Adipose tissue Mesenchymal Stem Cells attenuated neuroinflammation on Alzheimer's disease model in rats

Shima Mehrabadi[1], Seyed Shahabeddin Sadr[1,2*]

1. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
2. Electrophysiology Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran

Introduction: The most important pathogenesis of AD is linked to Aβ deposition, microglia activation due to release of pro-inflammatory cytokines in AD. Studies showed that adipose tissue mesenchymal stem cell conditioned medium (ASC-CM) secrete various trophic and anti-inflammatory factors. Also when ASCs grow in hypoxic condition (physiologic condition), the anti-inflammatory and trophic factors can be released more in CM by ASCs. For this reason we used ASC in hypoxic condition (hASC-CM) in rat model of AD.
Material and Methods:In this study 40 rats were randomly divided to 4 group : control, sham group injected PBS intra hippocampal, Alzheimer group injected the Aβ1-40 intra-hippocampal and the Alzheimer-conditioned medium group, which was injected Aβ1-40 intra-hippocampal and 200µl intraperitoneal injection of CM (200µl) once a day for 7 days. Memory and learning evaluated by Morris water maze and Novel object recognition tests, for detection of beta-amyloid plaque, we used Congo-Red staining and neuronal survival was assessed by Nissl-staining.Inflammation markers measured (IL-1β and TNF-α) in the hippocampus, used ELISA kits.
Result: In treatment group memory significantly was improved.CM administration decreased beta-amyloid plaques and increased neuronal survival. Finally our result showed that CM reduced IL-1β and TNF-α in AD.
Conclusion: This study showed CM could improve memory deficit, increase survival neurons by inducing clearance of beta-amyloids and decreasing neuroinflammation in AD

P-611

The role of mesenchymal stem cell-derived Exosomes in treatment of Cardial diseases

Sahar Hormozi[1] , Neda Amin[2] ,Arsalan Jalili[3]

1. Dept. Of Cilinical Research, Pasteur Institute Of Iran, Tehran, Iran
2. Dept. Of Virology, Pasteur Institute Of Iran, Tehran, Iran
3. Dept. Of Stem Cell and Developmental Biology at Cell Science Research center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Background and objective: Cardiac diseases are one of the main causes of death the world. A great deal of research has proven the safety and efficacy of stem cell-based therapy for cardiac disease. Exosomes are nanoparticles enclosed by two layers of phospholipids, which are secreted by various cells under physiological and pathological

conditions, causing intercellular communication. They carry complex cargo such as mRNA, micro-RNA, and other substances such as anti-apoptotic and pro-angiogenic factors that can be transmitted to the recipient cells. The aim of this study is to evaluate the progression of exosomes_derived mesenchymal stem cells in cardiac injury, including therapeutic effects and functional mechanisms, Examining the necessary changes in exosomes_drived stem cell for better and more specific function.
Materials and Methods: Relevant English-language literature were searched and the necessary studies were carry out through PubMed search engine (2009-2019). For this purpose, the keywords "stem cells", "heart disease treatment", "engineered exosomes" were used.
Result: Exosomes produced in stem cells and their diffusion can effectively treat cardiac diseases, although engineered exosomes perform more efficiently. Changes in ligand fragments or topical peptides discovered by phagitis display and inoculation of exogenous enriched molecules have been used to improve the ability of exosomes to target specific tissues or organs of known receptors.
Conclusion: The results of our study indicate that exosomes derived_ mesenchymal stem cells and exosomes engineered by can specifically target myocardial and enhance the therapeutic effect on acute cardiac disease.
Keywords: Exosomes; Engineered Exosomes; Stem Cells; Mesenchymal Stem Cells (MSCs); cardial Diseases

P-612

Effects of Ischemic Renal Tissue as Conditioned Medium on Mesenchymal Stem Cell; an in vivo study in Acute Ischemic Kidney Injury model

Shahrzad Havakhah[1], Ahmad Reza Bahrami[2], Abolfazl Khajavi Rad[1,3*].

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
3. Neurogenic Inflammation Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: Acute kidney injury (AKI) occurred in 8-16% of hospital admissions. The results of studies showed mesenchymal stem cell (MSC) can improve renal ischemic-reperfusion injury (IRI). The aim of this study was to test the therapeutic potential effects of conditioned-medium (CM) treated MSC in a rat model of IRI/AKI.
Materials and Methods: MSCs were generated from the femur and tibia of 4 weeks old male Wistar rats and were confirmed by differentiation and FACS analysis. Passage 3 was used in all experiments. CM was prepared from ischemia renal tissues. MSCs were treated by 50 µg/ml CM for 24-h. The groups were: IRI, IRI with MSC or CM-MSC treated. After 40-min renal ischemia and reflow, ~2×106 MSCs were injected systemically or intra-parenchymaly. Blood and urine samples were collected at baseline and day 1 post-IRI.
Results: The results showed a rise in Cr to 3.4±0.2, 3±0.1, and BUN to 86.8±6.6 and 83.5± 4.6 mg/dl, and declined GFR to 0.15±0.1 and 0.15 (ml/min/100g BW) respectively in systemic and local ischemic rats after 24-h. Animals infused with MSC and CM-MSC, had significantly lower serum Cr, 1±0.09 and 0.9±0.09 in systemic and 1±0.07 and 0.9±0.03, also, BUN levels were 58±3 and 55±6 in systemic and 57±4 and 54±3 in local groups. GFR was measured in MSC and CM-MSC, systemic and local groups as 0.3, 0.32, 0.31 and 0.32 respectively.
Conclusion: Our data showed the kidney-protective effect of MSC in IRI/AKI experimental model and effects of ischemic renal tissue as conditioned-medium on MSCs properties.
Key words: Mesenchymal stem cell, Acute kidney injury, Conditioned-medium, Cell therapy.

P-613

Effect of Lycopene on serum antioxidant and inflammatory mediators in rat's model of experimental Multiple Sclerosis (MS)

Shekoufeh Atashpour[1,2], Hosein Kargar Jahromi[1,2], Mohammad Navid Vnda[3]

1. Zoonoses Research Center, Jahrom University of Medical Sciences, Jahrom, Iran
2. Research Center for Non.Communicable Diseases , Jahrom University of Medical Sciences, Jahrom, Iran
3. Student Research Committee ,Jahrom University of Medical Sciences, Jahrom, Iran

Background and Objective: Multiple sclerosis is a chronic autoimmune disease that has been widespread in recent years, as one of the worries of today's world. The aim of this study was to evaluate the effect of lycopene as an anti-cystide and lycopene neuzum agent on the progression of M.S. and the possible mechanisms involved.

Materials and Methods: In this experimental study, 40 male rats weighing 210±10 g were used. After induction of EAE (Experimental autoimmune encephalomyelitis), animals were randomly divided into 5 groups of 8 (control, MS, MS with lycopene 200, MS with lycopene neuzum 100 and 200 mg/kg). The parameters of MDA, TAC, TOS, TNF-α, IL10 and IL17 were measured one day after the last animal cattle. The results were analyzed by ANOVA and Duncan's tests at a significant level of $p \leq 0.05$.
Results: The mean concentrations of TOS, MDA and TNF-α and IL17 and mean scores of fifty-seventh day in all experimental and control groups were significantly higher than control, and in all experimental groups, there was a significant decrease in the control group shows. Mean concentration of TAC and IL-10 in all experimental and control groups was significantly lower than controls, and in all experimental groups, there was a significant increase compared to the control group.
Conclusion: Lycopene neuzum was more effective than lycopene as a potent antioxidant and, with anti-inflammatory properties, could relieve M.S in animal specimens.
Keywords: Multiple Sclerosis, Lycopene, Rat

P-614

Effect of botulinum toxin type A injection on pain symptoms, quality of life and sleep quality of patients with diabetic neuropathy: A randomized double-blind clinical trial

Zahra kamiab[1], Hossein Salehi[2], Alireza Vakilian[3], Moein Moussaei[4]

1. Assistant Professor, Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, & Social Medicine Department, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
2. Assistant Professor of Plastic & Reconstructive Surgery, School of Medicine, clinical research development Unit, Ali Ebene Abitaleb Hospital of Rafsanjan, Rafsanjan University of Medical Sciences, Iran.
3. Associate Professor of Neurology, School of Medicine, Non-Communicable Diseases Research Center, Ali Ibn Abitaleb Educational and Treatment Hospital, Rafsanjan University of Medical Sciences.
4. Medical student, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

Background and Objective: Neuropathic pain is one of the most common problems in diabetic patients. In this study, the effect of type A botulinum toxin, on neuropathic pain, quality of sleep and life of diabetic patients with sensorimotor polyneuropathy were studied.
Materials and Methods: This randomized, placebo-controlled trial study was carried out in a double-blind (patient-researcher) study. This study was performed on 32 patients with type 2 diabetes. Neuropathy was confirmed by DN4 questionnaire and nerve conduction study. They were randomly assigned to two intervention and control groups based on the random numbers table. After selecting the subjects, we used Short Form-36 Quality-of-Life Questionnaire, Neuropathic Pain Scale, visual analogue scale and The Pittsburgh Sleep Quality Index questionnaires before and after 3 months of 100 units botulinum toxin type A injection (as intervention group) or same amount of chloride sodium (as control group) to the subjects' feet. The data were analyzed by SPSS-20 software using independent two-sample t-test, chi-square test and one-way repeated measures ANOVA.
Results: Twelve male and 20 female patients participated in this study. There was a significant difference in the mean VAS, PSQI, physical dimension of the quality of life and some NPS indices over time (12 weeks) (P value <0.001).
Conclusion: The results of this study showed that botulinum toxin type A reduces neuropathic pain, improves the quality of life and sleep in people with diabetic neuropathy.
Keywords: Neuropathic pain, Quality of life, sleep quality, Botulinum Toxin A, Diabetes, Rafsanjan

P-615

Effect of Oleuropein on Morphine-induced working Memory Impairments in Rats

Farhad Shibani[1,2], Ali Sahamsizadeh[2], Jalal Hasanshahi[2], Mohammadreza Rahmani[1], Ayat Kaeidi[2]

1. Physiology-Pharmacology Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
2. Department of Physiology and Pharmacology, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Background and Objective: Pervious findings showed that morphine treatment in an increasing doses manner cause oxidative stress and neurodegeneration in the hippocampus area of the brain. The hippocampus has an important role in the process of learning and memory. This study was done to investigate the effects of oleuropein (main olive leave polyphenol compound) against morphine-induced working memory impairments in male Wistar rats.
Materials and Methods: using the Y-maze spontaneous alternation tests (to evaluation the working memory), we explored the pro-cognitive effect of oleuropein (5, 15 and 30 mg/kg, i.p., 4 weeks) in rats which treated with morphine sulfate (45 mg/ kg, for 4 weeks, s.c.). In order to evaluate the oxidative stress in hippocampus tissue, malondialdehyde (MDA) level, superoxide dismutase (SOD) and, glutathione peroxidase (GPx) activity were assessed. Furthermore, we investigated the effects of oleuropein on brain derived neurotrophic factor (BDNF) protein expression in the hippocampus tissue using ELIZA method.
Results: The data showed that treatment with oleuropein (15 and 30mg/kg) improves the impairment of working memory in morphine-treated animals. Also, oleuropein treatment (15 and 30mg/kg), decreased the oxidative status in hippocampus tissue of morphine-traded rats. Chronic morphine or oleuropein treatment have no any significant effects of hippocampus BDNF protein expression.
Conclusion: Oleuropein can improve the working memory performance in morphine-treated animals. Cellular mechanisms underlying the observed effects could be at least partially related to the inhibition of oxidative stress in the hippocampus of morphine treated animals.
Keywords: Morphine, working Memory, Hippocampus, Oxidative stress.

P-616

Lead neurotoxic effects reverses by protective effects vitamin E in hippocampal synaptic plasticity in rats

Ruhollah Karamian

Vitamin E (VE) is an antioxidant that could have protective effects against Pb intoxication. Lead (Pb) exposure during development is associated with impaired cognitive function and long-term potentiation (LTP). In this study, we examined the protective effects of vitamin E against Pb-induced LTP impairments. Forty-six adult male Wistar rats were randomly divided into 6 treatment groups: (1) control; (2) Pb exposure; (3) VE; (4) Pb þVE; (5) Pb exposure followed by VE 2 months after exposure; (6) VE followed by Pb exposure 1 month after treatment. Rats were exposed to Pb through daily consumption of Pb-contaminated distilled water; VE was administered by daily gavage for 3 months. After this period, the population spike (PS) amplitudes and the slopes of excitatory postsynaptic potentials (EPSPs) were measured in the dentate gyrus (DG) area of the hippocampus in adult rats in response to electrical stimulation applied to the perforant pathway in vivo. Blood samples were also collected to evaluate malondialdehyde (MDA) levels, total antioxidant capacity (TAC), and total oxidant status (TOS). Biochemical analyses demonstrated significant increases in plasma MDA and TOS levels in the Pb-exposed group compared to the control group. VE–protected groups revealed significant increases in TAC levels. Our results demonstrate that Pb decreased EPSP slopes and PS amplitudes compared to the control group, whereas VE increased these parameters compared to the control group. Coadministration of VE with Pb exposure inhibited Pb-induced effects. These findings suggest that VE via its antioxidant activity reverses Pb-induced impairments of synaptic plasticity in the DG.
Keywords: Lead acetate, Hippocampus, Vitamin E, Dentate gyrus, Long-term potentiation, Antioxidants, Rat

P-617

Role of changes in cardiac metabolism following endotoxemia-induced cardiac dysfunction

Hamid Soraya[1], Alireza Garjani[2] , Alexander S. Clanachan[3*]

1. Department of Pharmacology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran
2. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran
3. Department of Pharmacology, Faculty of Medicine and Dentistry, 9-70 Medical Sciences Building, University of Alberta, Edmonton, Alberta, Canada

Background and Objective: To determine whether drug-induced alterations in cardiac metabolism may be a viable strategy to reduce endotoxemia-mediated cardiac dysfunction, we assessed endotoxemia-induced changes in glucose and fatty acid metabolism. Materials and Methods: Endotoxemia was induced in male Sprague-Dawley rats by lipopolysaccharide (4 mg/kg, i.p.) 6 hrs prior to heart removal for ex vivo assessment of left ventricular (LV) work and rates of glucose metabolism (glucose uptake, glycogen synthesis, glycolysis and glucose oxidation) and palmitate oxidation. Results: Endotoxemic hearts had impaired LV function as judged by echocardiography in vivo (% ejection fraction, 66.0±3.2 vs 78.0±2.1, $p<0.05$) or by LV work ex vivo (2.14±0.16 vs 3.28±0.16, Joules.min-1.g dry wt-1, $p<0.05$). However, rates of glucose uptake, glycogen synthesis, glycolysis, and glucose oxidation were not altered. Palmitate oxidation was lower in endotoxemic hearts in proportion to the decreased workload, thus metabolic efficiency was unaffected. In hearts reperfused following global ischemia, untreated hearts had impaired recovery of LV work (52.3±9.4%) whereas endotoxemic hearts had significantly higher recovery (105.6±11.3%, $p<0.05$). During reperfusion, fatty acid oxidation, acetyl CoA production and metabolic efficiency were similar in both groups. Conclusion: As impaired cardiac function appeared unrelated to depression of energy substrate oxidation, it is unlikely that drug-induced acceleration of fatty acid oxidation will improve mechanical function. The beneficial repartitioning of glucose metabolism in reperfused endotoxemic hearts may contribute to the cardioprotected phenotype.
Key Words: Endotoxemia, cardiac function, glucose metabolism, palmitate metabolism

P-618

The effect of nobiletin on inflammatory response, oxidative stress, and apoptosis in a model of Parkinson's disease induced by intranigral injection of lipopolysaccharide in the rat

Sedigheh Keshtkar[1], Zahra Kiasalari[2], Maryam Khorasani[1], Marzieh Fakour[1], Reihane Ghasemi[1], Mehrdad Roghani[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Department of Physiology, Shahed University, Tehran, Iran.

Background and Objective: Nobiletin is a flavonoid in citrus. The antioxidant, anti-inflammatory and anti-apoptotic properties of nobiletin have been observed. The aim of the present study was to investigate the effect of nobiletin (NOB) on inflammatory response, oxidative stress and apoptosis in an experimental model of Parkinson's disease (PD) induced by intranigral injection of lipopolysaccharide (LPS) in rats.
Materials and Methods: Male rats (n = 28) were divided into four groups: sham, sham under treatment of NOB, lesion and lesion treated with NOB. To achieve unilateral lesion of the nigrostriatal system, rats received 5 µg of LPS into the right substantia nigra. NOB was administered p.o. at a dose of 10 mg/kg/day from one hour after surgery till one week later. One week post-surgery, oxidative stress markers, inflammatory factors, and severity of apoptosis were measured.
Results: The results showed that treatment with NOB significantly decreased malondialdehyde (MDA), reactive oxygen species (ROS), increased glutathione (GSH), superoxide dismutase (SOD) activity, decreased inflammatory factors including nuclear factor-kappa, Toll-like receptor 4, tumor necrosis factor and also decreased DNA fragmentation in LPS group.
Conclusion: Administration of NOB to LPS-induced PD reduces oxidative stress, inflammation and apoptosis, which may potentially be of benefit for ancillary therapy of PD.
Keywords: Nobiletin, Oxidative stress, Inflammation, Apoptosis, Parkinson's disease, Lipopolysaccharide

P-619

Protective effect of Nigella sativa on Cisplatin-induced memory and learning impairment in male ra

Marzieh Kafami[1], Masoud Hoseinzadeh[2], Yasin Mohamad Janloo[3], Fatemeh Ataei[3], Sahar Roshan[3]

1. Cellular and Molecular Research Center, Department of Physiology and Pharmacology, Faculty of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran
2. Department of Physiology and Pharmacology, School of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran.

3. Student Research Committee, Sabzevar University of Medical Sciences, Sabzevar, Iran.

Introduction: Cisplatin (CP) is one of the most common drugs used in clinics to treat different types of cancer. The rationale of our study was to investigate the efficacy of Nigella sativa on learning and memory impairments in Cisplatin-induced cognitive impairment.
Material and methods: The thirty two male rats divided into four groups: Group I (Control; n=8) received 0.9% saline once per day for two weeks intraperitoneally (i.p); Group II received Cisplatin (3mg/kg/2 weeks, ip, n=8); Group III received Cisplatin (3mg/kg/2 weeks) and Nigella sativa (200 mg/kg/2 weeks, i.p, n=8); Group IV received Nigella sativa (200 mg/kg/2 weeks). At the end of the experiment, the memory and learning were evaluated by Morris water maze (MWM) and passive avoidance (PA) tests.
Results: Cisplatin increased the escape latency and traveled path in MWM ($P < 0.001$). Cisplatin also shortened the latency for enter the dark room of PA as well as the time spent in the target quadrant in probe trial test of MWM ($P<0.05$- $P< 0.001$). All the effects of Cisplatin were reversed by Nigella sativa ($P < 0.05$-$P < 0.01$).
Conclusion: Our findings indicate that Nigella sativa ameliorates Cisplatin-induced spatial learning and memory impairment.
Key words: Nigella sativa, Cisplatin, Memory, Morris water maze test, Passive avoidance

P-620

Upregulation of the hippocampal connexin43 during memory consolidation

Nazila Koravand, Siamak Beheshti

Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran

Background and Objective: Studies have shown that intercellular communication via gap junction channels has a crucial role in the learning process. This communication can change by opening and closing state of the channels or by a change in the expression levels of the connexin subunits. In this study, we measured the expression levels of connexin43 (Cx43) as an astrocytic connexin in the hippocampus of rats, during spatial memory consolidation.
Materials and methods: Adult male Wistar rats weighing 250 g were used. Animals were trained with the Morris-water maze task, using a two-day protocol. At different times post-training (1, 3 and 24 h), the rats were decapitated and their hippocampus was removed and freeze in liquid nitrogen, immediately. The control group was not trained in the water maze and just had a swimming experience. The mRNA expression level of Cx43 was measured by the real-time PCR method.
Results: One-way ANOVA indicated a significant increase in the expression levels of the hippocampal Cx43 during spatial memory consolidation. Post-hoc comparison showed that the expression levels of Cx43 increased at 3 h post-training compared to the control group.
Conclusion: The results indicate that the intercellular communication between astrocytes increase via Cx43 made gap junction channels and this communication has a role during spatial memory consolidation. This is inconsistent with a previous result that showed an impairment of the spatial memory in Cx43 knockout rats.
Keywords: Connexin43, Hippocampus, Glia, Morris Water Maze

P-621

Homosynaptic and Heterosynaptic Plasticity in Visual Cortical Neurons

Masoumeh Kourosh Arami[1,2], Bin Jiang[1], Yuchio Yanagawa[3]

1. Brain Science Institute, RIKEN, Wako, Japan
2. Department of Basic Sciences, Allied Medical College, Iran University of Medical Sciences, Tehran, Iran
3. Department of Genetic and Behavioral Neuroscience, Gunma University Graduate School of Medicine, Maebashi, Japan

Background and Objective: Most neurons in layer VI of the visual cortex project to the dorsal lateral geniculate nucleus (dLGN). These corticogeniculate projection neurons (CG cells) receive top-down synaptic inputs from upper layers (ULs) and bottom-up inputs from the underlying white matter (WM). Use-dependent plasticity of these synapses in layer VI of the cortex has received less attention than in other layers.
Materials and Methods: In the present study, we used a retrograde tracer injected into dLGN to identify CG cells, and, by analyzing EPSPs evoked by electrical stimulation of the UL or WM site, examined whether these synapses show long-term synaptic plasticity. Theta-burst stimulation-induced long-term potentiation (LTP) of activated synapses (hom-LTP) and long-term depression (LTD) of nonactivated synapses (het-LTD) in either pathway.
Results: The paired-pulse stimulation protocol and the analysis of coefficient variation of EPSPs suggested postsynaptic induction of these changes except UL-induced het-LTD, which may be presynaptic in origin. Intracellular injection of a Ca+2 -chelator suggested involvement of postsynaptic Ca+2 rise in all types of long-term plasticity. Pharmacological analysis indicated that NMDA receptors and type-5 metabotropic glutamate receptors are involved in WM-induced and UL-induced plasticity, respectively. Analysis with inhibitors and/or in transgenic mice suggested an involvement of cannabinoid type 1 receptors and calcineurin in UL-induced and WM-induced het-LTD, respectively.
Conclusion: These results suggested that hom-LTP and het-LTD may play a role in switching the top-down or bottom-up regulation of CG cell function and/or in maintaining the stability of synaptic transmission efficacy through different molecular mechanisms.
Keywords: Homosynaptic, Heterosynaptic Plasticity, Visual Cortex, Layer VI, Layer II/III, White matter

P-622

Evaluation the effect of chronic toxoplasmosis on synaptic plasticity in rats

Bahere Kiani[1,2], Mohammad sayah[1] , Katane Abrari[2] ,Hamid Gholami Pourbadie[1], Jalal Babaie[3], Majid Golkar[3]

1. Department of Physiology & Pharmacology, Pasteur of Iran, Tehran, IRAN
2. Department of Animal Biology, Faculty of Biology, University of Damghan, IRAN
3. Department of Parasitology, Pasteur of Iran, Tehran, IRAN

Introduction: Toxoplasma gondii is an intracellular parasite. One-third of world's populations estimated to be infected with Toxoplasma gondii. Recent studies indicate a major role of this parasite in etiology of neurologic disorders including psychosis, epilepsy and cognitive disorders. We have recently demonstrated the proconvulsant and epileptogenic effect for this parasite. Limbic system including hippocampus is among the main brain areas involved in emotion and cognition. The effect of rats infected with T. gondii on synaptic plasticity in the hippocampus was examined in this study.
Methods: Male Wister rats were infected with T. gondii by i.p. injection of 500 parasite cysts. The synaptic plasticity in the hippocampus of rats with chronic infection (8 weeks after cysts injection) was determined by field potential recording. Rats with latent infection (chronic phase) and rats without infection (250-300g) are used to study changes in synaptic plasticity.Rats were anesthetized by urethane (Sigma, 1.5 g/kg, i.p) and placed in a stereotaxic apparatus (Stoelting, USA). A bipolar stimulating electrode, consisting of a pair of twisted stainless steel Teflon-coated wires (125 mm inner diameter/150mm external diameter, Advent Co., UK) with tips horizontally separated 500 µm apart, was positioned at the medial perforant path (AP: -8.1, ML: 4.3, DV: 3.3), and a similar recording electrode was positioned at the dentate gyrus (DG) area (AP: -3.8, ML: 2.4, DV: 3-3.5). Both electrodes were slowly lowered through the cortex and upper layers of hippocampus. Lowering of electrodes was continued until a standard DG signal was detected. Electrodes were left still for 30min to ensure stability of the signal. Population spike (PS) was measured in the granule cell layer upon stimulation of the medial perforant pathway. Using a constant current isolation unit (A365, WPI, USA), a 0.2 µs monophasic square wave was applied to produce the stimulating signal at desired magnitudes. Field potential responses were then amplified using differential amplifier (DAM 80, WPI, USA) with band pass filtered between 1 Hz and 3 kHz, digitized at 10 kHz, and recorded and analysed using homemade software. PS amplitude was calculated as the distance between the first positive wave and peak of the first negative deflection. All recordings were the average of 5 single pulses with pulse intervals of 30s. PS amplitude was plotted against different magnitudes of stimulating currents to obtain the input/output (I/O) curve. Baseline synaptic activity was then recorded in every 5 min for at least 30 min by applying test stimulus (TS), which was a stimulation of the perforant path at a current that produced 40% of the maximum response according to the I/O curve. Long term potentiation (LTP) was induced by a high-frequency stimulation (HFS) consisting of 10 trains of 20 pulses at 200 Hz with 80% of maximum intensity, delivered every 10. LTP induction criteria were a 25% increase of the PS amplitude compared to the baseline. Post-HFS evoked field potential was recorded every 5 min for 2 h. Data were analyzed by two-way ANOVA. A p value of less than 0.01was considered to represent a significant difference.
Results: PS amplitude increased about 38% of baseline in control group, whereas it is augmented 80% of baseline in the infected rats (Fig. 1). The difference was significant statistically ($p<0.0001$). The slope of EPSP increased about 20% of baseline in uninfected rats (control group). However, it is increased to about 40% of baseline in infected rats (Figure 2). The difference was significant statistically ($p<0.0001$).
Conclusion: It can be suggested that Toxoplasmagondii lead to changes synaptic plasticity in the hippocampus rats. Increase excitability of neurons is the result of this research. This study can be used as a starting point for more extensive studies.

P-623

Naloxone reversible effect of immobilization stress on learning and memory in rat

Mehdi Geraily Afra[1], Farideh Bahrami[1,2], Zahra Bahari[1,2], Hedayat Sahraei[1,2]

1. Department of Physiology and Medical Physics, Faculty of Medicine, Baqiyatallah University of Medical Science, Tehran,Iran.
2. Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran.

Background and Objective: Stress can disrupt the physiological homeostasis of biological organisms which follow by behavioral impairment; especially it can induce deficits in learning and memory process. Furthermore, opioid can modify learning and affect, mood and emotions, processes that have been regulated in amygdaloidal system. In this

study we examine the blocking effect of opioid receptors in amygdala on learning and memory deficits induced by immobilization stress.
Materials and Methods: Forty tow male Wistar rats were subjected to 2 hours of immobilization per day in a narrow, uneven and stony place for 3 consecutive days. After every session of immobilizing the rats were trained in Barnes maze. For treatment the Naloxone 0.01 and 0.05 (µM) were injected in to amygdala during the examination.
Results: The results of this study showed that stress could delay the learning procedure and 24hours memory retention. The injection of Naloxone with 0.01 and 0.05 (µM) concentrations in amygdala improved learning and memory. This improvement was better with 0.05 concentration of Naloxone. Furthermore, treatment of stress exposed animals with Naloxone 0.01 and 0.05 (µM) also indicated progress in learning and memory, which there were no significant changes between 0.01 and 0.05 (µM) concentrations.
Conclusion: Injection of Naloxone in to amygdala could improve learning and memory in stress condition.
Key word: Immobilization, learning and memory, Naloxone, Amygdala

P-624

Evaluation of anti-inflammatory effect of aqueous extract of Cuminum cyminum L. fruit with formalin-induced inflammatory model in male rats

Sahar Golabi*, Asma Mohammadi, Narges Chamkouri

Abadan Faculty of Medical Sciences, Abadan, Iran

Background and Objective: Inflammatory pain is caused by tissue damage and inflammation. Formalin is one of the most important substances used to induce inflammation. Recognition and development of anti-inflammatory drugs of natural origin is currently receiving much attention. Cumin has anti-inflammatory potential. Given the importance of understanding more precisely the mechanisms that trigger and promote inflammation in order to find better, more complete, and less complicated ways to improve inflammation and inflammatory pain, High and sometimes severe side effects of chemical treatments, the growing importance of medicinal plants in different fields of medical sciences and the abundant and various application of cumin medical sciences, the aim of this study was to investigate the anti-inflammatory effect of aqueous extract of Cumin fruit in male rats.
Materials and Methods: thirty-six rats were used in different groups. Aqueous extract of cumin fruit was prepared in doses of 200, 500, 1000 mg/ kg. Inflammation was induced by subcutaneous injection of formalin in the animal's right hind paw and inflammatory pain was assessed. One-way ANOVA was used for data analysis.
Results: Different doses of the extract reduced the acute and chronic inflammation. The most significant decrease in acute phase was dose 200 and in chronic phase was dose 1000.
Conclusion: The aqueous extract of Cumin fruit has an acute and chronic anti-inflammatory effect and is dose dependent.
Keywords: Acute inflammation, chronic inflammation, formalin, cumin, aqueous extract

P-625

Isorhamnetin exerts neuroprotective effects in STZ-induced diabetic rats via attenuation of oxidative stress, inflammation and apoptosis

Mina Goudarzi

Objective: Isorhamnetin, a derivative of quercetin, exerts antioxidant and anti-inflammatory effects in different diseases and we examined its protective effects against diabetes-related changes in a brain.
Methods: A single dose of a freshly prepared solution of Streptozotocin (STZ) (60 mg/kg body weight) was intraperitoneally injected to establish STZ-induced diabetic model in male Wistar rats. The animals were randomly divided into four groups: control, control+ isorhamnetin, diabetic, diabetic+ isorhamnetin. Isorhamnetin at dose of 10 mg/kg body weight was intraperitoneally administrated for 12 weeks. Formalin and tail immersion tests were

performed to evaluate severity of pain. Astrogliosis markers such as GFAP and APO-E4, DNA fragmentation, MDA level, and TNFα expressions were evaluated using ELISA assay. Neuronal density in hippocampus region was evaluated using Nissl staining. The method of Ellman was used to measure brain acetyl-cholinesterase activity. Fluorescent probe 2, 7-dichlorofluorescein diacetate (DCFH-DA) was used to detect reactive oxygen species (ROS)
Results: Isorhamnetin significantly reduced pain, blood glucose levels and increased body weight than control. Moreover, Isorhamnetin inhibited astroglial activation, acetyl-cholinesterase activity, oxidative stress, apoptosis and inflammation.
Conclusion: These findings suggested that isorhamnetin has potential effects as neuroprotective agents against diabetes-related changes in a brain.
Keywords: Isorhamnetin, Diabetes mellitus, Streptozotocin, astrogliosis; neuroprotective effects
Abbreviations: Diabetes mellitus, DM; reactive oxygen species, ROS; Streptozotocin-induced type 2 DM, STZ-induced T2DM; dentate gyrus, DG; Brain-derived neurotrophic factor, BDNF; Superoxide dismutase, SOD; Malondialdehyde, MDA; Tumor necrosis factor-alpha, TNF-α; Glutathione peroxidase, GPx; Thiobarbituric acid-reactive substance, TBARS.

P-626

Involvement of the opioid receptors of cuneiform nucleus in regulation of cardiovascular responses during normal and hemorrhagic conditions

Reza Mohebbati[1], Mohammad Naser Shafei[2]

1. Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: The opioid receptors regulate cardiovascular responses especially in hemorrhage. Presence of this receptor in the cuneiform nucleus (CnF) has shown. The present study evaluates the cardiovascular effect of μ and Δ opioid receptors of the CnF in normal and hypotensive hemorrhagic rats.
Materials and Methods: Morphine (μ agonist), naloxone (μ antagonist), [D-Pen2,5]-Enkephalin hydrate) (DPDPE) (Δ agonist) and naltridol (Δ antagonist) were microinjected into the CnF in basal and hemorrhagic conditions and cardiovascular responses were evaluated. Hemorrhage induced by blood withdrawal from femoral artery and 2 min after that drugs microinjected. Time course and peak changes (Δ) of the mean arterial pressure (MAP), systolic blood pressure (SBP) and heart rate (ΔHR) were recorded by a Power Lab instrument and compared with the control and hemorrhage groups by repeated measurement ANOVA.
Results: In basal condition, morphine significantly decreased ΔSBP, ΔMAP and ΔHR than the control ($P<0.05$) and naloxone significantly increased them ($P<0.05$) while Δ antagonist and agonist have not any significant effect. Hypotension and tachycardia induced by hemorrhage ameliorate by morphine ($P<0.05$) and naloxone deteriorated hypotension ($P<0.05$). The naltridole reduced tachycardia induced by the hemorrhage while DPDPE has not significant effect.
Conclusion: Activation of μ opioid receptor improves the cardiovascular parameters during hemorrhage in CnF nucleus but Δ opioid receptor seems that has not important role in modulation of hemodynamic during and after hemorrhage in this nucleus.
Keywords: Cuneiform nucleus, Opioid receptor, Hemorrhage, Blood pressure

P-627

Assessment of the protective effects of huperzine-A in a rat model of temporal lobe epilepsy induced by kainic acid

Parvaneh Mohseni-Moghaddam[1], Seyed Shahabeddin Sadr[2], Mehrdad Roghani[3]

1. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Electrophysiology Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran
3. Neurophysiology Research Center, Shahed University, Tehran, Iran

Background and Objective: Temporal lobe epilepsy (TLE) is one of the most prevalent types of epilepsy in human. Huperzine A has been reported to possess antioxidative and anti-inflammatory properties; however, its role in TLE induced by kainic acid has not been determined.
Materials and Methods: The current study investigated the protective effects of huperzine A (0.1 mg/kg) in kainic acid-induced model of TLE. Altogether 6 groups were used and each group was divided into two subgroups. Six subgroups were studied for evaluating NLRP3 Inflammasome-Related Inflammation and oxidative stress during acute phase. The other six subgroups were used to assess learning and memory behaviour and investigation of the neuronal death and acetylcholinesterase activity in chronic phase.
Results: We found that huperzine A significantly prevented the seizure intensity and spatial learning and memory deterioration. However, kainic acid injection could not affect memory related to novel object recognition. Additionally, huperzine A inhibited acetylcholinesterase activity. Regarding oxidative stress, catalase and SOD activities increased after huperzine A treatment, while MDA and nitrite levels significantly reduced. This drug decreased NLRP3 expression and also diminished caspase-1 activity and IL-1β level in hippocampal tissue.
Conclusion: Altogether, our data showed that huperzine A could be a potential protective substance to ameliorate seizure severity and sapatial learning and memory deficits related to epilepsy via attenuating neuroinflammation and protection of neurons.
Keywords: Cognitive dysfunction, Huperzine A, Inflammasome, Oxidative stress, Temporal lobe epilepsy

P-628

Adjustment of mitochondrial dynamics by Mitochondrial ATP-sensitive potassium channel after temporal lobe epilepsy

Ali Mohammad Khanizadeh

Background and objective: Temporal lobe epilepsy is the prevalent form of epilepsy that is highly repetitive and is resistant to anti-epileptic drug. There are different contributing causes of epilepsy such as inflammation, infection, stroke, and mitochondria dysfunction. However, the underlying mechanism of mitochondria dysfunction is not well understood in epilepsy.
Mitochondria functions are under the influence of mitochondrial dynamic which of consists of mitochondrial fission and fusion.
Some studies have shown that mitoKATP channels play an important role in mitochondrial dynamics. This channels have antioxidant, anti-apoptotic properties in the brain.
Material and methods: Epilepsy was induced by i.c.v injection of kainic acid (KA). 5-HD as selective mitoKATP blocker (10/mg/kg/day) was administered intraperitoneally. Three days later, animals were sacrificed. Their brain sections were then stained with Cresyl violet to assess the necrotic number of neurons in CA3 and Hilus the hippocampus.
5-HD decreases latency to seizure and increase seizure intensity (<0.01). Immunohistochemistry was used to detect DRP1 and FIS1 level was evaluated by real time PCR.
The histological analysis showed that 5-HD decreased the number of neurons in CA3 and Hilar areas (P<0.001). A significant increase of DRP1 positive cells in KA+5-HD group compare to control and KA groups (p<0.001) was observed. Real time PCR analysis demonstrated that ۵-HD significantly increased FIS1 expression (p<0.001).
It was concluded that mitoKATP have neuroprotective effect in epilepsy and probably one of its neuroprotective mechanisms is by modulating mitochondrial dynamics.

P-629

The effect of intraperitoneal injection of alpha-lipoic acid on memory deficit in the methamphetamine-induced neurotoxicity

Hossein Mohammad Pour Kargar , Hamed Valizadeh, Hossein Ghods

Islamic Azad University, Damghan Branch, Damghan, Iran.

Background and Objective: Alpha-lipoic, as a cofactor, is essential for aerobic metabolism and also acts as a potent antioxidant in the body. It was cleared that oxidative stress responsible for cognitive deficit in acute exposure to methamphetamine. In this study, preventive effect of intraperitoneal injection of alpha-lipoic acid on memory impairment in the model of methamphetamine-induced neurotoxicity was investigated.
Materials and Methods: 45 rats were allocated to 6 groups: control, saline + saline, saline (as methamphetamine solvent) + sunflower oil (as alpha-lipoic acid solvent), methamphetamine + sunflower oil, and two

methamphetamine groups under treatment with alpha-lipoic acid (10, and 40mg/kg). Rats received methamphetamine repeatedly (20 mg/kg, ½ hour interval) and alpha-lipoic acid was injected 30 min, 24 h and 48 h after methamphetamine. Passive avoidance test was used for evaluation of memory. Data were analyzed using SPSS.
Results: Statistical analysis showed that injection of saline or sunflower oil did not affect number of entrance into the dark part or time of spending in dark. Methamphetamine induced memory impairment and increased both of them. But alpha-lipoic acid injection significantly reduced them in the dose-dependent manner.
Conclusion: Our results showed that antioxidant activity of alpha-lipoic acid could prevent memory deficit in the methamphetamine-induced neurotoxicity.
Keywords: Methamphetamine, Alpha-lipoic acid, Oxidative stress, Memory

P-630

Paraoxon-induced anxiolytic activity is associated with alterations in expression of apoptosis-related genes in rat hippocampus

Moslem Mohammadi[1], Zohreh Zare[2], Sakineh Shafia[3]

1. Associate Professor, Department of Physiology, Molecular and Cell Biology Research Center, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
2. Assistant Professor, Department of Anatomical Sciences, Molecular and Cell Biology Research Center, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
3. Assistant Professor, Department of Physiology, Molecular and Cell Biology Research Center, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.

Background and Objective :Exposure to organophosphate (OP) compounds leads to behavioral alterations. Paraoxon is the active metabolite of the OP insecticide, parathion. In order to determine whether paraoxon has effects on anxiety, anxiety-like behaviors were assessed in paraoxon-exposed rats. Protein expression of apoptosis-related genes has also been measured in hippocampus.
Materials and Methods :Adult male Wistar rats were intraperitoneally injected with paraoxon (0.3, 0.7, or 1 mg/kg) or corn oil as vehicle. At 14 or 28 days after exposure, behavioral tests were done using elevated plus-maze (EPM) or open field tests. Thereafter, animals were sacrificed and both hippocampi were dissected out for measuring expression of apoptosis related genes, including Bax, Bcl-2, and caspase-3, using western blotting.
Results :Animals treated with convulsive doses of paraoxon (0.7 and 1 mg/kg) showed an increase in percentages of time spent and entries into open arm in the EPM as well as an increase in the time spent in central area of the open field. These results demonstrated reduced anxiety-like behaviors. There was a significant increase in Bax and caspase-3 levels in rats receiving 0.7 and 1 mg/kg of paraoxon at both time points. A significant decrease in the Bcl-2 protein levels was observed in 0.7 and 1 mg/kg groups after 14 days and in 1 mg/kg group after 28 days.
Conclusion: The results indicate that exposure to convulsive doses of paraoxon induced anxiolytic-like behaviors. It is possible that apoptosis-induced brain damage after administration of convulsive doses of paraoxon contributes to decrease in anxiety like behaviors.
Keywords: paraoxon; anxiety; apoptosis; hippocampus; elevated plus-maze

P-631

Persistent peripheral inflammatory pain changes spatial memory function via hippocampal neuronal apoptosis

Mola Mohammadi[1,2], Zaringhalam[1,2*]

1. Physiology Department, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Cognitive impairment is commonly associated with the pain experience. This impairment represents a major obstacle to daily activities and rehabilitation, especially in the chronic pain population. It has been suggested that inflammatory persistent pain led to learning and memory impairment, but little is known about molecular mechanisms involved in between them. Therefore, the aim of this study was the investigation of apoptotic cell death and spatial memory variation during persistent peripheral inflammation. Animals were randomly distributed to 3 groups, control, Complete Freund's Adjuvant (CFA) (received 100 µL CFA), CFA+Minocyclin groups (received

100 µL CFA+40mg/kg/day minocycline). These groups also divided to 3 subgroups day 0, 7(CFA7) and 21(CFA21) to assess different time points of study. Each subgroup included 6 rats. Our results indicated that CFA-induced inflammatory pain impaired spatial learning and memory associated with an increase hippocampal apoptotic cell death in regions of CA1 and dentate gyrus during first week of study. Whereas, Function of CFA-treated rats in the probe trial at third week indicated better performance in memory retention associated with slower apoptotic cell death rate. Also administration of Minocycline can effectively reduce hippocampal neurons death which in turn improved spatial learning and memory in our model. Therefore, we can suggest that peripheral inflammatory pain impaired cognitive functions through apoptotic neuron death in the hippocampus.

P-632

Peroxisome proliferator-activated receptor alpha (PPARα) activation by fenofibrate protects neurovascular functions and structure in pentylenetetrazole-induced kindling seizure in mice

Mohammad Taghi Mohammadi[1,2], Nahid Sarahian[1], Shamsi Darabi[3]

1. Department of Physiology and Biophysics, School of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran
2. Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
3. Department of Physiology, Faculty of Medicine, Qom University of Medical Sciences, Qom, Iran

Background and Objective: Based on the pleiotropic functions of peroxisome proliferator-activated receptor-alpha (PPARα), we evaluated the neuroprotective effects of PPARα agonist, fenofibrate, on the brain injuries induced by pentylenetetrazole (PTZ)-induced kindling seizure.
Materials and Methods: Adult male NMRI mice were randomly assigned into four groups (n=14) as follows; control, untreated kindled mice (PTZ) and two fenofibrate-treated kindled groups. Repeated intraperitoneal injections of PTZ (65 mg/kg), every 48 hours till day 21, were used to develop the kindling seizure. Treated mice were administered orally fenofibrate at doses of 30&50 mg/kg/day. Plasma corticosterone and brain levels of brain-derived neurotrophic factor (BDNF), malondialdehyde (MDA) and mRNA transcription of p53, as well as blood-brain barrier (BBB) permeability, were evaluated at termination of the study.
Results: PPARα activation considerably improved seizure latency and anxiety-like behaviors in treated kindled mice. Fenofibrate at doses of 30&50 mg/kg significantly ($P<0.001$) decreased plasma corticosterone (56.88±0.80&54.81±0.29 ng/mL, respectively) compared to PTZ group (74.96±1.60 ng/mL). It also significantly ($P<0.001$) decreased BDNF levels in both treatment groups (8.13±0.14&8.74±0.09 ng/mL, respectively) compared to PTZ group (9.68±0.20 ng/mL). High dose of fenofibrate significantly decreased MDA content and mRNA expression levels of p53 in treated kindled mice by 75% and 28%, respectively, compared to PTZ group ($P<0.05$ and $P<0.01$, respectively). Similarly, 50 mg/kg fenofibrate significantly ($P<0.05$) decreased Evans blue extravasation into brain in treated kindled mice (8.72±0.96 µg/g) compared to PTZ group (15.31±2.18 µg/g).
Conclusion: PPARα agonist, fenofibrate, improves the neurovascular functions and structure at molecular levels in kindling seizures.
Keywords: PPARα, Neurotrophin, Corticosterone, Oxidative damage, Apoptosis

P-633

Involvement of nuclear transcription factors in rat hypothalamus in the development of morphine tolerance

Shiva Mohammadi Talvar, Mohammad Zobeiri, Kaivan Masoudi, Shamseddin Ahmadi

Department of Biological Science, Faculty of Science, University of Kurdistan, Sanandaj, Iran

Background and Objective: The interface of the mesocorticolimbic dopamine system with other structures such as the hypothalamus is critical to long lasting molecular changes driving addiction. Increasing evidence has supported a contribution of the nuclear transcription factors in the development of addiction. We aim to examine the gene expression of NFκB, CREB and AP1in the hypothalamus of morphine-tolerant rats.
Materials and Methods: Male Wistar rats were used and randomly allocated to either saline-treated or morphine-treated groups. The experimental groups received a regimen of 8 days treatments of saline (1 ml/kg) or morphine

(10 mg/kg) twice daily. Induction of analgesic tolerance to repeated injections of morphine was assessed with a hotplate test of analgesia on day 8 of the schedule. On day 8, each rat was deeply anesthetized, decapitated and the hypothalamus was dissected immediately. The gene expression of NFκB, CREB and AP1 was examined by using a real-time PCR method.
Results: The results of the hotplate test of analgesia revealed that morphine treatments for 8 days induced tolerance to the analgesic effect of the opioid. The qPCR results indicated that the gene expressions of the CREB and AP1 in the hypothalamus of the morphine tolerant group were significantly increased compared to the saline-treated group but the gene expression of NFκB was not altered.
Conclusion: We conclude that the increases in the expression of nuclear transcription factors including CREB and AP1 involved, at least partly, in the development of molecular changes underlying morphine addiction and tolerance in the hypothalamus.
Keywords: Morphine tolerance, Hypothalamus, Nuclear transcription factors, CREB, AP1

P-634

Silk protein exhibits anti-depressant and anxiolytic properties through regulation of cerebral oxidative stress, neuroinflammation and apoptosis in a mouse model of spatial restraint stress

Javad Mahmoudi[1], Fereshteh Farajdokht[1], Ahad Banagozar Mohammadi[2], Saeed Sadigh-Eteghad[1], Seyed Mehdi Vatandoust[1]

1. Neurosciences Research Center, Tabriz University of medical Sciences, Tabriz, Iran.
2. Department of Traditional Medicine, Faculty of Traditional medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Background and objectives: Chronic stress induces a wide range of neurochemical and neurobehavioral alternations, resulting in mood disturbances. This study examined the effects of silk protein (Sericin), on anxiety- and depressive-like behaviors, oxidative stress, inflammation, and apoptosis in the prefrontal cortex (PFC) and hippocampus (HIP) of spatial restraint stress-subjected mice.
Materials and methods: Mice were randomized into 5 groups: control, restraint stress (RS), RS+ sericin100, RS+sericin150, and RS+sericin200. Animals in the stress groups were subjected to chronic spatial restraint stress (3 h/day for 21 days). Sericin-treated mice were received sericin (100, 150, and 200 mg/kg/day, gavage for 21 days) along with immobilization. Anxiety-like behaviors were assessed by elevated plus maze (EPM) and open field test (OFT), and depressive-like behaviors were evaluated by the forced swim test (FST) and tail suspension test (TST). Serum levels of corticosterone, mitochondrial membrane potential (MMP), and markers of oxidative stress, pro-inflammatory cytokines, and apoptosis-related proteins were evaluated in the PFC and HIP regions.
Results: Silk Sericin prolonged time spent in open arms of EPM apparatus and increased number of central entries in OFT. Moreover, it reduced immobility time in TST and FST. Furthermore, sericin decreased ROS and MDA levels, restored MMP, and enhanced total antioxidant capacity and enzyme activity of GPx and SOD, and decreased NF-κB, TNF-α, and IL-1β levels in HIP and PFC Additionally, sericin reduced corticosterone concentration and inhibited mitochondrial-dependent apoptosis pathway.
Conclusion: These findings provide evidence for the protective effect of sericin therapy against neurochemical and behavioral changes induced by restraint stress.
Keywords: Spatial restraint stress, Depression and anxiety-like behaviors, Sericin, Neuroinflammation, Apoptosis, Oxidative stress

P-635

Amygdala– and serum– neurotrophic factor levels depend on rearing condition in male rats

Belal Mosaferi[1], Shirin Babri[2], Gisou Mohaddes[3]

1. Department of Basic Sciences, School of Nursing and Midwifery, Maragheh University of Medical Sciences, Maragheh, Iran
2. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
3. Neuroscience Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Background and Objectives: Early life experiences could determine brain and behavioral development. Neurotrophic factors are likely to mediate the effects of the experience on brain structures and function. Brain-derived neurotrophic factor (BDNF) plays a central role in psychiatric disorders.
Materials and Methods: To investigate the effects of early rearing condition on the amygdala – and serum – BDNF levels, we reared male Wistar rats from weaning (postnatal days 21) to adulthood (postnatal days 119) in three different rearing conditions: (1) enriched, (2) standard and (3) isolated.
Results: We found that long-term post-weaning environmental enrichment leads to lower amygdala – and serum – BDNF levels as well as lower brain weights. Grouped rearing in standard laboratory cages enhanced body weight.
Conclusion: Thus, early rearing condition might play a crucial role in adult healthiness by predetermining individual BDNF profiles.
Keywords: amygdala; brain-derived neurotrophic factor; early life experiences; environmental enrichment;

P-636

Effects of Achillea biebersteinii Hydro-Alcoholic Extract on Anxiety Like-Behavior and Reproductive Parameters in Rat Model of Chronic Restraint Stress

Yasin Bagheri[1], Sina Moshtagh[2], Alireza Barati[2], Zahra Sabbaghi Rostami[2], Mohammad Bakhshi[2]

1. Young Researchers and Elite club, Tabriz Branch Islamic Azad university, Tabriz, Iran.
2. College of Veterinary Medicine, Islamic Azad University, Tabriz Branch, Tabriz, Iran.

Background and Objective: Achillea biebersteinii belongs to Asteraceae and has biological and medicinal properties. The objective of the present study was to elucidate the effect of the AT on anxiety behavior and reproductive characteristics, using male rats subjected to chronic restraint stress (CRS).
Materials and Methods: For this purpose, male Wistar rats (n=45) were allocated into five groups: control, one group received normal saline (2 ml/kg; p.o) with CRS and 3 groups received Achillea biebersteinii hydro-alcoholic extract (100, 200 and 300 mg/kg/day; p.o.) with CRS for 21 consequence days.
In the end, the testes tissue of rats in whole groups were removed and sperm was collected from the epididymis and prepared for analysis. The organs were weighed and the biochemical parameters assessed. Whereas, the rat's behavior was assessed in the elevated plus maze (EPM).
Results: The findings of this research revealed that extract of Achillea biebersteinii with different dose increased the entries and the time of open arm and decrease the entries and the time of close arm exploration in the EPM. Also indicated significant changes in fertility capacity, sperm parameters (motility, viability, and count), LH, FSH and testosterone levels in the Achillea biebersteinii extract treated rats compared to CRS rats ($p<0.05$).
Conclusion: These effects could be related to the bioactive molecules and secondary metabolites like alkaloids and flavonoids in the plant.
Keywords: Achillea biebersteinii, Chronic restraint stress, Anxiety like-behavioral, Sperm parameters, Rat

P-637

The Effect of Intracerebroventricular Administration of Calcitonin Gene Related Peptide and Rat-Calcitonin on CGRP and rCT mRNA in Periaqueductal Gray Matter of Formalin Tested Healthy and Diabetic Rats

Olya Moshiri[1], Javad Sajedianfard[1], Saeid Hosseinzadeh[2], Kaveh Rahimi[1], Saeideh Ahmadi Jokani[1]

1. Department of Basic Science, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.

2. Department of Food Hygiene and Public Health, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.

Background and objective: This study evaluates the effect of intracerebroventricular (ICV) administration of Calcitonin Gene Related Peptide (CGRP) and Rat-Calcitonin (rCT) on CGRP and rCT mRNAs' expression in periaqueductal gray (PAG) of healthy and diabetic rats which were subjected to formalin test.
Material and Methods: In this study, 48 male Sprague Dawley rats were assigned to eight groups (n=6). For induction of diabetes, streptozotocin (45mg/kg) was applied intraperitoneally. The animals in the diabetic and non-diabetic groups underwent stereotaxic surgery. One week after surgery, CGRP and rCT peptides with 1.5 nmol (5 µL) were injected (ICV) daily for 7 days. Twenty minutes after the last injection, 50µl of 2.5% formalin was injected subcutaneously into the right hind paw.
Pain related behaviors were recorded immediately for 60 minutes. The PAG nucleus was removed to evaluate the changes in CGRP and rCT related mRNAs' expression.
Results: In healthy rats, pain was reduced in acute, middle and chronic phases of formalin test. While, in diabetic rats, pain was reduced in the acute and middle phases of formalin test.
Conclusion: The ICV injections of CGRP and rCT peptides attenuated the formalin noiciceptive effect in healthy and diabetic rats due to increased expression of the mRNA of these peptides in PAG.
Keywords: mRNA, rCT, CGRP, Diabetes, pain.

P-638

Effect of scopolamine and mecamylamine on depressive-like behavior of rivastigmine in the tail suspension test

Azadeh Mesripour, Hasan Fakhr-hoseiny, Valiollah Hajhashemi

Department of Pharmacology and Toxicology, School of Pharmacy and Pharmaceutical Sciences, Isfahan university of Medical Sciences, Isfahan, IRAN

Background and objective: Rivastigmine is a, reversible non-competitive inhibitor of acetylcholinesterase used to treat mild to moderate dementia in Alzheimer's disease (AD) patients. Rivastigmine can decrease the severity of depression in AD patients. Apart from the monoamines hypothesis of despair, it is well known that depression is a disease of cholinergic domination. Thus regarding the antidepressant effect of rivastigmine, the aim was evaluating the influence of scopolamine (muscarinic cholinergic receptors antagonist) and/or mecamylamine (nicotinic cholinergic receptors antagonist) co-administration on the depression-like behavior in mice. Material and methods: depression-like behavior was evaluated by a despair model the tail suspension test in male mice, that was performed 30 min after drug administration. Immobility as an index of despair was recorded at the last 4 min of the trial. Rivastigmine (0.75 mg/kg, sc), scopolamine (0.5 mg/kg, ip) and/or mecamylamine (1 mg/kg, ip) were administered. Results: Rivastigmine by reducing the immobility time (90 ± 5.6 sec vs control 126s ± 1.9 sec, $p< 0.001$) proved to have antidepressant effects. The combination treatment of rivastigmine and scopolamine also significantly reduced the immobility time to 84 ± 0.5 sec ($p<0.001$compared with control). Mecamylamine prevented the antidepressant-like effects of rivastigmine when they were co-administered (immobility time= 131± 1.1 sec). Ultimately by administrating scopolamine and mecamylamine together with rivastigmine immobility time decreased significantly to 63±11 sec ($p<0.001$). Conclusion: It is possible that nicotine cholinergic receptors are prominent in the antidepressant effects of rivastigmine. Thus nicotine receptor stimulants could be considered for further researches regarding antidepressants.
Keywords: rivastigmine, depression, acetylcholine, tail suspension test

P-639

Morphine affects long term potentiation induced by different stimulation patterns at the Schaffer collateral-CA1 synapses of rat hippocampal slices

Masoumeh Mosleh, Javad Mirnajafi-Zadeh, Yaghoub Fathollahi

Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

Background: Morphine exposure affects hippocampal dependent learning and memory. Long-term potentiation (LTP) provides a compelling cellular model for learning and memory. Current experiments were therefore designed to study whether morphine would influence LTP induced by three types of LTP inducing protocols, differently.
Materials and Methods: Male Wistar rats (215–230 g) were made dependent by chronic administration of morphine in drinking water. Transverse hippocampal slices were prepared and incubated in morphine free/morphine containing aCSF. Stimulating and recording electrodes were placed on Schaffer collaterals of CA3 region and pyramidal cell dendrites of CA1 region, respectively. Field EPSP slopes were measured before and after LTP induction with 3 different LTP inducing protocols: high frequency stimulation, primed bursts and theta burst stimulation.
Results: Presence of morphine on the slices significantly increased the amount of LTP induced by three protocols compared to control slices. There was no significant difference in the amount of LTP among three protocols in control slices while significant difference was observed in the presence of morphine on the slices. Finally in morphine dependent rats LTP magnitude was significantly less than 2 other groups.
Conclusion: Morphine differentially modulates synaptic plasticity induced by different LTP inducing protocols.
Keywords: Morphine, stimulating pattern, Schaffer collaterals

P-640

Behavioral effect of yttrium oxide nanoparticles on improved spatial memory deficits by amyloid beta in male Wistar rats

Marzieh Meyari[1], Shahrbano oryan[1], Delaram Eslimi Esfahani[1], Akram Eidi[2], Adel Salari Esker[1,*]

1. Department of Animal Science, Faculty of Biological Sciences, Kharazmi University, Tehran, Iran
2. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran

Background and Objective: Amyloid-beta (Aβ) accumulation in the brain play a central role in Alzheimer's disease (AD) pathogenesis. The common late-onset form of AD is characterized by an overall impairment in Aβ clearance. Nanoparticles (NPs) have shown the significant effects on the beta-amyloid fibrillation, due to crossing the blood-brain barrier. According to neuroprotective effects of yttrium oxide nanoparticles (Y2O3 NP) on nerve tissues, in this study, we assessed behavioral effect of yttrium oxide nanoparticles on improved spatial memory deficits by amyloid beta, in male wistar rats.
Materials and Methods: In the present investigation, 42 male wistar rats (200 to 250 gr) were used. We injected Aβ1-40 bilaterally into the hippocampus of rats to mimic rat model of AD. Treatment was performed for 21 days with intraperitoneal injection of nanoparticles after induction of AD. Morris water maze test was used for behavioral study and assessment of learning and space memory of animals.
Results: The spatial memory index in AB group decreased significantly, compared to control and sham groups. In contrast, treatment groups with Y2O3 NP found the hidden platform in less time and less distance than Alzheimer's rats, which indicate improvement of spatial memory in Alzheimer's models.
Conclusion: These results indicate that Y2O3 with antioxidant activity could significantly ameliorate Aβ1-40-induced spatial learning and memory impairment in hippocampal neurons, suggesting that administration of yttrium oxide could provide a therapeutic approach for AD.
Keywords: Alzheimer, Yttrium oxide, Amyloid plaques, Morris water maze

P-641

Modified bilateral common carotid occlusion: A proper model for studying memory deficit?

Mehrnoush Moghaddasi[1], Majid Taati[2], Soheila Pourkhodadad[3]

1. Department of Physiology, Razi Herbal Medicines Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran
2. Department of Pathobiology, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran
3. National Cell Bank, Pasteur Institute of Iran, Tehran, Iran

Background and Objective: Reduction of cerebral blood flow has been shown is involved in the physiopathological mechanisms of cognitive decline in age-related disease. Several animal models have been developed to study the effects of chronic cerebral hypoperfusion (CCH). CCH can be induced in the rat by permanent occlusion of the two common carotid arteries, simultaneously. A modified method has been suggested in which the two-stage occlusion of two common carotid arteies, with a 1-week interval has been established. our study was designed to examine spatial learning and memory impairment following CCH induced by the modified 2VO method.

Materials and Methods: The animals were divided into two groups. Hypoperfusion groups (n = 36), cerebral hypoperfusion was induced by modified 2VO, the second group served as sham-operated controls (sham, n = 36). Then the animals in both groups were divided into three groups, the first group after 30 days, the second and third groups after 45 day and 60 days, respectively, their cognitive function was evaluated using the Morris water maze test (MWM).
Results: There was no significant differences in swim speed between the hypoperfusion and sham groups. Our results showed the escape latency and traveled distance in the hypoperfusion groups were decreased significantly in comparison with control groups after 30 days. Additionally, there was a significant difference in time spent in the target quadrant between the two groups ($p<0.05$). After 45 days, the escape latency and travelled distance was significantly less than sham groups, but the probe results were not significant between two groups. And finally after 60 days, there were not significant differences between two groups regarding the escape latency, travelled distance and time spent in the target quadrant.
Conclusion: in the modified 2VO, a stronger compensatory system is assumed since there is more time for compensating of the reduced blood flow. it appears that applying young rats and more delicate method recovered the learning and memory to the control level.
Key words: common carotid occlusion, modified two vessel occlusion, learning and memory, morris water maze

P-642

The effects of mental exercise and Nepeta menthoides on depression like behavior induced by reserpine

Maryam Malekian[1], Faezeh Rezaei[1], Batool Rahmati[2], Mohsen Khalili[2]

1. Department of Physiology, School of Medicine, Shahed University, Tehran, Iran
2. Neurophysiology Research Center, Shahed University, Tehran,Iran

Background and Objective: Many studies demonstrate that cognitive empowerment reduces the risk of depression. Anti-depressant properties of Nepeta menthoides as an herbal medicine has also been reported. This study aims to determine the effects of mental exercise and Nepeta menthoides on reserpine induced depression in rats.
Materials and Methods: Male rats were divided into 8 groups: 1-Saline, 2-Reserpine,3-Reserpine + Fluoxetine,4-Nepeta,5-Nepeta +Reserpine, 6-Mental exercise,7-Mental exercise+ Reserpine, 8-Mental exercise + Nepeta + Reserpine. Reserpine was administered at a dose of 0.2 mg/kg for 14 days.At the same time, the animals received Nepeta at the dose of 200 mg/kg and radial maze training. Then the results were assessed through forced swimming test (FST), sucrose preference, elevated plus maze and open field tests.
Results: Reserpine enhanced immobility and decreased active swimming time significantly, in the FST, while mental exercise combined with Nepeta were able to antagonize the effect of reserpine. Reserpine also lowered sucrose preference ratio which were recovered in mental exercise, Nepeta and combined treatment groups. Time spent and % of entrance in to the open arms have been increased by Nepeta and mental exercise relative to reserpine. Decreased locomotor activity due to reserpine had been improved in mental exercise and Nepeta groups. The mental exercise was also found to increase number of rearing as exploratory behavior.
Conclusion: Nepeta menthoides and mental exercise alleviated the depression symptoms caused by Reserpine.
Keywords: Depression, Reserpine, Mental Exercise, Nepeta menthoides

P-643

The effect of rosmarinic Acid on Liposaccharide-induced memory deficit in rat

Soroush Mazloomi[1], Tajmah Mombeini [2*], Mehrdad Roghani[3]

1. School of Medicine, Shahed University, Tehran, Iran
2. Department of Pharmacology, School of Medicine, Shahed University, Tehran, Iran
3. Neurophysiology Research Center, Shahed University, Tehran, Iran

Background and Objective Alzheimer disease (AD) is the most common type of dementia, and is currently incurable; Current treatments for AD produce only a modest amelioration of symptoms. Rosmarinic acid is a polyphenol with anti-inflammatory, antioxidant and neuroprotective properties. The aim of this study was to

investigate possible effect of rosmarinic acid (RA) on lipopolysaccharide-induced memory and learning deficit in rat.
Materials and Methods: 32 male rats were randomly divided into 5 groups: control, rats treated with saline and RA 20 mg/kg (RA20), tars treated with LPS, and two LPS groups treated with RA at doses of 5 and 20mg/ kg (LPS-RA5 and LPS-RA20). Rats treated were received saline or RA, daily by gavage for seven days. For induction of memory deficit, the LPS dissolved in normal saline at dose of 1mg/kg was injected intraperitoneally on the first day, one hour before the administration of drugs. After 24 h of the last dose, for evaluation of memory, passive avoidance test was performed.
Results: Results showed that in the LPS-RA20, treatment with RA had no significant effect on the initial latency. However, step-through latency was significantly increased, compared with the LPS group.
Conclusion: The results of this study indicated the beneficial effects of RA on improvement of memory in rats.
Keywords: Rosmarinic acid, Lipopolysaccharide, passive avoidance, rat

P-644

Minocycline mitigates tremor syndrome and defect of cognitive and balance induced by harmaline

Marzieh Maneshian[1,2], Farinaz Nasirinezhad[1], Fatemeh Mohammadi[2], Mina Behzadi[2], Majid Asadi –shekaari[2], Mohammad Shabani[2*]

1. Department of Physiology, Physiological Research Center, Iran University of Medical Sciences, Tehran, Iran
2. Intracellular Recording Lab, Kerman, Neuroscience Research Center, Neuropharmacology Institute, Kerman University of Medical Sciences, Kerman, Iran

Minocycline has been shown to exert anti-inflammatory, anti-apoptotic, and antioxidant effects. Preclinical data suggest that minocycline could be beneficial for treating common neurological disorders, including Parkinson's disease and multiple sclerosis. In the current study, the effects of minocycline on harmaline-induced motor and cognitive impairments were studied in male Wistar rats. Rats were divided into four groups of ten animals each. Harmaline was used for the induction of tremor. Minocycline (90 mg/kg, i.p.) was administered 30 minutes before the saline or harmaline. Tremor intensity, spontaneous locomotor activity, passive avoidance memory, anxiety related behaviors and motor function were assessed. The results showed that minocycline could recover tremor intensity and step width, but failed to recuperate the motor balance. The memory impairments observed in harmaline treated rats were somewhat reversed by administration of minocycline. The cerebellum and inferior olive nucleus were studied for neuronal degeneration using immunohistochemistry and transmission electron microscopy techniques. Harmaline caused ultrastructural changes and neuronal cell loss in inferior olive and cerebellar Purkinje cells. Minocycline exhibited neuroprotective changes on cerebellar Purkinje cells and inferior olivary neurons. These results open new therapeutic perspectives for motor and memory impairments in ET and complementary studies are needed to clarify the exact mechanisms.
Keywords: Essential tremor, Minocycline, Motor function, Memory

P-645

Neuroprotective effect of sumac extract on recognition memory impairment in rat model of Alzheimer's disease

Marzieh Mosavi mehr[1], Akbar Hajizadeh Moghaddam[1], Vahid Hasantabar[2], Sedigheh Khanjani Jelodar[3]

1. Department of Biology, Faculty of Basic Sciences, University of Mazandaran, Babolsar, Iran.
2. Department of Organic-Polymer Chemistry, Faculty of Chemistry, University of Mazandaran, Babolsar, Iran
3. Faculty of Biology, Shahid Beheshti University, Tehran, Iran.

Background and Objective: Alzheimer diseases (AD) is the most common cause of dementia wordwild. Sumac (Rhus coriaria L.) extract contains a high level of polyphenols such as gallic acid, hydrolysable tannins,

anthocyanins, and flavones. In this study, we investigate the neuroprotective effects of sumac extract on recognition memory impairment in a streptozotocin (STZ)-induced Alzheimer rat model.
Materials and Methods: Alzheimer's disease induced by intracerebroventricular administration of streptozotocin. Wistar rats were administrated with sumac extract at doses of 40 mg/kg for three weeks. Passive avoidance test was used for evaluation of learning and memory.
Results: Based on our results, a rat model of Alzheimer's disease (AD) exhibited recognition memory impairment ($P<0.001$). Sumac extract was significantly reversed recognition memory impairment compared to the STZ group ($P<0.001$).
Conclusion: These findings indicated that administration of sumac extract ameliorates STZ-induced learning and memory deficits through enhancing the antioxidant defense system.
Keywords: sumac extract; memory impairment; Streptozotocin; rat

P-646

Zinc supplementation during pregnancy improves working memory impairment and inflammatory response in an animal model of schizophrenia.

Ronak Mousaviyan[1], Faezeh Alizadeh[2], Nahid Davoodian[3]

1. Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2. Department of Biochemistry, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
3. Molecular Medicine Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Background and objective: Schizophrenia is a neuropsychiatric illness affecting one percent of the world population. Among the multitude factors, maternal exposure to infectious agents such as lipopolysaccharide (LPS) has been shown to increase the risk of schizophrenia in the next generation. Due to the important role of Zinc in brain function, in the present study, we utilized maternal LPS injection on gestational days (GD) 15 and 16 as a model for schizophrenia to investigate whether zinc supplementation can prevent LPS-associated alterations.
Material and method: On GD 15 and 16, pregnant rats received intraperitoneal injection of LPS (500µg/kg) and supplemented with ZnSO4 (30mg/kg) throughout pregnancy by gavage.at postnatal day 60, Y-maze was used to assess working memory of male offspring. The expression level of Tumor necrosis factor α (TNFα) and inducible Nitric oxide synthase (iNOS) was evaluated by q-PCR. Furthermore, immunostaining was carried out for ionized calcium-binding adapter molecule 1 (Iba1) in the frontal cortex.
Results: Working memory impairment as well as increased mRNA level of TNFα and iNOS, and microglia reactivity was detected for male offspring which prenatally exposed to LPS. However, maternal zinc supplementation could reverse the mentioned deficits.
Conclusion: The present study supports the idea that the deleterious effects of prenatal LPS exposure could be attenuated by zinc supplementation during pregnancy.
Key words: Schizophrenia, lipopolysaccharide, zinc supplementation, microglia

P-647

Chronic administration of vitamin E ameliorate oxidative stress in the hippocampus of pups from alcoholic mothers

Rahebeh Mahdinia

Background and Objective: Prenatal exposure to ethanol produces fetal alcohol syndrome (FAS) involve abnormal CNS development including loss of neurons, decreased brain mass and neurobehavioral deficits such as impaired memory and learning. Previous studies suggested that generation of oxidative stress, depletion of protective endogenous antioxidants, or both of them are the important mechanism underlying FAS. The aim of this study was to investigate the effects of vitamin E, as a potent antioxidant on oxidative stress markers in the hippocampus of pups from alcoholic mothers.
Materials and Methods: Pregnant Wistar rats received ethanol (4g/kg) and vitamin E (100, 200 and 400 mg/kg) on day 1 of gestation until weaning by oral gavage. At the end of treatment (postnatal day 28), the activities of several antioxidant enzymes including superoxide dismutase (SOD), glutathione peroxidase (GPx) and the amount of glutathione (oxidized and reduced forms) in the hippocampus were assayed. Also, malondialdehyde (MDA) and carbonyl levels were measured as markers of lipid and protein oxidation in the hippocampus of pups.

Results: Our Results demonstrated that ethanol exposure could induce lipid and protein oxidation, and decrease glutathione peroxidase activity, glutathione levels, GSH/GSSG ratio in the rat hippocampus. Further, vitamin E can ameliorate these effects.
Conclusion: We conclude that vitamin E can ameliorate oxidative stress levels in the hippocampus of pups from alcoholic mothers.
Keywords: Ethanol, Vitamin E, Oxidative stress, Fetal alcohol syndrome, Hippocampus

P-648

Protective effect of Hydralazine on a cellular model of Parkinson's disease: a 2 possible role of hypoxia-inducible factor (HIF)-1α

Mehrnaz Mehrabania[1], Mohammad Hadi Nematollahi[2,3], Kobra Bahrampour Juybari[4], Mojde Esmaeili Tarzi[5], Ali Mohammad Sharifi[6], Hamze Paseban[7], Mohsen Saravanih[8,9], Solmaz Mirzamohammadi[10*]

1. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Kerman Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
3. Department of Clinical Biochemistry, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran
4. Department of Pharmacology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran
5. Cardiovascular research center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
6. Department of Pharmacology and Razi Drug Research Center, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
7. Herbal and Traditional Medicines Research Center, Kerman University of Medical Sciences, Kerman, Iran
8. Cellular and Molecular Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
9. Department of Clinical Biochemistry, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
10. School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran

Background and Objective: Parkinson's disease (PD) is a chronic neurodegenerative disease that is commonly associated with a low level of the cerebral hypoxia-inducible factor (HIF-1α). Hence, activating the hypoxia-signaling pathway may be considered a favorable therapeutic approach for PD treatment. The present study explored the efficacy of hydralazine, a well-known antihypertensive drug, for restoring the impaired HIF-1 signaling in PD, with the aid of 6-hydroxydopamine (6-OHDA)-exposed SH-SY5Y human neuroblastoma cells.
Materials and Methods: To obtain the effects of various concentrations of hydralazine and 6-OHDA on the viability of SH-SY5Y cells, MTT-assay was performed. Then, the protective effect of hydralazine against 6-OHDA was assessed by MTT and apoptosis detection assays. Eventually, expressions of HIF-1α, VEGF, tyrosine hydroxylase (TH) and dopamine transporter (DAT) at protein levels were measured by western blotting.
Results: Hydralazine was non-toxic at the concentration of ≤50 μM in SH-SY5Y cells. Furthermore, it significantly attenuated apoptotic death induced by 6-OHDA. At a non-toxic concentration, hydralazine significantly up-regulated expressions of HIF-1α, VEGF, TH, and DAT proteins in the treated cells in comparison with the 6-OHDA-exposed group.
Conclusion: The present data suggested that pharmacological priming with hydralazine via up-regulation of HIF-1α and related neuroprotective target genes could attenuate the deleterious effects of 6-OHDA on the SH-SY5Y cells.
Keywords: Parkinson disease, Hydralazine, HIF-1α, 6-OHDA, SH-SY5Y cells

P-649

Effect of clavulanic acid on memory dysfunction: In vitro and in vivo assay

Soghra Mehri[1], Hossein Hosseinzadeh[1], Samaneh Silakhori [2], Saeedeh Adelkhah[2]

1. Pharmaceutical Research Center, Institute of Pharmaceutical Technology, Mashhad University of Medical Sciences, Mashhad, Iran
2. School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
3. School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: Clavulanic acid (CA) as a non-competitive inhibitor of β-lactamase has weak antibiotic activity. Important properties of CA including good oral bioavailability, low antibiotic activity and good CNS penetration have nominated this compound for evaluation neuroprotective effects.

Trimethyltin chloride (TMT) is a potent neurotoxic agent in both human and animals producing significant and selective neurodegeneration in the limbic system and is particularly toxic to the hippocampal formation, which finally induces profound memory impairment. Therefore, the effect of CA against TMT-induced neurotoxicity in PC12 cells and in rat (as a model of memory impairment) was evaluated.
Materials and Methods: Cell viability, reactive oxygen species production (ROS) and the level of apoptotic proteins were evaluated using MTT assay, DCFH-DA method and western blot analysis, respectively.
Memory impairment was induced using single dose administration of TMT. CA (50, 100 and 200 mg/kg) was administrated IP for 20 days. Learning and memory function were determined using the Morris water maze test. GSH and MDA contents and the level of proteins that are involved in apoptosis pathway were determined.
Results: TMT reduced cell viability, increased ROS production and induced apoptosis in PC12 cells while CA protected against TMT-induced toxicity. Administration of CA significantly recovered memory dysfunction induced by TMT. In addition, oxidative stress and the levels of apoptotic proteins were reduced in rat hippocampus following administration of CA.
Conclusion: Inhibition of oxidative stress and modulation of apoptosis pathway proteins were considered as main mechanisms behind neuroprotective effects of CA.
Keywords: Clavulanic acid, Trimethyltin, Memory impairment, Apoptosis

P-650

Antagonism of the ghrelin receptor in the rat brain downregulate the hippocampal Htr1A receptors of serotonin

Atefeh Mirzabeh, Siamak Beheshti

Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran

Background and Objective: Ghrelin affect memory formation. We have previously shown that antagonism of the ghrelin receptors in the rat brain impair memory consolidation. However, the underlying mechanisms are not well-known. It was shown that ghrelin can influence serotonergic signaling in the brain. We aimed to evaluate the effect of i.c.v injection of a ghrelin receptor antagonist (D-Lys-3-GHRP-6) on the gene expression levels of the hippocampal Htr1A receptors of serotonin.
Materials and methods: Fifteen adult male Wistar rats weighing 250 g were implanted with cannulas in their lateral ventricles. Three groups of animals (n=5) received D-Lys-3-GHRP-6 (0.5 and 5nM) or saline. Twenty-four hours thereafter, their hippocampus was removed. The Htr1A gene expression levels were measured using a quantitative Real-time PCR method.
Results: One-way ANOVA indicated a significant decrease in the expression levels of Htr1A receptors of serotonin. Post-hoc comparison showed that D-Lys-3-GHRP-6 (5nM) downregulated the gene expression levels of the hippocampal Htr1A receptors, compared to the control group.
Conclusion: It seems that part of the impairing effect of i.c.v injection of D-Lys-3-GHRP-6 on memory consolidation might be due to a decrease in the Htr1A receptors of serotonin in the hippocampus of rats.
Keywords: D-Lys-3-GHRP-6, Hippocampus, Htr1A, Serotonin

P-651

Roles of GABA of the KF nucleus in generating the cardiovascular chemoreflex, a cardiovascular and single-unit study

Nafiseh Mirzaei Damabi[1], Masoumeh Hatam[1] and Ali Nasimi[2]

1. Department of Physiology, Shiraz University of Medical Science, Shiraz, Iran
2. Department of Physiology, Esfahan University of Medical Science, Esfahan, Iran

Background and Objective: The Kölliker-Fuse (KF) nucleus is part of the parabrachial complex, located in the dorsal lateral pons. It is involved in the respiratory chemoreflex but its role in the cardiovascular chemoreflex has not been established yet. This study was performed to determine the role of GABAA receptors in cardiovascular chemoreflex in anesthetized rat.

Material and Methods: Experiments were done on urethane (1.4 g/kg,ip) anesthetized male rats. The femoral artery and vein were cannulated for recording blood pressure (BP), heart rate (HR), and drug administration. Extracellular single unit action potentials simultaneously recorded. The chemoreflex evoked by i.v. injection of KCN(80 µg/kg) before, 5, 15 and 40min bilateral microinjection saline (100nl) , Cobalt chloride (5mM/100 nl), bicuculline(BMI) (1 mM) in to the KF. The KCN exhibited short excitatory response on KF neurons with a short pressor followed by bradycardic responses.
Results: Microinjection of saline had no significant effect on pressor and bradycardia responses. Microinjection of CoCl2, a synaptic blocker, into the KF significantly were attenuated both responses by confirming the role of the KF in generating the reflex. Blockade of GABAA receptors by BMI potentiated both blood pressure and heart rate responses.
Conclusion: In conclusion, the KF plays a major role in generating cardiovascular chemoreflex and GABAergic system of the KF inhibits both components of this reflex through GABAA receptors. Single-unit results were also presented and their correlation with the homodynamic findings was discussed.
Keywords: Kölliker-Fuse, Chemoreflex, Bicuculline, CoCl2

P-652

The neuroprotective effect of Ketone body on a model of nervous lesion (M.S.) in the mice

Vahideh Mirzaei

Background and objective: Multiple Sclerosis (M.S.) is an inflammatory demyelinating disease of the central nerves system in which neuropathic pain is recognized as a major symptom,. The neuropathic pain is the least understood and most difficult to treat. We showed that in a chronic- relapsing animal model of M.S., experimental autoimmune encephalomyelitis (EAE), characteristic neuropathic behaviors such as hyperalgesia and allodynia. There is growing evidence that ketone bodies have broad neuroprotective effects.
Although the mechanisms underlaying the neuroprotectivity of ketone bodies have not yet been fully elucidated. Based on the neuroprotective effects the ketone body injection ,betahydroxybutyrate (BHB), has been used in the treatment of EAE.
Materials and Methods: 30 female C57BL/6 mice were allocated to 3 groups: Control, EAE. Group and EAE. Group under treatment with BHB. (5.0 mM/kg/d) for 9 consecutive days. Neuropathic pain behaviors were analysed such as thermal hyperalgesia, mechanical allodynia and tail flick.
Results: The results showed that the BHB. Injection has great effects in the neuropathic pain behaviors. Our findings demonstrate that BHB. Injection in EAE. Mice reduced thermal hyperalgesia and mechanical allodynia, even more strikingly in the decrease of the score of EAE.
Conclusion: Our results showed that exogenous BHB. Can prevent neuropathic pain and has neuroprotectivity effects in a animal model of M.S.(EAE.).
Keywords: Ketone body, EAE. , M.S. , Neuropathic pain, Neuroprotectivity

P-653

Changes in fatty acid composition in spinal cord of ethidium bromide-treated rats as a multiple sclerosis (MS) model; GC-MS evaluation

Nafise Sadat Mirshafieyan[1], Majid Hassanpour-ezatti[*1], Hossien Dehgan[2]

1. Department of Biology, Basic Sciences School, Shahed University, Tehran Iran
2. Medicinal Plants Research Center, Shahed University, Tehran, Iran

The compositions of fatty acids (FAs) in nervous tissues of animal models of MS may have important roles in the process and mechanisms related to the onset and progress of this disease. The purpose of this study was to evaluate the effects of ethidium bromide (ET), which used for induction of neurodegenerative symptoms in rats, on spinal

FAs profile in rats. The present study used gas chromatography-mass spectrometry (GC-MS) analysis of fatty acid methyl esters (FAMES) to profile all detectable FA species present in rats spinal cord tissue homogenate after treatment with intraspinally injection of ET (0.02mg/ml). Quantitative analysis was done on spinal cord samples of normal and ET-treated rats (n=6 per group). GC-MS analysis of FAMES detected a total of 24 FAs and of these, 13 were fully quantifiable. The results showed significant alterations in ET-treated rat spinal cord FA concentrations. A total of 3 FAs were elevated in ET-treated samples with arachidic, oleic and eicosenoic acid increased most (100%; P=0.033). Docosahexanoic acid, Vaccenic acid and linoleic acid concentrations were decreased (47%; P=0.018) which accordance with the findings of others in other region of nervous after the onset of MS. Furthermore, our results appear to indicate that alteration of FAs at spinal level in ET model of MS in rats. These preliminary findings pinpoint FAs disturbances at spinal cord level have been occurred and may be potentially important in the pathology of MS.
Keywords: Fatty acid, Gas Chromatography-Mass Spectrometry, Ethidium bromide, Multiple Sclerosis, Spinal cord, Rats

P-654

Anti-inflammatory effects of levothyroxine in a rat model of multiple sclerosis

Mohammad Ali Mirshekar

Department of Physiology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

Objective: Multiple sclerosis (MS) is a CNS autoimmune disease. since metformin (Met) play a crucial role in development and physiological function of the CNS and reduces memory impairment, the effect of Met on the improvement of cognitive deficits of MS induced by lysolecithine was studied in rats.
Materials and Methods: 40 Wistar rats randomly divided into five groups, sham, Met, MS group, MS group receiving Met and positive control group. The Shuttle Box and Morris water maze were used to investigate passive avoidance and spatial memory. Also, the hippocampus level interleukin-6 (IL- 6) and TNF alpha were measured by a special kit.
Results: IL- 6 and TNF-α in the Met treated group showed a significant reduction compared to the MS group. Behavioral evaluation also showed that Met significantly improved the ability to store information and remind them in the passive avoidance and to improve spatial memory in the Morris water maze.
Discussion: It seems that treatment with Met is able to prevent cognitive deficits. Positive effects of Met may be due to decrements in TNF-α and IL- 6 concentrations as pro-inflammatory factor. these results suggest that Met can be used as an effective ingredient in the treatment of MS.
Keywords: Multiple sclerosis, Met, Inflammation, Cognition

P-655

In-vivo evaluation of some hybrid derivatives based on dimethyl fumarate-benzothiazole scaffold as candidates for Multiple Sclerosis (MS) treatment

Seyedeh Azin Mirmotahhari[1], Farshid hassanzadeh[1], Mahboubeh Rostami[1], Mehdi Aliomrani[2], Hajar Sirous[3]

1. Master of Science student of Medicinal Chemistry, Department of Medicinal Chemistry, School of Pharmacy and pharmaceutical Sciences, Isfahan University of Medical Science, Iran
2. Department of Medicinal Chemistry, School of Pharmacy and pharmaceutical Sciences, Isfahan University of Medical Science, Iran
3. Department of Pharmacology and Toxicology of Pharmacy and pharmaceutical Sciences, Isfahan University of Medical Science, Iran
4. Bioinformatics Research Center, School of Pharmacy and pharmaceutical Sciences, Isfahan University of Medical Science, Iran

Background and Objective: Riluzole and dimethyl fumarate(DMF) are two the most important approved drugs for Multiple Sclerosis control. The mechanism of Riluzole, a benzothiazole derivative, is attributed to its inhibitory effects on the glutamate release by antagonizing the NMDA(N-Methyl-D-Aspartate) receptor. The DMF in turn up-regulates an array of anti-oxidative pathways.
We described some new hybride derivatives, which have at once both inhibition of NMDA and anti-oxidative activities. The binding models for these molecules to NMDA active site were assessed by molecular docking. Then the best compounds were synthesized and the in-vivo evaluations in C57/BL6 mice were done.
Materials and Methods: 49 designed derivatives were studied in-silico using AUTODOCK 4.2 software package. Then synthesis of designed compounds were done. For in-vivo studies, C57BL/6 male mice was randomly divided into 11 groups and were fed with food containing cuprizone for 5 weeks. The first group were checked after 5weeks to ensure that the disease was induced. The second group were fed with a normal diet after 5 weeks to examine the process of myelination. To the third and fourth group, after 5 weeks, Riluzole and DMF were injected intraperitoneally for 7 days respectively. To the fifth group, a mixture of both drugs were injected. To groups 6 to 11,the synthesized compounds were given. All the groups were anesthetized and their brains were removed. Brain sections stained with luxol fast blue and the images were analyzed.
Results: Our findings including ΔGbind,were expressed. The NMR and FTIR spectrum of derivatives confirmed the synthesis of structures. Also images of brain confirmed that the derivateives were effective.
Conclusion: These hybrid molecules have more efficacy and fewer side effects in comparison with previous individual drugs.
Keywords: Multiple Sclerosis , NMDA , Riluzole , Dimethyl fumarate , Invivo studies , Molecular docking , Synthesis

P-656

A survey of the effects of diosmin on learning and memory following the use of paraquat herbicide poisoning in a model of rats

Mohammad Ali Mirshekar[1,2], Somayeh Miri[1], Ali Shahraki[*3]

1. Department of Physiology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
2. Clinical Immunology Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
3. Department of Biology, Faculty of Sciences, University of Sistan and Baluchestan, Zahedan, Iran;

Objective: Exposure to herbicide paraquat (PQT) is a potential risk factor for cognitive impairment. Many cognitive behaviors, including spatial memory, passive avoidance, balance, and motor performance, may be affected by PQT. This study aimed at determining cognitive behaviors, motor function, and malondialdehyde (MDA) content of the hippocampus after i.p. injection of PQT in rats and evaluating the effects of diosmin (DM) in preventing PQT effects on cognitive behaviors and MDA level in the hippocampus.
Methods: In this study, 32 male Wistar rats were divided randomly into four groups: control, PQT (4 ml/kg), DM (100 mg/kg), and DM+PQT. PQT (4 mg/kg, i.p.) was used three times a day for one week to develop a cognitive deficit model. The rats were pretreated using DM (100 mg/kg) for seven days before PQT administration. Passive avoidance task (PAT), rotarod test, and spatial memory tests were also performed. The MDA level was measured in the hippocampus of different groups to determine lipid peroxidation.
Results: Based on the findings, 100 mg/kg of DM increased the step-through latency, total time in the target quarter, and bar latency in the cognitive deficit model ($P<0.01$ and $P< 0.001$, respectively). The hippocampal concentration of MDA was significantly lower in the DM+PQT group, compared with the PQT group ($P<0.001$).
Conclusion: DM could effectively prevent cognitive deficits (spatial memory and passive avoidance) and motor dysfunctions induced by PQT administration. Also, MDA concentration reduced in the hippocampus induced by i.p. injection of PQT. The present study suggests DM as a suitable compound for memory restoration in cases of PQT poisoning

P-657

Paroxetine attenuates cerebral ischemia/reperfusion injury in rat via its anti-inflammatory and antioxidant effects

YazdanNaderi[1*], SiavashParvardeh[2], MasoumehSabetkasaei[2], Ehsan Aali

1. Department of Pharmacology, School of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran
2. Department of Pharmacology, School of Medicine, ShahidBeheshti University of Medical Sciences, Tehran, Iran

Cerebral ischemia is often associated with sensory-motor impairment and memory deficit. Previous studies have demonstrated that paroxetine, the antidepressant drug, exhibits anti-inflammatory and antioxidant effects. In this study, we investigated the protective effects of paroxetine on neuronal damage and activation of microglial cells induced by cerebral ischemia/reperfusion in the rat.Cerebral ischemia/reperfusion injury was induced by transient bilateral common carotid artery occlusion. TheWistar rats were assigned to sham, ischemia, and paroxetine-treated

groups. Paroxetine(10 mg/kg) was administered intraperitoneallyonce daily for 7 days subsequent to surgery. In order to evaluate spatial memory in rats, Morris water maze test (MWM) was conducted. The viability of pyramidal neurons in the hippocampus was assessed by Nissl staining method. Microglial activation and production of pro-inflammatory cytokines (IL-1β,TNF-α) wereexamined using Iba1-immunostaining and ELISA methods, respectively. Oxidative stress was evaluated by measuring the levels of malondialdehyde(MDA)in homogenates of hippocampal tissue.In MWM test, paroxetine significantly enhanced learning performance in rats subjected to cerebral ischemia/reperfusion. Nissl staining showed an increase in the number of surviving pyramidal neurons in paroxetine-treated group. Our findings indicated that paroxetinesignificantly suppressed ischemia-induced microglial activation and decreased the IL-1β and TNF-α levels in the hippocampus. In addition, paroxetine inhibited lipid peroxidation and decreased MDA levels in homogenates of hippocampal tissue. These results establish that paroxetineexert a protective effect against cerebral ischemia/reperfusion-induced damage to hippocampal neurons and memory impairment in rats through anti-inflammatory and antioxidant effects.
Keywords:Brain ischemia;Microglia; Cytokine; Memory; SSRI

P-658

Effect of acute administration of caffeine and the role of nitric oxid pathway on neuropathic pain threshold in a rat model of chronic constriction injury

Naderi Tehrani M*, Heydari Azh, Hamidi Gh, Nasrollahi S

Physiology Research Center, Kashan University of Medical Sciences, Kashan, I. R. Iran

Objective: Neuropathic pain caused by nervous system damage or system dysfunction. The pathogenesis and the mechanism underlying neuropathic pain remains unclear.
This study was designed to determine whether acute administration of caffeine was effective in alleviating symptoms of neuropathic pain.
Materials and Methods: Neuropathic pain was induced by chronic constriction injury (CCI) of the sciatic nerve in rats(8 group ,n=8), which resulted in thermal hyperalgesia and allodynia. Caffeine (non selective antagonist of adenosine receptors), 10,50 and 100 mg/kg ,l- NAME (non-selective NOS inhibitor) at a dose of 30 mg / kg and L-Arginine (precursor NO) at a dose of 100 mg / kg alone and 30 minutes before Received the best dose of caffeine (50 mg/kg) , IP, were administered on the 4, 7,14,21and28th and days after surgery . Behavioral tests were done at 30 min after drug injections
Results: caffeine at the dose of 50 mg / kg and 100 mg Kg / kg significantly decreased thermal hyperalgesia . In the LNAME received groups, hyperalgesia, and thermal allodynia Significantly decreased. The levels of nitric oxide metabolites (NOx) increased significantly in that groups of 10, 50, 100 mg / kg of caffeine compared to the control group.
Conclusion: Our results suggest that caffeine can be considered a potential therapeutic for the treatment of neuropathic pain.

P-659

The effect of ethyl acetate extract of oleo-gum-resin of ferula assa-foetida L. on painful diabetic neuropathy in adult male rats

Samad Nazemi[1], Hamid Rudsarabi[2], Hasan Azhdari Zarmehri[3]

1. Department of Physiology & Pharmacology, School of Medicine, Sabzevar University of medical Sciences, Sabzevar, Iran.
2. Student Research Committee, Sabzevar University of Medical Sciences, Sabzevar, Iran
3. Department of Basic Sciences and Neurosciences Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

Background and Objective: Painful diabetic neuropathy is a well-known and often progressive complication in both types of diabetes which does not respond well to the common pain medications. Using medicinal herbs can help to

find new pain medications with more efficacy and less side effects. This study aimed to evaluate the effect of ethyl acetate extract of Asafoetida on painful diabetic neuropathy induced by streptozotocin (STZ) in adult male rats.
Materials and methods: In this experiment, 40male Wistar rats (230-280g) were used. Diabetes was induced by intraperitoneal (ip) injection of single dose of STZ (60mg/kg). Animals were randomly divided into five groups including: control, diabetic and 3diabetic groups were treated with the Asafoetida extract at dose of 25, 50, 100 mg/kg for 25 days. To evaluate the neuropathic changes, Tail-flick and von-Frey tests were performed on post diabetic days (PDD) 0, 7, 14, 21 and 28, ($P<0.05$).
Results: Behavioral results showed that, diabetic neuropathy was established in PDD21. Asafoetida extract with the dose of 50 mg/kg ($P<0.05$) and 100mg/kg ($P<0.01$) prevented the induction of thermal hyperalgesia, whereas this response was observed only for the dose of 100mg/kg in the case of mechanical allodynia ($P<0.05$). In addition, blood glucose concentration in the extract treated groups was decreased in a dose-dependent manner ($P<0.05$).
Conclusion: Ethyl acetate extract of asafoetida can prevent the development of painful diabetic neuropathy. Further studies are required to identify the bioactive components present in this extract and their mechanisms of action in reducing diabetic neuropathic pain.
Keywords: Neuropathic pain; Diabetes; STZ; Hyperalgesia; Allodynia

P-660

Protective effects of fullerene nanoparticles on learning and memory, histopathological changes of brain and genes expression of mTOR and HIF-1α in streptozotocin-induced experimental diabetes mellitus

Fariba Namdar

Background and Objective: Diabetes induces brain injury with a wide profile of micro and macrostructural changes, leading to neurodegeneration, neurovascular deterioration, neuroinflammation and progressive cognition dysfunction. Present study evaluated the effects of fullerene nanopaticles on cognitive functions, histopathological changes of brain and genes expression of mTOR and HIF-1α in streptozotocin-induced experimental diabetes mellitus.
Materials and Methods: Male Wistar rats (190-220 g) were randomly divided into four groups (each n=8); normal, treated normal, diabetic, and treated diabetic groups. Diabetes was induced in the rats by an intravenous injection of streptozotocin (40 mg/kg). Treated rats received orally fullerene nanoparticles at dose of 1 mg/kg/day for eight weeks. At the end of experiment, histopathological changes, antioxidant parameters and genes expression of mTOR and HIF-1α in hypocampus as well as learning and memory were assessed.
Results: Chronic hyperglycemia (blood glucose >400 mg/dL) significantly decreased learning and memory functions in diabetic rats. Hyperglycemia decreased the mTOR expression by 61% and increased HIF-1α expression by 65% in accompany with histopathological changes of hypocampus in diabetic rats. Treatment with fullerene improved learning and memory functions of diabetic rats without changing blood glucose. Fullerene also increased mTOR expression by 48% and decreased HIF-1α expression by 29% in accompany with improvement of histopathological changes and antioxidant parameters of hypocampus in treated diabetic rats.
Conclusion: Our findings indicated that fullerene nanoparticles effectively prevented diabetes-induced dementia and cognitive decline in diabetes. It is suggested that mTOR increment and HIF-1α reduction may play a crucial role in improvement of cognitive functions.
Keywords: Diabetes mellitus, Fullerene, HIF-1α, Cognision, Hypocampus

P-661

The effect of hydro-alcoholic extract of Curcuma longa on pain and Pentylenetetrazol induced seizure mice

Fatemeh Nabi[1*], Fatemeh Taleahmad[1], Mahdi Alizadeh[1], Fariba Ansari[1], Mohsen Khalili[2], Zahra Kiasalari[2]

1. School of Medicine, Shahed University, Tehran, Iran.
2. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective: Pain is an abrasive sense. Considering that there is no proper treatment for pain and epilepsy, while chemical drugs have adverse effects, we decided to study the effect of the Curcuma longa on pain and seizure.
Materials and Methods: Forty-five NMRI male mice were randomly allocated to 5 groups, Control, positive control and three groups under treatment with curcuma longa extract (25, 50 and 100 mg/kg). Formalin and Tail immersion tests were used to measure pain volume and for kindling we used PTZ-induced seizure mice.
Result: Curcumin extract in all doses (25, 50 & 100 mg/kg) effectively reduced acute pain in Formalin test. Obtained data from tail immersion test showed that all doses were effective to reducing acute pain in 5 and 10 min after extract injection. However, Curcuma extract at all doses and especially at 50 mg/kg could reduce onset seizure time in PTZ kindling test.
Conclusion: Our data showed that all doses of Curcumin extract can reduce acute pain. Also anticonvulsant activity of the extract was shown at dose of 50 mg/kg.
Keywords: Pain, Seizure, Mice, Curcumin

P-662

Tauopathy in spinal cord injury: a systematic review

Elnaz Nakhjiri[1], Behzad Abedi[2], Hamid Soltani-Zangbar[3], Koorosh Shahpasand[4], Parviz Shahabi[3]

1. Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran
2. Medical Bioengineering Department, School of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
3. Neurosciences Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
4. Department of Brain and Cognitive Sciences, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Objective: Spinal cord injury (SCI) is one of the major causes of death and disabilities among all traumas. Many CNS biomarkers are being evaluated for their potential to assess the severity of SCI. The ideal biomarker would be a molecular marker specific for injured nervous tissue that would provide a reliable assessment of the presence and severity of injury. Tau, a microtubule-associated protein abundant in the axonal compartment of neurons, is candidate biomarker. Following axonal injury, tau becomes modified primarily by hyperphosphorylation and cleavage into smaller fragments. These posttrauma products can leak into the CSF or bloodstream. We focused on the potential for hyperphosphorylated and cleaved tau as sensitive biomarkers of injury.
Methods: This study aims to systematically review the literature on publications that have investigated prognostic biomarkers in either the blood or CSF of animals and humans following SCI.
Results: The PubMed search identified 123 publications, of which 20 were selected and critically reviewed.
Conclusion: Few studies have aimed at the discovery of biomarkers within the CSF or blood in this field. Several studies using various animal models and some with small human patient cohorts have begun to pinpoint biomarkers in the CSF and blood with putative prognostic value. Increased sample size will be required to validate these biomarkers. Posttraumatic tau products, such as c-tau and p-tau are attractive candidates as SCI biomarkers, and future research should focus on the potential of these tau products to serve as biomarkers for SCI.
Keywords: Tau, Biomarker, Spinal cord injury, Systematic review

P-663

Comparison the convulsive potential of pentylentetrazol and pilocarpine

Giti Nasudi [1], Mahmoud Elahdadi Salmani[1], Narges Hoseinmardi[2], Taghi Lashkarbolouki[1], Iran Goudarzi[1]

1. Department of animal biology, Faculty of biology, Damghan University, Iran
2. Department of Physiology, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Iran

Background and Aim: Seizures are caused by sudden, abnormal electrical activity in the brain, which can damage the brain. Seizure models affect the brain differently, which may have a negative impact on the outcome of the

experiments. The greater the severity of the seizures, the greater the damage to the brain. Therefore, in this study, the convulsive effects of pentylentetrazol and pilocarpine will be compared.
Methods: In this experimental study, 24 adult male Wistar rats were allocated into two groups. In the first group, seizure was induced by a single intravenous injection of petylentetrazole (30 mg/Kg i.v). The second group, seizure was induced by a single intraperitoneal injection of lithium and pilocarpine (3 mEq of lithium followed 20 hours by 30 mg/Kg of pilocarpine). The latency from injection to the first convulsions and from that point to tocic-clonic (TC) behaviors were ascribed as latency 1 and 2. The duration of the TC was measured as a criterion for seizure intensity.
Results: The results of this study showed that the latency1 And 2 for the onset of seizures, induced by pentyltentetrazole, decreased significantly compared with the pilocarpine group ($P<0.001$). Duration of seizures ($P<0.05$), the percentage of tonic-clonic seizures and mortality rate in the pentyltentetrazole group increased significantly.
Conclusion: Based on the results of this study, the pentylentetrazole provokes a higher seizure intensity and quicker attackes than the pilocarpine model and this may impose a negative strong impact on the brain structure and function.
Keywords: Pentylentetrazole, Pilocarpine, Convulsion.

P-664

Orexin 1 receptors in the nucleus accumbens' shell reversed the devastating effect of olanzapine on effort-based decision-making in the rat

Saeedeh Nasrollahi , Alireza Abed , Sara karimi , Monire Naderi tehrani , Gholamali Hamidi*

Physiology Research Center, Kashan University of Medical Sciences, Kashan, Iran; Department of Physiology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, Iran

Effort-based decision making, a common form of cost-benefit decision making, requires one to decide how much effort to expend for a certain amount of reward. Orexin is a crucial neuropeptide in the physiological aspect specially variety of effective and cognitive processes. The nucleus accumbens (NAc) is a region of neural system that serves effort-based decision making and Orexin 1 receptor (OX1R) is distributed extensively throughout nucleus accumbens shell (AcbS). Olanzapine (OLZ), a typical antipsychotic drug, has a high affinity to D2 as an antagonist and also partial agonistic-like action at D2 receptors has been reported. We examined the interaction of OLZ with orexinergic receptor 1 in AcbS on effort-based decision making in cost–benefit T-maze task. Two goal arms were different in the amount of accessible reward. The animals had to pass the barrier for receiving high reward in one arm (HRA) or obtain a low reward in the other arm without any cost. Before surgery, all animals were selecting the HRA on almost every trial. During test days, the rats received local injections of either DMSO 20% /0.5µl, as vehicle, or SB334867(30, 100, 300 nM/0.5µl), as selective OX1R antagonist, within the AcbS. Other group received OLZ (10µg/rat) / vehicle alone or SB334867 (300 nM/0.5µl), 5 min before administration of OLZ. The results showed that administration of OLZ in the AcbS alters rat's preference for high reward in effort-based decision- making. On the other hand, blocked of the OX1R (300 nM/0.5µl) in this region could reverse the effect of OLZ, however, administration of the OX1R antagonist alone in the AcbS led to decreasing rat's preference for high reward. This result indicates that orexin-1 antagonist might affect some effects of antipsychotic drugs

P-665

Effects of probiotic (combination of Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) on memory processes in LPS-induced rats

Marjan Nassiri-Asl[1*], Ghazaleh Mohammadi[2], Leila Dargahi[3], Amir Peymani[4]

1. Department of Pharmacology, Qazvin University of Medical Sciences, Qazvin
2. Department of Molecular Medicine, Qazvin University of Medical Sciences, Qazvin, Iran;
3. NeuroBiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Medical Microbiology Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

Background and Objective: In recent years, the role of gut microbiota in pathogenesis of several neurodegenerative disorders including Alzheimer's disease (AD) has been demonstrated. Therefore, targeted modification of gut microbiota composition by probiotics seems to be a beneficial and promising approach to improve these conditions via gut-brain axis. In this regard, there are limited evidences about the effect of probiotics on cellular and molecular pathways associated with AD.
In addition, identification of effective probiotics on different types of mechanisms involved in AD is needed. This study was designed to assess the effects of probiotic (L.helveticus R0052+B.longum R0175) on inflammation, apoptosis and memory processes in LPS-induced rats.
Materials and Methods: In rats, maltodextrin or probiotic (109 CFU/ml/rat) was administered by gavage for 14 consecutive days and then saline or LPS (1 mg/kg, i.p) was injected. After 4 hours, memory retention was evaluated by passive avoidance test, subsequently serum and hippocampal samples were collected for assessment by ELISA and western blotting.
Results: Probiotic pretreatment significantly decreased both serum and hippocampal levels of TNFα and IL1β in LPS-exposed rats. Probiotic administration also remarkably up-regulated Procaspase-3 while down-regulated Cleaved caspase-3 expression in hippocampus of LPS-induced rats. In addition, decremental effect of LPS on memory was attenuated through increasing of BDNF and step through latency. However, this positive effect of probiotic was not significant at behavioral level.
Conclusion: Probiotic pretreatment (L.helveticus R0052 + B.longum R0175) could be considered as a beneficial intervention to improve neuroinflammation-associated disorders, similar to AD.
Keywords: Probiotic; Neuroinflammation; Apoptosis; Memory; Lipopolysaccharide; Alzheimer's disease

P-666

Functional coupling of the brain mitochondrial ATP-sensitive large conductance Ca+2-activated K+ channel (mitoBKCa) to respiratory chain in amyloid-β Alzheimer model rats

Maryam Nazari[1, 2], Nihad Torabi[1, 2], Javad Fahanik-Babaei[2], Adele Jafari[3], Afsaneh Eliassi[* 1, 2]

1. Department of Physiology, Medical School, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Neurophysiology Research Center& Department of Physiology, Guilan University of Medical Sciences, Rasht, Iran

Introduction: Previously, we showed that the 211 pS mitoBKCa channel activity was negatively altered in Aβ toxicity. In the current study, the 565 pS mitoBKCa channel function and respiratory chain activity considered in a model of Aβ toxicity.
Material and methods: Aβ1–42 (4 μg/μl/side) was injected intracerebroventricularly in male Wistar rats (220-250 g). After 14 days, mitochondrial inner membranes extraction incorporated into bilayer lipid membrane (BLM). L-α Phosphatidylcholine was extracted from fresh egg yolk to form BLM in a 150 μm diameter hole. All recordings were filtered at 1 kHz and stored at a sampling rate of 10 kHz for offline analysis by PClamp10. Additionally, we determined the activities of mitochondrial complexes I and IV, ROS and Δψ levels in control and Aβ groups.
Results: The conductance and open probability of the Alzheimer's channel reduced 2.5 folds compared to control group. Our data explained an equivalent gating charge (Zd) = -5.8 ± 1.1 and Vmid = 27.2 ± 1.15 in Aβ model compared to Zd = 2.49, and Vmid = -74.08 mV in control rats which caused a right shift in the channel voltage dependence. Furthermore, Alzheimer disease reduced mitochondrial activities of complexes I and IV, Δψ and increased ROS production.
Conclusion: Current study reports the possible structural and functional coupling of the mitoBKCa channel with the mitochondrial respiratory chain. Our results may provide new insights into the cellular mechanisms underlying mitochondrial dysfunctions in Aβ neurotoxicity.
Keywords: Amyloid-β, Mitochondria, BKCa channel, Respiratory chain.

P-667

Conditioned medium obtained from human amniotic mesenchymal stem cells attenuates focal cerebral ischemia/ reperfusion injury in rats

Donya Nazarinia[1], Nahid Aboutaleb[1*], Raheleh Gholamzadeh[1], Solmaz Nasseri Maleki[1], Mahin Nikougoftar[2]

1. Physiology Research Center and Department of Physiology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, Iran

Background and objective: Stroke is a cerebrovascular disorder that results in a high degree of mortality and morbidity around the world. Previous studies have shown that conditioned medium (CM) obtained from mesenchymal stem cells (MSCs) might exert neuroprotective effects against different neurodegenerative disorder. The present study was performed to investigate whether the amniotic mesenchymal stem cells-conditioned medium (AMSC-CM) can confer neuroprotection against focal cerebral ischemia/ reperfusion (I/R) injury by improving neurological function and reduction of infarct volume
Materials and methods: A rat model of middle cerebral artery occlusion (MCAO) was created and the animals were divided into three groups including sham, MCAO and MCAO+ hAMSC-CM. The AMSC-CM at the dose of 1 µl was intravenously administrated to rats. Infarct volume neurobehavioral functions, were assessed 24 h after reperfusion using 2, 3,5-Triphenyltetrazolium chloride (TTC) staining and neurological scores, respectively.
Results: intravenously administration of AMSC-CM markedly reduced infarct volume compared to MCAO group ($P < 0.05$). Additionally, treatment with AMSC-CM significantly reduced neurological motor disorders compared to MCAO group ($P < 0.05$).
Conclusion: Collectively, our results demonstrated that hAMSC-CM contributed to neuroprotection following ischemic stroke by reduction of infarct volume and improving neurobehavioral functions. These findings suggest the validity of AMSC-CM as a good therapeutic agent for acute stage stroke.
Key words: cerebral ischemia/ reperfusion; amniotic mesenchymal stem cells; conditioned medium; infarct volume; neurological motor disorders

P-668

Protective effect of piperine on hippocampal synaptic plasticity impairment in streptozotocin-induced model of Alzheimer's disease

Nazifi Masoomeh[1], Ashrafpour Manouchehr[2], Oryan Shahrbano[1], Eslimi Delaram[1]

1. Department of Animal Sciences; Faculty of Biological Sciences; Kharazmi University; Tehran; Iran
2. Neuroscience Research Center; Health Research Institute and Department of Physiology; School of Medicine; Babol University of Medical Sciences; Babol; Iran

Background and Objective: Alzheimer's disease is an neurodegenrative disorder associated with defictis in cognition and synaptic plasticity. The present study examined the effect of chronic piperine treatment on synaptic plasticity at dentate gyrus in rat model of intracerebroventricular-streptozotocin (ICV-STZ) induced Alzheimer's disease (AD).
Materials and Methods: Adult male rats were randomly assigned into 5 groups. For induction of Alzheimer model, rats were injected with ICV STZ bilaterally, on days 1 and 3 (3 mg/kg. Following the four week treatment with piperine, the local field potentials in the dentate gyrus were recorded in response to perforant path stimulation. Field excitatory post-synaptic potential (fEPSP) slope and population spike (PS) amplitude were analyzed.
Results: There were no significant differences in the baseline activity of granule cells between the groups. Long-term potentiation (LTP) was significantly decreased in the ICV-STZ group. Piperine treatment restores ICV-STZ-induced impairments in induction and maintenance of LTP with a significant potentiation of both fEPSP slope and PS amplitude components throughout the recording period.
Conclusion: The positive effect of piperine on the synaptic transmission supports its previously reported behavioral effects on improvement of impaired spatial memory in the Alzheimeric animals.
Keywords: piperine; Long-term potentiation; Alzheimer's; streptozotocin

P-669

Neuroprotective effect of quercetin on oxidative stress and apoptosis of motor neurons in cultured spinal cord slices of adult mouse

Hamid Reza Noghli, Hamid Reza Momeni, Niloufar Darbandi

Department of biology, faculty of Science, Arak University, Arak, Iran.

Background and Objective: Oxidative stress is one of mechanisms involved in apoptosis of motor neurons during neurodegenerative diseases and spinal cord injuries. Despite of extensive researches, there is no universally accepted

treatment for these diseases. Therefore, the aim of this study was to investigate if quercetin, as a powerful antioxidant, with reducing oxidative stress is able to delay the apoptosis of motor neurons in cultured spinal cord slices.
Materials and Methods: Thoracic region of spinal cord of adult mouse was cut into 500 µm slices. The slices were then divided to three groups: 1. Freshly prepared slices (0 hour); 2. Control slices; 3. Slices treated with quercetin (100 µM). The control and the treated slices were cultured in a medium for 6 hours in a CO2 incubator. Morphological features of apoptosis in the motor neurons were studied using fluorescent staining. The amount of malondialdehyde (MDA) and Ferric reducing antioxidant power (FRAP) were assessed for evaluating lipid peroxidation and total antioxidant power respectively.
Results: After 6 hours, the motor neurons displayed morphological features of apoptosis compared to the control group. At this time point, quercetin not only delayed morphological features of apoptosis in the motor neurons but also significantly compensate the changes MDA and FRAP in the cultured slices.
Conclusion: Since quercetin was able to reduce lipid peroxidation, increase the total antioxidant power and delay the morphological features of apoptosis, it is possible that oxidative stress is responsible for apoptosis of motor neurons.
Keywords: Apoptosis, Oxidative stress, Quercetin, Motor neuron, Spinal cord slices

P-670

Modulating proteoglycan receptor PTPσ using intracellular sigma peptide improves remyelination in demyelinated optic chiasm of mice

Parvin Niknam[1], Yaghoub Fathollahi[1], Mohammad Javan[1, 2*]

1. Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
2. Department of Brain and Cognitive Sciences, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

Background and Objective: Multiple sclerosis (MS) is an autoimmune disease characterized by myelin and axonal damage in the central nervous system. Glial scar is a hallmark of this disease which is rich of inhibitory molecules. Dominant component of glial scar is chondroitin sulfate proteoglycans (CSPGs) that inhibits repair of damaged area through various receptors including protein tyrosine phosphatase sigma (PTPσ). Given the role of PTPσ in mediating the inhibitory effects of CSPGs on oligodendrocyte remyelination, in this study we investigated the effect of PTPσ inhibition, on myelin repair in an animal model of myelin destruction in mouse optic chiasm.
Material and methods: We inhibited PTPσ receptor in LPC-induced focal demyelination of mouse optic chiasm by systemic administration of intracellular sigma peptide (ISP), as an inhibitor of PTPσ signaling. Then, we investigated the effect of ISP on myelin repair using histological, immunofluorescence techniques.
Results: LFB (myelin-specific dye) staining, FluoroMyelin (myelin marker) staining and immunostaining against myelin antigen (Myelin basic protein (MBP)) indicated that ISP treatment resulted in decreased demyelination at 14 dpi. In addition toluidine blue staining on semi-thin coronal sections of optic chiasm and g-ratio analysis showed an increased g-ratio in LPC group while LPC+ISP group showed reduced amounts of g-ratio toward the control.
Conclusion: Current study showed that the animals which were challenged with a demyelinating insult by LPC and received daily treatment with ISP, showed reduced demyelination and enhanced remyelination at 14 dpi.
Keywords: Multiple sclerosis, CSPG, oligodendrocyte, PTPσ, Myelin repair, Demyelination, Remyelination.

P-671

Effect of quercetin, ghrelin and exercise on the expression of genes BDNF, cytochrome b and caspase3 model of Parkinson in male mice MPTP- induced

Neda Nikokalam Nazif[1], Maryam Khosravi[1], Ramesh Ahmadi[2], Maryam Bananej[1], Ahmad Majd[1]

1. Department of Biology, Faculty of Biological Sciences, North-Tehran Branch, Islamic Azad University, Tehran, Iran.
2. Department of Physiology, Qom Branch, Islamic Azad University, Qom, Iran.

Background and objective: Parkinson's disease is a neurodegenerative disease of central nervous system, characterized by dopaminergic neuronal loss in the nigrostriatal pathway with clinical symptoms. In this study quercetin, ghrelin and exercise have a neuroprotective effect to prevent the greater loss of substantia nigra dopaminergic neurons improves the brain function.

Materials and Methods: Thirty -six mice were randomly allocated to 6 groups: control, MPTP (25 mg/kg i.p), MPTP+ quercetin(25 mg/kg), MPTP +ghrelin (0.0004mg/kg i.p), MPTP+ exercise, and MPTP + quercetin+ ghrelin+ exercise. To induce PD model, MPTP 25 mg/kg (25 mg per 5 cc normal saline) was injected intrapritoneally (i.p.) for four days and catalepsy was assessed by test bars. Quercetin (25 mg / kg) was gavaged for 42 days and ghrelin was injected (i.p., 0.000 4mg/Kg) for 42 days.Mice in exercise group were forced to have treadmill exercise (5 days a week for 20 minutes at a speed of 24 meters per minute at zero slope). After behavioral evaluation, mice were anesthetized, brains were removed, and the expression of genes BDNF, cytochrome b and caspase3, was evaluation using Specified kits. Data were analyzed using SPSS.
Results: The catalepsy was significantly reduced in MPTP mice treated with quercetin, ghrelin and exercise.Treatment with quercetin, ghrelin and exercise groups the most BDNF,cytochrome b, caspase3 expression genes and the least MPTP group BDNF,cytochrome b, caspase3 expression genes was observed.
Conclusion: Our results showed that a combined treatment with quercetin, ghrelin and exercise could be a potential treatment for Parkinson's disease.
Keywords: Parkinson's disease, Quercetin, Ghrelin, Exercise, Expression of genes.

P-672

Effect of melatonin on diabetic retinopathy in rats

Vahid Nikoui[1], Saeed Mehrzadi[1], Karim Hemati[2], Mohammad Yahya Karimi[1], Azam Hosseinzadeh[1], Azam Bakhtiarian[3], Golrokh Malihi[4], Muhammad Imran Khan[5], Mario Giorgi[6], Masood Naseripour[7]

1. Razi Drug Research Center, Iran University of Medical Sciences, Tehran, Iran.
2. Department of Anesthesiology, Critical Care and Pain Medicine, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
3. Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.
4. Fargol Research Group, Ballwin, MO, USA.
5. Department of Pharmacy, Kohat University of Science and Technology, 26000 Kohat, Pakistan.
6. Department of Veterinary Sciences, Veterinary Teaching Hospital, University of Pisa, Via Livornese (lato monte), San Piero a Grado, Italy.
7. Eye Research Center, Rassoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran.

Background and Objective: Diabetic retinopathy is a complication of diabetes, which damages the blood vessels in the retina. The aim of the present experiment was to evaluate the effects of oxidative stress factors and melatonin on diabetic retinopathy in rats.
Materials and Methods: Male rats were randomly divided into three groups of control, diabetic, and diabetic treated with melatonin (10 mg/kg) orally for two weeks. Ten weeks after streptozocin-induced induction of diabetes, retina were removed and studied for malondialdehyde (MDA) levels and superoxide dismutase (SOD) activity. One-way analysis of variance (ANOVA) followed by Tukey's post-hoc test was used for statistical analyses. $P \leq 0.05$ was considered statistically significant.
Results: Induction of diabetes significantly boosted the MDA levels and decreased the SOD activity in retina compared to control group ($P \leq 0.05$). However, treatment of diabetic animals with melatonin could not reverse them, significantly ($P > 0.05$).
Conclusion: It is concluded that oxidative stress factors play a dramatic role in diabetic retinopathy.
Keywords: Melatonin, Diabetic retinopathy, Oxidative stress factors

P-673

Effect of acute L-Carnitine administration on pentylenetetrazole (PTZ) -induced clonic and tonic seizure thresholds in mice

Sayyed Morteza Vaghefi[1,2], Azhdar Heydari[2,3], Hassan Jamali[1,2]

1. Student Research Committee, Kashan University of Medical Sciences, Kashan, I.R. Iran
2. Physiology Research Center, Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, I.R. Iran
3. Department of Physiology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, I.R. Iran

Background and Objective: L-Carnitine is a unique nutritional supplement for athletes that has been recently studied as a potential treatment for certain neuropsychiatric disorders. However, its efficacy in seizure control has a few

investigated. Thus, the aim of the current study was to investigate the effects of acute administration of L-Carnitine on pentylenetetrazole (PTZ) -induced clonic and tonic seizure thresholds in mice.
Materials and Methods: Male NMRI mice weighing 25-30 g (n=10 in each group) were used in this study. L-Carnitine was administrated at doses of 50, 100, 150 and 200 mg/kg via gastric gavage 4 hour before the seizure induction. Intravenous infusion of PTZ was used to induce seizure signs and latencies to the occurrence of general clonus and tonic hind limb extension were recorded to calculate the threshold doses.
Results: L-Carnitine at doses of 50, 100 and 150 mg/kg did not significantly change PTZ-induced seizure thresholds of the clonic or tonic hind limb extension. On the other hand, L-Carnitine at dose of 200 mg/kg significantly increased seizure thresholds of clonic ($P<0.001$) and tonic hind limb extension ($P<0.05$).
Conclusion: The results of the present study confirm and extent the previous reports that some doses of L-Carnitine have anticonvulsant effect. Profound effect of L-Carnitine on seizure threshold of clonic in this study may represent the different sensitivity of forebrain and hindbrain seizure circuitry to L-Carnitine. Considering the anticonvulsant effect of L-Carnitine, more investigations should be carried out to clarify the exact mechanisms.
Keyword: L-Carnitine, Pentylenetetrazole, Seizure

P-674

Dose-dependent anticonvulsant and protective effects of metformin in kainate induced temporal lobe epilepsy

Somayeh Vazifekhah[1], Farnaz Nikbakht [*2], Paria Hashemi [1], Ali mohammad khanizadeh [1]

1. Department of Physiology, School of medicine, Iran University of Medical Sciences. Tehran. Iran
2. Cellular and molecular research center and Department of Physiology, School of medicine, Iran University of Medical Sciences. Tehran. Iran

Metformin, the most commonly prescribed antidiabetic drug, has been shown to be effective in controlling seizures in some studies. However, there are some reports of proconvulsant activity of metformin in diabetic patients. The aim of the present study was to investigate the effects of metformin dosage on anti-seizure and neuronal protective activity. Male Wistar rats were randomly divided into 5 groups as follows: 1-control/vehicle group, 2- Kainic acid (KA), 3-metformin+KA (50 mg/kg), 4-metformin+KA (100 mg/kg), 5- metformin+KA (200 mg/kg). Temporal lobe epilepsy (TLE) was induced by injection of 0.5 µg kainite into the left lateral ventricle. Metformin was administered orally for two weeks before the induction of TLE.
We found that metformin at higher doses (100 and 200 mg/kg) significantly suppressed the progression of seizure in TLE and ameliorated the neuronal loss in the hippocampus induced by KA. However, the low dose of metformin had no effect. We concluded that metformin may be a potential agent for the treatment of epilepsy and seizure and this effect is dose dependent.
Keywords: Metformin, epilepsy, dose dependent, neuroprotection, anticonvulsant

P-675

Role of insulin-like growth factor 2 (IGF-2) in memory impairment following intracerebral hemorrhage

Farzaneh Vafaee[1, 2], Asadollah Zarifkar[3], Masoumeh Emamghoreishi[4], Mohammad Reza Namavar[5]

1. Neuroscience Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Neuroscience, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran
3. Department of Physiology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
4. Department of Pharmacology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
5. Clinical Neurology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction: The insulin-like growth factor 2 (IGF-2) is a growth factor and anti-inflammatory cytokine that playing a key role in memory consolidation. The present study aimed to examine the variations in distribution and gene expression of the IGF-2 on different days following acute hippocampal damage and investigate the role of IGF-2 on memory impairment and cell death resulting from intracerebral hemorrhage (ICH).
Materials and Methods: ICH was induced by injection of 100 μL of autologous blood into the left hippocampus of 64 male Sprague-Dawley rats. Recombinant IGF-2 was injected inside the damaged hippocampus 30 min after the induction of ICH. Then, on postoperative days 1, 3, 7, and 14, behavioral tests were performed and a sample of brain tissue was collected to immunohistochemical and RT-PCR examinations.
Results: Passive avoidance memory had a significant reduction in ICH group compared to sham groups and recombinant IGF-2 led to significant improve in this memory, but no significant difference was observed in recognition memory. Immunohistochemical data showed that the IGF-2 distribution was increased in ICH groups, but significantly reduced in IGF-2 group. The expression of IGF-2 gene was increased in all groups compared to the controls, but no significant difference was seen between sham and ICH groups. The injection of IGF-2 led to a significant decrease in gene expression.
Conclusion: The dispersion and gene expression of the IGF-2 are likely to increase in order to improve the damage. Moreover, the injection of IGF-2 can improve memory and alleviate the infarct.
Keywords: Intracerebral hemorrhage; Insulin-Like Growth Factor 2; Learning and Memory; Hippocampus

P-676

The Effect of extract of Prangos Ferulacea on Behavioral, Motor and Cognitive Functions in Autistic Model Rats

Arefe Vafaeinejad[1,2], Mehrnoush Rahmani[1,2], Abbas Ali Vafaei[2], Abbas Ali Taherian[2], Ali Rahidypour[2]

1. Student Research Committee, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran
2. Research Center Physiology, Semnan University of Medical Sciences, Semnan, Iran

Introduction: Previous studies have shown that autism, or self-preservation, is a type of neurodegenerative disorder commonly seen in social communication and relations. Previous studies suggested that Prangos Ferulacea (PF) had potent antioxidant effects and probably had a beneficial effect on autism related disorders. Accordingly, the aim of this study was to determine the effect of extract of PF on behavioral, motor and cognitive functions in autistic model rats in experimental rats.
Materials and Methods: In this experimental study, valproic acid was injected on day 12 of pregnancy (when the embryonic development of the neural tube occurs) for induction of autism. Also, some groups were injected with PF (25 And 50 mg / kg body weight) or vehicle intraperitoneally. On the other hand, all rats were tested on days 30 and 60 (Elevated Plus Maze, Hot plate, Rotarod, Open field and T Maze). Data were analyzed using SPSS.
Results: Data analysis showed that injection of valproic acid can cause behavioral disorders including decreased social interactions, increased repetitive behaviors, increased pain tolerance thresholds, increased anxiety, decreased exploring behaviors, reduced balance power and motor learning, and cognitive change in rat infants undergo postnatal evaluation, which is usually done on days 30 and 60, and the administration of extract of PF can significantly modify these abnormalities. ($P<0.05$).
Conclusion: These findings showed that PF can modify behavioral, motor and cognitive functions in autistic model rat and may be effective in the pharmacological treatment of autistic dysfunction.
Keywords: Autism, Prangos Ferulacea, Valproic acid, Rat

P-677

Effects of different addictive foods on memory in male rats

Ghazaleh Hadian*, Maryam Radahmadi, Hojjatalah Alaei, Parham Reisi

Department of Physiology, Medical School, Isfahan University of Medical Sciences

Introduction : Lifestyle factors such as food diet influenced memory. In addition, people have major interest to some palatable foods (such as different kinds of chocolate and sugar). Hence, they interest to intake them repeatedly. These foods were considered as addictive foods. This study investigated the effect of different addictive foods such as kinds of chocolate with various percentage of cocoa and sugar (from low to high), and even sugar on the short, mid and long-term memories in male rats.

Materials and Methods: Male Wistar rats were randomly allocated to five groups of control, dark chocolate (97% cocoa), milk chocolate (60% cocoa), white chocolate (10% cocoa) and sugar (0% cocoa) for 14 days. Memory was evaluated using by passive avoidance test at intervals of 1, 7, and 14 days after a foot shock.
Results: Intake of dark and milk chocolates significantly improved short-term memory (after 1 day) and particularly mid- term memory (after 7 days). Also, only the dark chocolate showed a significant enhancement on long-term memory (after 14 days). White chocolate and sugar did not have significant effects on three kinds of memory.
Conclusion: The percentage of cocoa in the kinds of chocolates is very important on three kinds of memory. However, the effects of dark and milk chocolate were stronger on improvement of mid-term memory than short and long-term memory. Also, only effects of dark chocolate was permanent through days 1-14 after induction of foot shock. White chocolate and sugar as addictive food impaired memory.
Keywords: Chocolate, Sugar, Memory, Rats.

P-678

Evaluation of the neuroprotective, anticonvulsant, and cognition improvement effects of apigenin in model of temporal lobe epilepsy: Involvement of the mitochondrial apoptotic pathway

Paria Hashemi[1], Farnaz Nikbakht[2] , Javad Fahanik Babaei[1] , Somaye Vazifekhah[1]

1. Department of Physiology, School of medicine, Iran University of Medical Sciences. Tehran. Iran
2. Cellular and Molecular research center and Department of Physiology, School of medicine and, Iran University of Medical Sciences. Tehran. Iran

Background and Objective: The Cognitive deficit is a common problem in epilepsy. A major concern emergent from the use of antiepileptic drugs includes their side effects on learning and memory. Herbal medicine is considered a complementary and alternative therapy in epilepsy. Apigenin is a safe flavone with antioxidant properties. However, there is little information about the beneficial effect of apigenin in epilepsy. Therefore, in the present study effects of apigenin on memory deficit was evaluated in a rat model of temporal lobe epilepsy.
Materials and Methods: Forty-four rats were randomely divided to 4 groups: Control vehicle, apigenin-sham, kainic acid, apigenin+kainic acid. Apigenin was orally administered (50 mg/kg) for six days. Reference and working memory were examined via Morris water maze and Y maze task spontaneously. Data were analyzed using SPSS.
Results: Results showed that apigenin had significant anticonvulsant activity ($P<0.01$) and restored the memory-deficit induced by kainic acid ($P<0.05$). Furthermore, apigenin significantly increased the number of living neurons in the hilus ($P < 0.001$). Immunohistochemical analysis showed that apigenin reduced the release of cytochrome c ($P< 0.01$).
Conclusion: These results suggest that apigenin restores memory impairment via anticonvulsant and neuroprotective activity by inhibitory effect on intrinsic apoptotic pathway.
Keywords: Apigenin; Anticonvulsant; Cognition; Neuroprotection; Temporal lobe epilepsy; cytochrome c

P-679

Intra-hippocampal L-NAME low dose did not affect morphine antinociception in the rat formalin test

Mahboobeh Hashemi[1], Manizheh Karami[2*], Mohammad Reza Zarrindast[3,4]

1. Ph.D student, Dept of Biology, Faculty of Basic Sciences, Shahed University
2. Dept of Biology, Faculty of Basic Sciences, Shahed University
3. Dept of Pharmacology, Faculty of Medicine, Tehran University of Medical Sciences
4. Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Tehran, Iran

Introduction: This laboratory has shown previously that intra-hippocampal CA1 injections of L-arginine, a nitric oxide (NO) precursor, can attenuate the morphine-induced antinociception in rat formalin test. We investigated the NG-Nitro-L-arginine Methyl Ester (L-NAME), the NO synthase inhibitor, intra-CA1 injection to interfere with the morphine anti-pain effect using rat formalin test.
Methods: Male Wistar rats in group control received subcutaneous (s.c.) injections of formalin (50 µl at 2.5%) once prior to testing. Morphine identified dose (6 mg/kg) was injected intraperituneally (i.p.) 10 min before injection of formalin. L-NAME (0.25-2 µg/rat) pre-administered (5 min) prior to the morphine injection pre-testing. Early and late phases of the formalin test were calculated and compared with the morphine as well as the control data.
Results: Morphine in comparison to the control induced a significant anti-pain response both in early and late phases; however, L-NAME low (0.25 µg/rat) rather higher doses did not reverse that response.
Conclusion: L-NAME low dose, based on the finding, most probably cannot interact with the modulator NO, so, it did not affect the antinociception induced of morphine in the rat hippocampal CA1.
Key Words: Morphine, L-NAME, NO, Antinociception, Formalin test

P-680

The effects of Lithium chloride and cathodal/anodal transcranial Direct Current Stimulation on the level of p-CREB/CREB in PFC of male NMRI mice

Mojgan Hamdami[1], Nida Jamali-Raeufy[1], Turan Dokht Balouchnejad Mojarrad[1], Mohammad Nasehi[2] , Solmaz Khalifeh[2]

1. Department of Medical Physiology, Iran University of Medical Sciences, Tehran, Iran.
2. Cognitive and Neuroscience Research Centre, Amir-Almomenin Hospital, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran.

Background: Lithium clinically used to treat mental diseases albeit it has cognitive impairment side effects, however, research has consistently shown that microinjection of lithium has neuroprotective effect thus effect on molecular factors like cAMP Responsive Element Binding protein (CREB) that has crucial role in synaptic plasticity, in addition, there has been an increasing interest in brain stimulation methods such as transcranial direct current stimulation (tDCS). tDCs changed the neural activity of brain areas with applying two-electrode placed around the stimulation region on the scalp. In spite of the aim of this study is to provide a conceptual, theoretical framework based on molecular changes induced by Lithium and anodal/cathodal tDCS in male NMRI mice.
Methods: Six groups include 4 mice is taken in this study, for tDCS(cathodal/anodal) mice implanted electrode was placed on the skull over the Left prefrontal, after recovery period they had consecutive three days Lithium/saline intraperitoneally injection followed by, tDCS administered for 20minutes with 2mA. All animals were sacrificed on the last day of the experiment, the PFC was dissected and placed in a liquid nitrogen tank immediately, later tissues were transformed for further analysis of CREB by Western Blotting Technique. Data analyzed with SPSS. Results: The level of p-CREB/CREB increased significantly after Lithium administration, however in mice which received Lithium and cathodal tDCS level of protein decreased although anodal tDCS solely increased p-CREB protein level.
Conclusion: Present study showed inducing the effect of Lithium injection on p-CREB protein level as same as anodal, while decreased by cathodal.
Keywords: Lithium; CREB; Cathodal tDCS; Anodal tDCS; PFC

P-681

Opium protects brain against ischemic injury through reducing inflammation and enhancing antioxidant defense in male rat

Salimeh Yarahmadzehi, Mohammad Ali Mirshekar, Hamed Fanaei

Department of Physiology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

Objective: Brain ischemia is an arterial vascular disorder. The second cause of death in the world. In this study, the effect of oral consumption of opium on the inflammation status, oxidative stress, infarction volume and neurological function after the stroke in male rats were investigated.
Materials and Methods: In this study, a total of 48 male Wistar rats were used in a range of 250-280g. Rats were randomly selected and divided into 3 groups of 16 animals. Animals were evaluated for neurological examination 24 hours after stroke. The cerebral edema and the size of the infarction region were evaluated by Image j software, and the concentration of TAC, MDA, TNF-α , and CRP of the brain tissue was measured as an indicator of inflammation and oxidative stress.
Results: TAC concentration in the opium group was significantly higher than that of the stroke groups. Also, the TNF-α CRP MDA concentration in the opium group was significantly lower than that of the stroke groups. The rate of cerebral edema and ischemic region in the opium group was significantly lower than that of the stroke groups. Also, the opium group had better neurological performance than the stroke group.
Discussion: Based on the results of this study, the use of opium by enhancing the antioxidant capacity and weakening immune responses after cerebral ischemia can reduce the amount of damage.
Keywords: Opium, cerebral ischemia, inflammation, oxidative stress

P-682

Effect of betahistine on depression induced by PTZ in kindled mice

Azadeh Yazdi*[1], Mohammadmahdi Doostmohammadi[2], Farshid Pourhossein Majareshin[2]

1. Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
2. Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran

Background and Objective: Epilepsy is a brain disorder characterized by repeated and spontaneous convulsion. Epidemiological studies have shown the higher prevalence of depression and anxiety-like behavior in epileptic patients than healthy people. Central histamine plays a critical role in anxiety and depression. The histaminergic system enhances an antidepressant- like responses mainly via activation of the H1 receptor and inhibition of the H3 receptor. Betahistine acts as a histamine H1 receptor agonist and H3 receptor antagonist. These effects lead to an increase in histamine level of the brain. In the current study, we evaluated the impact of betahistine administration in depression induced by PTZ in kindled mice.
Materials and Methods: Kindling model was induced by i.p. injection of PTZ (36 mg/kg) once every 48 h until stage 5 of the seizure on three consecutive trials was achieved. Different doses of betahistine (1, 10, 20 mg/kg) were administrated every day started eight days before PTZ injection continued until scarification. Forced swimming test was evaluated in both kindled (control) and treated groups.
Results: The finding showed that repetitive and chronic administration of betahistine at dose 10 mg/kg significantly decreased the depression-like behavior induced by PTZ in forced swimming test ($P< 0.05$). However, dose 1 and 20 mg/kg did not have any antidepressant effect.
Conclusion: Chronic pretreatment of betahistine at dose 10 mg/kg decreases the depression in mice.
Key words: betahistine, histamine, depression, epilepsy, PTZ

P-683

The effect of very low frequency electromagnetic waves on the formalin-induced pain in male rats

Elham Yousef Haghi[1], Shiva Khezri[1], Saeed Nafisi[2]

1. Department of Biology, Faculty of Science, Urmia University, Urmia, Iran

2. Department of Basic Science, Faculty of Veterinary Medicine, Urmia University, Urmia, Iran

Background and purpose: Two-phase square waves can affect the receptors to release all types of neurotransmitters such as; dopamine, serotonin, histamine, and so on. Serotonin acts on the pain receptors and opiate system, causing analgesia. Pain is a prevailing problem so that the existing homeopathic remedies are not usually useful. On the other hand, the use of drugs has its own side effects. The aim of this project was to evaluate the effect of low frequency electromagnetic waves on the formalin-induced pain in male rats.
Materials and Methods: 12 male Wistar rats were divided into two groups. The first group was free of irradiation and the second group was subjected to a frequency of 20 Hz for 60 minutes. 20 µl Formalin 5% was injected under the skin of the left foot. The response to formalin effects was recorded in 5 min intervals from 0-5 min (as early phase) and 15-30 min (as late phase). Data were analyzed using one-way ANOVA and post hoc Tukey test.
Results: The results of this study showed that low frequency electromagnetic waves significantly reduced the pain caused by formalin injection. Reduction of symptoms and decreasing in the duration of the time spent licking in the acute and chronic phase was observed in rats exposed to electromagnetic radiation at a frequency of 20 Hz ($P<0.05$).
Conclusion: Low-frequency electromagnetic waves are effective in pain reduction and can be used to relieve pain.
Keywords: Pain, Low frequency electromagnetic waves, Formalin test, Rat

P-684

The effect of repeated ICV injections on brain inflammation and anxiety

Yousefvand SH[1], Hamidi F[1*], Zendehdel M[2], Parham A[1], Hashemzadeh M[2]

1. Department of Physiology, Department of Basic Sciences, Faculty of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran

2. Department of Physiology, Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

Background and Objectives: Due to the increasing development of the poultry industry, having enough information about how to centrally regulate appetite in birds is important. Investigating the mechanisms involved in the central control of appetite in birds is done by ICV injection of biological compounds. In ICV injection in birds, it has been mentioned that only one experiment (one injection) should be done on each bird. This study examines this subject.
Materials & Methods: The present study was performed on 24 male Ross 308 broiler chickens. Stereotaxic surgery was performed on all of the animals. After 5 days of recovery, birds every day for a week received ICV injection, and their behavioral changes were examined.
Results: No behavioral changes were observed in the first and second days of the experiment. From the third day onwards, the birds show a degree of anxiety, and in the following days these symptoms were more severe and eventually led to the animal death. Repetitive ICV injections may cause inflammation of the brain tissue, and resulting in anxiety symptoms in the animal. Do next ICV injection by intensifying these symptoms, can cause the death of the animal.
Conclusion: Repeated ICV injections can cause brain inflammation and anxiety in the animal. Therefore, on every chick just has one experiment (injection) be done.
Keywords: Bird, Appetite, ICV injection, inflammation, anxiety.

P-685

Evaluation of Anti-Fungal Activity of Two Species of Cousinia

Arash Mahboubi[1], Ebrahim Salimi Sabour[2*], Faraz Mojab[2]

1. Department of Pharmaceutics, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2. Department of Pharmacognosy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: The increasing pattern of anti-fungal resistance had led to difficult and expensive treatment of infectious diseases, beside that there are many concerns about side effects associated with the anti-biotic therapy. Flora of Iran is one of the richest floras in SW of Asia and it has 1800 endemic species from 8000 taxa. The genus Cousinia with 600-700 species is the largest genera of flowering plants in Central and Western Asia. C. harazensis Rech.f., C. calocephala Jaub. & Spach are endemics to Iran.
Material and Methods: Aerial parts of plants were collected from Lasem (Mazandaran Province) in July 2018. The air-dried and milled whole plants were macerated for 24 hours in methanol 80% and this rout was repeated for four times. Primary anti-fungal effects of methanol extracts against two pathogenic fungi, including: Candida albicans (ATCC: 10231) and Aspergillus fumigatus (PTCC: 5009) were evaluated by disc diffusion method and MIC and MFC values were determined by agar dilution method described by CLSI.
Results: Results of disk diffusion showed that these extracts don't have effect. Via agar dilution method extracts can inhibit growth of examined fungi strains. According to results of MIC value test, effect of extract of C. harazensis against A. fumigatus was 62.5 mg/ml and it was the best results. About MBC results, main of effective concentrations was 250 mg/ml.
Conclusion: This research showed that Cousinia harazensis can be used for future works such as: phytochemical screening, bio-assay guided fractions, etc.
Keywords: Cousinia harazensis, C. calocephala, Disk diffusion, Agar dilution methods, MIC, MFC

P-686

Curcumin ameliorates methotrexate-induced testicular oxidative stress in the rat

Maryam Sharayeli[1], Sima Nasri[1*], Reihane Ghasemi Tarei[2], Fariba Ansari[2], Mehrdad Roghani[3]

1. Department of biology, School of Basic science, Payame Noor University, Tehran, Iran.
2. Department of physiology, School of medicine, Shahed University, Tehran, Iran.
3. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective: Methotrexate (MTX) leads to toxic side effects in tissues such as testis. Curcumin is the active and principal ingredient of Curcuma longa with multiple protective effects. In this study, the effect of curcumin on MTX-induced testicular oxidative stress was investigated in the rat.
Materials and Methods: In this experimental and interventional study, 28 male rats were randomly divided into 4 groups of control, MTX, MTX+curcumin50, and MTX+curcumin200. MTX was i.p. administered once at a dose of 20 mg/kg. Treatment groups received curcumin at doses of 50 or 200 mg/kg/day (p.o.) for two weeks. Finally, testicular oxidative stress parameters including malondialdehyde (MDA), glutathione (GSH), catalase, and superoxide dismutase (SOD) were assessed.
Results: Our findings showed that curcumin at a dose of 200 mg/kg could significantly reduce testicular level of MDA and enhance SOD activity with no significant change of GSH and catalase following MTX challenge.
Conclusion: Curcumin is capable to attenuate MTX-induced oxidative stress in the testis and part of its beneficial effect is through improvement of antioxidant status.
Keywords: Curcumin, Methotrexate, Testis, Oxidative stress

P-687

Three Novel Candidates as Mu Opioid Receptor Antagonists: An In Silico Study

Hadis Shahriari[1], Maysam Fadaei-kenarsary[2]

1. Toxicology Department, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences
2. Neuroscience Research Center, Kerman University of Medical Sciences

Background and Objective: Morphine overdose is a lethal condition that is reversible by administration of mu opioid antagonists like naloxone. This treatment can be associated with side effects like opioid toxicity recurrence. We aimed to design novel chemical compounds as potential mu opioid receptor (MOR) antagonists.

Materials and Methods: We used Chemdraw, Hyperchem and Autodock Tools softwares to design, optimize and dock these compounds to the receptor. We designed 11 chemical compounds that 3 of them were successfully docked. None of these 3 compounds were found in Google scholar, Google search engine and other databases. Exclusion criteria included unsolved non-integral charge, half electron approximation in geometry with minimum energy, non-bonded atoms and optimization errors.
Results: The obtained results of the molecular docking simulation using the mu opioid receptor (PDB code: 4DKL) showed lowest binding energies (LBEs) and estimated Inhibition constants (KIs). Three novel compounds including a 8-Carboxamidocyclazocine analogue (LBE= -8.99 kcal/mol, Ki=256.85 nM) and two triazole derivatives (LBE= -9.21 kcal/mol, Ki=178.45 nM and LBE= -8.66 kcal/mol, Ki=445.88 nM) were suitably fitted in the active site of MOR in comparison with the main ligand (LBE=-10.13 kcal/mol, Ki=37.78 nM) in MOR. In parallel, LBEs and KIs of 3 novel compounds and standard antagonist naloxone (LBE=-8.21 kcal/mol, Ki=960.18 nM) in temperature of 298.15 K were compared.
Conclusion: All of three novel compounds had better potential antagonist properties than standard antagonist naloxone. The best antagonist candidate among them was 7-amino-3-(cyclopropylmethyl)-6,11-dimethyl-1,2,3,4,5,6-hexahydro-2,6-methanobenzo[d]azocine-8-carboxamide. We suggest further studies to evaluate these potential antidotes in morphine overdose.
Keywords: Mu opioid receptor, Antagonist, Morphine, Naloxone, Molecular Docking Simulation

P-688

Biofilm inhibition activity of CuO/ZnO nanoparticles by cold tolerant Microbacterium sp.

Bashir Ahmad Aseem[1], Bahar Shahnavaz[1*], Mansour Mashreghi[1], Ftemeh B.Rassouli[2], Alireza Zenhari[1]

1. Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran
2. Novel Diagnostic and Therapeutics Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, 9177948974, Iran

Background and Objective: Bacterial biofilm play one important in the pathogenesis and virulence of diseases. Therefore, biofilm control of bacteria is one of the essential and vital goals of medicine.
Material and Methods: One cold tolerant bacterium, namely Microbacterium sp. was isolated and identified from high altitude. This bacterium can biosynthesize CuO and ZnONPs extracellularly at 20 °C. Biofilm inhibition was determined by the crystal violet assay. 1.5×106 CFU/mL of S.epidermidis overnight culture was exposed to CuO and ZnONPs solution with different concentrations on 96 microplate wells. To monitor the adherence of bacterial cells, the crystal violet was added. An ELISA microtiter plate reader at 590 nm determined adherent biofilm and percentage of biofilm inhibition was calculated. The biofilm inhibitory effect of the two NPs was confirmed at different concentrations. An increase in the percentage of biofilm inhibition was observed with the increase in the concentration of CuO and ZnONPs as compared to the negative control.
Results: For S.epidermidis, the biofilm formation was found to be inhibited by up to 100% at ZnONPs of 250 µg/mL. While, CuONPs at 250 µg/mL concentration able to inhibit only %12 of bacterial biofilm. However, even at a concentration of 16 µg/mL, there was 10% anti-biofilm activity.
Conclusion: The results suggest that the CuONPs synthesized from cold tolerant Microbacterium sp. exhibit specific biofilm inhibition and could reduce severity of disease due to S.epidermidis infections.
Keywords: Biofilm inhibition, CuO/ZnO nanoparticles, Microbacterium sp

P-689

Neopterin increase in Obstructive Sleep Apnea Patients

Samaneh Sheikhi Kouhsar[1], Mohammadreza Bigdeli[1,2], Yadollah Shakiba[3], Khosro Sadeghniiat[4]

1. Department of Animal Sciences and Biotechnology, Faculty of Life Sciences and Biotechnology, Shahid Beheshti University, Tehran, Iran
2. Institute for Cognitive and Brain Sciences, Shahid Beheshti University, Tehran, Iran
3. Regenerative Medicine Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

4. Occupational Sleep Research Center, Baharlu Hospital, Tehran, Iran

Background and Objective: Obstructive Sleep Apnea is one of the common sleep disorders which has been less widely considered by scientists and people, but in recent years, many studies have been conducted to identify pathological processes in the OSA. On of underlying mechanism of the disease is oxidative stress, which is due to periodic hypoxia in these patients. Neopterin synthesis by human macrophages and is indicative of a pro-inflammatory immune status. High neopterin production is associated with increased production of reactive oxygen species, neopterin concentrations also allow to estimate the extent of oxidative stress elicited by the immune system.
Materials and Methods: In this study, 100 OSA patients and 100 healthy people participated. OSA patients All controls filled in the STOP-BANG, and Epworth Sleepiness Scale questionnaires, and patients performed polysomnography test. Neopterin serum concentration assessed by ELISA kit in OSA and controls. The ethical code for this project was IR.TUMS.VCR.REC.1395.1107.
Results: Neopterin concentration in OSA patients was significantly higher than the control group ($P<0.0001$). For more analysis, patients divided to sever and non-sever (mild to moderate) patients and. Then, Neopterin levels did not differ in two groups.
Conclusion: Our results showed hypoxia increase oxidative stress which is the result of immune system activation in these patients.
Keywords: Obstructive Sleep apnea, Oxidative Stress, Neopterin, Immune System

P-690

Dermal and Ocular Safety Assessment of Ordinary vs. Nano-form Titanium Dioxide (TiO2) in the Animal Models

Sadeghi-Hashjin G, Jafari SM, Koohi MK, Abdolmaleki Z & Hassankhani M

Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran & 2Faculty of Veterinary Medicine, Islamic Azad University - Karaj Branch, Karaj, Iran

Background and Objectives: Titanium dioxide (TiO2) is widely used in sunscreen formulations as either in ordinary or nano-form particles. The safety evaluations of nano-form TiO2 (NF-TiO2) were done by dermal exposure, acute dermal and eye irritation/corrosion, and skin sensitization in the animal models according to the guideline of Organization for Economic Co-operation and Development (OECD). The aim of this study was the evaluation of safety and toxicity of NF-TiO2 following acute sunscreen exposure.
Materials and Methods: TiO2 and NF-TiO2 (20-40 nm and 98% purity) were purchased in the anatase crystal phase, and five types of concentrations for sunscreens were made which were carried out in five different treatment groups in mice and rabbits.
Results: In acute eye irritation using rabbits, the only irritation effect was observed in the conjunctivae area within one hour after administration both in NF-TiO2 and TiO2 groups. In acute dermal irritation using rabbits did not show a significant difference among groups in different concentrations and durations. Similarly, in a skin sensitization test using mice, contact hypersensitivity (CHS) did not show a significant difference ($P<0.05$) among groups in 15% concentration of TiO2 in the different durations after application.
Conclusion: Experimental finding indicated that TiO2-NPs and TiO2 in sunscreens were relatively safe and did not induce statistically significant eye and dermal irritation and skin hypersensitivity.
Keywords: sunscreens, TiO2, dermal irritation test, eye irritation test, rabbit

P-691

Opium addiction during pregnancy through inflammation increases adverse pregnancy outcome

Hamed Fanaei[1,2], Samira Khayat[1]

1. Pregnancy Health Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
2. Department of Physiology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

Background and Objective: Recent studies have shown that opium addiction changes the activity of immune system. Considering that abnormal activity of the mother's immune system during pregnancy can endanger the health of the mother and the fetus, the aim of this study was to investigate the effect of opium addiction during pregnancy on pregnancy outcome and the level of inflammatory markers in the maternal serum and umbilical cord blood.
Materials and methods: This is a case-control study comparing pregnancy outcome and maternal serum and umbilical cord blood inflammatory markers (IL-6 and IL-10) levels in pregnant women with opium addiction and non-addicted pregnant women.
Results: Results of the present study showed that levels of IL-6 and IL-10 in maternal serum and cord blood in opium addicted group were significantly higher than control group. In addition, prevalence of adverse pregnancy outcomes such as NICU admissions, congenital anomalies, neonatal deaths, Meconium contaminated amniotic fluid, respiratory problems, neonatal resuscitation and low Apgar score were more in opium addicted group than control group.
Conclusion: The results of this study indicated that opium addiction in pregnant mothers leads to some degrees of inflammation and increases prevalence of adverse pregnancy outcome.
Keywords: opium, addiction, pregnancy outcome, inflammation, IL-6, IL-10

P-692

Adjuvant therapy with memantine enhances the antiproliferative effects of doxorubicin in MCF-7 breast cancer cells

Vahid Shafiei-Irannejad[1], Hamid Soraya[1,2], Negin Mahboubi[1,2], Maryam Kahyaei[1,2]

1. Cellular and Molecular Research Center, Cellular and Molecular Medicine Institute, Urmia University of Medical Sciences, Urmia, Iran.
2. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran.

Background and Objective: Combination therapy with new components has been considered as a promising strategy in breast cancer treatment. Doxorubicin is a potent and widely used anticancer agent which is routinely used in the treatment of breast cancer, however, treatment with this compound is accompanied with sever toxic side effects. To overcome this problem, in the current study we investigated the effects of memantine, an N-methyl-D-aspartate antagonist which is used in the treatment of alzhimers's disease, on the cytotoxicity and apoptosis-inducing effects of doxorubicin in MCF-7 breast cancer cells.
Materials and Methods: The viability of cells after treatment with memantine, doxorubicin and combination of these compounds was assessed with MTT assay. Flow cytometeric analysis of apoptosis following staining with annexin V/PI was performed after single and combination treatment with both compounds. To further investigate the effect of memantine on doxorubicin-induced apoptosis, DAPI staining was performed.
Results: Treatment with memantine significantly enhanced the cytotoxicity of doxorubicin in MCF-7 cells which is presented by decreased IC50 of doxorubicin in the cytotoxicty profile. This effect was confirmed by enhanced apoptosis-inducing effects of doxorubicin after treatment with memantine which is illustrated in the results of flow cytometery and DAPI staining.
Conclusion: Our results showed that combination of memantine with doxorubicin can be considered as a promising strategy for the treatment of patients suffering from breast cancer.
Keywords: combination therapy, breast cancer, apoptosis, memantine, doxorubicin

P-693

Adjuvant therapy with memantine enhances the sensitivity of A2780 ovarian cancer cells to cisplatin

Hamid Soraya[1,2], Vahid Shafiei-Irannejad[1], Maryam Kahyaei[1,2], Negin Mahboubi[1,2]

1. Cellular and Molecular Research Center, Cellular and Molecular Medicine Institute, Urmia University of Medical Sciences, Urmia, Iran.
2. Department of Pharmacology and Toxicology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran.

Background and Objective: Chemotherapy is an important tool for treatment of various types of malignancies including ovarian cancer. Cisplatin is considered as the first-line chemotherapy option for ovarian cancer, however, treatment with this drug is associated with adverse toxic effects to healthy tissues. To overcome this problem, one strategy is to combine cisplatin with safe compounds. Therefore, in this study we investigated the effects of memantine, an N-methyl-D-aspartate antagonist which is routinely used in the treatment of alzhimer's disease, on cytotoxicity and apoptosis induction of cisplatin in A2780 ovarian cancer cells.
Materials and Methods: MTT assay was performed to assess the viability of A2780 cells after treatment with cisplatin, memantine and combination of these drugs. To evaluate the effects of memantine on cisplatin-induced apoptosis, flow cytometeric analysis of apotosis following staining with annexin V/PI was performed. In addition to that, DAPI staining was performed to further analyse the apoptosis-inducing effects of cisplatin when combined with memantine.
Results: In our results a shift to left in the cytotoxicity profile of cisplatin after addition of memantine was observed, indicating that memantine could enhance the cytotoxicity and decrease the IC50 of cisplatin in A2780 ovarian cancer cells. These findings were further confirmed by the results of DAPI staining and flow cytometery analysis as indicated by more fragmented chromatin and migration of cells to apoptotic regions in combination treatment group.
Conclusion: Our findings suggested that memantine can be considered as a potent adjuvant for combination therapy in ovarian cancer chemotherapy.
Keywords: adjuvant therapy, ovarian cancer, apoptosis, memantine, cisplatin

P-694

Elucidation of the mechanisms of Ciprofloxacin-induced myopathy

Mohammad Reza Neshat and Jalal Pourahmad

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Ciprofloxacin is a second-generation fluoroquinolone antibiotic commonly used in therapy of many microbial infections. Rhabdomyolis is one of the serious side effects of ciprofloxacin. In this study, we investigated the effects of ciprofloxacin on isolated rat skeletal muscles mitochondria.
Materials and Methods: Rat skeletal muscles mitochondria were obtained by differential ultracentrifugation and incubated with different concentrations of ciprofloxacin (35,70 and 140 µM) .The activity of mitochondrial complex II was assayed via the measurement of MTT reduction. The mitochondrial ROS measurement was perfomed using the fluorescent probe DCFH-DA. The Rhodamine 123 (Rh 123) redistribution technique was used for MMP measurement. The concentration of cytochrome c was determined through using the Quantikine Rat/mouse cytochrome c Immunoassay kit. Data were analyzed using the Graph pad prism software, version 6.
Results: Our results demonstrated that ciprofloxacin induced a rise in mitochondrial reactive species (ROS) formation and mitochondrial membrane potential (MMP) collapse before mitochondrial swelling ensued in isolated skeletal muscles mitochondria. In addition collapse of MMP and mitochondrial swelling produced release of cytochrome c via outer membrane rupture or mitochondrial permeability transition (MPT) pore opening.
Conclusion: According to the results, we suggested that ciprofloxacin- induced myopathy is the result of a disruptive effect on mitochondrial respiratory chain and induction of ROS-mediated apoptosis signaling in skeletal muscle cells.
Keywords: ciprofloxacin, mitochondria, myopathy, ROS

P-695

The effect of Zataria multiflora on pulmonary function tests, respiratory symptoms, bronchodilator drugs use and hematological parameters in chronic obstructive pulmonary disease

Vahideh Ghorani[1], Omid Rajabi[2], Majid Mirsadraee[3], Mohammad Hossein Boskabady[1]

1. Neurogenic Inflammation Research Center and Department of Physiology, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Department of Drug and Food Control, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Department of Internal Medicine, Faculty of Medicine, Islamic Azad University-Mashhad Branch, Mashhad, Iran.

Objective: The preventive therapeutic effect of Zataria multiflora on pulmonary function tests, respiratory symptoms, inhaled bronchodilator drugs use, and hematological parameters in chronic obstructive pulmonary disease patients was assessed. Methods: 45 patients divided to three groups including placebo group (P), groups

received 3 and 6 mg/kg/day Z. multiflora extract (Z3 and Z6), (n=14 in P and Z3 groups and n=17 in Z6 group). Patients consumed prepared drugs in a double-blind manner 3 times a day for two months. Pulmonary function tests (MEF25-75), respiratory symptoms, inhaled bronchodilator drugs use and hematological parameters were evaluated pretreatment, one and two months after starting treatment. Results: Two-months treatment with Z. multiflora did not affect MEF25-75 values. However, respiratory symptoms including activity limitations at home, confidence in leaving the home, sleep, and energy as well as CAT score were significantly improved 1 and 2 months after treatment with both doses of Z. multiflora compared to step 0 ($p<0.05$ to $p<0.001$). Inhaled bronchodilator drugs use was also significantly reduced at the end of 2-month treatment with both doses of extract ($p<0.05$). Total white blood cells in Z3 group after 2-months and in Z6 group in two steps were significantly decreased compared to step 0 ($p<0.05$ to $p<0.001$). Neutrophil counts were significantly decreased in both treated groups in step II compared to step I ($p<0.05$ to $p<0.01$). Other hematological indices did not significantly change during treatment period. Conclusion: The results suggest a preventive therapeutic effect for this plant which could be due to its anti-inflammatory property.
Keywords: Zataria multiflora, chronic obstructive pulmonary diseases, pulmonary function test, hematological parameters, respiratory symptoms

P-696

Anti-inflammatory effect of lycopene in lipopolysaccharide-induced model of acute kidney injury in C57BL/6 mouse

Atefeh Ghorbanpour[1], Sepide Salari[1], Tourandokht Baluchnejadmojarad[2], Mehrdad Roghani[3]

1. School of Medicine, Shahed University, Tehran, Iran.
2. Department of Physiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
3. Neurophysiology Research Center, Department of Physiology, Shahed University, Tehran, Iran.

Background and Objective: Acute kidney injury (AKI) is a prevalent complication following sepsis and finally leads to loss of kidney function. Lipopolysaccharide (LPS) is usually used to induce AKI. Lycopene is a carotenoid pigment in fruits like tomato with anti-oxidant, anti-inflammatory, and protective effects. This study was done to evaluate anti-inflammatory potential of lycopene in a model of AKI induced by LPS in the mouse.
Materials and Methods: Male C57BL/6 mice (n=32) were divided into 4 groups including control, LPS, and LPS groups receiving lycopene (5 or 20 mg/kg). For induction of AKI, LPS was injected i.p. at a dose of 10 mg/kg. After 24 h, mice were killed and serum BUN and creatinine and inflammation-related specific markers including nuclear factor-kB (NF-kB) and toll-like receptor 4 (TLR4) were determined.
Results: Our findings indicated that lycopene could significantly lower serum BUN and creatinine and reduce renal NF-kB and TLR4.
Conclusion: It is concluded that lycopene could attenuate LPS-induced AKI and part of its advantageous effect is through amelioration of some inflammation-related parameters.
Keywords: Acute kidney injury, Lipopolysaccharide, Lycopene, Inflammation

P-697

Evaluation of the effect of oral administration of Quercus, Cirsium vulgare and Falcaria vulgaris hydroalcoholic extracts on prevention of gastric ulcer caused by ethanol by studying the levels of caspase 9, c-fos, c-myc and Bcl-2 in rats

Mahbobeh Kamrani Mehni, Javad Sajedianfard, Said Hossainzade

Department of Basic Sciences, School of Veterinary Science, Shiraz University, Shiraz, Iran.

Background and objective: Gastric ulcers are open sores that develop on the inside lining of stomach due to harmful element. Nowaday, treating gastric ulcer with herbal medicines has been a significant achievement. We examined the effect of hydroalcoholic extracts of these plants on caspase 9, c-fos, c-myc and Bcl2 genes by using Real Time PCR in gastric ulcer induced by ethanol.

Materials and Methods: 30 male rats were randomly allocated into 6 groups: Control group (intact animals), Sham group (distilled water was gavaged for 14 days. Negative control group (omeprazole was administered at for 14 days (20 mg/kg)). Experimental groups (hydroalcoholic extracts were gavaged for 14 days (500 mg/kg)). And gastric ulcer was induced by ethanol gavage 1 ml/200 g/kg. Then caspase 9, c-myc, and Bcl2 were measured by using Real time PCR. Data were analyzed by using SPSS.
Results: Analysis of Real Time PCR showed that the expression of C-fos and c-myc and caspase 9 increased in sham group and decreased in all experimental groups. Bcl2 expression acted just the reverse.
Conclusion: It can be concluded that protective effects of hydroalcoholic extracts of of considerable plants on ethanol-induced gastric ulcers and can regulated the expression of these genes.
Keywords: Quercus, Cirsium vulgare, Falcaria vulgaris, Gastric ulcer, genes

P-698

The role of bone marrow mesenchymal stem cells in the expression of TLR2 and TLR4 in acute kidney injury induced by renal ischemia-reperfusion in rats.

Zeinab Karimi[*1], Sara Hashemi[2], Sahar Janfeshan[3], Leila Malekmakan[1]

1. Shiraz nephro-urology research center, Shiraz University of Medical Sciences, Shiraz, Iran
2. Department of Anatomy, School of Medicine Burn and Wound Healing Research Center Trauma Research Institute
3. Department of Biology, Zarghan Branch, Islamic Azad University, Zarghan, Iran

Introduction: Renal ischemic reperfusion injury (IRI) leads to both functional and pathological damage and associated with oxidative stress and inflammatory response. Tool like receptors are part of innate immune system and involve in inflammatory responses. Bone marrow mesenchymal stem cells (BMSCs) are pluripotent cells that capable to regenerate other tissues. Therefore in present study we investigated the effect of BMSCs in improvement of renal function in rats.
Methods: Rats were randomly divided into 3 groups; control (n=6), renal ischemia-reperfusion (n=6) and renal ischemia-reperfusion that received 2×106 BMSCs from their caudal vein. We examined the level of BUN/Cr in serum, and TLR-2, TLR-4 by using real time-pcr method.
Results: Renal ischemia-reperfusion resulted in tissue damage and decreased renal function (increased BUN/Cr) and because of inflammatory response the expression of TLR-2 and TLR-4 increased. BMSCs effectively improved renal function and decreased the level of BUN/Cr.
Conclusion: Our results showed that renal ischemia-reperfusion caused renal damage and increased TLR2, 4 expression and BMSCs restore renal function.
Key words: TLR2, TLR4, renal ischemia-reperfusion, acute kidney injury

P-699

The effect of maternal stress on pain in adult male rats and the possible effect of oxytocin treatment

Nayereh Askari , Manizheh Dogani , Shima Karimi Afshar

Department of physiology, faculty of biology, shahid bahonar university, kerman, iran

Background and Objective: Stress affects brain activity and causes long-term changes in various nervous systems. Stress can cause long-term analgesia or hyperallergy.
Oxytocin is a 9-amino acid hormone that is produced in the mammalian superovulatory hypothalamus and stored in the pituitary.
Injection of oxytocin into the CNS sites causes analgesia and oxytocin decreases pain sensitivity by reducing mood.

Materials and Methods: In this study, 90healthy Wistar rats (120-150 gr) were assigned randomly into three groups (n=8 per group): Adult male that received maternal stress (control group), Adult male that in addition to maternal stress received food deprivation , Adult male that in addition to maternal stress received food Inequality.
Finally, these three groups of rats were divided into three subgroups: the group not treated with oxytocin, the group treated with 10 dose of oxytocin and the group treated with 20 dose of oxytocin. The hot plate and tail flick was used to measure the pain threshold of rats.
Results the pain threshold in rats that receiving inequality stress and food deprivation was significantly reduced compared to rats receiving only maternal stress, which This is more noticeable in rats that received dietary inequality stress. Oxytocin also slightly increased pain threshold, This increase is most commonly seen in groups receiving 20 dose of oxytocin and in tail flick assays.
Conclusion: our results showed that while Stress reduces pain threshold in adult male rats, doses of 1 and 2 oxytocin increase the pain threshold.
Key words: Pain, Oxytocin, Anthropometry, Food deprivation and Food inequality

P-700

Bioinformatics studies of polyphenolic compounds of Pistacia and grapes to inhibit proteinase kinase BRAF in colorectal cancer

Ziba Karimi Sadr, Masumeh Jamali Gandomani

Research Centre for Biosciences, Malek-Ashtar University of Technology, Tehran, Iran.

Background and Objective: Colorectal cancer is the third cause of cancer-related death. Accumulating line of evidence has represented that the proteinase kinase BRAF is involved in the development of this cancer. This protein which is produced by a mutation in the BRAF gene, is a promising target molecule to produce drugs which has been the focus of many research area. Polyphenyl compounds that have antioxidant properties can be a good candidate for this process. The goal of this study was to investigate the pharmacodynamics of polyphenol compounds in Pistacia Atlantica and Brazilian grapes on BRAF protein using docking in order to prevent and manage colorectal tumors.
Materials and Methods: The crystallography of BRAF protein was prepared as the 5csw.pdb file from the PDB protein data bank. Then the 5csw. gpf and 5csw.dpf files were prepared using the autodock tools 4 software, and finally, these files were loaded in Cygwin software to obtain the protein 5csw.dlg file.
Results: The results from the rmsd table indicated that cyanidin with a binding energy of -9.07 kcal/mol had the highest affinity to the active site of the BRAF protein. Furthermore, the amount of material needed to inactivate the BRAF protein is 224.86 nanomolar.
Conclusion: Our results depicted that cyanidin in grapes is approved as an inhibitory BRAF protein in colorectal cancer and can appropriately be bonded to active protein position.
Keywords: Colorectal Cancer, BRAF Protein Kinase, Polyphenolic Compounds, Bioinformatics

P-701

Effect of different dark chocolate diets on memory in chronic psychical stressed rats

Elham kalantarzadeh*, Maryam Radahmadi, Parham Reisi

Department of Physiology, Medical School, Isfahan University of Medical Sciences

Background and Objective: Psychical stress adversely influences brain functions while dark chocolate probably exhibits positive effects on memory processes. This study investigated the effects of different dark chocolate diets on the memory in chronic psychical stressed rats.
Materials and Methods: Thirty five male rats were randomly allocated to five groups (n =7): Control, isolation stress, isolation stress with compulsory dark chocolate diet (only dark chocolate without chow), isolation stress with optional dark chocolate diet (both dark chocolate and chow were available for rat) and isolation stress with restricted dark chocolate diet (chow and only 4 gr/rat chocolate were available for rats). Experimental period was 14 days. Latency was evaluated as brain function using the passive avoidance test one-day after foot shock.

Results: Results revealed that compulsory dark chocolate diet significantly increased latency in chronic isolation stress group. Whereas, the optional dark chocolate and restricted dark chocolate diets no significantly increased memory in stress group.
Conclusion: Based on the results obtained, only the beneficial effects of compulsory dark chocolate diet observed on memory improvement in chronic psychical stressed rats. Whereas, the optional dark chocolate and restricted dark chocolate diets had not helpful effects on improvement of memory in psychical stress conditions.
Keywords: Dark Chocolate, Diet, Memory, Stress, Rat

P-702

Evaluation of the prescription pattern of proton pump inhibitors in a tertiary hospital

Zahra Kiani, Kobra Naseri

Assistant professor, Birjand University of Medical Sciences

Background: Proton pump inhibitors (PPIs) are one of the most commonly prescribed drug classes worldwide. Due to their high efficacy in reducing acid-related symptoms and low perceived adverse effects, PPIs are often overused which associated with potential adverse effects and great health spending. The aim of this study was to evaluate the prescription pattern of PPI and compare to approved indications in a teaching hospital.
Methods: In this retrospective cross-sectional observational study, 365 inpatients were randomly selected in four wards including of cardiology, general medicine, neurology and infectious wards of a 300-bed tertiary care teaching hospital over 6 months from November 2018 to March 2019. Demographic characteristics and medical histories were recorded and analyzed using SPSS version 16.
Results: Hospital records of three hundred and sixty-five patients were evaluated. At least one PPI was prescribed for 77% of patients during hospitalization, from which 50% were received parenteral pantoprazole. 85% of patients who coadministered aspirin and NSAIDs were also received PPI. The average prescribed daily dose (PPD) of each PPI was calculated, which was 1.81, 0.98, 0.98 and 0.67 for pantoprazole vial (40mg), pantoprazole tablet (20 mg), pantoprazole tablet (40 mg), and omeprazole capsule (20 mg), respectively. The appropriateness of PPIs according to American Hospital Formulary (AHF) was 83%, while parenteral form of pantoprazole was prescribed inappropriately in 202 (93%) patients.
Conclusion: According to our data, PPIs especially parenteral forms were prescribed inappropriately in our hospital. Therefore, educational courses and more audits are necessary to improve the prescription pattern of PPIs.

P-703

Combination of ascorbic acid and calcitriol attenuates airway remodeling in a murine model of chronic asthma

Farzaneh Kianian[1], Seyed Morteza Karimian[1], Mehri Kadkhodaee[1], Nasrin Takzaree[2], Behjat Seifi[1], Hamid Reza Sadeghipour[1,*]

1. Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Anatomy and Histology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

Objective: Airway remodeling is one of the most refractory problems in asthma that results in the decrease of lung function. Therefore, this study investigated the protective effects of ascorbic acid in combination with calcitriol on airway remodeling in ovalbumin-induced chronic asthma.

Methods: BALB/c mice were randomly assigned into seven groups. 1) Control; 2) Asthma; 3) Ineffective C (39 mg/kg ascorbic acid); 4) Ineffective D (1.5 µg/kg calcitriol); 5) Effective C (130 mg/kg ascorbic acid); 6) Effective D (5 µg/kg calcitriol); 7) Combination (39 mg/kg ascorbic acid + 1.5 µg/kg calcitriol). All animals, except in the control group, were sensitized and challenged with OVA. In all treatment groups, animals were administrated vitamins 30 min before each challenge. One day after the last challenge, lung tissue samples were stored for examining the histopathology.
Results: Asthma caused significant increases of goblet hyperplasia and subepithelial fibrosis. Co-administration of ineffective doses of ascorbic acid and calcitriol reduced the mentioned histopathological changes.
Conclusion: Combination of ascorbic acid with calcitriol in ineffective doses mitigates airway remodeling due to additive effects.
Keywords: Asthma; Ascorbic acid; Calcitriol; Goblet hyperplasia; Subepithelial fibrosis

P-704

The effect of facilitatory kinesiotape on erector spinae muscle activity in healthy men

Navid Fallahzadeh, Sakineh Goljaryan, Maryam Moghadam Salimi, Fariba Ghaderi

Tabriz University of Medical Sciences

Background and Objective: Kinesiotape is a type of tensile bond that is used in rehabilitation clinics for pain control and body and joint realignment. The kinesiotape effects depend on the amount of stretching and the muscle that the kinesiotape is attached to, which is either excitatory or inhibitory. So far, a few studies have examined the effect of kinesiotape on the level of erector-spinae muscle activity. The aim of this study was to evaluate the effect of excitatory mode of kinesiotape on longissimus muscle in healthy, non-athlete 18-25-year-old men.
Materials and Methods: 40 people participated in this study. The subjects were randomly divided into two groups of excitatory and sham kinesiotape. Kinesiotaping in form I with 30% stretch was applied to the right longissimus muscle. Before and after kinesiotape and 48 hours later, before and after kinesiotape removing, muscle activity was measured by surface EMG during muscle extension.
Results: There was an increase in the level of muscle activity before and after the kinesiotape, but this increase was not significant. Also, the level of muscle activity did not differ significantly between the two groups.
Conclusion: Using I-Shape Kinesiotape with 30% stretching, although it did not facilitate longissimus muscle in healthy men ages 18-25, the increase in muscle activity was observed. It seems that the reasons for the lack of significant changes in the level of muscle activity were the location of the electromyography electrodes and the attitude of the individuals towards the effect of kinesiotape.
Key words: Kinesiotaping, Muscle Facilitation, Erector Spine

P-705

The protective effects of long term NaHS administration on sperm parameters, testicular morphometry, testicular H2S levels, oxidative stress markers in varicocele male rats

Keivan Lorian

Background: Varicocele, is characterized by abnormal dilation and tortuosity of veins of the pampiniform plexus. Hydrogen sulfide, an endogenous gaseous signaling molecule, has various anti-oxidant and inflammatory functions in different parts of body. The aim of the current study was to evaluate the protective effects of NaHS on sperm parameters, testicular morphometry and testicular H2S levels and oxidative stress markers in varicocele male rats.
Methods and materials: Eighteen rats were randomly assigned to 3 experimental groups: 1) sham 2) varicocele 3) varicocele + sodium hydrosulfide. Experimental groups were underwent partial ligation of the renal vein to induce experimental varicocele. Animals in varicocele + sodium hydrogen sulfide group received 30 µmol/l NaHS in drinking water for 8 weeks. After 8 weeks in all rats, caudal epididymis was used for collecting sperms in order to assess sperm parameters (motility and count). The left testis was excised, dissected free of surrounding tissue for measuring oxidative stress markers (MDA level and SOD activity) and testicular H2S levels. Testicular morphometry (diameter and thickness) was assessed.

Results: Varicocele caused significant decrease in sperm parameters, oxidative stress markers (increased testicular MDA levels and decreased testicular SOD activity), decreased testicular H2S levels and testicular morphometry compared to sham group. NaHS administration improved above parameters.
Conclusion: This study revealed that reduction in testicular H2S is a contributor factor in varicocele. Protective effects of NaHS administration were observed in current study. This treatment may be a promising strategy for protection against varicocele-induced male infertility in clinical practice.
Key words: varicocele, NaHS, oxidative stress

P-706

Evaluating the expression of ERα66 and its novel variant ERα36 in drug-resistant lactotroph pituitary adenomas by gender

Fatemeh Mahboobifard1, Farahnaz Bidari-Zerehpoosh2, Zahra Davoudi3, Mahshid Panahi4, Leila Dargahi5, Mohammad H. Pourgholami6, Gieve Sharifi7, Neda Izadi8, Masoumeh Jorjani9,*

1. Department of Pharmacology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Pathology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Skull Base Research Center, Loghman Hakim Hospital, Shahid Beheshti University of Medical Science, Tehran, Iran
4. Department of Pathology, Firoozgar hospital, Iran University of Medical Sciences, Tehran, Iran
5. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6. Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
7. Department of Neurosurgery, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
8. Department of Epidemiology, School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran
9. Department of Pharmacology and Neurobioloy Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Objective: Dopamine agonist therapy is a successful approach in most lactotroph pituitary microadenomas (microprolactinomas). However, the noticeable rate of drug-resistance, especially in male macroprolactinomas requires novel medical approaches. The regulatory effects of estradiol on pituitary homeostasis are well-documented, but the expression patterns of ERα66 and its novel isoform ERα36 are not yet clear in prolactinoma patients.
Materials and Methods: In this retrospective cohort study, 62 prolactinoma patients from three hospitals, who underwent surgery from 2011-2017 were evaluated. ERα36 and ERα66 expression were detected by immunohistochemistry. Snap-frozen tumors and normal pituitaries were also examined by western blotting for the detection of estrogen receptors. Data were analyzed using STATA.
Results: A broad expression of ERα36 was identified in normal pituitaries. The median scores of ERα36 and ERα66 expression were significantly higher in normal pituitaries than tumors. Four phenotypes of ERα36 and ERα66 expression were explored in tumors, with regard to sex and dopamine resistance. The Low ERα66/Low ERα36 phenotype was the most frequent among dopamine-resistant tumors. Low ERα66 expression was associated with dopamine agonist resistance. Multivariate logistic regression analysis showed that the inversely significant association of ERα66 with dopamine resistance remained significant after adjustment for sex as a potential confounder.
Conclusion: The results indicate that the decreasing trends of ERα36 and ERα66 expression from normal pituitaries to tumors are associated with dopamine resistance.
Keywords: Lactotroph pituitary adenoma; Prolactinoma; ERα36; ERα66, Dopamine resistance

P-707

Regular exercise and psychosocial stress modulate angiogenesis in heart failure

Seyed Mohammad Mortazavi[1,2], Fatemeh Moradi[3], Reyhane Sadegh zade[4], Mohammad Reza Vaez Mahdavi[4,5], Mehrdad Roghani[4], Parvaneh Mohseni Moghaddam[6]

1. Department of Veterinary Medicine, Sanandaj Branch, Islamic Azad University, Sanandaj, Iran.
2. Department of Dentistry, Faculty of Medicine, University of Medical Sciences and Health Services, Zanjan, Iran.
3. Phsiology Department, Faculty of Medicin, Zanjan University of Medical Sciences, Zanjan, Iran
4. Phsiology Department, Shahed University , Tehran, Iran
5. Equity and Health Research Center, Shahed University, Tehran, Iran.
6. physiology Department, Faculty of Medicin, Tehran University of Medical Sciences, Tehran, Iran

Background and Objective: Today human may meet psychosocial invironmental inevitable stresses from various stress sources and detrimental effects of this type of stress it's not covered in health, moreover cardiovascular health is affected by multi deteriorations of health such as stress coping system, exercise and physical activity, so we supposed that regular exercise maybe modulates psychosocial stress consequences in heart.
Materials and Methods: 35 rat were randomly divided into 5 groups: Control group, Heart failure group, psychosocial stress plus Heart failure group, Exercise plus Heart failure group, Psychosocial stress, exercise plus heart failure group. Gene expression of angiogenic factors such as hypoxia inducible factor-1a (HIF-1a), vascular endothelial growth factor A (VEGFA) and endothelial nitric oxide synthase (eNOS) were measured.
Results: Psychosocial stress and Heart failure decreased gene expression of angiogenic factors such as HIF-1a, VEGFA and eNOS ($P<0.05$). socially stressed rats had more decreases in gene expression of angiogenic factors in comarision with heart failure ($P<0.001$). 4 weeks regular exercise training caused more improvement and promotion of gene expression of angiogenic and vascular growth factors; HIF-1a, VEGFA, eNOS in heart failure ($P<0.001$).
Conclusion: Psychosocial stress can attenute angiogenesis and vasular growth factors production in heart failure. Regulare exercise through increasing of gene experssion of angiogenic factors will be more effective in heart failure consequences. So for experience more healty situation both reduse of various stresse sources and regulare exercise are recommended.
Keywords: Regulare Exersice; Heart Failure; Psychosocial stress; Angiogenesis, Vasular growth factors

P-708

Association between frequency of early ovarian hyperstimulation syndrome (OHSS) and vitamin D levels in follicular fluid of non-obese PCOS and healthy women

Fatemeh Masjedi, Sara Keshtgar

Department of Physiology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Background and Objective: Ovarian hyperstimulation syndrome (OHSS) is an unintended complication of controlled ovarian stimulation (COS). Polycystic ovary syndrome (PCOS) is a common endocrinologic disorder and COS in these women remains a challenge, because of potential risk of OHSS. Vitamin D (Vit.D) therapy in women with PCOS significantly decreases OHSS complications. Due to lack of research on the basic association of this vitamin with incidence or severity of OHSS, we decided to evaluate the relationship between follicular fluid (FF) 25(OH)D levels and OHSS frequency in women with normal and polycystic ovaries.
Materials and Methods: One hundred-fifty PCOS women were compared with 130 age- and body mass index-matched healthy controls. GnRH antagonist protocol was the main treatment option used in both groups. After oocyte retrieval, remaining follicular aspirates from each patient were pooled and centrifuged and 25(OH)D level was assessed. Early OHSS was diagnosed by a gynecologist. Spearman correlation coefficient, Chi-square test and independent t-test were used for data analysis with GraphPad Prism for Windows.
Results: The frequency of OHSS was significantly greater and FF 25(OH)D levels was significantly lower in PCOS women than those of controls. In women with healthy and polycystic ovary, OHSS frequency had a significant negative correlation with FF 25(OH)D levels.
Conclusion: PCOS is a risk factor for OHSS and women with lower levels of FF 25(OH)D experienced more early OHSS frequency. We suggested vit.D therapy before COS result in a decrease in the incidence and severity of OHSS.
Keywords: Ovarian hyperstimulation syndrome (OHSS), Vitamin D, Follicular fluid, Polycystic ovary

P-709

L-carnitine and cholesterol-loaded cyclodextrin attenuate vitrification induced reactive oxygen release in sheep epididymal sperm

Leili Mavalizadeh[1], Mohammad Reza Tabandeh[1], Farid Barati[2]

1. Department of Basic Sciences, Division of Biochemistry and Molecular Biology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.
2. Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran.

Background and Objective: Vitrification is a method for improving sperm cryopreservation. The coincidental effect of increasing membrane cholesterol content and improvement of antioxidant status on vitrified sheep epididymal sperm quality has not been assessed. In this study the effect of cholesterol- loaded cyclodextrin (CLC) with L-carnitine (LC) on quality of sheep epididymal sperm after vitrification was evaluated.

Materials and Methods: Sheep epididymal sperms (20 ×106 sperm /ml) in different vitrification media containing a) CLC (1 mg/ 60 ×106 sperm), b) LC 5mM, c) LC 10 mM, d) CLC+LC 5 mM, e) CLC+LC 10 mM f) basic medium (sucrose +Tris) were loaded in 0.5 ml French straws and cooled on nitrogen vapor, then immersed in liquid nitrogen for one week. After thawing some sperm parameters including vital activity (MTT assay), lipid peroxidation level (TBA assay) and ROS levels (NBT assay) were analyzed.
Results: The vitrified sperms in the presence of CLC and 5 mM or 10 mM LC showed significant lower degree of lipid peroxidation and ROS production in concomitant with higher vital activity.
Conclusion: In conclusion our results demonstrated that vitrification of ram sperms in the presence of CLC and LC could attenuate the oxidative stress and this method can be used for improvement of sperm freezing of animal or human in future.
Key words: Vitrification, L-carnitine, Cholesterol-Loaded Cyclodextrin, Sperm, Sheep

P-710

Effect of oxytocin on cerebral damage, spatial memory and apoptosis in a rodent model of cerebral stroke

Shahein Momenabadi[1,2], Abedin Vakili[1,2],Mahdi Zahedi khorasani[1,2], Abbas Ali Vafaei[1,2], Zohreh Mazaheri[3]

1. Research Center of Physiology, Semnan University of Medical Sciences, Semnan, Iran.
2. Department of Physiology, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran.
3. Basic Medical Science Research, Histogenotech Company, Tehran, Iran

Background and Objective: Oxytocin (OXT) is a classic hormone that recently offers as a new therapeutic strategy for variety of mental disorders. In addition, new document has been found that OXT may have a positive impact on brain ischemia. Therefore, the present study was designed to determine the outcome of intranasal application OXT at various doses on brain damage, neurological function and exploring possible molecular mechanisms in acute phase of stroke in mice.
Material and methods: Cerebral ischemia generated by middle cerebral artery occlusion (MCAO) for 60 min and 24h reperfusion in mice. OXT at doses of 1, 2, 4 and 8 IU/per mouse were given intranasally at starting of ischemia. Infarct size, neurological outcome and spatial memory were evaluated by standard methods. TUNEL positive cell (apoptosis) in cortex and hippocampus was measured by fluorescent immunohistochemistry staining 24h after stroke. Results: OXT at doses of 4 and 8 IU/per mouse significantly reduced infarct size by 42% and 52%, respectively, and improved neurological and spatial memory ($P < 0.001$),while other doses did not change ($P > 0.05$).Treatment with OXT in therapeutic dose (8 IU/per mouse)significantly diminished TUNEL positive cell in the brain ($P < 0.001$).
Conclusion: Finding of current study indicated intranasal exposure to OXT limited ischemic injury that was associated with recovery of neurological function and spatial memory. The protective effects of oxytocin may be due to the attenuation of apoptosis.
Key words: Cerebral ischemia, Oxytocin, spatial memory, Infarct size, Apoptosis, Mice

P-711

The effect of methanolic extract of fenugreek on learning and memory in an experimental model of Alzheimer's disease in the rat

Leila Nasiri[1], Hoora Zardooz[2], Zahra Kiasalari[3], Mehrdad Roghani[3]

1. Department of Biology, Faculty of Science, Shahed University, Tehran, Iran.
2. School of Medicine, Shahed University, Tehran, Iran.
3. Neurophysiology Research Center, Shahed University, Tehran, Iran.

Background and Objective:Alzheimer's disease (AD) is regarded as the most prevalent phenotype of dementia with debilitating disability in learning and memory. With respect to anti-oxidative and neuroprotective potential of

Trigonellafoenum-graecum (TFG; fenugreek), this study was conducted to evaluate the effect of its alcoholic seed extract on learning and spatial memory in an experimental model of AD induced by amyloid beta 25-35 in rats.
Materials and Methods: In this experimental study, 32 male Wistar rats were divided into 4 groups, i.e. sham, extract-treated sham, AD, and AD group treated with TFGextract. For induction of AD, β-amyloid 25-35 (at a dose of 10 µg/2 µl) was bilaterally microinjected into CA1 area of the hippocampus. The treatment groups received alcoholic extract of TFG (i.p.) at a dose of 200 mg/kg for 1 week till 1 h before the surgery. At 4th week post-surgery, learning and memory was assessed using passive avoidance test and spatial memory was evaluated in Y maze.
Results: Treatment of AD group with the extract significantly prevented the reduction of step-through latency and extract treatment had no significant effect on spatial memory. In addition, extract treatment did not have a significant effect in the sham group.
Conclusion: TFG extract pretreatment of Alzheimeric rats could improve the ability of information consolidation and retrieval in passive avoidance test, however it could not affect recognitive spatial memory.
Key words: Alzheimer's disease, Trigonellafoenum-graecum, Amyloid beta, Learning and memory

P-712

The Therapeutic Potential of Losartan in Colorectal Cancer

Nazari, E.[1] ,Hashemzehi, M.[2] ,Asghrzadeh, F.[3] ,Khazaei, M.[4]

1. Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
4. Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

Background: Colorectal Cancer (CRC) is a disease with high incidence rates and mortality. The Renin-angiotensin system (RAS) is a hormone system that is upregulated in CRC. In current study, we evaluated the therapeutic potential of Losartan as a known angiotensin receptor antagonist in CRC model.
Methods: We used animal model of CRC by injection of 2*106 CT-26 cells in the left flank to investigate anti-tumor effects of Losartan, 5-Flurouracil (5-FU) and losartan+5-FU (combination). After 14 days, tumor samples were used for the evaluation of oxidative stress-balance and angiogenesis using immunohistochemistry.
Results: Combination of Losartan and 5-FU significantly inhibited tumor growth and histological staining of tumor tissues showed more necrosis and reduction of fibrosis compare to control. Our results also indicated a significantly reduction of tumor vasculature and capillary density following treatment with Losartan and combination of losartan and 5-FU. In tumor tissue, Malondialdehyde (MDA) level was increased and total thiol and catalase activity were decreased in treated group which were more significant in combination group.
Conclusion: These data showed anti-cancer potential of Losartan in combination with a standard chemotherapy agent can be mediated by reduction of fibrosis and tumor angiogenesis, modulating of oxidant/anti-oxidant status, supporting further studies on this therapeutic approach for colon cancer.
Keywords: Losartan, Renin-angiotensin system, Colorectal Cancer

P-713

Wound healing effects of topical Vitamin K: A randomized controlled trial

Nader Pazyar[1], Gholamreza Houshmand[2], Reza Yaghoobi[1], Ali Asghar Hemmati[3], Zahra Zeinelil[4], Behnam Ghorbanzadeh[5]

1. Department of Dermatology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2. Department of Pharmacology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
3. Department of Pharmacology, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
4. Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran,

5. Department of Pharmacology, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran

BACKGROUND: The incidence of acute and chronic wounds has rapidly increased which treatment remains as health problem. Previously, we reported the healing effect of Vitamin K in experimental animal models. The aim of this study was to investigate the effects of topical Vitamin K on skin wound healing process in patients.
MATERIALS AND METHODS: Sixty‐three patients with indication for high‐frequency electrocautery were enrolled in this randomized controlled trial. The patients were divided randomly into three groups. All the patients underwent high‐frequency electrocautery treatment. Then, the patients in the A group received 1% Vitamin K cream, the patients in the B group received 1% phenytoin cream. Furthermore, the patients in the control group received Eucerin. The wound status (width and the time of recovery) and complications in the three groups were evaluated 2 weeks after procedure by a dermatologist.
RESULTS: The effects produced by the topical Vitamin K showed a significant ($P < 0.05$) healing when compared with Eucerin group in parameters such as wound contraction and time to full recovery. Moreover, the healing time did not differ between phenytoin and Vitamin K groups ($P = 0.16$).
CONCLUSION: A randomized, controlled trial suggests that topical application of Vitamin K significantly reduces healing time in patients.
Keywords: Phenytoin, skin, topical application, Vitamin K, wound healing.

P-714

Effects of Saffron Aqueous Extract on Hepatic Angiotensinogen Gene Expression and Insulin Resistance in Rats under Sub-chronic Stress

YeganehYazdani[1], Maryam Radahmadi[2], Roshanak Roustazade[1], Mohammad Kazemi[3]

1. Medical Students' Research Center, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
2. Department of Physiology, Medical School, Isfahan University of Medical Sciences, Isfahan, Iran.
3. Department of Genetics and Molecular Biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

Background and Objectives: Stress induces insulin resistance (IR) through such mechanisms as Renin-Angiotensin System (RAS) induction, gene expression, and hormonal changes. Unlike stress, saffron alleviates IR. This study investigates angiotensinogen (Agt) gene expression and IR in subchronically stressed rats treated with saffron.
Materials and Methods: Male Wistar rats were allocated to the four control, restraint stress (6h/day/7days), and two stress-saffron (30 and 60 mg/kg/i.p/7 post-stress days) treatments. The glucose oxidase method, ELISA, and Real-time quantitative PCR were used at day 15 to measure serum glucose, insulin, and hepatic angiotensinogen gene expression, respectively, with homeostasis model assessment of IR (HOMA-IR) employed as an IR index.
Results: Compared to the control, the stress group exhibited significant ($P<0.01$) increments in Agt expression although it recorded similar glucose and insulin levels. While saffron led to significantly enhanced glucose levels ($P<0.001$ and $P<0.01$ in 30 and 60 mg/kg, respectively) with a corresponding elevated HOMA-IR with 60 mg/kg ($P<0.05$) compared to the control, the effect on insulin was non-significant. Compared to the stress-only group, the treatments with 30 and 60 mg saffron/kg recorded higher glucose and insulin levels, respectively, which led to increased HOMA-IR values ($P<0.05$ and $P<0.01$ in 30 and 60 mg/kg, respectively). Hepatic Agt gene expression increased under saffron treatment compared to both control ($P<0.001$) and stress-only ($P<0.01$ and $P<0.05$ in 30 and 60 mg/kg, respectively) groups.

P-715

Induction of cytotoxicity and apoptosis in FLT3 mutant expressing cells using novel pyrimido cyanoacrylates and quinoline derivatives

Mohammad-Ali Sobhanifar

Background: Aberrant activation of FMS-like tyrosine kinase 3 (FLT3) is associated with acute myeloid leukemia (AML). Leukemic cells expressing constitutively active FLT3 mutants are resistance to the current cancer therapies (radiotherapy and chemotherapy); hence, there is an increased interest to identify new agents for the treatment of

AML. The main aim of this study was evaluating cytotoxic effects of novel pyrimidocyanoacrylates and quinoline derivatives on FLT3 overexpressing cells.
Materials and Methods: Five novel pyrimidocyanoacrylates & 2-chloro 3-carbaldehyde quinolone derivative compounds, E1QAC1, E1QAC2, E1QAC3, E1QAC4, and E1QAC5 were designed and synthesized at the Department of Chemistry, Faculty of Sciences, Ferdowsi University, Mashhad, Iran. FDC-P1 cells expressing human wild-type FLT3 (FD-FLT3-WT) and internal tandem duplication (ITD) mutants (FD-FLT3-ITD) used in this study. The cells maintained in DMEM medium supplemented with 10% fetal calf serum (FCS) and murine granulocyte-macrophage colony stimulating factor (mGM-CSF). Potency for induction of cytotoxicity (IC50 value) and apoptosis was determined after treating the cells with concentration of the compounds by resazurin assay. Bax and Bcl2 activation status was also investigated by Western blot analysis.
Results: All the compounds had concentration-dependent effects on inhibition of cell proliferation and induction of apoptosis in both cell lines. E1QAC4 was the most potent compound for inhibition of cell proliferation (with IC50 value of 19 µM) and apoptosis induction in the FLT3-WT cells. However, FD-FLT3-ITD cells were nearly five-times more resistant to all the compounds (except than E1QAC2) that the FLT3-WT expressing cells. Western blotting results also showed that FD-FLT3-ITD cells had lower levels of Bax and higher levels of Bcl2 than the FD-FLT3-WT cells
Conclusion: The five novel heterocyclic compounds (E1QAC1-5) had cytotoxic effects and induced apoptosis in FD-FLT3 cells. Therefore, it is worthwhile to consider them as potential lead compound for development of new therapeutic agents for AML patients.
Keywords: FMS-like tyrosine kinase 3, Cell proliferation inhibition, Autophosphorilation inhibition, Small molecule inhibitors, Tyrosine kinase domain, FLT3 ligand, Tyrosine kinase domain inhibitors.

P-716

Effect of vitamin D on severity of morphine dependence in the conditioned place preference model in rat

Mahbubeh Saeedfar[1], Gholamreza Ghavipanjeh[2], Abolfazl Ardjmand[2]

1. Student Research Committee, Kashan University of Medical Sciences, Kashan, Iran
2. Physiology Research Center, Institute for Basic Science, Kashan University of Medical Sciences, Kashan, Iran

Aim: A large corpus of studies reveal the pivotal role of vitamin D (Vit.D) in the evolution and function of the brain. Both the Vit.D receptor and enzyme synthesizing the active form of Vit.D are found in some regions in rat brain (e.g. nucleus accumbens and other reward-related centers). Moreover, evidence show the involvement of Vit.D in the evolution of dopaminergic neurons in the nucleus accumbens, the increase in the expression of thyrosine hydroxylase and the regulation of dopaminergic processes. Hence, it is presumed that Vit.D can be considered as an effective therapeutic approach for narcotic addiction and substance abuse.
Methods: Male Wistar rats (220-220g) were assigned in 6 groups (control, vehicle, Mor, Mor+vit.D250, Mor+vit.D500, Mor+vit.D1000). Morphine (5 mg/kg) was used as an effective dose. Following each conditioning session in CPP, the animals received intraperitoneal Vit.D (250,500 and1000 U/kg).
Findings: The coadministration of Vit.D and the effective dose of Mor caused a significant increase in the place preference index in acquisition phase (One way ANOVA, $p < 0.05$).
Conclusion: Considering the increased place preference index induced by Mor, it can be concluded that Vit.D acts via the same path that the Mor does, so that can potentiate the Mor effect.
Keywords: Vitamin D, Morphine, Dopamine, Place preference, Rat

P-717

Experimental evaluation of mouse hind paw edema induced by Iranian Naja oxiana venom

Ramin Seyedian[1], Hossein Fatemikia [2]

1. Department of Pharmacology, Bushehr University of Medical Sciences, Bushehr, Iran
2. Department of Physiology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Background and Objectives: Iranian Naja oxiana known as cobra snake inhabits in northwestern part of Iran. This study was set out to evaluate the edematogenic potency of the crude venom with intraplantar injection in mice. Additionally, the inhibitory effects of three different drugs (promethazine,dexamethasone, and piroxicam) on paw edema were examined.
Materials and Methods: Paw edema was induced by intraplantar injection of different concentrations of the venom (0.5-10µg dissolved in 50µl of normal saline) in mice. It was estimated by measuring the increase of this parameter (%) with a digital caliper. Drugs were pretreated and the rate of changes in paw thickness was measured after the

venom injection. Meanwhile, the pathological findings in the treated paws were evaluated with Hematoxylin&Eosin (H&E) staining.
Results: Paw thickness reached its maximum amount within 5 minutes and resolved after an hour. This venom had no gelatinase activity with zymography method ruling out its role in edema . It caused nonhemorrhagic diffuse edema with infiltration of inflammatory cells (leukocytes and lymphocytes) in dermis. Pretreatment with drugs intraperitoneally inhibited the venom-induced (1µg/paw) edema significantly, while unexpectedly all mice died a day after piroxicam injection.
Conclusions: This in vitro and in vivo preliminary study was shown for the first time that Naja Naja Oxiana venom induced nonhemorrhagic edema in a short time. Dexamethason (phospholipase A2 inhibitor, 1mg/kg) and promethasin (H1 inhibitor, 5mg/kg) decreased the venom induced edema ($P<0.001$). More studies need to be carried out to define the different mediators in venom induced edema formation.
Keywords: Iranian Naja oxiana, gelatinase, paw edema, envenomation.

P-718

Preparation of a soft contact lens model based on molecularly imprinted for timolol using computational method and experimental design

Faezeh Shakermahani[1], Mehdi Ansari[2], Payam Khazaeli[3]

1. Student Research Committee, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran
2. Pharmaceutics Research center, Kerman University of Medical Sciences, Kerman, Iran
3. Pharmaceutics Research center, Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: Molecular imprinting is a method for the preparation of polymeric systems with predetermined affinity and/or selectivity for specific molecules. The technique involves the formation of complexes between template molecules and functional monomers, followed by polymerization in the presence of cross-linker and an appropriate solvent. Soft contact lenses release the drug molecules to the postlens tear film, this results in a prolonged contact with the cornea surface.
Glaucoma disease is an abnormality in the production and drainage of aqueous humor which causes an elevation in the intraocular pressure (IOP). Timolol, a nonselective beta blocker, treats glaucoma by lowering the pressure inside the eye by inhibiting the production of aqueos humor.
Materials and Methods: In this project we used Hydroxy ethyl methacrylate and Methacrylic acid as functional monomers, Ethylen glycol dimethacrylate as cross-linker and timolol as template. In order to achieve the optimum amounts we used Gaussian program for computational modeling.
Timolol MIP was made by precipitation method and also non-imprinted polymer was made without the presence of timolol. Drug release and loading capacity of MIP was evaluated. Finally experimental design model gave us the best conditions for optimum loading.
Results: Timolol MIP showed a better selectivity and affinity for the polymer network. It had more drug loading capacity and drug release in comparison with the NIP.
Conclusion: The timolol MIP can be used as soft contact lenses in order to treat glaucoma.
key words: Contact lens, Molecular imprinting factor, Timolol

P-719

L-carnitine oral administration effects on genes expression in the liver and serum adiponectin levels in rat model of type 2 diabetes

Beydolah Shahouzehi[1,2], Yaser Masoumi-Ardakani[1]

1. Physiology Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
2. Cardiovascular Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: Diabetes is a chronic disease and considered as a public health problem globally. L-Carnitine is synthesized in liver and promotes fatty acids oxidation. Currently it is used as a supplement against weight gain. L-Carnitine value is reduced in diabetic patients and there are some studies which showed its beneficial effects in diabetes. But the mechanism of these beneficial effects is not clear. We evaluated oral L-carnitine supplementation on AMPK and PPARγ expression in the liver and adiponectin and insulin values in serum of diabetic rats.

Materials and Methods: Twenty-four male rats were randomly divided into three groups (n=8) as follow; Group I, control which did not receive any treatment, group II, Diabetic control which received STZ (45 mg/kg) and nicotinamide (200 mg/kg) by i.p injection, group III, diabetic rats which received 600 mg/kg/day carnitine orally for 35 days.
Results: L-carnitine supplementation reduced fasting glucose compared to control and diabetic groups (p=0.001, p=0.0001 respectively). Insulin level in the diabetic group significantly reduced compared to the control group. L-carnitine supplementation increased adiponectin levels compared to diabetic non treated rats (p=0.0001). HOMA-IR, as a method to measure insulin resistance, significantly increased in the diabetic group and reduced in the group that received oral L-carnitine supplementation.
Conclusion: we found that L-carnitine administration has valuable effects on type 2 diabetes rats' model. These promising effects are conducted through up regulation of PPARγ and AMPK and also elevation of serum adiponectin levels which has insulin sensitizing effects.
Keywords: L-carnitine, diabetes, AMPK, PPARγ

P-720

Both injection doses and slow release of progesterone are effective on histopathological changes after TBI.

Shirazpour Sara[1], Khaksari Mohammad[2*], Iranpour Maryam [3]

1. Neuroscience Research Center, Neuropharmacology I(1)nstitute, Kerman University of Medical Sciences, Kerman, Iran
2. Endocrinology and Metabolism Research Center, Institute of Basic and Clinical Physiology Sciences, Kerman University of Medical Sciences, Kerman, Iran
3. Pathology and Stem Cell Research Center, Department of Pathology , Kerman University of Medical Sciences, Kerman, Iran

Background and Objective: Progesterone is an ovarian steroid that has neuroprotective effects. In this study, we investigated these effects on some of the pathological parameters after traumatic brain injury (TBI) including: the edema stroma, neuron apoptosis, and vascular congestion.
Materials and Methods: Female ovaricetomized rats were divided into 8 groups: intact, sham, TBI, vehicle, LP (low dose of progesterone), HP (high dose of progesterone), CP (progesterone capsules), and Cveh (vehicle capsules). In LP,and HP groups receiving progesterone or vehicle, as a single dose (ip)2 hours, and in CP, and Cveh receiving implant capsules 6 hours following a diffuse TBI (Marmarou's method).Edema stroma, vascular congestion and neuron apoptosis in the Brain tissue were evaluated by Hematoxilin and Eosine method.
Results: The score of edema stroma, vascular congestion and neuron apoptosis in TBI, and vehicle groups are significantly increased compared to the sham group ($P<0.001$).That this increase, reduce in the LP, HP and CP – treated rats ($P<0.01$, $P<0.001$ and $P<0.05$, respectively). In addition, score of neuron apoptosis in the HP group is lower than LP group ($P<0.05$). The percentage changes in edema stroma and vascular congestion in the HP - treated group was significantly lower than in CP- treated groups ($P<0.05$).
Conclusion: Based on our histopathologic findings, we conclude that after TBI, both LP and HP, and CP were effective in reducing edema stroma, neuron apoptosis and vascular congestion.
Keywords: TBI, Progesterone, Edema stroma, Neuron apoptosis, Vascular congestion.

P-721

Sub-chronic administration of brewed coffee on rat behavior and cognition and oxidative stress Alzheimer's disease model

Gohar Sedaghat[1], Mohammad Ali Mirshekar[2,3*], Mahsa Amirpour [1], Farzaneh Montazerifar[1], Somayeh Miri[2], Shadi Shourestani[1]

1. Department of Food Sciences and Nutrition, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
2. Department of Physiology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
3. Clinical Immunology Research Center, Zahedan University of Medical Sciences, Zahedan, Iran

Background and Objective: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by intracellular neurofibrillary tangles and neuro-inflammation. Growing experimental evidence indicates diverse

biological effects of brewed coffee (BC) including antioxidant, neuroprotective and anti-inflammatory. However, the underlying neuroprotective mechanism of BC is still largely elusive. Keeping this in mind, the present study was aimed to investigate the neuroprotective effects of BC on STZ-induced AD.
Materials and Methods: We observed that path length and latency time and path length increased in STZ induced AD while BC administration enhanced these indices in the BC-STZ group. Results: After treatment with BC, latency times in groups with memory impairment enhanced in shuttle box and MWM tasks. Biochemical factors including lipid peroxidation marker and tumor necrosis factor-α increased in STZ induced AD and BC treatment ameliorated these. Total anti-oxidant concentration level has reduced in AD rats and otherwise, BC treatment has prevented its reduction.
Conclusion: Our study demonstrated that BC pretreatment significantly improved spatial learning and memory functions, effectively mitigated ICV-STZ mediated neuronal oxidative stress and improved neurobehavioral functions. Moreover, BC attenuated hippocampal neuro-inflammatory response in the hippocampus. Thus, our study further provides evidence for the therapeutic supplementation of BC for various neurodegenerative disorders including AD.
Keywords: Brewed coffee; Alzheimer, Inflammation, Oxidative stress, Rat

P-722

Oral administration of Auraptene and Umbelliprenin controls inflammation in a CFA-induced inflammatory rat model

Zhila Taherzadeh

Introduction: This experimental study was designed to evaluate systemic and local anti-inflammatory effects of auraptene and umbelliprenin, natural coumarin derivatives, in CFA- induced inflammatory rat model.
Methods & Materials: Arthritis was induced by complete Freund's adjuvant. Treatment with different doses of Umbelliprenin and Auraptene and indomethacin and prednisolone were given to rats intragastrically once a day from day 0 to day 28 .In the present study the effects of Auraptene and Umbelliprenin on arthritic profiles based on clinical score, paw edema size, histological changes, and activity of inflammatory mediators using CFA-induced arthritic rat are reported. Paw swelling was measured over 4days period using a plethysmometer. The effect of Auraptene and Umbelliprenin on the production of nitric oxide, prostaglandin E2, and inflammatory biomarkers (TNF-α, IFN-γ, IL-2, IL-10, IL-4, TGF-β and IL-17) were determined.
Results: Treated with Auraptene 64 and 32mM / kg produced the highest therapeutic effect in reducing the systemic inflammation in rats ($P < 0.05$). Also, the lowest edema and inflammation at the end of the study were observed in the group received Auraptene 64 mM / kg ($P<0.001$). In the treated groups, level of inflammatory cytokines (IL-2, IL-17, TNF-α, IL-4, IL-10) [except for Interferon gamma and TGF-β], as well as PGE2 and nitric oxide were significantly different compared to negative control group ($P<0.0001$). Also, histological studies, including the frequency of granuloma and keratosis, proliferation and infiltration of inflammatory cells, were not significantly different between the treatment groups ($P>0.05$).
Conclusion: Overall, according to the results of this study we can conclude that Auraptene and Umbelliprenin were able to effectively reduce systemic inflammation by affecting the production of inflammatory and anti-inflammatory cytokines, and reduced the foot Edema as an indicator of local inflammation.

P-723

The effect of methadone on blood glucose, lipids and glucose-modulating hormones in methadone-dependent Wistar rats

ZoyaTahergorabi[1], HadisehRahmani [2], Zahra Ghiravani[3]

1. Associate Professor, Medical Toxicology and Drug Abuse Research Center (MTDRC), Departmentof Physiology, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran
2. Member of Student Research Committee, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran.
3. Instructor of Physiology, Department of Physiology, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran.

Background and Objective: A growing body of evidence indicates that opioids regulate mechanisms activated during the stress response. This study was aimed to investigate the effect of methadone dependency on blood glucose, lipids and glucose-modulating hormones in methadone-dependent Wistar rats.

Materials and Methods: This study was performed on 40 Wistar rats weighing 150-350 g, in four methadone exposure and control groups of both males and females. All rats were weighed at the beginning and end of the study and their fasting blood glucose was measured using a glucometer. In order to induce addiction, methadone was injected intraperitoneal for 10 consecutive days at 5mg/kg dose. The control group received the same volume of only normal saline. At the end of the study, the rats were sacrificed and their blood serum collected to measure cortisol, glucagon, adrenaline and lipid profile levels.
Results: There was a significant decrease in the mean final blood glucose of methadone-treated versus control male rats (P = 0.02). There was no significant glucose difference, however, in female rats. Furthermore, a decrease in the mean serum levels of triglyceride (P=0.01), cortical(P=0.02), and adrenaline(P=0.03) occurred in male rats of methadone-dependent compared with control animals, but there was no significant difference in these values in female rats.
Conclusion: Our results showed that methadone significantly reduced serum glucose as well as triglyceride levels only in male rats, this being associated with a reduction in the level of counter-regulating hormones of carbohydrate metabolism. Changes in lipid profiles, however, occurred independently of gender.
Key words: Methadone, Glucose-modulating hormones, Wistar rats, Blood glucose

P-724

Effects of Pumpkin seed on sexual function, blood factors and sex hormones in male rats

Meysam Alamdari Far[1], Abdollah Abdollahpour[2], Jamshid Ghiasi Ghalehkandi[1]

1. Faculty of Veterinary Medicine and Animal Sciences, Islamic Azad University of Shabestar, Shabestar, Iran.
2. Faculty of Veterinary Medicine, Islamic Azad University of Tabriz, Tabriz, Iran.

3. Background and Objective: The purpose of this study was to investigate the effects of the pumpkin seeds in experiments based on completely randomized design.

Materials and Methods: 72 male rats with 4 times of treatment, repeated 3 times and each repetition contains 6 male rats with a period of 60 day. During the first week all of the groups fed with basic ration in order to adapt them to the environment and thereafter groups fed with experimental ration for the next 9 weeks. At the end of the week 8, after exclusion of the food intake, 6 rats were selected randomly from each group and blood samples were collected and then rats were killed with disjointing the necklace and their abdominal cavity was opened and their testicles and epididymis were removed. The values of the Cholesterol, Glucose, Triglyceride, total protein, Albumin, Urea, HDL, LDL and sexual hormones (Testosterone, LH, FSH) and survivability rate of sperms were determined in laboratory.
Results: The results showed that pumpkin seeds significantly decreased the concentration of Glucose, Cholesterol, Triglyceride, Urea, LDL, Testosterone and LH ($P<0.05$) and significantly increased the concentration HDL ($P<0.05$), but had no significant effect on the concentration of total protein, Albumin and FSH. Furthermore effect of pumpkin seed on survivability rate of sperms were significant ($P<0.05$).
Conclusion: The results showed that using the experimental ration containing 0.6 gr per kg pumpkin seed in comparison with treatment group had the most decrease in the number and survivability rate of sperms.
Keywords: Pumpkin seeds, Biochemical factors, Testicles, Function of sexual hormones, Male rat

P-725

Gender-related relation between metabolic syndrome and S447X and HindIIIpolymorphisms of lipoprotein lipase gene in northern Iran

Elaheh Abdollahi

Background and Objective: Metabolic syndrome is a cluster of conditions that increase risk of cardiovascular morbidity and mortality. Among genetic factors that contributed to incidence of metabolic syndrome, polymorphisms of lipoprotein lipase (LPL) are major candidates especially because of their effect on obesity and dyslipidemia. S447X (rs328) and Hind III (rs320) polymorphisms of LPL gene have been reported to change LPL activity. This study investigates the effects of these gene polymorphisms on factors affecting metabolic syndrome in northern population of Iran.

Materials and Methods: Studied population included 223 adults consisting 90 women and 133 men with body mass index (BMI) ≥ 30 kg/m2 as obese subjects, and 156 healthy participants as a control group with BMI <25 that included 68 women and 88 men. All factors causing metabolic syndrome were evaluated. In addition, DNA was extracted from blood samples and HindIII and S447X LPL gene polymorphisms were screened by polymerase chain reaction-restriction fragment length polymorphism method (PCR-RFLP).
Conclusion: The present study proves that some genotypes of HindIII were associated with a reduced risk of developing low HDL-C only in men, while the protective effects of S447X on hypertriglyceridemia were only seen in women. The point is that this relation is affected by the weight profile of the participants. It can be concluded that there is a gender-related relation between the polymorphisms of LPL gene and the risk factors for incidence of metabolic syndrome in the northern population of Iran.
Keywords: Metabolic syndrome, Obesity, lipoprotein lipase (LPL) Polymorphism, S447X, HindIII

P-726

Survey on the anti-fungal activity of a synthetic econazole derivative in mice

Masoumeh Ezzati Givi[1], Masoud Ghorbanpoor[2], Marzieh Namazi[3]

1. Department of Pharmacology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Iran.
2. Department of Pathobiology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Iran.
3. Faculty of Science, Shahid Chamran University of Ahvaz, Iran.

Background and Objective: Fungal infections become a public health problem due to the increase in populations at risk, particularly among severely immunocompromised patients. candida albicans is a common human fungal pathogen capable of causing serious systemic infections that can progress to become lethal. recently, the incidence of resistance to antifungal treatment of Candida spp. has increased rapidly, which is of serious concern for healthcare professionals. The aim of this study was to assess the anti-fungal activity of a new synthetic econazole derivative in mice with cutaneous candidiasis.
Materials and Methods: First the MIC and MFC of the new econazole derivative was assessted by disk diffusion and microdilution methods. Then antifungal effect of this topical synthetic compound was investigated in the animal models of cutaneous candidiasis. Treatment groups included synthethic drug, commercial available antifungal drug and control groups. Drugs were applied once per day for 3 days. Wound repair process was assessed clinically and pathologically. The systemic absorption of this synthetic compound was also investigated.
Results: The MIC and MFC of the derivative of econazole were 8 µg/ml. The Invivo resoult showed the decreased size of the wounds by new synthetic econazole compared with control groups. The results indicated a lack of the systemic absorption of this compound.
Conclusion: The results of this study indicated the significant therapeutic effect of the investigated synthethic compound on superficial candida infection.
Keywords: candidiasis, Econazole, Balb/C mice

P-727

Hormetic Effect of some Phytochemicals in Myeloid Cell Leukemia Type-1 Gene Expression by overcompensation stimulation method

Omid Gholami, Zahra Kafi, Davood Mahdian

Cellular and Molecular Research Center, Faculty of Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran

Background and Objective: Hormesis is a new concept in dose–response relationship. Despite of traditional dose–response curves, there is a low-dose stimulation and a high-dose inhibition in this case. Hormesis effect in apoptosis induction/inhibition by natural compounds is reported previously. Here, we searched this effect for myeloid cell leukemia type-1 (Mcl-1) gene expression by phytochemicals 7-isopenthenyloxycoumarin (7-IP), arctigenin (Arg), and hesperidin (Hsp). This phenomenon is reported for the first time.
Materials and Methods: First we tested the cytotoxicity of various doses of these compounds against K562 leukemia cell lines for different times by 3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide method. After that

we explored the effect of various doses of these phytochemicals on Mcl-1 gene expression for different times by real-time polymerase chain reaction method.
Results: We found that these phytochemicals have cytotoxicity against K562 cell line. Hesperidin is the most cytotoxic agent. We also found that these natural compounds have hormetic effect on Mcl-1 gene expression. The hormetic model in Mcl-1 gene expression is overcompensation stimulation.
Conclusion: We conclude that 7-IP, Arg, and Hsp are cytotoxic against K562 cancerous cells and induce/inhibit Mcl-1 gene expression by hormesis dose–response relationship.
Keywords: 7-isopenthenyloxycoumarin, arctigenin, hesperidin, myeloid cell leukemia type-1 (Mcl-1), hormesis

P-728

Evaluation of protective effects of methylene blue on testicular damage induced by cisplatin

Fatemeh Gholami Jourabi[1], Siamak Yari[1], Ali Heidarianpour[2]

1. Department of Biology, Faculty of Science, Bu-Ali Sina University, Hamedan, Iran.
2. Department of Exercise Physiology, Faculty of Physical Education and Sport Sciences, Bu-Ali Sina University, Hamedan, Iran

Objective/Background: Cisplatin (CP) is an effective chemotherapeutic drug, but generation of reactive oxygen species (ROS) has limited its usefulness due to its toxicity to normal cells including testis cells. Methylene blue (MB) is a reducing agent that can act as a powerful antioxidant and also as an enhancer of the electron transport chain preventing formation of mitochondrial oxygen free radicals. This research was designed to investigate the protective effect of MB on CP-induced toxicity on reproductive system of male rats.
Materials & Methods: in this study, 35 male rats were divided into 5 groups: control, CP (5 mg/kg) given intraperitoneal as single dose), CP+ MB (4 mg/kg by Subcutaneous injection), CP+MB (2 mg/kg) and MB (4 mg/kg). Experimental period was 7 days. After treatment, serum from all groups were collected for biochemical analysis. Histological examination and sperm parameter inclouding: sperm count, viability and motility were evaluated.
Results: our data indicate a significant reduction in the sperm count, motility, viability in cisplatin group but MB ameliorate this reduction in CP+MB group. The MB treated group showed an improved histological appearance in compared to CP group. In addition, serum testestrone level in CP group reduced significantly and MB with high and low dose prevent this reduction.
Conclusion: In conclusion, our study showed that MB can correct the histological damages caused by cisplatin, improve the sperm parameters and the amount of testosterone hormone.
Key words: Cisplatin, Methylene blue, Testis, Rat

P-729

Assessment of Protective effects of carvacrol and rutin on haloperidol-induced oxidative stress and genotoxicity, in peripheral blood lymphocytes

Mehdi Evazalipour[1], Hediye Fatemi[2], Alireza Ahmadi Shad[2], Ehsan Zamani[3*]

1. Department of Pharmaceutical Biotechnology, School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran
2. Student Research Committee, School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran
3. Department of Toxicology and Pharmacology, School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran

Background and Objective: Haloperidol (HP) is a widely used antipsychotic drug that its long-term use may lead to complications such as genotoxicity. One of the suggested mechanisms for this toxicity is oxidative stress whose role in causing genetic damage was evaluated in this study by using carvacrol and rutin (as potent antioxidants) in human peripheral blood lymphocytes (PBL).

Materials and Methods: PBL samples of a healthy man were prepared and were divided into 5 groups: control group (receiving normal saline), HP group (5 ng/ml), HP and rutin (50µM) group, HP and carvacrol (100µM) group, HP and vitamin E as positive control group. Micronucleus test and comet assay were performed to determine genotoxicity. In addition, we assessed lipid peroxidation and glutathione oxidation to investigate oxidative stress.
Results: The micronucleus test showed a significant increase in micronucleus frequencies for the group exposed to HP, and an increase tail length was observed in the comet assay (compared with control group). Interestingly, rutin or carvacrol significantly decreased genotoxic effects of HP. Furthermore, the group treated with rutin or carvacrol showed inhibition in oxidative stress by decreasing lipid peroxidation and glutathione oxidation as well as vitamin E.
Conclusion: The results of our study indicate that haloperidol causes genotoxicity due to oxidative stress. Analysis of micronucleus and comet assay data prove that carvacrol and rutin significantly reduce the extent of these genetic damages by their antioxidant properties.
Keywords: Haloperidol, Rutin, Carvacrol, Oxidative stress, Genotoxicity, Micronucleus, Comet assay

P-730

Learning to obtain food on specific time dramatically provokes plasma ghrelin-induced dopamine release in the hippocampus of adult male rats

Maedeh Ghasemi[1*], Nasrin Mehranfard2, Alireza Halabian3, Maryam Radahmadi1, HojjatAllah Alaei[1]

1. Department of Physiology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
2. Neurophysiolog Research Center, Urmia University of Medical Sciences, Urmia, Iran
3. Department of biology, School of Science, Isfahan University, Isfahan, Iran.

Introduction: Ghrelin is about more than just as a “hunger” hormone. It’s also central to learning feeding behavior through dopamine release or signaling in the brain. Here, we examined whether endogenous ghrelin response to a combination of chronic scheduled –caloric dietary will affect hippocampal dopamine level and there is a relation between circulating ghrelin, the hippocampal dopamine and memory performance.
Methods: Forty male Wistar rats (180-200gr) were distributed into four groups (n=10), freely fed (control) and three scheduled-fed groups with different caloric intakes; high fat, standard and restricted diet. At the end of study (on day 16), passive avoidance test (for learning and memory) as well as circulating ghrelin were evaluated. The hippocampus homogenates were analyzed using HPLC with electrochemical detection to quantitate dopamine levels.
Results: Anticipation of a meal on specific time intensely provoked the hippocampus dopamine release rather than fasting condition. Dopamine level was the highest in scheduled-restricted feeding ($P< 0.01$). There was a significant positive correlation between the hippocampal dopamine and circulating ghrelin in all scheduled-feeding groups. A positive correlation just was found between plasma ghrelin level and memory performance for freely fed and scheduled- standard groups ($P<0.001$).
Discussion: Current data emphasis the fact that nutritional balance and incentive signals of diet are critical determinants of memory performance in scheduled diets, not just ghrelin concentration.
Key word: Scheduled –dietary, Ghrelin plasma level, Dopamine, Hippocampus, memory

P-731

The effect of selegiline on acute toxicity of aluminium phosphide in rats

Adeleh Maleki[1,2], Nastaran Rahimi[1,2], Ahmad Reza Dehpour[1,2*]

1. Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran.
2. Department of Pharmacology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Background and Objective: Aluminium phosphide (AlP); rice pill, is a highly toxic substance with a high mortality rate and no effective antidote. Selegiline is a monoamine oxidase inhibitor with antioxidant and anti-apoptotic properties. Since AlP has detrimental effects on cardiac physiology and mitochondrial function, we aimed to investigate the protective effects of selegiline on the AlP-induced oxidative damage and injuries in rats.

Materials and Methods: AlP (8, 12 mg/kg) was given to male Wistar rats (weighing 200–250 gr) by gavage to induce toxicity. Selegiline (1, 5 and 10 mg/kg) injected intraperitoneally in the treatment groups 1 hr after AlP poisoning. The rats, which survived after 24 hr, anesthetized, then cardiac tissues were removed, and the mitochondrial function were assessed. Pathological analysis on the stomach and duodenum was also evaluated.
Results: Our results suggest that selegiline treatment following AlP intoxication, reduced oxidative stress (decrease the reactive oxygen species and malondialdehyde), and increased glutathione in the cardiac tissue of rats exposed to AlP. Further, the mitochondrial membrane potential ($\Delta\Psi m$) collapse reversed after treatment with selegiline. The histopathological evaluation revealed that selegiline eliminated the inflammation and injuries induced by AlP in the stomach and duodenum.
Conclusion: Selegiline treatment can ameliorate the AlP-induced cardiac and gastrointestinal injuries in rats via boosting redox status and mitochondrial function with no significant effect on survival. We suggest that using selegiline, apart from other clinical treatments, may improve the quality of treatment process for AlP toxicity.
Keywords: Aluminium Phosphide; Mitochondria; Selegiline; Cardiac Toxicity; Rat

P-732

The effect of maternal treatment of troxerutin during pregnancy on serum level of apelin and stereological structure of testis in male offspring with obese mother

Keyvan Mehri[1], Shirin Babri[1,2], Gholamreza Hamidian[3], Zohreh Zavvari Oskuye[1], Roghayeh Diba[1]

1. Department of Physiology, Tabriz University of Medical Sciences, Tabriz, Iran.
2. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
3. Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.

Background and Objective: Paternal obesity is associated not only with an increased incidence of infertility, but also with an increased risk of metabolic disturbance in adult offspring. The aim of this study was to evaluate the effect of maternal treatment of troxerutin on serum level of apelin and microscopical structure of testis in male offspring with obese mother.
Materials and Methods: Three-week-old female Wistar rats (n=40) received high-fat (HFD) or control diet for eight weeks. After maiting, pregnant females animals were divided in two sub-groups which treated or non-treated with troxerutin (150 mg/kg/day during pregnancy). HFD continued to the end of lactation. After weaning, the male offspring were fed by normal diet until 12 weeks of age and then uthenized and their serum was collected for measurement of apelin by ELISA. Their testes were fixed in 10% formalin for microscopical analysis. Total volume of testis and germinal epithelium and total number of spermatogenic, Sertoli and Leydig cells were estimated by stereological techniques. ANOVA test and Tukey's post hoc were performed for data analysis by SPSS.
Results: The results showed that HFD reduced serum level of apelin significantly compared to control groups. It was also revealed that administration of troxerutin in HFD group could significantly increase apelin. Our stereological analysis of testis indicated that there were no significant changes in microscopical structure of testis among experimental groups.
Conclusion: Our study indicated that troxrutin treatment during pregnancy can improved methabolic disturbance in reproductive system by modulation of serum apelin in male offspring.
Keywords: Troxerutin, Maternal high-fat diet, Apelin, Testis, Stereology

P-733

The comparison of mice autologous serum and bovine BSA impact on on quality and 2PN embryos numbers of NMRI mice in IVF medium

Sima Nassri, Akbar Karimi, Fatemeh Eslamian

Department of Biology, Payame Noor University, Tehran, Iran

Background and Objective: The in vitro embryo production technology permits to produce a large amount of embryo in various evolutionary levels and hence biological, reproductive and biotechnology scientists are interested in it. Some of applications of this technique as follows: infertility treatment especially in human, establishing new methods for determining the gender of fetus, treatment of diseases using stem cells, pharmaceutical purposes, research in all aspects of simulation and etc.The aim of this research is the comparison of mice autologous serum and BSA(Bovine Serum Albumin) impact on quality and 2PN embryos numbers of NMRI mice in In Vitro Fertilization (IVF) medium that by these experiments can be used the best serum in IVF medium to make a huge difference in patient cost, time, health and safety and the quality and quantity of embryos. Materials and Methods: This study use BSA and maternal autologous serum in IVF medium. The effect of BSA serum, autologous serum media on development of mice embryo are done in two groups with three repetition. Data differences in groups were considered at least $p < 0.05$ significantly. Results: Percentage of embryos received autologous serum was less than control group that is contain of BSA serum.Conclusion: Due to these results, preparation of BSA is more applicable for increasing quality and numbers of 2PN embryo quality compared to autologous serum.
Keywords: 2PN embryo, Autologous serum, BSA, IVF medium

P-734

The effect of troxerutin on caspase 3 and glucokinase expression of the liver in streptozotocin-induced hyperglycemic adult male rats

Azadeh Nochalabadi

Background and Objective: Hyperglycemia induces apoptosis in hepatocytes and glucokinase (GK) plays a key role in glucose utilization in the liver. Troxerutin is a natural bioflavonoid which our previous studies showed that it has anti-diabetic properties. This study was conducted to evaluate the effect of troxerutin on caspase 3 and GK gene expression of the liver in diabetic rats.
Materials and Methods: Fifty adult male wistar rats were divided into 5 groups including control, troxerutin, diabetes, diabetes+troxerutin and diabetes+insulin. Diabetes was induced by 55 mg/kg streptozotocin. Diabetes+insulin group received 4-6 U/day insulin NPH. Troxerutin and diabetes+troxerutin groups received 150 mg/kg troxerutin via oral gavage for 4 weeks. At the end of experiments, animals were uthenized and their liver were fixed in formalin 10% and after routine paraffin embedding processes, caspase 3 expression were studied by immunohistochemical technique. A part of each liver was located in RNA later solution for Real-time PCR analysis of GK gen expression. ANOVA test and Tukey's post hoc were performed for data analysis by SPSS.
Results: the results showed that diabetes induction increased caspase 3 expression and reduced GK gen expression in liver tissue significantly. It was also revealed that administration of troxerutin could decrease caspase 3 expressin similar to insulin. Our results indicated that troxerutin significantly increased GK gen expression more than insulin therapy.
Conclusion: Our study showed that troxrutin can restrain diabetes side effect in liver and be considered as a therapeutic strategy for improvement of structure and function of liver in diabetic patients.
Keywords: Troxerutin, Diabetes, Caspase 3, Glucokinase, Liver

P-735

Evaluation of the effects of using peroxisome proliferator-activated receptor alpha (PPARα) on brain infarction, brain swelling and edema in focal- transient cerebral ischemia in rat

Hadi Vahidi[1], Ali Noroozzadeh[1], Mohammad Taghi Mohammadi[1,2]

1. Department of Physiology and Biophysics, School of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran
2. Neuroscience Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

Background and Objective: Increasing evidence has demonstrated that activation of peroxisome proliferator-activated receptor alpha (PPARα), which belongs to the nuclear receptor family of ligand-activated transcription factors, following cerebral ischemia exhibit neuroprotective functions including anti-oxidative, anti-apoptotic and

anti-inflammatory effects. Hence, the aim of present study was to evaluate the pretreatment effects of PPARα agonist, fenofibrate, on brain infarction, tissue swelling and brain edema in an experimental model of ischemic stroke.
Materials and Methods: Experiment was performed in three groups of rats (N=24); sham, control ischemic and treated ischemic groups. Brain ischemia was induced by 90 min middle cerebral artery occlusion (MCAO) followed by 24 hours reperfusion. Rats received orally fenofibrate at dose of 200 mg/kg/day for 4 days before induction of MCAO. Neurological deficit score (NDS), infarct volume (TTC staining method), tissue swelling and brain edema were assessed 24 hours after termination of MCAO.
Results: MCAO induced neurological dysfunction (2.83±0.16) and brain infarction in control ischemic group (282±30 mm3) in accompany with brain swelling (15.13±2.29 %) and edema (17.23±1.97%). Administration of fenofibrate in ischemic treated rats significantly reduced neurological dysfunction (2.14±0.14), brain infarction (92±28 mm3), brain swelling (5.49±1.44) and edema (4.35±1.42%) compared to control ischemic group.
Conclusion: Our findings indicated that activation of PPARα by specific agonist, fenofibrate, effectively declines the cerebral ischemia-reperfusion injuries as well as brain swelling and edema in an experimental model of ischemic stroke.
Keywords: Ischemic stroke, Fenofibrate, PPARα, Brain infarction, Brain edema

P-736

Noscapine protects rat H9c2 cardiomyocytes against oxygen and glucose deprivation-reperfusion injury

Hannaneh Mohammad Rezaei[1], Gelareh Vahabzadeh[2], Hamidreza Soltani[3]

1. MSc. Student of Toxicology, Department of Pharmacology and Toxicology, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, Iran (IAUPS)
2. Department of Pharmacology, Iran University of Medical Sciences, Tehran, Iran
3. Cellular and Molecular Research Center (CMRC), Iran University of Medical Sciences

Background and Objective: This study aimed to investigate the effect of noscapine (1-5 µM), an alkaloid from the opium poppy, on H9c2 cells against 120 minutes oxygen–glucose deprivation/Reperfusion (OGD/R), an in vitro model of ischemia.
Materials and Methods: In vitro Ischemia/Reperfusion injury model was established on H9c2 cells underwent oxygen glucose deprivation (OGD) followed by reperfusion to simulate cardiomyocytes ischemia/reperfusion injury. Cells were transferred to glucose-free DMEM (Dulbecco's Modified Eagle Medium) and were exposed to hypoxia in a small anaerobic chamber. Cell viability and nitric oxide (NO) production were analyzed by MTT assay and modified Griess method respectively.
Results: The results showed that noscapine significantly enhanced the survival of H9c2 cells following OGD/R. The cardiotoxicities produced by 120 minutes OGD/R tested were significantly inhibited by 1 µM noscapine. Increasing noscapine concentration up to 5 µM produced a concentration-dependent inhibition of cardiootoxicity. Subsequently, noscapine remarkably was able to reduce nitric oxide production compared with the H9c2 cells exposed to 120 min OGD/R.
Conclusion: Taken together, these data suggested that pretreatment with different concentrations of noscapine exerted cardio protective effects exposed to120 minutes OGD/R-induced injury in H9c2 cells, at least partly via attenuation of nitric oxide production.
Keywords: Noscapine, Oxygen-glucose deprivation, H9c2 cells, nitric oxide

P-737

STUDY OF THE EFFECT OF CISPLATIN ON SPERM PARAMETERS AND TESTICULAR HISTOLOGY AND SUPPORTIVE EFFECTS OF PROPOLIS

Hadis Hashemi, Siamak Yari, Roya karamian

Department of Biology, Faculty of Science, BU-Ali Sina University, Hamedan, Iran.

Background/ objective: Cisplatin (CP) is a potent drug which, has been used against cancers. Contrary to its antineoplastic activities, CP has many adverse effects such as testicular damages. Reactive Oxygen Species (ROS) is known to provide a mechanism for the pathogenesis of CP-induced testicular damage. Propolis is a honeybee product contains phenolic and flavonoids compounds, which have been shown an antioxidative property. This study aimed to investigate the potentially protective effects of propolis extract on CP-induced testicular damages.

Materials and Methods: In this study, 35 male rats were divided into five groups(n=7each). Group1 control. Group2 received single intraperitoneal injections of CP at 5 mg/kg. Groups3 CP+ 100 mg/kg/day propolis (orally). Group4 CP+ 400 mg/kg/day propolis (orally) .Group5 400 mg/kg/day propolis (orally) treatment period was 7 days. After treatment,serum from all groups were collected for biochemical analysis and sperm parameters including: sperm count, viability and motility were evaluated. Histological evaluation whit eosin and hematoxilyn were performed.
Result: This study indicated that sperm count, viability and motility in CP+Propolis group are significantly higher than CP group. Serum testestron level in CP group reduced and propolis ameliorated this reduction. In addition, the propolis treated group showed an improved histological appearance in compared to CP group.
Conclusion: In conclusion, it was found that propolis acts as a potent antioxidant agent prevent testicular injury.
Keywords: Cisplatin, Propolis, Testis, Rat.

P-738

Investigation of the hypoglycemic antioxidant effect of four rice bran species in Iran

Maryam Hemati[1], Reyhane Sariri[2], Shirin Shahangian[3]

1. Department of Biology, University of Guilan
2. University Professor, Faculty of Sciences, Department of Biology, University of Guilan
3. Assistant Professor, Faculty of Sciences, Department of Biology, University of Guilan

Background and Objective: The growing interest on the replacement of synthetic antioxidants with natural ones has directed many researches toward the plant-derived raw materials. The special attention is focused on inexpensive and residual sources from food and agricultural industries. In the present study, the antioxidant, anti-bacterial and anti-amylase properties of the acetone, methanol and ethanol extract from bran of four rice varieties of Guilan province, including Hashemi, Tarom, Neda, Dasht were investigated.
Materials and Methods: Anti-amylase activity was evaluated by Bernfeld method using DNS reagent. DPPH and FRAP methods were used to determine the antioxidant activity of the extracts. Total phenol, flavonoid and anthocyanin contents were also measured. Antibacterial properties were studied using disk diffusion method and quercetin estimated by HPLC chromatography.
Results: The results showed that highest ferric reducing ability belongs to acetone extract of Dasht wastes (1/36 mM Fe (II)/g DW) and the highest percentage of free radical inhibitory belong to the acetone extract of Neda variety. Also, the highest amounts of phenol (0.79 mg GAE/g DW) flavonoids (55.49 µg QE/g DW) and anthocyanins (0.016 mg/g DW) belonged to the acetone extract of Dasht variety. Tarom variety showed the most efficient anti-bacterial activity on Escherichia coli and Micrococcus luteus bacteria, whereas Neda and Dasht varieties showed anti-bacterial potential against Pseudomonas Aeruginosa and on Staphylococcus aureus. Amylase activity test resulted in the conclusion that extracts prepared using mixed solvent possessed a considerable hypoglycemic activity.
Conclusion: In the present investigation, we found some considerable antioxidant, antibacterial and hypoglycemic activity from rice brans. Based on the results obtained from wastes of rice in this research, it could be concluded that many other natural wastes should be examined for various possible pharmaceutical and medical activities.
Keywords: Rice bran, antioxidant, diabetic

P-739

A practical guide for inducing a rat model of osteoporosis using ovariectomy

Nasibeh Yousefzadeh

Background and Objective: Osteoporosis is characterized by low bone mineral density and deterioration of the bone microarchitecture. Osteoporosis affects 200 million people worldwide and 34% of women older than 50 years. Since osteoporosis-induced fractures are associated with a high economic burden and increased morbidity and mortality, developing new strategies for prevention and treatment of osteoporosis are warranted. To do this animal models are appropriate tools. The aim of this study is therefore to provide a practical guide for inducing a rat model of osteoporosis using ovariectomy (OVX). Materials and Methods: Related articles on ovariectomized rat model of

osteoporosis between 1975 and 2019 were searched in PubMed. Advantages and disadvantages of the model are presented and points related to human studies are highlighted. Results: For management of osteoporosis, animal models of osteoporosis are appropriate tools, of which ovariectomized rat model of osteoporosis is the most commonly used model. OVX in rat is induced by dorsolateral surgery method and verified after 1-3 weeks by decreased serum estradiol levels, decreased uterine weigh, increased body weight, and disappearance of regular estrus cycle. Conclusion: Current data show that response of rat bones to OVX are dependent on the age of rat at the time of OVX (rats aged 6 months are more appropriate), type of bone (trabecular bone is recommended), site of bone (proximal tibia, lumbar vertebrae and femur are recommended) and duration of OVX (14, 30 and 60 days after OVX are recommended for proximal tibia, femoral neck, and lumbar vertebral body).
Keywords: Animal model; Bone; Osteoporosis; Rat.

P-740

Evaluation of antiviral properties of Yarrow alcoholic extract in ovo inoculation of Newcastle disease virus

Javad Rezanejad [1], Adel Feizi[2]

1. College of Veterinary Medicine, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
2. Assistant Professor, Department of Clinical Sciences, Tabriz Branch, Islamic Azad University, Tabriz, Iran

Yellow Yarrow (Achillea biebersteinii) is a kind of plants belonging to the Astraceae family which found in Europe, Turkey, Iran and Central Asia. In addition to its traditional application, this plant is remarkable due to its extract characteristics in modern medicine and various industries. The aim of this study was to evaluate the antiviral properties of alcoholic extract of yarrow on Newcastle disease virus.
Material and methods: for this purpose, the plant extract was prepared at 200 and 400 mg/ml dilutions and inoculated with virus (500µl of extract plus 500 µl of each virus dilution) into 9-day-old fertilized egg by Allantois fluid injection method. The eggs were kept at 350c and after 7 days, the EID50 virus and virus + extract composition were calculated by REED and MUNCH method.
Results: results showed that yellow yarrow extract at 200 and 400mg/ml dosage decreased the potency of the virus 50 and 100 times compared to the virus group respectively.
Conclusion: in this study, since at the beginning, the extract were adjacent to the virus and then injected into the eggs; it is likely that the plants antiviral properties may be influenced on the structure or ligands of the virus, so that it prevented the virus binding to the cell. It may also affect the process of virus replication within the cell. Due to the antiviral properties of yellow yarrow, this plant can be used for various industries, especially pharmaceuticals.
Key word: Achillea biebersteinii, Newcastle, egg

P-741

The effect of testosterone enanthate on Liver tissue in adult male rats

Fereshte Ebrahimian

Testosterone-enanthate is highly used by athletes for body building, because of its metabolic effects, many researches have shown that the high concentration of this component in the plasma may effects natural activity of endocrine glands and function of different organs especially liver.

In this study the effect of high dose of T.E. on liver function in strain rats has been considered. 50 adult male rats were divided in to 5 groups (n=10) as follow.

A. Gonadectomized rats which received TE (5mg/100g B.W.) intraperitoneally weekly, up to 9 weeks.
B. Control group (gonadectomized) received TE
C. Gonadectomized group received equal volume of the solvent (olive oil)
D. Control group (non-gonadectomized) received solvent.
E. Control group without any injection or surgery

After 63 days, liver tissue samples were collected from all groups, and serial sections were prepared for H&E staining. The central vein, interlobular connective tissue, hepatocyte sinusoid were studied for histomorphology.
The results show a significant difference ($p<0.05$) in diameter of above structures in group A in comparison with the control group. The results also express that T.E. can cause diameter increase of central vein, interlobular connective tissue, hepatocyte & sinusoid which is can be the reason of the liver dysfunction and congestion.

P-742

The Protective Effect of Sesame Oil on Doxorubicin Induced Nephrotoxicity

Abolfazl Khajavi Rad[1, 2*], Zahra Samadi Noshahr[1], Somaye Mahzari, Sara hosseinian[1, 2], Samira Shahraki[1], Mahnaz Allahyari[1]

1. Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
2. Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Objective: The aim of the present study was to investigate the effect of sesame oil (SO) against doxorubicin (DOX)-induced nephropathy in the rat.
Materials and methods: In this study, two doses of SO (3 and 6 ml/kg) were administrated orally for 6 consecutive weeks and DOX (5mg/kg) was intravenously injected on the 4th day of the experiment.
Results: DOX caused significant proteinuria and hyperlipidemia compared to control group ($p<0.001$). Significant decrease in total thiol contents and a significant increase in malondialdehyde (MDA) levels ($p<0.001$). Oral administration of SO significantly reversed DOX-induced proteinuria and hyperlipidemia compared to DOX group ($p<0.001$). Furthermore, compared to the DOX group, SO significantly increased the activity of total thiols content and decreased in MDA concentration ($p<0.01$).
Conclusion: The current study suggests that SO is able to improve kidney function as well as kidney tissue oxidative damage in DOX-induced nephrotic the rat.
Key words: Doxorubicin, Sesame Oil, Nephropathy, Oxidative Stress.

P-743

Efficacy of repetitive daily normobaric hyperoxia preconditioning against gentamicin-induced nephrotoxicity in rats

Khalil Pourkhalili[1], Samad Ansari[1], Zahra Akbari[1], Zeynab karimi[2], Soodabeh Zendeboodi[3], Mohammad Reza Farzaneh[4]

1. Department of Physiology, Faculty of Medicine, Bushehr University of Medical Sciences, Iran.
2. Nephro-Urology Research Center, Shiraz University of Medical Sciences, Iran.
3. Department of Internal Medicine, Bushehr University of Medical Sciences, Iran
4. Department of Pathology, Faculty of Medicine, Bushehr University of Medical Sciences, Iran.

Background and Objective: Gentamicin (GM) induced nephrotoxicity is one of the most common causes of acute kidney injury and limits its administration. Evidences suggest that pre-treatment with oxygen increases the activity of antioxidant enzymes and protects tissues against damage. In this study, the effect of daily normobaric heperoxia pre-treatment on alleviating gentamicin induced nephrotoxicity has been investigated.
Materials and Methods: 28 male Wistar rats were randomly divided into 4 groups (n=7): Control (received room air); Gentamicin (100 mg/kg, IP, for 9 days); Hyperoxia60 (60 min daily pretreatment with 95% oxygen and then 100 mg/kg gentamicin, IP, for 9 days) and Hyperoxia180 (180 min daily pretreatment with 95% oxygen and then 100 mg/kg gentamicin, IP, for 9 days). Then 24 h urine was collected and on day 10 the animals were sacrificed for serum, urine and renal tissue sampling.
Results: Results showed that hyperoxia significantly enhanced renal antioxidative capacity and decreased serum creatinine, BUN, potassium and renal failure index. Histological examination also showed that tissue damage in the hyperoxia groups was lower compared to the gentamicin group. However hyperoxia effect on body weight, kidney-to-body weight ratio, urine volume, blood urea nitrogen and glomerular filtration were not significant.
Conclusion: Although pre-treatment with hyperoxia enhances the antioxidant capacity of renal tissue and improves some of the functional and histopatological parameters of the kidney, it failed to completely eliminate the adverse effects of gentamicin induced nephrotoxicity. More studies are needed to determine the clinical effect of hyperoxia on gentamicin induced nephrotoxicity.
Keywords: Gentamicin, nephrotoxicity, normobaric hyperoxia, antioxidant

P-744

Effect of dietary nitrate or nitrite supplementation on PTZ- induced clonic seizure threshold in mice

Azhdar Heydari[1,2], Abolfazl Ardjmand[1,2], Shima Davoudi[3]

1. Physiology Research Center, Institute for Basic Sciences, Kashan University of Medical Sciences, Kashan, I.R. Iran
2. Department of Physiology, Faculty of Medicine, Kashan University of Medical Sciences, Kashan, I.R. Iran
3. Department of Physiology, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, I.R. Iran

Background and Objective: Nitric oxide (NO) has anticonvulsant or proconvulsant properties in different seizure models. Recently, nitrate-nitrite-NO pathway has been considered as an alternative route for NO production. Nitrate and nitrite are metabolized to NO or NO-like species to exert their biological effects Thus, the aim of this study was to evaluate the effect of dietary nitrate or nitrite supplementation on pentylenetetrazole (PTZ)- induced clonic seizure threshold and levels of total nitric oxide metabolites (NOx) in mice.
Materials and Methods: In this study, 40 NMRI male mice (n=8 in each group) were randomly divided into one control and 4 experimental groups receiving nitrate or nitrite at doses of 50 and 100 mg/l in drinking water for 21 days. Control animals were provided with tap water for 21 days. Seizure threshold was measured by intravenous (i.v.) infusion of PTZ. The NOx levels were measured using Griess method in the brain tissues.
Results: Only nitrate at a dose of 100 mg/l significantly ($P<0.001$) increased PTZ- induced clonic seizure threshold. The NOx levels significantly increased in all groups receiving nitrate or nitrite at doses of 50 and 100 mg/l ($P<0.05$).
Conclusion: The results of our study showed that the protective effect of nitrate on PTZ- induced seizure is partly mediated by NO-cGMP pathway. Nevertheless, it seems that some NO- independent pathways to be involved in this protective effect of nitrate on seizure threshold.
Key words: nitric oxide, nitrate, nitrite, pentylenetetrazole, seizure

P-745

Study of the effect of intracerebroventricular injection of kaempferol and its intraction with type B GABA recrptor on pain in male rat

Maryam esmaeili salem, Mohammad Zarei, Siamak shahidi, safoora raufi

Neurophysiology research center, Hamadan university of Medical sciences, Hamadan, Iran.

Background and Objective: kaempferol is one of the most important herbal active constituent with antinociceptive and anti inflammatory effects. The aim of this study was to evaluate the effect of intracerebroventricular injection of kaempferol and its interaction with Gaba type B receptors on pain in male rats.
Materials and Methods:In this experimental study, male rats (200-250 g) were divided to the following groups: sham(DMSO),naloxan, morphine, kaempferol at dosages of 0.5,1, and 1.5 mg/rat, baclofen, CGP35348, baclofen plus kaempferol (1 mg/rat) and CGP 35348 plus kaempferol (1 mg/rat). After cannula implantation in cerebroventricular area, the rats received target components and then evaluated by pain assessment test (tail flick test). data were analyzed by one-way anova followed by Tukey,s post-test.
Results:The result showed that administration of both kaempferol doses (0.5 and 1 mg/rat) had significant effect in comparisonto the control group on the tail flick test ($p < 0.05$)
Conclusion:The kaempferol probably has acute antinociceptive effects and exert this activity at least in part by activating GABA B receptors.
Keywords:kaempferol, GABA type B receptors, pain, central nervous system

P-746

Investigation of level of BDNF and NGF in brain and spinal cord in experimental endometrioses in rat and therapeutic effect of royal jelly on them

Fatemeh dejan, Mahnaz Taherianfard

Physiology division of Department of Basic Sciences, School of Veterinary Medicine, Shiraz University, Shiraz,Iran

Background and Objective: Endometriosis defines as the presence of endometrial gland and stroma in extra uterine places. It seems that changes in the BDNF and NGF concentrations in the spinal cord (SP) and brain to be the cause of endometriosis. The aim of present study was investigation of the effect of royal jelly (RJ) on the SP and brain BDNF and NGF concentrations in rat models of endometriosis.
Materials and methods: 32 Sprague Dawley, female rat's were randomly assigned to 4 groups as follow: Control; intact rats, Sham; animals operation was done without endometriosis induction, positive control; induction of endometriosis without any treatment, treatment; induction of endometriosis + 21 day orally administration of RJ 200mg/kg. Assessments of BDNF and NGF levels were done by ELISA test.
Results: according to present data endometriosis induction lead to production of mass in the peritoneum that significantly was larger in positive control than that experimental group .In brain positive control was significantly ($P<0.001$) higher than that other groups; BDNF in experimental group had not significant difference with control and sham. In positive control, NGF was significantly lower than that other group, while NGF in experimental group had not significant difference with control and sham groups. In SP both BDNF and NGF had no significant differences between all groups ($p>0.05$).
Conclusion: RJ can reduce the size of mass in endometriosis. It seems that endometriosis induction accompanying with increases in brain BDNF and decrease in brain NGF, while oral administration of RJ can improve these disorders.
Key words: Endometriosis, brain-derived neurotrophic factor, nerve growth factor, royal jelly

P-747

Chlorogenic acid inhibited growth in 4T1 cancer cell line and induced apoptosis

Zahra Changizi[1], Azam Moslehi[2], Ali Haeri Rohani[1], Akram Eidi[1]

1. Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran

2. Department of Cellular Molecular Research Center, Qom University of Medical Sciences, Qom, Iran

Background and Objective: Chlorogenic acid is an herbal compound with various effects like antiviral, antioxidant, and anticancer effect with low toxicity, which inhibits cell proliferation. Clinical studies had shown that chlorogenic acid has a positive effect on the different types of cancers treatment. So, this study evaluates chlorogenic acid effects on 4T1 breast cancer cells.
Materials and Methods: In this study, cell proliferation was measured using an MTT assay on 4T1 cells. Afterwards, other assays like Annexin V/PI, Bax, and Bcl-2 were detected by immunocytochemistry; also Caspase-3 and P53 proteins expression were carried out by flow cytometry.
Results: 200 µM of chlorogenic acid concentration showed the highest level of cytotoxicity toward 4T1 cells. Percentage of cell viability data were significant in 100 µM ($P<0.05$) and 150, 200 µM ($P<0.001$) doses. The evaluation by using Annexin V/PI showed cell apoptosis in 100 µM ($P<0.05$), 150 µM ($P<0.01$), and for 200 µM ($P<0.05$ and $P<0.01$). Immunocytochemistry results showed the upregulation of Bax and also the downregulation of Bcl-2 in 4T1 cells treated with chlorogenic acid ($P<0.001$). The expression level of P53 and Caspase-3 increased during the chlorogenic acid treated the 4T1 cells ($P<0.001$).
Conclusion: Our findings demonstrated that chlorogenic acid plays a notable role on apoptosis inducing in the 4T1 cells through regulation of apoptotic proteins.
Keywords: Chlorogenic acid, 4T1 cell, Apoptosis, Bax, Bcl-2, P53, Caspase-3

P-748

P-749

Effect of handling on migraine of mother-deprived neonatal rats

Abbas Tajabadi, Mehdi Abbasnejad, Saeed Esmaili Mahani, Razieh Kooshki, Parastoo Nikkhouy

Department of biology, Faculty of Scinces, Shahid Bahonar University of Kerman

Background and Objective: Previous studies showed that separating pups from their mother even for short time causes a serious behavioral problem. Here we evaluated the effect of pup rat handling on migraine in pups whith separated from mather.
Material and method: In the current experimental study, 28, one day aged rat pups were used. The pups were handled durig 1 to 21 days after birth time. At the age of 1 rats were divided in four groups: control, sham-vehicle, handling and mather-deprived, using Nitroglycerine for migraine induction. The test grooming was used for pain assessment.
Result: The data showed that mother- deprived-induced migraine intensity(P <0. 005)was significantly redused by handling (P<0.001).
Conclusion: It seems that handling of mather-deprivied neonatal rats, at the age of puberty has prevention effect on migraine hedache.
Key words: neonatal handling, deprivation, migraine, Rat.

P-750

Effect of maternal stress and oxytocin treatment on anxiety-like behaviors

Asma Alimolaie

Back ground and objective: research shows that prenatal stress can have significant effects on pregnancy, maternal health and human development across the lifespan. These effects may occur through the influence of prenatal stress-related physiological changes on the developing fetus. Much evidence suggests that anxiety-like behaviors is a consequence of prenatal stress. The Oxytocin hormone which is produced in the central nervous system and some tissues plays an important role in reduced anxiety and depression caused by stress. The purpose of this study was to investigate that treatment by Oxytocin could be improve anxiety caused by maternal stress.
Material and Methods: Pregnant rats were exposed to 60 minutes' restraint stress twice a day for eight days in late phase period of pregnancy. Male offspring of wistar rats (n=8 per group) were randomly divided into 3 groups. During puberty, two group of rats were treated with oxytocin at doses of 10 and 20 macro (intranasal) for 2 weeks. The control group did not receive stress. Learning and memory were examined by Open field and Plus maze tests.
Results: The results this study showed that maternal stress decrease has significant (P<0.01) in entrances, time and distance in Plus maze and Open field tests. Also treatment whit Oxytocin increased significantly in the time and distance traveled in the open arm of plus test and in the open field tests. (P<0.01)
Conclusion: Research has shown that maternal stress combined with treatment with oxytocin decrease on anxiety behavior.
Keywords: stress, anxiety, maternal stress, oxytocin,

P-751

The effect of oxytocin on maternal stress-induced impairment of spatial memory in adult rats

Fatemeh Ashrafganjoie[1] ,Sara Emadian[1], Manizheh Dogani[1] , Nayere Askari[1,2]

1. Department of Biology, Faculty of Sciences, Shahid Bahonar University of Kerman, Kerman, I.R. Iran

2. Immunoregulation Research Center, Shahed University, Tehran, I.R. Iran

Background and Objective: Several studies focus on the effects of maternal stress in adulthood. Relatively little is known about the early neurodevelopmental consequences of such experiences and their predictive value. Studies have shown that oxytocin is involved in the development Learning and memory. The purpose of this study was to investigate the Effect of maternal stress and oxytocin treatment on spatial learning and memory.
Material and Methods: Pregnant rats were exposed to 60 minutes' restraint stress twice a day for eight days in late phase period of pregnancy. Male offspring of wistar rats (n=8 per group) were randomly divided into 3 groups. During puberty, two group of rats were treated with oxytocin at doses of 10 and 20 macro (intranasal) for 2 weeks. The control group did not receive stress.
Learning and memory were examined by Morris water maze test.
Results: Our results indicate that maternal stress impairs learning and memory in water maze test. Also treatment whit Oxytocin improve memory in the maternal stressed group.
Conclusion: according to these data, maternal stress impaired spatial learning and Memory but treating with oxytocin inversed maternal stress-induced impairment of spatial memory.
Key words: Maternal stress, Oxytocin, Learning, Memory.

P-752

The Protective Effects of Ginger (Zingiber officinale Roscoe) Extract on Toxicity Induced by Ethanol in Rat brain

Khadijeh Nasiri[1], Abolfazl Akbari[2], Marjan Chahardahcherik[3], Mojtaba Heydari[4]

1. Department of Exercise Physiology, Faculty of Sport Science, University of Mazandaran, Babolsar, Iran.

2. Department of Physiology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.

3. Department of Biochemistry, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.

4. Research Centre for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Background and Objective: Ginger (Zingiber officinale Roscoe) is widely used in traditional medicine and can improve brain activity. This study was conducted to evaluate the effect of ethanol-induced oxidative stress in the cerebrum and cerebellum and the prophylactic effect of ginger extract on these organs by measuring the antioxidant enzymes activity including: glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT), and malondialdehyde (MDA).
Materials and Methods: Twenty eight adult male Sprague-Dawley rats were randomly divided into four groups and treated for 28 consecutive days as follows: control, ginger (1g/kg/day, by gavage), ethanol (4g/kg/day, by gavage) and ginger+ethanol (received ethanol after administration of ginger). At the end of study, animals were killed and encephalon and cerebellum were quickly removed and homogenated to evaluate biochemical parameters.
Results: The results showed that oxidative biomarkers in ethanol group have significant changes compared with other groups ($p<0.05$), while pretreatment with ginger could significantly ameliorate the level of these factors in ginger+ethanol group compared to ethanol group ($p<0.05$).
Conclusion: It can be concluded that ginger had protective effect against encephalon and cerebellum damage induced by ethanol in rats.
Keywords: Ethanol, Oxidative Stress, Ginger, Cerebellum, Encephalon

P-753

The cardioprotective effects of aminoguanidine on lipopolysaccharide induced inflammation in rats

Ali Akbar Asghari[1], Farimah Beheshti[1], Mahmoud Hosseini[1], Maryam Mahmoudabady[1,2]

1. Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

2. Neurogenic Inflammation Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran

Background and Objective: Systemic inflammation and sepsis are accompanied by production of huge amount of cytokines. Myocardial dysfunction is a recognized manifestation of this syndrome. Nitric oxide (NO) is considered to act as a precursor of free radicals to have a role in inflammation.
Materials and Methods: Fifty male Wistar rats were distributed into groups of 10 animals in each: (1) control (2) LPS (3) LPS-AG50, (4) LPS-AG100 and (5) LPS-AG150. Injection of LPS (1 mg/kg) was done for 5 weeks and 30 min before LPS administration AG (50, 100 and 150 mg/kg) was injected. Application of drugs was intraperitoneal.
Results: LPS evolved cardiovascular toxicity indicated by augmentation the level of nitric oxide (NO) metabolites, interleukin (IL)-6 and malondialdehyde (MDA) and lowering the content of total thiol groups, catalase (CAT) and superoxide dismutase (SOD) activity in serum, heart and aortic tissues. In AG treated groups' noxious effects of LPS did not observe in these organs.
AG reduced MDA, NO metabolites and IL- 6, whereas augmented total thiol, CAT and SOD activity in the heart, aorta and serum.
Conclusions: AG, as inducible NO synthase inhibitor (iNOS) reduced oxidative stress and inflammation induced via injecting LPS and maybe consider as cardioprotective in this regard.
Keywords: Lipopolysaccharide, aminoguanidine, oxidative stress, cardioprotective

P-754

Investigating the effect of low frequency stimulation of olfactory bulb on seizure severity and working memory improvement in kindled rats

Javad Mirnajafi-Zadeht*, Marzieh Khodadadi, Amir Shojaei

Department of physilogy Tarbiat modares university

Background: Low- frequency stimulation (LFS) is a potential therapeutic method for controlling the seizures in drug-resistant epileptic patients. In the present study, the effect of LFS applying in olfactory bulb (as a region that have high structural and functional connections with the limbic system) on hippocampal kindled seizures and working memory impairments was investigated.
Material and method: Adult wistar rats (280±20g) were randomly divided into Kindled and Kindled+LFS groups. In all animals, stimulating and recording electrodes were implanted into the CA1 region of the dorsal hippocampus and stimulating electrodes were placed in the olfactory bulb bilaterally. All animals underwent semi rapid kindling procedure. In Kindled+LFS group 4 trains of LFS (each train contains 200 pulses, 0.1 ms pulse duration at 1 Hz) were applied at 3 minutes, 6 h, 24 h, and 30 h after the last kindling stimulation. 24 h after the last LFS, kindling stimulations were applied 6 times and seizure severity was evaluated. The Y-maze test was also conducted on all animals in order to measure the working memory behavior.
Results: Application of LFS significantly reduced the seizure behaviors, decreased the after discharge duration and increased the latency to stage 4 seizures. In addition, LFS administration restored the impairment in working memory.
Conclusion: the olfactory bulb can be considered as an appropriate candidate area for applying LFS in order to reduce the seizure severity.

P-755

Formability of prions and disease development mechanisms by PrPsc

Navid Shahbazi Shiran

Student of Medical Laboratory Sciences, Faculty of Medicine and Paramedical Sciences, Ardabil University of Medical Sciences, Ardabil, Iran

Objective: This review paper mainly aims to develop a new rationale and knowledge as well as an analysis and evaluation of information published in the literature.

Methods: In this descriptive-analytical study, data were collected through a combined survey and documentation method (including identification, examination, classification, analysis, and conclusion of information) concerning the research topic.
Prion diseases are a group of fatal diseases with lethal disorders that affect animals and humans. These diseases cause progressive deterioration, damage, and atrophy of the central nervous system. In addition to common symptoms of the disease, its adverse effects extend to actions and behaviors. The brain appears porous and spongiform in autopsy. The causative agent of this disease was unknown for a long time. Over time, the cause of the disease was introduced as slow viruses, virions, etc. by various hypotheses. Finally, Stanley Prusiner (1987) proposed the single protein hypothesis, indicating that only a single protein PrPsc is the cause of the disease without the presence of nucleic acid. The pathogenic PrPsc is created from the spatial and three-dimensional deformation of a natural protein called PrPc, which presently has an unknown function and its encoding gene is located on chromosome 2.
PrPSC protein is an abnormal PrPC isoform with abundant beta-sheets that is resistant to the cellular protease action. Thus, they are accumulated in neurocytes and tend to attach each other creating amyloid filaments that ultimately destroy neurocytes. The disease symptoms appear depending on the region destructed in the brain. Scrapie was the first discovered group of this disease, which was prevalent in sheep aged 2-5 years.
Conclusion: Pathogenic prions are similar to normal PrP in terms of chemical composition, which have brought about problems in the disease treatment as they do not induce immune response in the body and have a long incubation period.
Keywords: Prion, Disease, Protein, Nervous system, Spongiform encephalopathy.

P-756

Comparison of inflammatory Response between low and high scored mustard gas injured victims in Sardasht

Atefe Mirzaei [1], Mohammad Reza Vaez Mahdavi[2*], Tooba Ghazanfari[3], Abolfazl Rahimi[4]

1. Islamic Azad University, Tehran Medical Branch, Tehran, Iran
2. Department of Physiology, Shahed University, Tehran, Iran
3. Immunology Research Center, Shahed University, Tehran, Iran
4. Islamic Azad University, Tehran Medical Branch, Tehran, Iran

Background and Objective: 8025 of the 12000 residents in Sardasht exposed to Mustard Gas invasion of Sadam-Iraqui army in 1987.
A national study called SICS was designed, in which different immunological and physiological variables in exposed citizens of Sardasht were evaluated, and this study is one of the branches of this project.
Materials and Methods: 326 mustard gas-exposed citizens and 124 individuals from the control group were chosen. Injuring score of exposure in considered as percent of injury by Iranian Veteran foundation. inflammatory cytokines levels IL-1α, IL-1B, IL-1Ra و TNF-α by ELISA were measured and analyzed.
Results: Serum level of Pro-inflammatory Cytokines decreased in exposed group compared to control group. In individuals who had lower score of injury, it was more significant.
Conclusion: Exposure to Mustard Gas can be considered as a stress, so that even after 20 years of the exposure, this stress stimulated glucocorticoid system and diminished pro-inflamatory cytokines. This stimulation in 5-25% scored victims, is weaker than in 30-70% injured. As a result, this weaker response is not enough to activate negative feedback necessary to decrease glucocorticioids to normal. This subsequently induce cortisol-escape, which means long term elevated level of serum cortisol, maintaining some sustained levels of stress, called as chronic stress. This finding demonstrates sustained chronic stress and cortisol-escape specially in lower scored victims, and not in higher scored individuals. In this condition the pro-inflammatory immune system will be inhibited. In such condition, cortisol is frequently secreted, and long-term glucocorticoid abnormalities lead to immune suppression and increase the probability of diabetes, cardiovascular and infectious diseases and inflammation.
Key words: Sulfur Mustard, Inflammatory, Glucocorticoid, Victims, Sardasht

P-757

The study of married and single females, received a training course on Principles of health maintenance based on Persian medicine, in terms of physical pain, social function and general health.

Zakaria Rohani Yazdeli, Mohammad Reza Vaez Mahdavi

Clinical Trial Research Center, Shahed University, Tehran, Iran

Background and Objective: When females are training in the principles of health maintenance, they not only care about their health, but also apply the principles for other members of their family to improve their health. The current research was aimed to examine the impacts of training of the principles of health maintenance in Persian medicine on physical pain, social function and general health among rural, married and single females.
Materials and Methods: In this study, 703 females ranging from 20 to 55 years old, 58 single and 645 married females, received training in the principles of health maintenance based on Persian medicine by Health Workers. Before and after carrying out training, the quality of their life is measured and recorded with the help of questionnaire SF36 survey.
Results: The results indicated that training had a significant impact on reducing physical pain, boosting social performance. However, training insignificantly affected general health while the health scores had increased. When the performance of single and married females was compared, the finding showed that there was not significant difference between these 3 dimensions even though married females' social performance before getting trained was higher than that of single females.
Conclusion: It can be concluded that lifestyle and social education decrease physical pain and the feeling of pain, respectively.
Keywords: Training, Persian medicine, Physical pain, Social function

P-758

Effect of long term application of probiotics on brain damage and spatial learning and memory in a mouse model with cerebral hypoperfusion

Abedin Vakili[1,2], Hamideh Rahmati[1],Shahein Momenabadi[1],Abbas Ali Vafaei[1,2],Ahmad Reza Bandegi[3], Zohreh Mazaheri[4]

1. Research Center of Physiology, Semnan University of Medical Sciences, Semnan, Iran.
2. Department of Physiology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran
3. Department of Biochemistry, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran.
4. Basic Medical Science Research, Histogenotech Company, Tehran, Iran

Background and Objective: Probiotics are referred to species of living microscopic organisms may help conserve the normal balance of the digestive system and/or manage diseases. This study designed to examines the effect of 21 days consumption of probiotics on hippocampus injury, spatial and learning memory and some potential molecular mechanisms in a mouse model with cerebral hypoperfusion.
Materials and Methods: Cerebral hypoperfusion was established in the mouse model by bilateral common carotid artery occlusion for 20 min and 24 h reperfusion. Mixtures of several probiotic bacteria at concentrations of 107, 108 and 109 CFU/day were orally administrated for three weeks before the BCCAO. Spatial and learning memory, histological damage and apoptosis were assessed in the CA1, CA3 and dentate gyrus (DG) of the hippocampus 24 h after ischemia. The malondialdehyde (MDA) content and brain-derived neurotrophic factor (BDNF) level were measured by ELISA technique.
Results: Prophylactic of probiotic considerably reduced the number of apoptotic cells and neuronal death in the CA1, CA3 and DG of the hippocampus at all three concentrations ($P<0.001$). In addition, probiotics reduced spatial memory impairment and neurological dysfunction only at the 109-CFU/day ($P<0.01$). Nonetheless, probiotics did not change the levels of BDNF and MDA in the hippocampus ($P>0.05$).
Conclusion: Our findings showed daily prophylactic ingestion of probiotics reduced hippocampus damage and prevented the spatial learning and memory deficit by suppressing apoptosis in the mouse model with cerebral hypoperfusion. Probiotic supplementation may be suggested as a useful preventive dietary strategy for groups susceptible to cerebrovascular diseases.
Key words: Cerebral hypoperfusion, Ischemia, Probiotic supplementation, Apoptosis, BDNF, spatial memory, Mice.

P-759

To study and comparison effect of involuntary exercise on hippocampal BDNF in male and female PTSD rats

Sakineh Shafia[1] , Ali Rashidy-Pour b Abbas Ali Vafaei[2], Moslem Mohammadi[1]

1. Department of Physiology , Mazandaran University of Medical Sciences, Sari, Iran

2. Laboratory of Learning and Memory, Research Center and Department of Physiology, Semnan University of Medical Sciences, Semnan, Iran

Background and Objective: PTSD is a syndrome resulting from the exposure to a life-threatening event. PTSD have detrimental effects on anxiety, cognitive abilities, and extinction and hippocampal BDNF.BDNF is a neurotrophin. Neurotrophins are neuronal growth factors, that responsible for control of neuronal survival, differentiation and synaptic plasticity in nervous system. They have important role in physiology, develop and pathology in mental disease. BDNF has a role in depression, anxiety and PTSD. Estradiol, testosterone have important role in BDNF mRNA expression in hippocampus and on BDNF function. The risk of psychosis in women is twice that of men. There are differences in emotional related neuronal circuits between two sexes. Physical activity is known to improve symptoms of neuropsychiatric disorders. we investigated difference in response to involuntary exercise in hippocampal BDNF in male and female PTSD rats.
Materials and Methods: Rats were divided to SPS and Sham groups. SPS rats were exposed to restraint (2h), forced swimming (20min) and ether anesthesia and were then kept undisturbed for 14 days. After that, they were subjected to moderate treadmill running (5 day per week) then followed for BDNF measurement.
Results: Male SPS rats exhibited reduced hippocampal BDNF. Moderate treadmill exercise, alleviated the SPS-induced alterations in hippocampal BDNF. In the female sex, SPS did not reduce hippocampal BDNF. Comparison between two sexes showed that exercise increased BDNF in male SPS rats than female SPS rats.
Conclusion: Exercise has the beneficial effects on the BDNF synthesize and in female SPS rats estrogen has important role on hippocampal BDNF synthesize.
Keywords :Post-traumatic stress disorder (PTSD), Single prolonged Stress (SPS), Moderate exercise, Brain-derived neurotrophic factor (BDNF)

P-760

Methadone affecting on lifespan and reproductive ability in Drosophila melanogaster

Zahra Rostami, Majid Hassanpour-Ezatti*, Sara Khabazan

Dept. Biology, Basic Sciences School, Shahed University

Background: Environmental conditions together with genetic makeup constitute main modulator of organismal lifespan and reproduction. Methadone (Meth) has elicited antitumor activity by down regulating the threshold of apoptosis but it induces adverse side effects such as genotoxicity. Opioid receptor activation induced alteration in expression of the PI3K, TOR, iNOS, and NF-κB genes that involved in lifespan and reproduction mechanisms in some organisms.
Objective: In the present study we examine the effects of methadone consumption on life-span and reproduction of Drosophila melanogaster wild-type flies.
Material and methods: Parental generation was exposed to (0.1, 1 and 5 µM/g culture media) of Meth. The development time from egg to pupa and from pupa to adult as well as fertility was evaluated.
Results: Flies reared on Meth-supplemented diet had significant dose dependently lower lifespan. The effects of Meth on the next, non-exposed generation caused significant reduction in the number of organisms reaching the pupal, imaginal and adult stages. The imagoes of first generation exposed to Meth showed some anomalies in body size and malformations, such as deformed wings and abdomens, smaller black abdominal zone. Meth had significantly reduced the reproductive output of parents and F1 progeny.
Conclusion: The results suggest that Meth can permanently reduce lifespan and reproductive potential in this animal model.
Keywords: Reproduction, Life Cycle, Lifespan, Drosophila melanogaster

P-761

Cardioprotective effects of nicotinamide-mononucleotide in combination with postconditioning modalities in aged rats: involvement of mitochondrial function and biogenesis

Reza Badalzadeh[1,2], Leila Hosseini[2], Manouchehr Seyedi Vafaee[3] , Mojgan Rajabi[4], Aniseh Javadi[5]

1. Molecular Medicine Research Centre, Tabriz University of Medical Sciences, Tabriz, Iran
2. Department of Physiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
3. Department of Nuclear Medicine, Odense University Hospital, Odense, Denmark
4. Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran
5. Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

Introduction: Ischemic heart diseases are the major reasons for disability and mortality in elderly. Here, we tried to examine the combination effects of preconditioning with nicotinamide-mononucleotide (NMN) and postconditioning with ischemia (IPost) or melatonin on cardioprotection and mitochondrial function in ischemia/reperfusion (I/R) injury of aged male rats. Methods: Aged Wistar rats were randomly allocated to seven groups (n=6/each) including: sham, control, NMN-receiving, IPost-receiving, melatonin-receiving, and combination therapies (NMN+melatonin or NMN+IPost). On Langendorff apparatus, isolated hearts were underwent 30-minutes ligation of LAD coronary artery to induce regional ischemia followed by 60 minutes of reperfusion. NMN (100mg/kg/day/i.p.) was administered for 28 days before I/R. At the onset of reperfusion, IPost was applied by 6 cycles of 10 seconds alternative occluding and opening of LAD, and melatonin (50µm) was added to perfusion solution for 15 minutes. Myocardial hemodynamic and infarct size (IS) were measured and left ventricular samples were obtained to evaluate cardiac mitochondrial function and biogenesis. Results: Melatonin-postconditioning and NMN had significant cardioprotective effects in aged rats, and they improved hemodynamic parameters, and reduced IS and LDH as compared with control group ($P<0.05$-$P<0.001$). However, IPost failed to induce protective effects. Pretreatment with NMN significantly increased the cardioprotection by IPost and melatonin ($P<0.01$). As compared to individual treatments, the combination therapies significantly reduced mitochondrial ROS levels and improved mitochondrial membrane potential and expression profile of genes regulating mitochondrial biogenesis (PGC-1α, Sirt1/3, Nrf1/2). Conclusion: Combination of NMN with IPost and melatonin can be a promising strategy to attenuate myocardial I/R damages in aged hearts. Restoration of mitochondrial function and biogenesis may substantially contribute to this cardioprotection.
Keywords: Aging; Myocardial reperfusion injury; Nicotinamide mononucleotide; Melatonin; Mitochondria, Postconditioning

P-762

Interaction of central nitrergic and oxytocinergic systems on food intake regulation in neonatal layer-type chickens

Mina Khodadadi[1], Anahita Vosughi[2*], Morteza Zendehdel[3], Homeyra Zandieh[4]

1. Assistant Professor, Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.
2. PhD candidate, Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.

3. Full Professor, Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tehran, ehran, Iran.

4. Graduated DVM student, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran.

Background and Objective Various neurochemical pathways are participating in the regulation of food intake in mammals and birds. Both oxytocin (OT) and nitric oxide (NO) are known as hypophagic agents in birds. Therefore, our hypothesis is a possible interaction between nitrergic and oxytocinergic systems on food intake in neonatal layer-type chickens. Materials and Methods This study consisted of 6 experiments and each experiment had 4 groups (n group=12, 5-day-old). In all experiments, intracerebroventricular (ICV) injections were infused with either control diluent or drug solution in 3-hour food deprived (FD3) chickens. Then the birds had ad libitum access to the food and water and cumulative food intake (gr) was measured based on the percentage of body weight (%BW). In experiments 1 to 3, ICV injections of L-arginine (as a precursor of NO, 200, 400 and 800 nmol), L-NAME (as a NOS inhibitor, 100, 200 and 400 nmol) and OT (2.5, 5 and 10 µg) were performed respectively. In experiment 4, each group received any ICV injections of L-NAME (100 nmol), OT (10 µg) or a co-injection of L-NAME (100 nmol) + OT (10 µg). In experiments 5, ICV injections of L-arginine (200 nmol), OT (10 µg) or a co-injection of L-arginine (200 nmol) + OT (10 µg) were infused to any group. Experiment 6 was similar to experiment 5, although the dose of OT was 2.5 µg in all the treatments. Results this study showed that ICV injection of L-NAME (100 nmol) significantly attenuated hypophagic effect of OT (10 µg) ($P<0.05$), however, ICV co-injection of L-NAME (100 nmol) and OT (10 µg) did not change the food intake ($P\geq0.05$). On the other hand, ICV injection of L-arginine (200 nmol) significantly amplified hypophagic effect of OT (10 µg) ($P<0.05$) and ICV co-injection of L-arginine (200 nmol) and OT (2.5 µg or 10 µg) decreased food intake significantly ($P<0.05$). Conclusion NO might mediate the hypophagic effect of OT in FD3 neonatal layer-type chickens.
Keyword: Oxytocin, L-NAME, L-arginine, Food intake, Bird

P-763

Co-administration effects of nitrite and sodium hydrosulfide on oxidative stress in type 2 diabetic rats

Asghar Ghasemi[1], Sevda Gheibi[2], Sajad Jeddi[1], Mattias Carlström[3], Khosrow Kashfi[4]

1. Endocrine Physiology Research Center, Research institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2. Maternal and Childhood Obesity Research Center, Urmia University of Medical Sciences, Urmia, Iran

3. Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

4. Department of Molecular, Cellular and Biomedical Sciences, Sophie Davis School of Biomedical Education, City University of New York School of Medicine, New York, USA

Background and Objective: Type 2 diabetes (T2D) is associated with increased oxidative stress as well as decreased nitric oxide (NO) bioavailability and deficiency in hydrogen sulfide (H2S). NO and H2S have been shown to exert protective effects against oxidative stress. In addition, there are important interactions between NO and H2S, and H2S increases NO bioavailability. The aim of this study was to determine the long-term effects of co-administration of nitrite and sodium hydrosulfide (NaSH) on oxidative stress in type 2 diabetic rats.
Materials and Methods: T2D was induced by a high fat-low dose streptozotocin regimen. Rats were divided into 5 groups: control, diabetic, diabetic+nitrite, diabetic+NaSH, and diabetic+NaSH+nitrite. Nitrite (50 mg/L in drinking water) and NaSH (0.28 mg/kg, daily IP injection) were administered for 9 weeks. At the end of the study, serum total antioxidant capacity (TAC), total oxidant status (TOS), glutathione (GSH), oxidized glutathione (GSSG), malondialdehyde (MDA), and activities of superoxide dismutases (SOD) and catalase (CAT) were measured.
Results: Compared to the non-treated diabetic rats, nitrite increased serum TAC levels and SOD and CAT activities. NaSH per se had no effect on serum oxidants and antioxidants levels. However, compared to the nitrite-treated diabetic rats, co-administration treatment resulted in further increases in serum TAC levels (155.9±9.5 vs. 132.8±8.1 μM, p=0.05) as well as SOD (45.0±2.3 vs. 36.8±4.5 U/mL, p=0.08) and CAT (7.1±0.6 vs. 5.8±0.5 U/L, p=0.04) activities.
Conclusion: Chronic nitrite administration decreased oxidative stress in type 2 diabetic rats. Co-administration of NaSH along with nitrite potentiated the anti-oxidant effects of nitrite.
Key words: Diabetes; NO, H2S; co-administration; oxidative stress; rat

P-764

Effect of combination therapy on resistance and apoptosis of melanoma cancer cell (B16f10)

Marjan Hajimoradi Javarsiani[1], Javad Sajedianfard[1*],Shagayegh Haghjoo Javanmard[2]

1. Department of Basic Sciences, School of Veterinary Medicine, ShirazUniversity, Shiraz, Iran,
2. Applied Physiology Research Center, Cardiovascular, Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran.

Background and Objective: Dacarbazine is considered as standard for treatment of melanoma, but resistance to anticancer therapy is a major cause of invasion of cancer stem cells. In vitro assays showed that Metformin interferes with cell viability, proliferation and apoptosis.
Materials and Methods: Melanoma cell line B16f10 was treated with Dacarbazine, Metformin and combination therapy. Cell viability was determined with MTT assay. The cytotoxicity effect of Dacarbazine was analyzed. To determine the effect of the drug on apoptosis the amount of total PARP and cleaved PARP were measured by western blot. The statistical significance of the differences was analyzed by one-way analysis of variance. The value of $P<0.05$ was considered significant.
Results: Cell viability, which was determined at various time intervals (24 and 48 h) and in the presence of different concentrations of the drug (≈0.7μM), was reduced by ~50% following 24 h. The proliferation rate was evaluated over 24-48 hours and 12 days using varying subcytotoxic and cytotoxic concentrations of Metformin (2-8μM) decreased in a dose-dependent manner. The results shown that resistance cell be slender spindles and better colonization. Metformin decreased the cytotoxicity of Dacarbazine accompanied by increased apoptosis.
Conclusion:This study showed that the drug combination induced significantly more apoptosis than when each drug is used individually. The present study demonstrates that treatment of B16 cells with metformin alone and with chemotherapy drug caused proliferation block and apoptosis and combination therapy with Dacarbazine decreased colonization. This study detect cPARP level could be affected by Metformin and DTIC. Metformin exerts potent anti-melanoma effect in vitro and can use with chemotherapy drugs.
Key Words: melanoma cancer cell (B16f10), resistance, apoptosis, combination therapy

P-765

The role of endocannabinoid system in the antidepressant and anxiolytic effects of exercise

Ali Ahmalalipour, Ali Fakhari, Leila Hosseinzadeh Anvar, Ghazal Khuhkan Saadi, Fatemeh Sheykhkanlu Milan, Mahdi Dolatyari, Siamak Rezavi, Ahmad Mobed

Research Center of Psychiatry and Behavioral Sciences, Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran

Background: The mechanism underlying the antidepressant effects of exercise remain unclear. Several credible mechanisms have been proposed, and one of the most famous suggested mechanisms is the endorphin hypothesis. The endorphin hypothesis explains the exercise has a positive effect on depression as a result of increased secretion of β-endorphin following exercise. Endorphin use opiate receptors and are related to a positive mood and an overall enhanced sense of well-being. However, because β-endorphin cannot cross the blood-brain barrier, it remains unclear if rise in plasma endorphins are directly linked to a reduction in depression. Recently, it has been shown that the phenomenon of "runner's high" or "euphoria",i.e. reduction in anxiety, which is often attributed to endorphin release, is not blocked by naloxone injection, an opiate antagonist. New studies suggest that other factors may be involved in the anxiolytic and antidepressant effects of exercise. One of the recently recognized system is the endocannabinoid system (EC) which is a prominent promoter of the emotional homeostasis, mediating the effects of different environmental signals including rewarding stimuli. Recent evidence suggests that changes in EC system could be involved in some actions of antidepressants. The pharmacological enhancement of EC activity appears to exert an antidepressant-like effect and a reduced activity of the EC system seems to be associated with the animal model of depression. Moreover, many studies have reported an interaction between antidepressants and the EC system. New findings suggest that exercise anxiolytic and antidepressant effects might depend on EC system. The enhanced anxiolytic and analgesic effects of exercise are shown to be absent in the EC receptor-deficient mice, lacking CB1 receptors in γ-aminobutyric acid neurins (GABA-CB1-/-). Therefore, recent findings suggest that EC system mediates some of the positives effects associated with exercise.
Keywords: endocannabinoid system, depression, exercise

P-766

Effects of Exendin-4 on Oxidative Stress and Metabolic Disorders Induced by Bisphenol A in Adult Male Mice

Golshan Afshari[1], Akram Ahangarpour[2], Seyyed Ali Mard[3]

1. Golestan hospital clinical research development unit. Ahvaz jundishapur university of medical sciences, Ahvaz, IR Iran
2. Department of Physiology, Cellular and Molecular Research Center, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran
3. Physiology Research Center, Research Center for Infectious Diseases of Digestive System, Department of Physiology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran

Background and Aim: Exendin-4 is a similar peptide to GLP-1 (Glucagon like peptide 1) and can interfere with various receptors of GLP-1. Bisphenol A (BPA), as an endocrine disruptor chemical, is used in a wide range of plastic products. The aim of this study was to clarify several exendin-4 aspects in treatment of metabolic disorders
Methods : In in vivo condition, the BPA (100 g/kg) and exendin-4 (4 nmol/kg/d) were administered for 20 days in four different groups, and blood glucose, insulin, lipid profile, adipocyte hormones and oxidative stress markers were examined using Elisa kits.
Results: The results indicate that co-administration of exendin-4 and BPA modified hyperglycemia ($p<0.001$) and hyperlipidemia ($p<0.01$) induced by BPA. Bisphenol A reduced antioxidant level, whereas exendin-4 improved these effects ($p<0.05$).
Conclusion: The findings of these studies suggest that the use of exendin-4 is useful in hyperglycemia, hyperlipidemia, and metabolic disorders, induced by BPA.

P-767

Early postnatal maternal deprivation affected maternal care and offspring body mass index

Homeira Zardooz[1,2], Roxana Karbaschi[1, 3], Soheila Maghamil, Fateme Binayil, Roya Ranjbar Saberl

1. Department of Physiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Neurophysiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3. Faculty of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Background and Objective: Early life growth impairment would cause long lasting health problems such as psychiatric and metabolic disorders during later life. One of the most important factors that cause neonatal growth impairment is maternal care deprivation. In this regard this study investigated the effect of repeated maternal deprivation on maternal care and body mass index (BMI) in offspring.
Materials and Methods: After birth, the pups were randomly divided into "control" and "maternal-deprived" groups. The maternal-deprived pups were separated from their mothers 3h/day at postnatal days (PND) 1 to 21, whereas the controls remained with their mothers. On PND-1 to PND-21, the body weight and length of the offspring were measured to calculate BMI. Moreover, some maternal behavioral parameters including grooming frequency, pup retrieval and first pup contact latencies were evaluated by pup retrieval test. After weaning the plasma corticosterone concentrations were measured in dams.
Results: In the dams deprived of pups, plasma corticosterone level increased, moreover after performing the pup retrieval test, they showed higher grooming frequency, pup retrieval and first pup contact latencies than the control dams. Wherease, maternal deprived offspring showed lower BMI than the controls.
Conclusion: It seems that owing to higher level of plasma corticosterone, the dams deprived of pups showed frequent grooming as a stressfull behavior. Accordingly, these dams showed longer latencies to first pup contact and retrieve pups back to the nest, compared to the control dams. Thus a poor maternal care might be the reason for lower BMI of the maternal-deprived offspring.
Keywords: maternal deprivation, maternal care, corticosterone, body mass index

P-768

Assessing the effect of valproate sodium on spatial learning and memory in morphine-tolerant rats

Seyed Hossein Marashi , Yaghoub Fathollahi

Introduction: Valproate can prevent dendrite malformation and spatial memory impairment in seizure model animals. Chronic morphine consumption causes side-effects such as drug tolerance, decrease in drug efficacy, spatial memory impairment, and dendrite malformation in the hippocampus. Valproate can prevent morphine drug tolerance. Therefore, we examined the effect of valproate on spatial memory impairment in morphine tolerant rats.
Methods and materials: Male wistar rats weighing 180 g at the beginning of experiment were used. All drugs were administered sub-cutaneously during the sixteen days of the experiment. Rats were randomly assigned to saline (2 ml/kg), morphine (3 mg/kg), valproate sodium (250 mg/kg), morphine valproate sodium, single shot morphine and single shot valproate sodium morphine. Analgesia was assessed during the first eight days using the Hargreaves apparatus. Short-term memory was tested using a y-maze on the ninth day. Five to seven days later, working memory was assessed using a y-maze with a different color. Results: While valproate sodium did not produce analgesia on its own, administrating this drug before each morphine shot did prevent tolerance expression. Chronic morphine impaired short-term spatial memory. Valproate sodium did not impair short-term spatial memory on its own, but administrating valproate sodium an hour before each morphine shot did not prevent this impairment either. No impairment was seen in single shot groups and no difference was seen in locomotion or working memory across the groups.
Conclusion: Chronic morphine (3 mg/kg) impairs short-term memory in the y-maze. Valproate sodium does not impair short term spatial memory on its own, but administering valproate sodium an hour before each morphine shot does not prevent impairment either.
Keywords: drug tolerance, morphine, valproate sodium, spatial memory, short-term, memory, working memory