

Memantine Attenuates Myocardial Remodeling and Lipid Peroxidation: A Cardioprotective Agent

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Abstract

Introduction: Heart failure is a common heart disease which is usually accompanied by ventricular hypertrophy and myocardial remodeling. The stimulation of NMDA receptors in cardiomyocytes by increasing reactive oxygen species (ROS) production can play pathological role. ROS can stimulate the heart fibroblast cells and can cause myocardial remodeling. Many studies have taken on the effect of antagonists of NMDA receptors such as memantine on CNS, but the therapeutic effects of memantine not been studied on the heart. The effect of memantine on cardiac remodeling such as Necrosis, Fibrosis, hypertrophy and also MDA level in isoproterenol-inducd heart failure was evaluated in present study.

Methods: Male wistar rats were randomly assigned to 4 groups of control, Isoproterenol (Iso) alone and pretreated with 5 and 20 (mg/kg/day) of memantine for 21 days by *ip* injection. Isoproterenol was injected subcutaneously at 7th day for induction of heart failure for 14 days. The wet harvested heart weight to body weight ratio was calculated to assessing the degree of myocardial weight gain. Histopathological examination were done on harvested heart and the pathological changes in the myocardial tissues were observed with Hematoxyline and Eosin (H&E) staining and Gomeri's one step trichrom method for evaluation of Necrosis and Fibrosis and malondialdehyde (MDA) for lipid peroxidation.

Results: Histopathological analysis showed a marked attenuation of myocyte necrosis and interstitial fibrosis in both treated groups with Memantine in comparison to Iso group (p<0.001). The heart weight to body weight ratio was also decreased significantly in treated group with 20 (mg/kg/day) of Memantine in comparison to Iso group (p<0.05). Additionally memantine at both doses reduced myocardial MDA level significantly in comparison to isoproterenol group (p<0.01).

Conclusion: The result of this study for the first time demonstrated cardioprotective effects of memantine and this action can be partially through attenuation of myocardial remodeling and oxidative stress.

Keywords: Memantine, Heart failure, Isoproterenol, NMDA receptors, Oxidative stress



Hydroalcholic Extract of Arum Orientale Decrease Cardiac Necrosis and Neutrophil's Activity in Myocardial Infarction in Rats

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Abstract

Introduction: Arum orientale, a traditional medicinal herb, is widely used in Iranian folk medicine for the treatment of various diseases such as respiratory infections. The present study was designed to investigate the anti-inflammatory effect of the hydroalcholic extract of Arum orientale, specially neutrophil recruitment and activity, on isoproterenol-induced myocardial infarction (MI) in rat.

Methods: Male wistar rats were randomly assigned to 5 groups of control, isoproterenol (MI), and treatment with 40, 80, and 160 mg/kg/daily of the extract given *ip* injection concurrent with MI induction. Isoproternol injection (150 mg/kg/daily) for 2 consecutive days (*sc*) was used to induce acute MI. Then, histopathological changes and inflammatory markers such as myocardial necrosis, neutrophil count and MPO activity (as a neutrophil's activity marker) were evaluated.

Results: Isoproterenol injection increased inflammatory response, as shown by a significant increase in myocardial necrosis, myocardial and peripheral neutrophil count and myocardial myeloperoxidase (MPO) activity. Hydroalcholic extract of Arum orientale with dose of 160 mg/kg/day significantly decreased myocardial necrosis (p<0.05), the number of myocardial and peripheral neutrophils (p<0.01, p<0.05 respectively) and also decreased myocardial myeloperoxidas enzyme (MPO) activity (p<0.05) in comparison to MI group.

Conclusion: Our results for the first time demonstrated possible cardioprotective effects of *Arum orientale* partially through it's anti-inflammatory effects.

Keywords: Arum orientale, myocardial infarction, isoproterenol, inflammation



Preparation, Characterization, and Cell Viability Study of C-MET Sirna-Loaded Chitosan Nanoparticles

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Abstract

Introduction: According to increasing incidence of cancer, gene therapy is becoming an incorporating tool to standard therapeutic protocols. Small interfering RNA (siRNA) can be useful for gene silencing in malignancy pathways. To deliver a specific siRNA to cancer cells, chitosan nanoparticles can be safe carrier with suitable entrapping characterizations (1). C-MET, belonging to receptor tyrosine kinase superfamily has an important role in tumor viability and invasion (2). In this investigation we prepared and characterized c-MET siRNA loaded chitosan nanoparticles and evaluated their cell viability on metastatic breast cancer cells (SKBR3).

Methods: For preparation of chitosan nanoparticles, depolymerized 140KDa chitosan (1mg/ml) was dissolved in DEPC water. 3μl of c-MET siRNA (19 μg/μl) was added to 1.2ml of carboxy methyl dextran (CMD) solution (1mg/ml). Prepared siRNA solution was added dropwisely to 3ml of chitosan solution under magnetic stirring (3). Formation of siRNA loaded nanoparticles was evaluated by electrophoresis on 2% agarose gel compared with naked siRNA. Transmission electron microscopy (TEM) was used to investigate morphology of nanoparticles. Particle size, poly dispersity index (PDI) and surface charge of the chitosan/siRNA nanoparticles were measured by dynamic light scattering (DLS) using Zetasizer. Cell viability evaluations were done through 24-hour and 48-houre MTT-assay on SKBR3 cells.

Results: Electrophoresis of siRNA loaded nanoparticles represented the validity of loading. Spherical morphology of nanoparticles was observed in TEM image which confirms the formation of nanoparticles. DLS and Zetasizer

results represented a narrow size distribution (PDI ~0.3), positive zeta potential (+25mV) and size range of about 70–110nm which indicate appropriate monodispersity, cellular uptake and pharmacokinetic properties, respectively. MTT-assay showed c-MET siRNA loaded nanorparticles had decreased cell viability comparing naked siRNA, declaring the protective effect of nanoparticles.

Conclusion: Applying siRNA in cancer therapy through safe carriers such as chitosan nanoparticles can cause improvements of standard existing treatments.

Keywords: Chitosan, c-MET siRNA, SKBR3 cells, breast cancer



15th IPSC Proceeding

IGF-1R siRNA-Loaded Chitosan Nanoparticles: Synthesis, Characterization and Cytotoxicity Studies

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Abstract

Introduction: Gene knockdown with short interfering RNA (siRNA) is progressive strategy in the treatment of cancer. Delivery of siRNA with nanocarriers is more acceptable approach in pharmaceutical researches. Cationic chitosan nanoparticles can entrap negatively charged siRNA and are appropriate vector for siRNA delivery (1). Type I insulin-like growth factor receptor (IGF-1R) has been recognized in tumorigenesis, metastasis and drug resistance. Therefore, IGF-1R is potent pharmacological target in cancer therapy (2). In this study, we synthesized

and characterized chitosan nanoparticles for IGF-1R siRNA delivery and cytotoxicity was investigated in metastatic breast cancer cells (SKBR3).

Methods: For synthesis of chitosan nanoparticles, depolymerized 140KDa chitosan (1mg/ml) was dissolved in DEPC water. 3μl of IGF-1R siRNA (19 μg/μl) was added to 1.2ml of carboxy methyl dextran (CMD) solution (1mg/ml). Prepared siRNA solution was added dropwisely to 3ml of chitosan solution under magnetic stirring(3). For confirmation of siRNA loading into nanoparticles, electrophoresis on 2% agarose gel was performed. For evaluation of the morphology of nanoparticles, TEM microscopy was used. Dynamic light scattering using zetasizer was used for measurement of the size, poly dispersity index (PDI) and zeta potential of nanoparticles. For assessing the cytotoxicity of nanoparticles, MTT bio-assay was used.

Results: Electrophoresis showed that siRNA was loaded into nanoparticles. Confirmation of nanoparticles' formation through TEM images represented their spherical morphology. Narrow size distribution (PDI ~0.22), positive zeta potential (+21mV) and mean diameters of 90nm were represented in DLS and Zetasizer results which show the proper monodispersity, cellular uptake and pharmacokinetic properties, respectively. Cell viability was significantly decreased by IGF-1R siRNA loaded nanoparticles in compare to naked IGF-1R siRNA, representing efficiency of the used carrier for siRNA delivery.

Conclusion: Incorporation of siRNA to standard of care in cancer treatment through appropriate vehicles can be an effective combination therapy which should be more investigated in future studies.

Keywords: siRNA, chitosan, nanoparticle, IGF-1R



15th IPSC Proceeding

Development a validation of a novel, simple, accurate spectrophotometric method for the determination of lead in human serum

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Abstract

Introduction: The determination of blood lead levels is the most useful indicator of the determination of the amount of lead being absorbed by the human body. Various methods, such as atomic absorption spectroscopy (AAS), have already been used for the detection of lead in biological fluid. In this study, a simple and accurate spectroscopic

method for the determination of lead has been developed and applied for the investigation of lead concentration in biological samples.

Methods: In this study, a silica gel column was used in order to extract lead and eliminate interfering agents in human serum samples. The column was washed with de-ionized water. The pH was adjusted to 8.2using phosphate buffer and then tartrate and cyanide solutions were added as masking agents. The lead content was extracted into the organic phase containing dithizone as a complexion reagent and the dithizone-Pb (II) complex was formed and approved by visible spectrophotometry at 538 nm.

Results: The recovery was found to be 84.6%. In order to validate the method, a calibration curve involving the use of eight concentration levels was calculated and proven to be linear in the range of $0.1\mu g/ml-1.5\mu g/ml$ with an R^2 regression coefficient of 0.9915. The largest error% values were found to be 3.18% and -6.4% for intra-day and inter-day measurements, respectively. The largest RSD% values were calculated to be 4.37% and 8.63% for intra-day and inter-day measurements, respectively. The limit of detection (LOD) was calculated to be 0.003 $\mu g/ml$ while the limit of quantification (LOQ) was found to be 0.016 $\mu g/ml$. The developed method has been applied to determine the lead content in the human serum of voluntary miners, and it has been proven that there is no statistically significant difference between the data provided from this novel method and the data obtained from previously studied atomic absorption spectroscopy (AAS).

Conclusion: The developed method is based on complexation between lead and dithizone and alterations in the maximum absorbance wavelength of dithizone and dithizone—lead formed complexes. The developed method was considered accurate, repeatable, sensitive, and applicable to determine lead contaminants in miners.

Keywords: Lead, Human Serum, Spectrophotometric detection, Complexation, Dithizone



15th IPSC Proceeding

Effects of Moderate Treadmill Exercise and Fluoxetine on Mrna Expression of Apoptosis – Related Proteins in a Rat Model Of Post-Traumatic Stress Disorder

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Abstract

Introduction: Post-traumatic stress disorder (PTSD) is a condition that develops after an individual has experienced

a major trauma. Currently, selective serotonin reuptake inhibitors (SSRIs) like fluoxetine are the first-line choice in

PTSD drug treatment but their moderate response rates and side effects indicate an urgent need for the development

of new treatment. Physical activity is known to improve symptoms of certain neuropsychiatric disorders. The

present study investigated the effects of moderate treadmill exercise, the antidepressant fluoxetine and the combined

treatment on mRNA expression of apoptosis - related proteins in a rat model of PTSD: the single prolonged stress

(SPS) model.

Methods: Rats were exposed to SPS (restraint for 2 h, forced swimming for 20 min and ether anaesthesia) and were

then kept undisturbed for 14 days. After that, SPS rats were subjected to chronic treatment with fluoxetine (10

mg/kg/day, for 4 weeks), moderate treadmill running (4 weeks, 5 day per week) and the combined treatment

(fluoxetine plus treadmill exercise), followed by apoptosis markers assessments.

Results: This study showed that SPS significantly increased the mRNA expression of the pro-apoptotic protein Bax

in the hippocampus, but that of Bcl-2 remained constant, resulting in a high Bax/Bcl-2 ratio. These alterations, in

turn, shifted the balance between pro-apoptotic and anti-apoptotic factors in favor of cell death. The mRNA

expression of Caspase 3 was also increased by SPS. We found that all treatments (fluoxetine, exercise and the

combined treatment) upregulated Bcl-2 mRNA and downregulated Bax and Caspase 3 mRNA in the hippocampus,

which shifted the balance between pro-apoptotic and anti-apoptotic factors in favor of cell survival.

Conclusion: The anti-apoptotic effects of the combined treatment (exercise + fluoxetine) were much stronger than

those of either treatment alone, suggesting a synergistic effect between them in the hippocampus.

Keywords: Single prolonged stress, Moderate exercise, Fluoxetine, Apoptosis



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Preparation and evaluation of cellular uptake of liposomes modified with cell

penetrating lipo peptides

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Abstract

Introduction: Liposomes are spherical vesicles composed of one or more lipid bilayer (s) entrapping an aqueous compartment. Their similarity to cell membranes makes them useful as a carrier. Despite the high promise of liposomes as drug carriers the cellular uptake is limited. By attaching specific targeting ligands to the liposomal surface to specifically interact with certain cell surface receptors the cellular uptake of liposomes can be enhanced. Among all these ligands Cell Penetrating Peptides (CPPs) have attracted the attention of ours. CPPs are short peptides that facilitate cellular uptake of various molecular equipments. They typically have an amino acid composition that either contains a high relative abundance of positively charged amino acids such as lysine or arginine or has sequences that contain an alternating pattern of polar/charged amino acids. These two types of structures are referred to as polycationic or amphipathic, respectively.

Methods: Four sequences of CPPs with 8 amino acids in each one were synthesized by solid phase synthesis (SPPS) method. Succinyl-cholesterol was prepared and the structures formation was confirmed by the means of NMR and FTIR. Succinyl-cholesterol was attached to peptide sequences, then CPP modified liposomes were prepared and their size distribution was assessed by Zetasizer and cellular uptake of liposomes was studied by florescence microscopy and flow cytometry.

Results: FTIR and 1H-NMR spectrums confirmed that all desired compounds were formed. Fluorescence microscope and flow cytometry graphs indicated an increase in cellular uptake corresponded to the high relative abundance of positively charged amino acids such as lysine or arginine on the liposome surface.

Conclusion: Some specific Synthesized CPPs as modifiers of surface of liposome increased cellular uptake massively, by 15.28 times, plain liposomes' while enhancement of some other sequences' was only by 0.53 timessignifying these sequence's minimal effect on the cellular uptake of liposomes modified with.

Key words: Cell Penetrating Peptides (CPPS), modified liposomes, Cellular uptake, MCF7.



15th IPSC Proceeding

Synthesis and Anticonvulsant Activity of 5-Substituted 1h-Tetrazoles aganist Pentylentetrazole-Induced Seizures

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Abstract

Introduction: Tetrazoles and their derivatives demonstrate a large range of biological properties, such as anti microbial, anti-inflammatory, and antihypertensive activities. Generally, their based-on-drugs are classified depending on substituent pattern in the tetrazole nucleus. Tetrazole nucleus is a vital heterocycle that is present in a variety of therapeutical agents, including those with anticonvulsant and antidepressant activities Methods (Times

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The Methods section should provide enough information to allow the work reported to be repeated. (Times New

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Results: Under the optimized reaction conditions, we chose a variety of structurally divergent nitriles to understand the scope and generality of the nano- $SnCl_4.SiO_2$ promoted [2+3] cycloaddition reaction to form 5-substituted 1*H*-

tetrazoles.

Statistical analysis revealed that pretreatment with the dose of 30mg/kg of T1, T3 and T7 compounds increased the

latency for the first myoclonic and generalized tonic-clonic seizure compared to vehicle-treated mice.

Conclusion: In the current study, nine compounds were selected to be screened for their preliminary anticonvulsant activity against subcutaneous PTZ induced seizures in mice. Secondly our results revealed that compounds *T1*, *T3*, and *T7* were proved to be the most active anticonvulsant members in this study with special high activity.

Keywords: 5-Substituted 1H-tetrazoles, Anticonvulsant, PTZ



15th IPSC Proceeding

Design, Synthesis and Biological Evaluation of Novel Benzo[C] Acridine-Diones as Anticancer Agents

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Abstract

Introduction: β-lapachone is the most favorable molecule of the lapachol group. It is cytotoxic to a variety of human cancer cells. Which are naturally more prone to oxidative damage in comparison to normal cells. On the other hand, Microtubules play essential role in mitosis and have long been considered as an important target for the development of novel anticancer drugs. Colchicine an alkaloid isolated from *Colchicum autumnale* and *Gloriosa superba* was the first drug identified to bind tubulin, and it binds at a specific site called the colchicine domain. In the present study we report the design and synthesis of novel benzo[c]acridine-diones possessing pharmacophoric elements of Colchicine and β -lapachone.

Results: A one-step reaction was used to prepare the target 7-(aryl)-8,9,10-trimethoxybenzo[c]acridine-5,6(7H,12H)-dione derivatives, 2-hydroxy-1,4-naphthoquinone, 3,4,5-trimethoxyaniline and substituted benzaldehydes were stirred in acetic acid and then combined in under microwave irradiation to obtain the target compounds. The compounds were characterized by nuclear magnetic resonance, infrared and mass spectrometry.

Conclusion: The cytotoxic activities of the synthesized compounds are under evaluation on different eight cancer cell lines including MCF-7, A2780, HeLa, HepG2, DU145, A549, houvec, PC3,lncap in comparison to reference compounds Colchicine and β-lapachone employing the MTT assay.

Keywords: β-lapachone, Colchicine, acridine-diones, Anticancer activity; Cancer Cells



15th IPSC Proceeding

Design, Synthesis and Biological Evaluation of Novel Quinoline Analogues as Potential Anticancer Agents and Tubulin Inhibitors

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Abstract

Introduction: Microtubules play essential role in mitosis and have long been considered as an important target for the development of novel anticancer drugs. In general, antitubulin agents exert their effects by binding to one of the three established drug domains on the tubulin heterodimer: the colchicine, the paclitaxel and the vinca alkaloid binding sites. Agents that target the colchicine's domain (e.g., colchicine and podophyllotoxin) or to the vinca alkaloid binding site (e.g., vincristine) are defined as inhibitors of tubulin assembly, that is, microtubule destabilizing agents. Some quinoline derivatives displayed potent anticancer activity targeting different sites like topoisomerase I, telomerase, farnasyl transferase, Src tyrosine kinase, protein kinase CK-II, aromatase, COX-2 and etc. In the present study some new quinoline derivatives have been designed and synthesized as tubulin inhibitors, these compounds all possess trimethoxy phenyl pharmacophore and some of our compounds possessing also 3-hydroxy4-methoxy phenyl pharmacophore which are present in some potent tubulin inhibitors.

Results: A four-step reaction was used to prepare the target 5,6,7-trimethoxyquinoline derivatives, at first step to obtain quinolin-4-ol derivatives, trimethoxy aniline, ethyl acetoacetate and polyphosphoric acid was stirred at 130°C in THF, then reaction of quinolin-4-ols with POCl3 led to the formation of 4-chloroquinoline derivatives. In the third step 4-chloroquinolines with substituted benzaldehydes were refluxed in toluene to obtain the target compounds. The compounds were characterized by nuclear magnetic resonance, infrared and mass spectrometry.

Conclusion: The cytotoxic activity of the synthesized compounds are under evaluation against four human cancer cell lines including MCF-7 (Human Breast Cancer Cells), MCF-7/MX (Resistant human Breast Cancer Cells), A-2780 (human ovarian carcinoma) and A-2780/RCIS (Resistant human ovarian carcinoma), employing the MTT assay.



15th IPSC Proceeding

Determination of Valproic Acic in Plasma Sample Using EME-HPLC-UV Analysis

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Abstract

Introduction: Electromembrane extraction (EME) is recently introduced as a new sample preparation technique that uses an electrical potential difference as driving force. This technique provides high analyte extraction and enrichment in a short time to enhance the instrument sensitivity without time consuming and expensive procedures. Thus, EME is a good technique for pre-concentration of valproic acid in biological fluids. Valproic acid is an anticonvulsant drug with poor UV absorption and EME can improve the sensitivity of HPLV-UV for the determination of valproic acid in biological fluids.

Methods: In this study, major parameters on EME procedure including solvent composition, voltage, pH of acceptor and donor solutions, salt effect, and time of extraction were evaluated and optimized. The proposed EME procedure followed by HPLC-UV was applied for the determination of valproic acid in human plasma sample.

Results: The drug was extracted from the donor aqueous sample solution (pH 5) to the acceptor aqueous solution (pH 13). The donor and acceptor phases were separated by a dipped hollow fiber in 1-octanol as SLM (supported liquid membrane). The potential difference of 60 V during 25 minutes was applied over the SLM as a driving force. The drug concentration enrichment factor was obtained >125 which enhanced the sensitivity of the method. Limit of detection and limit of quantitation were 0.2 and 0.5 μ g/mL, respectively. The proposed method was successfully applied to plasma samples with relative recovery of 75%.

Conclusion: For the first time, a simple EME-HPLC-UV was developed and validated for the determination of valproic acid in human plasma sample. The sensitivity of HPLV-UV method for the determination of valproic acid in biological fluids was improved by electromembrane extraction technique. Therefore, the proposed method can be used in pharmacokinetic and toxicological assessments, in the case of valproic acid.

Keywords: Biological fluids, Determination, Electromembrane extraction (EME), HPLC-UV, Valproic acid.



15th IPSC Proceeding

Electromembrane Extraction of Phenobarbital from Biological Samples

for Analytical Purposes

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Abstract

Introduction: Nowadays, the analysis of complex samples and analyte determination at low levels are the main

analytical problems. Sample preparation and extraction are the most important steps in the case of complex matrices.

Electromembrane extraction (EME) is a new sample preparation technique which is rapid, easy, effective,

environment-friendly, and compatible with analytical systems (HPLC, GC). Application of EME can enrich the

analyte concentration in a sample matrix and then can enhance the sensitivity of an analytical method.

Methods: In the present work, EME followed by HPLC-UV was developed and validated for the determination of

phenobarbital in biological samples. The major parameters on EME efficiency (solvent, voltage, pH of acceptor and

donor phases, and time of extraction) were evaluated and optimized. The developed EME procedure followed by

HPLC-UV was applied for the extraction and determination of phenobarbital in biological samples.

Results: Phenobarbital was extracted from aqueous sample solutions (pH 9), through a supported liquid membrane

consisting of 1-octanol impregnated in the walls of a polypropylene hollow fiber, to aqueous acceptor solution (pH

13) inside the lumen of the hollow fiber. The main operational parameters were optimized, and extractions were

carried out in 20 min using a potential of 40 V. Enrichment factors of >50 has been obtained for phenobarbital

during 20 min. The procedure allows detection and quantitation limits of 7.5 and 25 ng/mL, respectively. The

proposed method was successfully applied to the analysis of phenobarbital in human urine and plasma samples with

relative recoveries of 70-80%.

Conclusion: A simple EME-HPLC-UV was developed and validated for the determination of phenobarbital in

biological samples. This procedure can be used for the determination of this drug in pharmacokinetic studies and

therapeutic drug monitoring. This procedure can improve the system sensitivity to determination of phenobarbital in

low concentrations.

Keywords: Biological fluids, Determination, Electromembrane extraction (EME), HPLC-UV, Phenobarbital

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Preparation and Evaluation of Physicochemical Properties of Injectable
Propofol Microemulsion

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Abstract

Introduction: Propofol is a short acting agent used for induction and maintenance of anesthesia. It has several advantages like short duration of action, excellent quality of recovery and short elimination half-life that leads to low tendency of accumulation in the body. Due to poor water solubility, developing of an injectable formulation has been quite a big challenge. Micro emulsions offer several advantages like thermodynamic stability, low viscosity and spontaneity of formation, which all give them an edge over conventional emulsions. The main purpose of this

study is to develop a stable Propofol micro emulsion formulation.

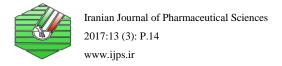
Methods: Four different formulations of micro emulsions were prepared by adding oil phase to the water phase under constant stirring and then homogenized using a high-pressure homogenizer (HPH). After assessment of active drug ingredient concentration and particle size analysis, three sets of samples were stored at room temperature, accelerated conditions and refrigerator. Physical stability was evaluated each month using SLS technique and

chemical stability was assessed with HPLC method for 6 months.

Results: Evaluation of chemical stability with HPLC method showed that active ingredient (2-6 diisopropyl phenol) is stable for 6 months at accelerated conditions and defined criteria (NLT 90% and NMT 110%) were met. Although particle sizes were under 5 micrometers at the end of 6 months period, visual appearance of some of the formulations was not satisfactory.

Conclusion: Our study showed that Propofol was chemically stable for 6 month under accelerated conditions. We are looking forward to enhance physical stability of micro-emulsion and perform in-vivo studies for the newly prepared formulations.

Keywords: Propofol, Microemulsion, HPLC, HPH



15th IPSC Proceeding

Effects of Moderate Treadmill Exercise and Fluoxetine on Mrna Expression of Apoptosis – Related Proteins in a Rat Model Of Post-Traumatic Stress

Disorder

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Abstract

Introduction: Post-traumatic stress disorder (PTSD) is a condition that develops after an individual has experienced a major trauma. Currently, selective serotonin reuptake inhibitors (SSRIs) like fluoxetine are the first-line choice in PTSD drug treatment but their moderate response rates and side effects indicate an urgent need for the development of new treatment. Physical activity is known to improve symptoms of certain neuropsychiatric disorders. The present study investigated the effects of moderate treadmill exercise, the antidepressant fluoxetine and the combined

treatment on mRNA expression of apoptosis - related proteins in a rat model of PTSD: the single prolonged stress

(SPS) model.

Methods: Rats were exposed to SPS (restraint for 2 h, forced swimming for 20 min and ether anaesthesia) and were then kept undisturbed for 14 days. After that, SPS rats were subjected to chronic treatment with fluoxetine (10 mg/kg/day, for 4 weeks), moderate treadmill running (4 weeks, 5 day per week) and the combined treatment (fluoxetine plus treadmill exercise), followed by apoptosis markers assessments.

Results and Discussion: This study showed that SPS significantly increased the mRNA expression of the proapoptotic protein Bax in the hippocampus, but that of Bcl-2 remained constant, resulting in a high Bax/Bcl-2 ratio. These alterations, in turn, shifted the balance between pro-apoptotic and anti-apoptotic factors in favor of cell death. The mRNA expression of Caspase 3 was also increased by SPS, we found that all treatments (fluoxetine, exercise and the combined treatment) upregulated Bcl-2 mRNA and downregulated Bax and Caspase 3 mRNA in the hippocampus, which shifted the balance between pro-apoptotic and anti-apoptotic factors in favor of cell survival.

Conclusion: The anti-apoptotic effects of the combined treatment (exercise + fluoxetine) were much stronger than those of either treatment alone, suggesting a synergistic effect between them in the hippocampus.

Keywords: Single prolonged stress, Moderate exercise, Fluoxetine, Apoptosis



15th IPSC Proceeding

Synthesis and Evaluation of Antimicrobial Activity of 2, 4-**Dinitrophenylpyrazoline Derivatives**

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Abstract

Introduction: The development of antibacterial agents is one of the greatest successes of 20th century medicine. Bacterial resistance development has become a very serious clinical problem for many classes of antibiotics. The increase in antibiotic resistance due to multiple factors shows the necessity for development and discovery of novel drugs. Pyrazolines and their derivatives are important biological compounds that display various properties such as

antibacterial, antitumor, antifungal and insecticidal.

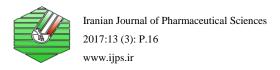
Methods: Synthesis of pyrazoline based on chalcones which is preparing by reaction of aldehydes and aromatic ketones in presence of NaOH. Chalcones on cyclization with 2,4-dinitrophenylhydrazine (claisen Schmidt)in presence of acetic acid and ethanol gave 2-pyrozoline. All the synthesized compounds were evaluated *in-vitro* for antibacterial activity against bacterial strains *Proteus vulgaris, Staphylococcus aureus* and *Salmonella typhimurium*

by MIC method.

Results: The structure of all products was confirmed using NMR and IR spectroscopy. All the synthesized compounds were evaluated *in-vitro* for antibacterial activity against bacterial strains *Proteus vulgaris*, *Staphylococcus aureus* and *Salmonella typhimurium* by MIC method.

Conclusion: In this study we describe synthesis and antibacterial activity assay of pyrozoline derivatives. The process of synthesis were done difficulty by examination several methods. All the synthesized compounds were evaluated *in-vitro* for antibacterial activity against bacterial strains by MIC method some derivatives whit NO₂ substituted has good antibacterial effect.

Keywords: Antimicrobial activity, resistance, synthesis, pyrazoline, chalcone



15th IPSC Proceeding

Investigation on the Water Solubility of Drugs with Diverse Structural and Physicochemical Properties in Presence of Anionic Surfactant of Sodium Lauryl Sulfate

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Abstract

Introduction: Micellar solubilization is a great method for increasing of drugs solubility in aqueous environments. At concentrations above the "Critical Micelle Concentration (CMC)" micelles are formed and they are able to increase the aqueous solubility of poorly soluble drugs. Anionic surfactant, sodium lauryl sulfate (SLS) is one of the common solubilizing agent in pharmaceutical sciences.

Investigation on the water solubility of drugs in presence of surfactants and the development of a relationship between drug solubility in presence of SLS and structural descriptors is an important issue for prediction and understanding mechanism of solubilization

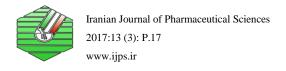
The aim of this study is experimental solubility determination of drug in presence of SLS and developing a model for finding a relation between solublization factor in presence of SLS and structural descriptors of drugs.

Methods: Samples are prepared by adding excess amount of 20 dugs (with diverse structural and physicochemical properties) to water and aqueous solution of SLS at different concentrations i.e. less than (0.1%) and above the CMC (0.5%, CMC of SLS at 37° C is 0.24%). They are placed in a shaker-incubator for 72-96 hours at 37° C. Then, the equilibrated samples filtered and analyzed at maximum wavelength by UV-spectrophotometry and the concentrations were calculated based on calibration curve. Afterward, the molecular descriptors of drugs were computed by different software and a relation between them and solublization factor in presence of SLS was investigated.

Results: The most of drugs showed a considerable increase in solubility at above the CMC (0.5%) of SLS. Therefore, the effective mechanism for solubilization by surfactants is formation of micelles. On the other hand, a good correlation was observed between structural descriptors and solubilization power in presence of SLS.

Conclusion: SLS is a good solubilization agent and the solubility in aqueous solution of SLS depends on various structural descriptors.

Keywords: Solubility, Surfactant, Sodium Lauryl sulfate, Structural descriptors



The Protective Effects of Astaxanthin on Cadmium Induced Toxicity in Sperm Parameters in Male Mice

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Abstract

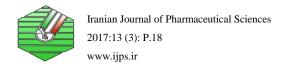
Introduction: Cadmium (Cd) is one of the most toxic environmental and industrial pollutants that induce toxicity in reproductive system [2]. Astaxanthin is a red carotenoid pigment [5] with antioxidant properties and pharmacological effects [3]. In this study we investigated the protective effects of AST on cadmium induced toxicity in sperm parameters in male mice.

Methods: Twenty-four male mice (20-25 g) were divided into four groups: control group (received nothing), sham group received olive oil for 14 days (astaxanthin was dissolved in olive oil), positive group received 3 mg/kg Cd once after the last injection of astaxanthin and treatment group received 10 mg/kg astaxanthin for 14 days. Cd, astaxanthin and olive oil were intraperituneally administrated in male mice. All the animals were sacrificed after 14 days. Sperm parameters (sperm count, sperm viability, motility and sperm abnormality) were evaluated after 14 days. Sperm viability and sperm abnormality was assessed using eosin-nigrosin staining. Sperm count and motility were examined using light microscopy.

Results: The result showed Cd significantly induced sperm abnormality and increased sperms with abnormal tail morphology compared to sham group. Moreover, Cd significantly reduced sperm count compared to sham group but couldn't alter sperm motility and sperm viability compared to sham group. Thus, exposure to Cd decreased sperm quality [1, 3]. Also, astaxanthin significantly decreased sperm abnormality and improve sperm tail morphology in mice that received Cd on the other hand; astaxanthin treatment could protect the number of sperms against Cd toxicity. Cd exposure induced oxidative stress and damaged to tests and increased lipid peroxidation in sperms [4,6] whereas astaxanthin as an antioxidant could protect sperm from oxidative damage [5].

Conclusion: Our findings indicate that astaxanthin could protect sperms against Cd toxicity thus it can be considered as a chemoprotective agent in male reproductive toxicity induced by Cd.

Keywords: Cadmium, Toxicity, Astaxanthin, Sperm, Antioxidant.



Fragment Pharmacophore-Based Screening: An Efficient Approach for Discovery of New MMP-9 Inhibitors

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Abstract

Introduction: Matrix metalloproteinase-9 (MMP-9) is a zinc dependent endopeptidase capable of degrading multiple components of the extracellular matrix including collagen, fibronectin, and elastin (1). The biological significance of MMP-9 has been described in multiple cellular processes including proliferation, wound healing, angiogenesis, migration, embryogenesis, cancer invasion, and metastasis (2). However, enhanced expression and activation of matrix metalloproteinase-9 (MMP-9) leads to different pathological outcomes in humans, including cardiovascular, inflammation, periodontal diseases, ischemic stroke, arthritis and metastasis of malignant tumor (3), therefore its inhibition has been considered as a potential therapeutic target. To date there are no FDA approved drugs targeting MMP-9, thus effort for finding novel MMP-9 inhibitors with improved selectivity, bioavailability and low toxicity is forcible to improve life quality of human. Recently, rational design of to MMP-9 inhibitors was made possible by the determination of high resolution structures of the MMP-9 active site. A hybrid strategy including docking, and pharmacophore based virtual screening were used to identify new MMP-9 inhibitors.

Methods: Structure based pharmacophore modeling strategy was employed to generate pharmacophore models which precisely describe physicochemical and structural features (functional groups), to enable the obtained set of compounds to interact properly in the target receptor ligand binding pocket.

Based on crystal structure of MMP-9 (PDB code: 4XCT), ten particular pharmacophore models were generated from the obtained poses using Ligand Scout v3.01. The models were then assigned individually as filters for pharmacophor based virtual screening over the ZINC database.

Results: Among compounds collected from ZINC libraries, 11223 compounds were selected for docking into the MMP-9 binding site. 16 compounds with the required interaction, critical amino acid residues and the binding free energies <-7 kcal/mol were identified as potential MMP-9 inhibitors.

Conclusion: Selected compounds can be considered as a proper candidate as lead compounds in order to develop new MMP-9 inhibitors.

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Laccase as a biocatalyst for the synthesis of bioactive compounds

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Abstract

Introduction: Quinazolinones and quinazolines are important family of nitrogen-containing heterocycles that play a significant role in the pharmaceutical community for their diverse range of pharmacological properties [1, 2]. They are useful building blocks for many natural products and pharmaceutical agents. In view of their various biological activities, numerous methods have been developed for the synthesis of these derivatives [3]. Laccase (benzenediol: oxygenoxidoreductase, EC 1.10.3.2), a multi-copper-containing oxidoreductase enzyme, is one of the enzymes that is being studied as a biocatalyst in organic synthesis. The range of laccase substrates can be extended by the simultaneous use of the enzyme and redox mediators.

Results: In order to develop an environmentally friendly method for the synthesis of biologically important heterocyclic compounds, the aerobic oxidation of 2-arylquinazolin-4(3*H*)-one and 2-arylquinazolin using laccase/DDQ (2, 3-Dichloro-5,6-dicyano-1,4-benzoquinone) and laccase/TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) as the catalytic system respectively are investigated (Scheme 1). Also the cytotoxic activities of the synthesized compounds are studied.

Conclusion: The advantages of these methods for the synthesis of quinazolins and quinazolinons derivatives are: the use of laccase enzyme and oxygen as eco-friendly biocatalyst and oxidant respectively and working in green conditions.

Keywords: Laccase, Biocatalyst, Mediator, Bioactive compound

APT^{AS1411} -ChitosanNPs-BODIPY-FL Nano-Fluorescent Imaging Agent

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Abstract

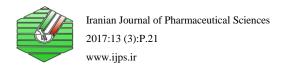
Introduction: Today, aptamer based drug delivery or imaging technology is being vastly continued as novel pharmaceutical approach *in vitro*/ in vivo. Aptamers depending on the types of defining receptors detects and treat diseases specifically and called smart devices in nanotheranostic applications.

Methods: In current project aptamer AS1411 (APT^{AS1411}) was successfully conjugated on Chitosan nanoparticle's (ChitosanNPs) surface and then labelled with BODIPY-FL a non-radioactive fluorescent agent.

Results: Size/ charge, AFM imaging, Mass and FTIR spectroscopic data were obtained and finally nano conjugate was assessed *in vitro* for cellular imaging and uptake plus toxicity assessments. The results showed a very successful economical synthesis validation for such nano- fluorescent imaging agent (size= 90 nm) in addition to a good promising cellular uptake of up to 67% in cancerous MCF-7 cells plus no significant p>0.05 HEK-293 cellular toxicity.

Conclusion: Besides of no cellular toxicity as well as good cellular uptake of such nanoconjugate it would be desirable as a novel *in vivo* fluorescent candidate agent for the next near future *in vivo* trials in animal models.

Keywords: APT^{AS1411}, ChitosanNPs, BODIPY-FL, Fluorescent, Imaging Agent



Application of Chemometrics in Determination of the Effects of Ionic and Non-Ionic Surfactants on Acid Dissociation Constant (Pk_a) of Meloxicam Using Spectrophotometric Method

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Abstract

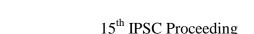
Introduction: The purpose of this study was to determine the acid dissociation constants (pK_a) of meloxicam in the presence of various surfactants including sodium lauryl sulfate (SLS) as an anionic surfactant, cetyl trimethyl ammonium bromide (CTAB) as a cationic surfactant and Triton® TX-100 (TX-100) as a non-ionic surfactant in different pre-determined concentrations.

Methods: The related pKa was determined spectrophotometrically at a constant ionic strength of 0.1 M at 25^oC. In order to investigate the effect of solvent on pKa of meloxicam, the pKa was also determined in different concentrations of ethanol, separately. The acid dissociation constant of all appropriate species were calculated using chemometric methods. In this study, DATAN[®] software was applied for analysis and interpretation of data.

Results: The acid dissociation constants (i.e. pK_a) for meloxicam as poorly soluble drug were reported as 1.22±0.56 and 4.00±0.12 for pKa_1 and pKa_2 , respectively. Results showed that by increasing the concentration of SLS up to 0.5% (w/v), both the pKa_1 and pKa_2 of meloxicam were increased and determined as 2.67±0.054 and 5.73±0.029, respectively while by increasing the concentration of CTAB, significant decrease was observed in pKa_2 of meloxicam to 2.53±0.16. Different concentrations of TX-100 posed non-significant changes in pKa_1 and pKa_2 . It was also reported that by increasing the concentration of ethanol as a co-solvent, both pKa_1 and pKa_2 of meloxicam were increased to 2.42±0.083 and 5.81±0.23, respectively

Conclusion: The results showed that pKa values of meloxicam were influenced as the concentration of SLS and CTAB were increased while increase in concentrations of TX-100 as a non-ionic surfactant had no significant effect on pKa of meloxicam. It was suggested that electrostatic interaction between ionic surfactant and dissociated species of the drug, considered to be a dominant mechanism for alteration of pKa.

Keywords: Acid dissociation constant, Meloxicam, Sodium Lauryl Sulfate (SLS), Cetyl Trimethyl Ammonium Bromide (CTAB), Triton TX-100





Molecular Docking Studies of Novel Coumarin-Pyridinium Salts As Good Inhibitors of Cholinesterase in Treatment of Alzheimer's Disease

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Abstract

Introduction: Alzheimer's disease is the most common cause of dementia. The word dementia describes a set of symptoms that can include memory loss and difficulties with thinking, problem-solving or language. These symptoms occur when the brain is damaged by certain diseases, including Alzheimer's disease. Decrease of acetylcholine level by acetylcholinesterase (AChE) is one of the most important causes of AD.AChE predominates in the healthy brain, whereas, butyrylcholinesterase (BuChE) is considered to play a minor role in regulating ACh level. However, inhibition of AChE and BuChE has been emerged as a versatile tool for the treatment of AD symptoms.

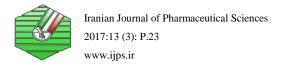
Methods: Docking studies were carried out using the AUTODOCK 4.2 program. For this purpose, the pdb structure of AChE (1EVE) and BuChE (4AQD) were taken from the Brookhaven protein database (http://www.rcsb.org). Subsequently, the water molecules and the original inhibitors were removed from the protein structure. The 3D structure of our compounds were provided using Marvine Sketch 5.10.4, 2012, Chem Axon (http://www.chemaxon.com) and converted to pdbqt coordinate by AUTODOCK 4.2 program.

Results: Docking study was conducted to determine the binding mode of the most active compound in the active site of enzyme. According to the interaction mode of our compound, benzyl moiety plays vital role in ligand recognition via π - π stacking through Phe330 and Trp84 amino acid residues. Carbonyl group oxygen formed hydrogen bonding with Ser124, respectively. However, the pyridine ring was oriented towards Trp84 via π - π stacking.

Conclusion: In our study, *in vitro* anti-ChE evaluation of synthesized coumarin-pyridinium salts (based Ellman's method) depicted selective anti-BuChE activity of the desired compounds. Also, molecular docking study of the

most active compound confirmed the favorite interactions with the active site of BuChE. It may offer remarkable results for the development of selective BChE inhibitors.

Keywords: Acetylcholinesterase, Alzheimer's disease, Butyrylcholinesterase, Coumarin-Pyridinium Salt, Molecular docking.



15th IPSC Proceeding

Melanoma Tumors Imaging Using 99mTc-HYNIC-Tricine-cyclopentapeptide

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Abstract

Introduction: Chemokine receptors (CKRs) belong to G-protein coupled receptors that binding to their chemokine ligands and lead the directional migration of cells. Recently it has reported that many malignant tumor cells express chemokine receptors. This overexpression is seen in cancers by origin of epithelial, mesenchymal and hematopoietic including breast, lung, lymphoma, melanoma, colorectal cancers. So synthesis and labeling of CXCR4 receptor targeted analogs as a tumor imaging agents has been encouraged.

Method: Herein ^{99m}Tc-HYNIC-Tricine-cyclopentapeptide was synthesis using a standard Fmoc strategy and thereafter it's labeling with ^{99m}Tc via a bifunctional chelating agent and tricine coligand was developed at 100°C. Radiotracer purity and stability in human serum were analyzed by RTLC and HPLC methods. Tumor cell binding was assessed and bioevaluation of radiotracer was studied in C57BL/6 mice bearing B16-F10 tumor.

Results: More than 95% labeling yield and serum stability up to 24 h were observed. Radiotracer related tumor accumulation was 3.61 ± 0.15 % ID/g at 1 h post injection.

Conclusion: High stability and specific tumor uptake are important characteristic of this radiotracer that could nominate this as a targeted imaging agent in the future.

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Qualitative and Quantitative Analysis of the Interaction of Antifungal Drugs and Albumin via Molecular Docking Method

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Abstract

Introduction: Albumin is the prominent protein of plasma and drug-albumin interaction causes changes in pharmac okinetics and toxicity of drugs (1). Studying drug-albumin interaction is an important and practical research field. N o systematic computational study has been dedicated to the interaction of antifungals with albumin despite their sign ificant role in pharmaceutical medications. In the present contribution, different antifungal drugs were examined by molecular docking to find possible binding sites with albumin and obtain structural information of drug-albumin complexes.

Methods: Molecular docking calculations were performed by AutoDock 4.2 software(2). Interaction patterns were a chieved by Ligplot. 3D structures of albumin with warfarin and diazepam as representatives of active sites 1 & 2 we re extracted from Brookhaven Protein Bank (2BXD & 2BXF).

Results: Results revealed that antifungals made hydrophobic contacts and H-bonds with albumin. It was found that within active site 2, Fenticonazole exhibited lowest free binding energy (-9.89 kcal.mol⁻¹) while Flucytosin showed I oosest binding to the albumin (-3.06 kcal.mol⁻¹). In the active site 1, Oxiconazole showed tightest binding (-9.01 kcal.mol⁻¹) while loosest contact was attributed to Fluconazole. However Fenticonazole could also achieve high score (-8.70 kcal.mol⁻¹) within active site 1 but results indicated that polar interactions might be important in binding to active site 1 since oxiconazole possessed oxime moiety. Binding maps indicated that higher affinity of Fenticonazole might be related to possible hydrophobic contacts via additional aromatic rings attached to sulfur atom.

Conclusion: Current computational results revealed that different antifungal drugs are important interfering agents s ince they may bind to human serum albumin with relatively high binding energies (< -6 kcal.mol⁻¹). Such studies mi ght aid in developing novel antifungal scaffolds, comparing the mechanism and binding affinity of antifungal drugs with albumin and also obtaining structural information about drug-albumin complexes.

Keywords: Antifungal, Albumin, Pharmacokinetics, Docking, Binding



The Preventive Effect of Gastrodin on Motor Impairment in Male Rats Following Induced Parkinsonism

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Abstract

Introduction: Parkinson disease (PD) is the second most common neurodegenerative disease and its main symptoms are resting tremor, rigidity, bradykinesia and postural instability (1). Gastrodin (GST) ,a natural phenol extracted from *Gastrodia eleta*, is used to treat headaches and is considered as an adjunctive therapy for epilepsy in traditional Chinese medicine (2). Since there is little information on the effect of GST on PD therefore,we decided to study the therapeutic effects of GST on male rats with induced parkinson.

Methods: PD was induced by unilateral injecting of 6-OHDA into SNc in male Wistar rats (240-200 g). Animals were pretreated with daily doses of intra cerebro ventricular injection (i.c.v) of gastrodin (20,40 and 80µg/2µl) for 5 consecutive days before intra nigral injection of 6-OHDA. 3 weeks after neurotoxin injection catalapsy and motor balance were assassed by bar test and rotarod, respectively.

Results: 6-OHDA injection significantly increased catalepsy and decreased motor balance in rats when compared with sham group. I.C.V injection of GST at doses (20, 40 and $80\mu g/2\mu l$) for five consecutive days before the injection of 6-OHDA prevented the increase in catalepsy and improved motor balance in 6-OHDA-parkinsonian rats, significantly (p <0.05).

Conclusion: It is suggested that gastrodin can prevent the progress of PD through inhibiting 6-OHDA-iduced catalaepsy and increasing motor balance. According to the results of the present study gastrodin can be suggested as an adjuvant therapy in the treatment of PD, but further studies are needed to confirm the effectiveness of gastrodin on PD.

Keywords: Gastrodin, 6-hydroxydopamine, Catalepsy, Motor balance, Rat



Docking Based Three-Dimensional Quantitative Structure-Activity Relationships (3D-QSAR) Studies of Selective Cyclooxygenase-2 Inhibitors

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Abstract

Introduction: Cyclooxygenase (COX) catalyzes prostaglandin biosynthesis from Arachidonic acid. Although non-estradiol anti-inflammatory drugs (NSAIDs) are widely used in inflammation related problems but inhibiting COX may have some unwanted effects, especially gastrointestinal problems. It has been found that there are two isoforms for COX; COX-1 and COX-2. COX-1 have a role in physiological functions such as GI mucosa secretions, vascular homeostasis and inducing platelet aggregation, while COX-2 is mostly responsible for inflammatory processes. Inhibiting COX-2 using Selective COX-2 inhibitors can be a solution to have minimal unwanted effects. In addition, there are evidences that show COX-2 gene expression increases in some cancerous cells that can result in cell apoptosis by increasing PG production.

In this research, a docking based 3D-QSAR was performed to achieve the needed structure features for inhibiting COX-2 and to predict new compounds activity.

Methods: A dataset of 26 with Methylsulfone pharmacophore compounds with potential of inhibiting COX-2 was taken and separated into a training set (20 compounds), for generating 3D-QSAR model, and a test set (6 compounds) for validating the quality of the model. The chemical structures of the molecules were built and optimized by Hyperchem 8.0 software. The docking process was performed using Autodock/Vina software (PDB: 3NT1). In order to calculate comparative molecular field analysis (CoMFA) and comparative molecular similarity indices analysis (CoMSIA) descriptors, SYBYL software was applied and finally QSAR model was built with partial least square (PLS) method.

We performed Leave-One-Out and Leave-Group-Out methods as an internal validation and test set as an external validation of model.

Results: Statistical parameters for the model shows leave-one-out (LOO) correlation coefficients were 0.51 for CoMFA and 0.57 for CoMSIA and the non-cross-validation coefficients were 0.96 for CoMFA and 0.95 for CoMSIA. The predictive correlation coefficient of test set was 0.63 for CoMFA and 0.80 for CoMSIA.

Conclusion: A 3D-QSAR model was built to predict various compounds activity to COX-2 and used to predict new designed structures.

Keywords: COX-2, 3D-QSAR, COMFA, COMSIA, Docking, PLS



15th IPSC Proceeding

Sesquiterpene Lactones from *Centaurea Behen* L. And *Rhaponticum Repens* (L.) Hidalgo; Cytotoxic and Antimicrobial Activities

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Abstract

Introduction : Sesquiterpene lactones (SLs), which have been isolated from numerous genera of the family Asteraceae, have a wide range of biological activities, especially cytotoxic and antitumor against cancer cells (1). This study aims to evaluate the *in vitro* cytotoxic, *in vitro* and *in vivo* anti-angiogenic effects, and antimicrobial activity of SLs from two plants belongs to Asteraceae family named *Centaurea behen* and *Rhaponticum repens* (L.). **Methods:** Structures of isolated compounds were assigned using 1H-NMR, 13C-NMR, HSQC, HMBC, and COSY spectra. Antimicrobial activity of compounds was tested by microdilution method. In addition, cytotoxicity of compounds against six cancer cell lines were assessed using an Alamar Blue[®] proliferation assay (2).

Results: Five SLs, including cynaropicrin (1), 4β ,15-dehydro-3-dehydrosolstitialin A (2), aguerin B (3), janerin (4), cebellin E (5), and the flavonoid hispidulin (6) were isolated from the *C. behen* (compounds 1-3) and *R. repens* (compounds 4-6). Cynaropicrin (1) and aguerin B (3) possessed cytotoxic activities against A2780 cell line with IC₅₀ values of 1.15 and 1.62 µg/mL, respectively, comparable to that of doxorubicin (IC₅₀= 1.17 µg/mL). The antiangiogenic study showed the remarkable inhibitory effect of cynaropicrin (1) and aguerin B (3) on the proliferation and migration of HUVECs. In addition, cynaropycrin and aguerin B exhibited significant angio-inhibitory effects in CAM assay. In addition, hispidulin (6) and cinaropicrin (1) showed potent antifungal activity with the MIC values of 31.75 and 62.5 µg/mL, respectively.

Conclusion: These findings may be useful for the development of novel chemotherapeutic agents for the treatment of cancers.

Keywords: Asteraceae; Centaurea; sesquiterpene lactone; cytotoxic; anti-angiogenic



15th IPSC Proceeding

Community Pharmacists' Attitudes toward Collaboration with Physicians

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Abstract

Introduction: For improving patient care, especially those with chronic diseases, and also reducing possible medication errors, health care providers must collaborate (1, 2). This study aims to assess pharmacist attitudes towards collaborative practice from the pharmacist's perspective in the Northeast of Iran.

Methods: A face-to-face survey was developed in community pharmacist that assessed following: 'interactional determinants', 'environmental determinants', and 'pharmacist determinants' which influence collaborative behavior of community pharmacists. A survey was offered to a sample of 124 pharmacists in Mashhad and some other cities of Khorasan Razavi province. Results were analyzed to determine how pharmacist attitudes and other variables, influence collaborative behavior.

Results: Survey response rates were 100%. Principal component analysis revealed the Attitudes Towards Collaboration Instrument for Pharmacists (ATCI-P) in our sample consisted of two factors: 'interactional determinants' and 'pharmacist determinants', both with good internal consistency (Cronbach's alpha = 0.83). The lowest and the highest score in the 'interactional determinants' domain was 19 and 35, respectively. Statistically, there was a significant difference in the average score of Mashhad and other cities (P-value = 0.006), and in the distance between the pharmacies and medical centers (P-value = 0.009). Multiple Linear regression analysis of the complete model was significant (R=0.36, P-value =0.005). The age and city (community size) were also found to be significant predictors of collaboration behavior (B = 0.300, p= 0.002 and B = 0.259, p= 0.004) respectively.

Conclusion: This work highlighted that the community pharmacists in Khorasan Razavi, Iran, have a great attitude toward collaboration with physicians and their collaborative behavior is influenced by the age, community size and distance from a medical center.

Keywords: community pharmacists, attitude, collaboration, physician, Khorasan Razavi, Iran



15th IPSC Proceeding

Determination of Composition, Antimicrobial and Antioxidant Effects of the Essential Oil Extracted From Aerial Parts of *Dracocephalum Moldavica*

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Abstract

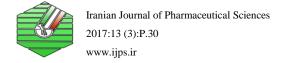
Introduction: Nowadays, due to widespread of antibiotic resistance worldwide, medicinal plants considered as valuable sources for investigating and manufacturing new antimicrobial agents. One of the most important medicinal plants in Iran is *Dracocephalum moldavica* which is growing in some cities, especially in Zanjan which was used for healing of gastric ulcer and as a dressing for prevention of infections on wounds.

Methods: Essential oil of aerial parts of plant was extracted by Hydrodistilation. Then, compounds were identified by GC-Mass. Antioxidant capacity was evaluated by measuring Radical Scavenging Activity by DPPH. In the next step, minimum inhibitory concentration and minimum bactericidal concentration of essence were evaluated against standard bacteria (*Enterococcus faecalis*, *Staphylococcus aureus*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Seratia marcescens*, *Salmonella* spp., *S. epidermidis*, *Listeria monocytogenes* and *Eschericia coli*) as well as Methicillinresistant *S. aureus*, Antibiotic-resistant *P. aeroginosa* and *E. faecalis* by microtiter assay.

Results: More than 40 compounds were characterized in essential oil. The most prominent ones were citral, limonene and carveol. Interestingly, antioxidant activity of essential oil was less than BHT (as a standard). Maximum inhibition zone was observed for *S. aureus* and *L. monocytogenes*, on the contrary, no antimicrobial activity was observed against *E. coli*. Maximum and minimum inhibition zone for antibiotic-resistant bacteria were obtained for *Staphylococcus* and *Enterococcus*, respectively. Furthermore, the lowest MIC values for standard and antibiotic-resistant bacteria was 20 Au/ml and the highest was (80 and 160) Au/ml, respectively. The lowest MBC values for standard and antibiotic-resistant bacteria was 20 Au/ml and the highest was (80 and 640) Au/ml, respectively.

Conclusion: The results represent weak antioxidant activity and significant antibacterial activity for essential oil of *D. moldavica*. Thus, the essential oil of the plant can be considered as a potential tool for controlling and prevention of infections in food and pharmaceutical industry.

Keywords: Dracocephalum moldavica, Antimicrobial activity, Antioxidant activity, MIC, MBC



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Evaluation of Toxicity Effects of Aqueous Extract of *Lippia Citriodora* **Leaves in Mice and Rats**

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Abstract

Introduction: *Lippia citriodora* (Lemon verbena) has a variety activity such as anti-inflammatory, anti-proliferative, anti-spasmodic, immonomudulatory, anti-oxidant, anti-nociceptive effects. As safety and toxicity of medicinal herbs is important for clinical uses, in this study, the acute and subacute toxicity of aqueous extract of this plant was studied in mice and rats.

Materials and Methods: In acute study, 12 male mice were injected intraperitoneally (i.p) once a day. For subacute study, the aqueous extract of *L. citriodora* was administrated i.p to male rats in daily doses of 50, 100, 200 mg/kg for 14 days. Then the blood samples (for haematological and biochemical parameters) were obtained and selected organs were prepared for pathological evaluation.

Results: The LD50 value of this plant was 5g/kg in acute toxicity study after i.p. injection in mice. In hematological test, a significant decrease in triglyceride level was seen in 50, 100, 200 mg/kg treated groups 53.66±2.5, 49.83±2.58, 50±1.93 mg/dl, respectively, compare with control group 92.6±4 mg/dl. (P<0.01, P<0.01 and P<0.05, respectively). No changes were observed in contents of blood cells. The histological studies indicate that the extract did not havet any significant toxic effects on heart, brain, spleen, liver, lung and kidney in rats. Hemorrhage was the only pathologic finding.

Conclusion: According to obtained results, this plant can be proposed for clinical treatment specially for decreasing the triglycerides.

Key words: Lippia citriodora, Acute Toxicity, Subacute Toxicity.



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Cirrhosis Improvement by Thalidomide: The Assessment of Suppressor of Cytokine Signalling (SOCS) 1 Expression.

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Abstract

Introduction: Cirrhosis is end-stage of liver diseases that defined as the histopathological development of

regenerative nodules encircled by fibrous septa. Cirrhosis progresses in response to chronic liver injury, which leads

to severe complications such as: Hepatorenal syndrome, Portal hypertension, Cirrhotic cardiomyopathy and Liver

failure finally. SOCS1 is a suppressor of cytokine signalling that modulates cytokine mediated immune responses.

Several studies have shown that, during hepatic chronic diseases and cirrhosis, expression of SOCS1 was decreased.

Thalidomide is an old drug, with immunomodulatory and anti-inflammatory. A main effect of thalidomide in

cirrhosis is reduction of hepatic fibro-inflammation. In this study, we evaluated thalidomide effect

on SOCS1 expression with regard to its beneficial effect in Cirrhosis.

Methods: Bile Duct Ligation (BDL) model of cirrhosis in rats was used in this study. Animals were grouped as:

Sham/saline, Sham/Thalidomide, BDL/saline and BDL/Thalidomide. In treatment groups, thalidomide

(200mg/kg/day), was administrated by intragastrial gavage for 21 consecutive days after operation. In day 22, then

rats' liver isolated and level of SOCS1 expression was measured by Realtime RT-PCR method. Also, liver

histopathology was performed by staining of liver sections with hematoxylin-eosin (H&E) and Masson trichrome.

Results: The results of histopathological findings, revealed a significant reduction in the extent and continuity of

fibrous bands in BDL/saline than BDL/thalidomide group. TNF-α and IL-6 are two main cytokines in development

of inflammation, necrosis and fibrosis in cirrhosis, which inhibition of these factors have been demonstrated by

thalidomide. Moreover, SOCS1, as a protective factor against liver inflammation, has a significant reduction in BDL

compared to the Sham group; furthermore, the level of SOCS1 in BDL/thalidomide group was higher than

BDL/saline group. It has been shown that, the SOCS1 gene promoters position is hypermethylated in cirrhosis. One

of the possible mechanisms on the overexpression of SOCS1 in thalidomide treatment is its

promoter's demethylation by thalidomide; so that, its function on SOCS1 gene promoters, has been shown by an

analogue of thalidomide previously.

Conclusion: Thalidomide improves necroinflammation and reduces the extensive fibrosis in BDL rats. A part of

this effect is probably mediated by increasing the expression of SOCS1 in BDL rats.

Keywords: Thalidomide, SOCS1, Cirrhosis, BDL.



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The Ferula Persica Oleo-Gom-Resin Nasal Formulation for Alzheimer Disease

Management: The Future of Tradition

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Abstract

Introduction: Acetyl choline is a neurotransmitter performed a significant role in neural transmission. The inhibition of acetyl choline esterase and subsequent increment level of acetyl choline are one of the goals in Alzheimer-disease treatment. The goal of this study is to prepare the nasal formulation (in traditional references called "Saout") from oleo-gum-resin of *Ferula persica* (Sakbinaj) with potential therapeutic effect in management of Alzheimer-disease.

Methods: By exploring in traditional references such as Qarabadin Salehi and Makhzanoladvieh; *Ferula persica* based on its obvious antiforgetfulness mentioned in traditional references and probably AchEI effect has been selected. Preparing the solution of oleo-gum-resin is our purpose at the first step of the investigation. There was no evidence of solubility of oleo-gum-resin. So the solubility determination of this resin has evaluated in different solvents with the wide range of polarity. The organoleptic properties, pH-profile, and conductivity of solution were evaluated over the time.

Result and Discussion: Based on the results, ethanol 70%, with 97% w/v has the most potential to solubilize the resin. In study of stability tests, organoleptic properties (odor, color, precipitate) fixed odor and color has observed. pH was 5.00±0.08 and conductivity was 340.07±3.92 mV with no significant change.

Conclusion: oleo-gum-resin has the best solubility in ethanol 70%. It means that most of the components of oleo-gum-resin are semi-polar. Ethanol is not an ideal co-solvent for nasal formulation, so it needs some modifications. Because of relatively low pH, it should be modified to reach the physiological value for prevention of irritation. The microbial control tests of final product are essential which all of these experiments are in progress. Preparing the nasal formulation from products with AchEI effect as formulation with rapid onset-of-action and less side effects, is a hopeful treatment of Alzheimer in future with the help of traditional products.

Key words: Ferula persica, Acetyl choline esterase inhibitor, Alzheimer disease, nasal formulation



The Effect of Lipid Nanoparticles Size on Skin Permeation and Hair Follicular Targeting of Cproterone Acetate

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Abstract

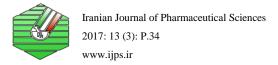
Introduction: Cyproterone acetate (CPA) is an anti-androgen drug with progesterone properties, used in acne, hirsutism and alopecia. Systemic administration of this drug may have various side effects, also topical delivery of conventional formulation would not have therapeutic value, because it has limited water solubility and limited skin permeation. So, Nanostructured lipid carriers (NLCs) were considered. Previous researches have emphasize on the effect of nanoparticles size on follicular targeting; so in this study CPA-loaded NLCs with different size ranges were prepared and their follicular targeting and skin permeation were assessed.

Methods: CPA-loaded NLCs were prepared by "solvent diffusion evaporation technique", and size optimization was done by Design-Expert software. Four different size ranges 100, 300, 600 nm and 6 micrometers lipid base nanoparticles were prepared. Skin permeation was measured using Franz cell and hamster flank organ skin. Also, *in vivo* follicular targeting was assessed using rhodamine-loaded NLCs with different size ranges, samples were applied on flank organ skin of hamsters then skin biopsies were prepared 0.5, 2, 4 hours after application, samples were fixed on glass slides and rhodamine penetration pathways were analyzed completely using fluorescent microscope (Olympus, BX51).

Results: It seems that lipid nanoparticles with average size range about 300 nm are able to target the hair follicles and sebaceous glands, which is completely in agreement with the previous researches. Also skin permeation was increased significantly by loading the drug in lipid nanoparticles with different size ranges in comparison with free CPA, due to change in penetration pathway.

Conclusion: Due to limited skin permeation of CPA, using appropriate delivery system enable us to deliver it to skin organelles such as hair follicles by controlling the mean size of the delivery system.

Key words: Cyproterone acetate (CPA), skin permeation, follicular targeting, nanostructured lipid carriers (NLCs), particle size.



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Flavonoids as future drugs for Parkinson's disease: a comprehensive review

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Abstract

Introduction: Parkinson disease (PD) is the most common movement disease which is characterized with the selective degeneration of dopaminergic neurons. Current investigations revealed significant interest in the growth of neuroprotective drugs from natural origins like flavonoids as a therapeutic approach for PD. This study reviews the therapeutic effects of flavonoids and their mechanisms in PD.

Methods: Electronic databases including PubMed, Scopus, and Cochrane library were searched with the keywords 'Parkinson's disease' in the title/abstract and 'plant', 'extract', 'herb', and 'flavonoids' in the whole text. Results were obtained from year 1966 to August 2015. Just English language articles were included in this review. Primary search results were screened by two independent investigators, and unrelated papers were excluded based on their title and abstract. Studies that assessed the effects of total extracts or different fractions were excluded. Papers on the efficacy of flavonoids in which the mechanism of action was not determined were also excluded because the aim of the current review is to collect different mechanisms of action in the antiparkinsonian effects of flavonoids.

Results: Flavonoids perform their antiparkinsonian effect through several mechanisms of action, including decreasing dopaminergic neuronal loss, tyrosine hydroxylase-positive neuronal loss and dopamine depletion,

suppressing apoptosis via the reduction of Bax/Bcl-2, caspase-3, -8, and -9, phosphorylation and expression of c-Jun N-terminal kinases and p38 and α -synuclein accumulation, reducing the expression of pro-inflammatory cytokines such as prostaglandin E2, nitric oxide and tumor necrosis factor- α , improvement of antioxidant status as well as the prevention of mitochondrial membrane potential MMP disruption. These findings suggest the potential future applications of flavonoids as therapeutic agents for the management of neurodegenerative disorders like PD. **Conclusion:** In conclusion, flavonoid therapy can be an encouraging candidate for the management of PD. Future well-designed clinical trials are essential to confirm the antiparkinsonian effects of flavonoids.

Keywords: Parkinson's disease; medicinal plant; natural product; neurodegenerative disease; flavonoid



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In Silico Investigation of Effective Mutations on Solubility and Stability of Recombinant Therapeutic Protein: Reteplase

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Abstract

Introduction: Reteplase is a thrombolytic drug which is a non-glycosylated deletion mutein of tissue Plasminogen Activator (t.PA), containing the kringle 2 and the protease domains of human t.PA. Reteplase has several prominent features such as longer half-life, strong thrombolytic ability, and high affinity fibrin binding and so on. However, a limitation in Reteplase production in large quantities is its relatively poor Solubility.

Methods: This study aimed at enhancing the stability and solubility of Reteplase using in silico design. For this purpose, the sequence of wild type Reteplase enzyme was modeled by Phyre2 server and the selected model was evaluated by procheck server. Using Popmusic server, five mutations including, E119I, E214I, E295M, D342M, and G368A were determined. These mutations probably should change solubility and stability of wild type protein, and

then they were created via RosettaBackrub server. Finally, 20 ns MD simulation were performed for each mutations and wild type at 300K under constant pressure and temperature (NPT) condition.

Results and Discussion: The results showed that the most variation at structural parameters like RMSD, Rg and intermolecular hydrogen bonds occur in E214I, E295M and G368A mutations. So, they likely are more unstable relative to wide type enzyme. On the other hand, the mutations did not show any significant change in number of hydrogen bonds between protein and solvent compared to the wild type except in D342M mutation. However, hydrophobic surface in mutations E119I, G368A increased in comparison to the wild type protein that can probably lead to raise aggregation.

Conclusion: The findings indicated that increased hydrophobicity of protein core not only leads to increased stability, but also increases the protein solubility compared to its wild type protein.

Keywords: Reteplase, Solubility, Stability, MD simulation, Mutation



15th IPSC Proceeding

Aptasensors: Promising Affinity Biosensors for *In Vitro* and *In Vivo*Applications

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Abstract

Introduction: Aptamers are single stranded oligonucleotides (ssRNA/ssDNA) with high selective affinity against target molecules or cells. Wide range of targets has been considered for aptamer selection through SELEX or non-SELEX process. Regarding to the high selective affinity of aptamers and their good compatibility with different types of chemical modifications and detection strategies, they have been exhibited worthwhile outcomes as the bioreceptor part of the biosensors that briefly termed as aptasensors [1-3]. As an affinity ligand, aptamers provide some advantages over monoclonal antibodies such as low cost of production, more stability, robustness and ease of chemical modification and surface attachment [4].

Methods: Published literatures until May 2017 extracted from Scopus, searching the keyword of aptasensors. About 1600 literatures were extracted and assessed.

Results: Various detection strategies have been verified in the design and development of aptasensors, including electrochemical, voltametric, potentiometric, optical/colorimetric, fluorescence, resonance energy transfer, SPR and etc [5-10]. As well, different types of targets have been evaluated using aptamer sensing technology. Small chemical molecules and metabolites, large biomacromolecules (proteins and peptides), whole cells including cancer cells, necrotic cells, pathologic bacteria or virus and even whole tissue or organisms could be considered for aptamer development [11-17]. *In-vitro* detection and quantification of small molecules/metabolites and protein/peptide biomarkers in biological fluid are mostly studied analytical aptasensors [18-21]. Moreover, in-vivo diagnosis of biomarkers has also proved using nanoparticle based aptasensors [3].

Conclusion: Electrochemical and colorimetric aptasensors are the most studied aptamer based detection systems for medical or analytical application. Nanoparticle based detection systems were one of the most attractive strategies in the design of *in vitro* and *in vivo* sensors. Sensing potential of aptamer-based systems could be add to the therapeutic ability of aptamers and result in to the theranostic systems. Aptasensors are simple, fast and sensitive systems for analytical detection and clinical diagnosis of clinically important biomarkers, physio-pathological metabolites, drugs and toxins.

Keywords: Aptamer; Affinity Ligand; Sensor; Analytical; Clinical; Diagnosis



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Effect of Omega-3 on the Prevention of Renal Scarring Caused by Acute Pyelonephritis in Children

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Abstract

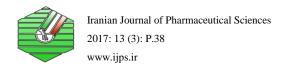
Introduction: Acute pyelonephritis caused by the inflammatory responses plays an important role in children renal damages. Omega-3 is a supplement that seems to have anti-inflammatory and antioxidant effects. Accordingly, the purpose of this study was to evaluate the effect of omega-3 in preventing the renal parenchyma scarring in children with acute pyelonephritis.

Methods: Fifty nine children (25 patients as intervention group and 34 patients as a control group) were participated in this study. After diagnosis of acute pyelonephritis based on urine tests and dimercaptosuccinic acid scans (DMSA scan), the control group received antibiotic and the intervention group received both omega-3 supplement and antibiotic. Pyelonephritis-induced renal scaring once before treatment and once 6 months after treatment was evaluated by using DMSA scan.

Results: The results of DMSA scan showed that there is no statistically significant difference between the two groups in terms of the scarring status of the left and right kidney parenchymatissue before the treatment process (P>0.05). DMSA scan results after 6 months of treatment showed that incidence of renal parenchyma scar between intervention and control groups only in the left kidney was significantly difference (P<0.05). Regardless left or right, kidney DMSA scan results showed that renal parenchyma scarring was significantly reduced after 6 month of treatment (P<0.05).

Conclusion: The results of this study showed that the use of omega-3 supplement along with appropriate antibiotic treatment can significantly decrease the rate and grade of renal scarring in children with acute pyelonephritis.

Keywords: Pyelonephritis, Omega-3, DMSA scan, Urinary tract infection, Antiinflammatory



Investigation of Hydrochlorothiazide Binding to Human Serum Albumin by Spectroscopic Methods

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Abstract

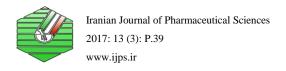
Introduction: Human serum albumin (HSA) has an extraordinary ligand-binding capacity, making it as a depot and suitable carrier for many endogenous and exogenous ligands including many drugs in the blood circulatory system [1]. Thiazide-type diuretics, such as hydrochlorothiazide (HCTZ), are among the first-line therapeutics for patients suffering from hypertension [2]. This study was designed to elucidate the interaction between HCTZ with HSA.

Methods: The binding of HCTZ to HSA was investigated by UV, circular dichroism (CD) and fluorescence spectroscopy in 50 mM sodium phosphate buffer, pH 7.4.

Results: The results of UV spectroscopy confirmed that a complex has been formed between the drug and HSA [3] whereas the analysis of the fluorescence data revealed that HCTZ strongly quenches the intrinsic fluorescence of HSA through a dynamic mechanism [4]. Binding constant (K_a) and the number of binding sites (n) were calculated by Stern-Volmer equation [5]. Thermodynamic analysis of the binding data indicated that the hydrophobic interactions played a major role in the binding process [6]. Computation of the protein surface hydrophobicity (PSH) index of the protein-drug complex using 1-anilinonaphtalene-8-sulfonate suggested that the protein PSH index was increased upon drug binding [5]. The results of far-UV CD experiments showed that the α -helical content of HSA was increased due to drug binding whereas near-UV CD results revealed occurrence of some reduction in the flexibility of the HSA tertiary structure [7]. Also, competitive binding studies using warfarin and ibuprofen suggested that binding of HCTZ occurred through the HSA subdomain IIA [8].

Conclusion: All the above data let us conclude that HCTZ binds to HSA via a 1:1 complex formation and the binding caused some alterations in the secondary as well as the tertiary structure of HSA.

Keywords: Human Serum Albumin; Hydrochlorothiazide; Fluorescence quenching; Protein surface hydrophobicity; Binding Study



Investigation of Different Surfactant Applicability for the Imidazolium Based Ionic Liquids Application in Protein Extraction from Plasma

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Abstract

Introduction: Room temperature ionic liquids (ILs), as green solvents, have gained interest in chemical and biological application. By possessing interesting characteristics such as negligible vapor pressure, high stability, ease of handling, and bio-compatibility they introduced as a possible alternative to conventional organic solvents(1). ILs application in liquid—liquid extraction of proteins can provide a green and cost effective method for proteomics and drug development studies. Serum albumin as the major soluble protein in body fluids is one of the most important protein which need to be extracted or removed from body fluids. In the present paper the capability of imidazoliume based ionic liquids in conjunction with different surfactants in the purification/removing of human serum albumin was studied.

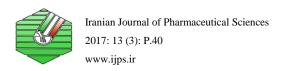
Methods: Aqueous two phase system based on back extraction used to extract HSA from human plasma. A three phasic system including human plasma, IL as a membrane bed for the extraction of HSA, and tris buffer solution containing surfactant as the stripping solution for the back extraction of HSA has been employed. The extraction efficiency was studied using gel electrophoresis.

Results: Extraction with SDS surfactant which used as stripping solution for the back extraction possessed better extraction capability in comparison with other surfactants i.e. Tween85. Tween80. Tween60. Brij-35. PVP K30. CMC-LD. Peg. BCD.

Conclusion: The applied method could successfully remove HSA from Human plasma, while a minor fraction of globulin proteins is extracted too. The results could be applied for the proteomics studies in which HSA and globulin free plasma is needed for the study. As the remained proteins are in solution and they are not treated with any solvent, structural studies of the remained proteins are possible.

Keywords: Ionic liquid, HSA, Human plasma, Gel electrophoresis





A Flourimetric and Molecular Docking Investigation of Mefenamic Acid Interaction with Human Serum Albumin

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Abstract

Introduction: Binding of drugs to the HSA affects their pharmacokinetic and pharmacodynamic properties(1) and investigation of the drug-HSA interaction molecular mechanism is important both for clinical and drug development applications. Mefenamic acid is a member of the anthranilic acid derivatives belongs to the NSAID drugs, and is used to treat mild to moderate pain (2, 3). Interaction mechanism of mefenamic acid with HSA (4) is studied by the application of flourimetric quenching titration method in this study.

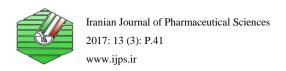
Methods: Mefenamic acid (MEF) binding to human serum albumin (HSA) was studied using fluorescence quenching titrations. Florescence spectra HSA in the absence and presence of MEF were obtained in the emission range of 300–450 nm using the excitation wavelength of 278nm. The emission intensities were used to calculate binding constant, number of binding site, binding rate constant of the binding. Förster (fluorescence resonance energy transfer (FRET)) were calculated using the consequent UV spectra.

Results: Results obtained from fluorescence data indicated that quenching mechanism was dynamic. Binding constant was 6.55E+07 and the number of binding sites was 1.51. Binding distance (r) between HSA– MEF was 3.78 indicating that energy transfer between flourofors and ligand is possible. The results confirmed by molecular docking studies in which showed better interaction of MEF with subdomain IIIA.

Conclusion: Results suggest that MEF could bind to HSA using a dynamic mechanism of interaction. In addition to the molecular binding mechanisms, energy transfer between MEF and HSA assisted stronger binding. Results of molecular docking could successfully be applied for detailed study of binding sites for HSA and all calculated parameters were in agreement with experimental values.

Keywords: Mefenamic acid, HSA, Interaction, Docking, Spectroscopy





A Simple and Fast Dispersive Liquid–Liquid Micro–Extraction Technique for The Pre–Concentration and Quantification of Vitamin D₃ in Dairy Samples Using a HPLC Method

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Abstract

Introduction: Cholecalciferol, vitamin D_3 (Vit D_3), is a fat-soluble vitamin that is essential for normal calcium metabolism and mineralization process in human body. In present work, a simple and fast dispersive liquid-liquid micro-extraction (DLLME)-HPLC-UV method has been developed and validated for the extraction, preconcentration and subsequently quantification of Vit D_3 in milk and yogurt samples.

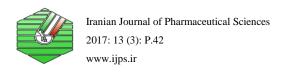
Methods: In order to be able to extract Vit D_3 from studied samples efficiently, the DLLME procedure was optimized with respect to the parameters affecting the extraction efficacy, where acetonitrile utilized for the cleanup purposes and carbon tetrachloride were selected as disperser and extracting solvents, respectively. The extracted samples were analyzed with a HPLC technique using a C_8 column (250mm \times 4.6mm, 5 μ m) at room temperature (25°C), mobile phase of acetonitrile / methanol (90:10% v/v) in isocratic elution mode at a flow rate of 1.2 mL/min and UV detection at 265 nm.

Results: The obtained results indicated that under the optimal conditions, the method was linear in the concentration range of 2 to 60 ng/ml with a LOD of 0.9 ng/ml and LOQ of 2 ng/ml; the method was accurate (-2.1% \leq RE% \leq +0.6%) and precise (1.2% \leq RSD% \leq 11.3%) and its recovery was in the range of 86.6 to 113.3%.

Conclusion: By taking the obtained results into the consideration, it can be said that the developed method could be applied as an easy to use and rapid technique in food quality control laboratories to inspect the amount of Vit D_3 in milk and yogurt samples, especially in fortified ones.

Keywords: DLLME, HPLC-UV, Vitamin D₃, Dairy products





A Simple and Fast Method for Adulteration Detection in Commercially Available Lime Juice Products in the Iranian Market

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Abstract

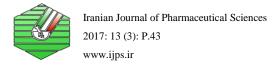
Introduction: Safety of food and beverage is one of the most important concerns in food industry. In the case of lime juice products, there is no access to a routine method for detection of possible adulterations; therefore, the main objective of the present work was to introduce a rapid, simple and cost-effective method applicable to detect possible adulterations in commercially available lime juice products.

Methods: In this study, eleven brands of marketed lime juice products were randomly purchased from local stores in Tabriz and fresh lime juice, as a control sample, was prepared by squeezing lime fruits using a plain juicer. Colorimetric analysis was carried out using Ehrlich's reagent and fingerprinting was done using a solid phase extraction – thin layer chromatography (SPE-TLC) technique, where Sep-Pak C18 cartridges were utilized to obtain samples' methanolic fractions which were analyzed on the silica gel plates using solvent systems of formic acidacetic acid-distilled water-ethyl acetate and chloroform-ethyl acetate and studied at two wavelengths of 366 and 254 nm before and after spraying aluminum chloride reagent.

Results: The obtained results from colorimetric analysis indicated appearance of orange-brown color pointing to the presence of limonoids in fresh lime juice and only five commercially available products. Regarding SPE-TLC fingerprinting, except for five products with identical or comparable TLC patterns to the fresh lime juice, other samples represented completely different TLC patterns suggesting the presence of adulterants in these products.

Conclusion: In conclusion, it can be said that the colorimetric analysis using Ehrlich's reagent followed by the SPE-TLC fingerprinting could be utilized as a simple and easy to use technique for preliminary screening of adulteration in lime juice products in food quality control laboratories.

Keywords: Colorimetric analysis, Ehrlich's reagent, Iranian market, Lime juice products, Solid phase extraction – thin layer chromatography fingerprinting



15th IPSC Proceeding

Development of a Validated Method for the Simultaneous HPLC Analysis of Letrozole, Naproxen and Propranolol from Human Plasma

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Abstract

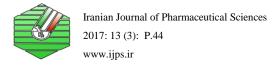
Introduction: Letrozole is an anticancer drug which is used for the treatment of breast cancer. Application of beta blocker and NSAID drugs in combination with anticancer drugs mainly after surgeries is common. Simultaneous extraction and analysis of drugs from body fluids is needed for clinical and drug development purposes. (1-3) The aim of this study is to develop a simple and fast HPLC method for the quantification of propanol, Letrozole and naproxen in human plasma after a simple protein precipitation procedure(4).

Methods: Spiked plasma sample was treated using NaCl (4%) and acetonitrile followed by vortex and centrifuge for the precipitation of proteins. supernatant was directly injected into HPLC system. The mobile phase was mixture of acetonitrile and di sodium hydrogen phosphate buffer (0.01M),(50:50, V/V) adjusted to pH 5.5 at flow rate of 1.5 ml.min ⁻¹. The total run time and wavelength were 6 min and 240 nm. The method was validated by evaluating its selectivity, sensitivity, linearity, accuracy, and precision according to US Food and Drug Administration guidelines.

Results: The result shows calibration curves were linear for the studied drugs in the range of 0.1-1 μ g.ml⁻¹, with correlation coefficients exceeding 0.99. intra –inter days precision (%CV) were <%15. The recovery values were between 89 and 99%. The stability study results showed this method had good stability according to the FDA guidelines.

Conclusion: The obtained results demonstrated that the reported method was sensitive ,selective , accurat and precise for simultaneous quantification of propranolol, Letrozole and naproxen in human plasma and it can be applied in clinic and in pharmacokinetic study .

Keywords: Plasma, HPLC, simultaneous, propranolol, Letrozole and naproxen



15th IPSC Proceeding

Investigation of Antibody-Drug Conjugates as a Novel Approach for Cancer Therapy

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Abstract

Introduction: Conventional chemotherapy drugs don't selectively act at the tumor site, this may lead to undesirable side effects and normal cells toxicity.

Antibody drug conjugates (ADC) is a novel therapeutic approach for cancer therapy. The structure of an ADC consist of a cytotoxic drug, monoclonal antibody that is specific for the cancer cell's antigens and a linker that bind the drug to the monoclonal antibody. The molecules are designed to selectively bind to target-expressing cells, so it can deliver the therapeutic agents directly to the tumor. ADCs are stable in systemic circulation and they can release their drug in response to pH, proteolytic enzymes etc.

Trastuzumab emtansine (kadcyia) and Brentuximab vedotin (Adcetris) have FDA approval for cancer therapy and more than 60 ADCs are currently in clinical trials. First generation of ADCs were suspended because of their immune response due to their murine-derived antibodies structure .this problem was solved by promotion of engineering technology for the generation of humanized and fully humanized antibodies.

Methods: Material of this review were obtained by searching PubMed and ScienceDirect with the following terms: "antibody drug conjugate", "immunoconjugates", "chemotherapy", "cancer", "monoclonal antibodies"

Results: ADCs enable selective targeting for cancer cells, improvement efficacy of therapy, reducing systemic toxicity and promotion of Pharmacokinetic (PK) and pharmacodynamics (PD) and bio distribution compared to traditional chemotherapy.

Conclusion: Antibody drug conjugates with two approval drugs for cancer therapy performing well in the clinic. More than 60 antibody drug conjugates are in clinical trial and probably added to approved drugs in the near future. paradigm of cancer treatment might shift to this class of drugs due to their advantages compared to the traditional drugs.

Keywords: Antibody-drug conjugate, monoclonal antibody, cancer, chemotherapy



15th IPSC Proceeding

Effect of Selegiline on the Hippocampal Ischemia-reperfusion Injuries and Cognitive Impairments following Global Ischemia in Male Rats

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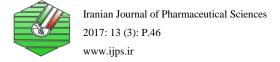
Abstract

Selegiline, a selective monoamine oxidase type B inhibitor, has been shown to have neurotrophic and anti-apoptotic properties and to protect neurons in experimental models of cerebral ischemia. The aim of this study was to investigate whether selegiline could enhance cognitive and functional recovery in stroke disease. The male rats were randomized in four groups: Control groups, Control + Selegiline (20 mg/kg), stroke induction groups and stroke+ Selegiline (20 mg/kg). Selegiline were added to water consumption after 4 day from starting of investigation.

In this regard, we tested whether 1) Administration of selegiline is able to inhibited abnormality behaviors related to global ischemia in Male Rats 2) Behavioral changes are associated with mitochondrial dysfunction in the hippocampus and 3) Administration of selegiline is able to alter immune-inflammatory factors in the hippocampus. Therefore, using valid and qualified behavioral tests for the assessment of stroke like behaviors such as novel object recognition test (NOR) were used for confirmation of stroke induction in male rats. Then, animals were sacrificed and hippocampi were dissected out and stored at -80 °C. The samples were divided into two different groups; first set of samples were used for preparation of tissue homogenate, on which measurement of oxidative stress

parameters and nitrite levels were performed. Second set of samples were fixed in 10% formalin, sectioned, and stained with hematoxylin and eosin (H&E) for pathological evaluations. The statistical analysis showed a significant improvement in most neuropsychological tests after two weeks in the study group. The between-group analysis revealed that involvement of oxidative stress, mitochondrial dysfunction and behavioral despair after stroke induction in animal models. The results of pathology confirmed our biochemistry data. Preliminary our results proposed statistically significant in animals between stroke induction and treated groups by selegiline. Our results predisposed selegiline has benefit effect in mitochondrial and behavioral function.

Keywords: Global ischemia, Rat, Selegiline, Stroke



15th IPSC Proceeding

Screening of Secondary Metabolites from Methanolic Extract of Flowers of Verbascum Sublobatum Murb. by Phytochemical Analysis

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Abstract

Introduction: There has been an increasing interest worldwide on therapeutic values of natural products. The nature provides the mankind vast therapeutic flora with a wide variety of medicinal potential. The revival of interest in plant derived drugs is mainly due to the current widespread belief that "green medicine" is safe and more dependable than the costly synthetic drugs many of which have adverse side effects. The need of the hour is to screen a number of medicinal plants for promising biological activity [1,2].

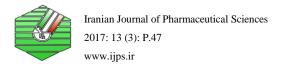
Methods: The aim of this study was to evaluate the bioactive compounds of methanolic extract of flowers of *Verbascum sublobatum* Murb. belonging to the family Scrophulariaceae. The flowers of *Verbascum sublobatum Murb*. were harvested in the highlands of Tonekabon, Iran and methanolic extract prepared by microwave assisted extraction (MAE) method. The present study reveals that the phytochemicals analysis of seven different chemical compounds Saponins (Foam Test), Flavonoids (Alkaline Reagent Test), Terpenoids (Salkowski Test), Phenols

(Ferric Chloride Test), Cardiac glycosides (Keller-Killani Test), Di-terpenoids (Copper acetate Test) and Tannins (Ferric Chloride Test) were tested in methanolic extract.

Results: This investigation has revealed that the methanolic extract of flowers of *Verbascum sublobatum* Murb. has high phytochemical contents like cardiac glycosides, tannins, saponins, flavonoids, terpenoids, phenols and Diterpenoids. These active constituents show different activities against different type of diseases like cancer, liver disorders, diabetes, atherosclerosis and inflammatory diseases etc. According to their characteristics, they can be involved into medicinal plant category.

Conclusion: Medicinal plants are universal and natural sources of active compounds which have tremendous effect in the society. Natural products either as pure compounds or as standardized plant extracts provide unlimited opportunities for new drug. Therefore, the flowers of *Verbascum sublobatum* Murb. incarnate might represent a new phytoconstituents and antioxidant source with stable, biologically active components that can establish a scientific base for modern medicine.

Keywords: Verbascum sublobatum Murb., MAE, Phytoconstituent, Biological activity, Modern medicine, Cancer.



15th IPSC Proceeding

Green Synthesis of Silver Nanoparticles Using Plantago Major L. Leaves

Extract At Room Temperature and Evaluation of Its Antibacterial Activities

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Abstract

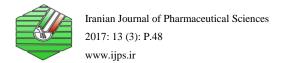
Introduction: Nanomedicine is a rapidly developing and promising field that makes best use of inert metals like silver, gold, and platinum to synthesize metallic nanoparticles with high therapeutic potential for various biomedical applications. Silver with its potent antimicrobial activity has been used in the synthesis of silver nanoparticles which finds extensive use in the preparation of creams, topical ointments, medical implants and drug delivery [1,2].

Methods: In this study the biosynthesis of silver nanoparticles using *Plantago major* L. leaves extract as a reducing agent by microwave irradiation method. The synthesized silver nanoparticles were characterized using various instrumental techniques including fourier transform infrared spectroscopy (FT-IR), ultraviolet-visible spectroscopy (UV-Vis), X-ray diffraction (XRD) and transmission electron microscopy (TEM). Later, the antibacterial activity of the synthesized silver nanoparticles was tested using both gram positive as well as gram negative bacteria i.e. *Staphylococcus aureus* (ATCC 25923) and *Escherichia coli* (ATCC 25922), respectively.

Results: The surface plasmon resonance (SPR) found at 445 nm confirmed the AgNPs synthesis. The FTIR results showed the presence of some biomolecules in extracts that act as reducing and capping agent for silver nanoparticles biosynthesis. The XRD peaks 38°, 44°, 64°, and 77° for leaves extract can be assigned the plane of silver crystals (111), (200), (220), and (311), respectively, and indicate that the silver nanoparticles are face centered cubic (FCC), and crystalline in nature. The particle size of the AgNPs was studied by TEM and showed the presence of AgNPs in the size range 25–50 nm. The synthesized AgNPs exhibited good antibacterial potential against gram positive and gram negative bacterial strains. The green synthesis an alternate method to physical and chemical synthesis is cost effective and eco-friendly.

Conclusion: Further, efficient antibacterial activity of the synthesized silver nanoparticles proves the application potential of green synthesis in the area of nano-medicine.

Keywords: Plantago major L., Green synthesis, Silver nanoparticles, Antibacterial activity, TEM, Nano-medicine.



15th IPSC Proceeding

Effects of Quercetin of Medlar Leaves on Passive Avoidance Learning and Memory on STZ-Induced Memory Impairement in Rats Model of Metabolic Syndrome

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Abstract

Introduction: Metabolic syndrome (MS) is a pre diabetes stage with 3 hallmarks of visceral obesity, dyslipidemia, and hypertension. The prevalence of MS in postmenopausal women is higher than premenopouse. Studies show that metabolic syndrome is also associated with memory disturbances (1). Anti-antioxidant flavonoids are good candidates for preventing Alzheimer's disease (2). The goal of this study was to investigate the effect of quercetin of medlar leaves, on streptozotocin-induced memory impairement, in rats' model of metabolic syndrome.

Methods: Forty eight female Wistar rats weighing 200-250 g, were divided into six group including: SHAM, OVX, OVX+STZ, OVX+SAL, OVX+STZ +FLA, OVX+STZ +SAL. At the initial, rats were ovariectomized, after 3 weeks induction model of metabolic syndrome, animals were cannulated using stereotaxic apparatus. Intracerebroventricular injection of STZ (3 mg/kg) was used to induce memory impairement (2). Then rats were received quercetin for 21days. All rats were tested for passive avoidance learning and memory in the shuttle box. Latency to enter to dark compartment and total time spent in that compartment were used in 3 minute as passive avoidance memory indices (2).

Results: Metabolic syndrome did not show significant difference on passive avoidance learning and memory (p=0.873). Intraventricular injection of streptozotocin significantly reduced passive avoidance learning and memory (p=0.001). Treatment of quercetin significantly improved passive avoidance learning and memory in rats model of Alzheimer's disease (p=0.001).

Conclusion: STZ injection causes memory impairment and treatment of quercetin can play a role to improve on it.

Keywords: Alzheimer, Shuttle box, Metabolic syndrome, Streptozotocin, Quercetin



15th IPSC Proceeding

Comparison of Sertraline with Rifampin in the Treatment of Cholestatic pruritus: a Randomized Clinical Trial

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^bDepartment of Internal Medicin Associated Professor of Gastroenterology and Hepatology, School of Medicin, Hamadan University of Medical Sciences, Hamadan, Iran. Abstract

Introduction: One of the most common and disabling symptoms of liver disease such as Primary sclerosing

cholangitis (PSC) and Primary Biliary Cholangitis (PBC) is pruritus that occurs on the skin surface for several

reasons. Various treatments including cholestyramine, rifampin, opioid antagonists, anti histamines and SSRIs are

used to control pruritus in these patients. Due to Rifampin drug interactions such as rifampin with sofosbuvir as well

as its important side effects such as hepatotoxicity and increased blood bilirubin level, clinicians attempted to find a

safer and better substitution. It is believed that if Rifampin taken especially for a long period of time, it leads to

severe complications for patients. According to previous studies sertraline is safer than Rifampin. In this study we

determined the safety and efficacy of sertraline in comparison with Rifampin in management of cholestasis-

associated pruritus.

Methods: In a single blinded randomized clinical trial a total of 36 patient of PSC and PBC were divided into two

equal groups, one group received 100 mg/day sertraline and the other group received Rifampin 300 mg/day for 1

month. Pruritus visual analog scale (PVAS) was recorded at baseline and after one month of intervention, also, ALT,

AST, ALP and total bilirubin of all patients were measured at baseline, second and fourth week of intervention.

Result: over the follow up period, pruritus had relieved in both groups, but there was no significant differences

between sertraline and Rifampin in pruritus management (P value=0.740), also there was no significant differences

between these two interventions in total bilirubin level changes (P value=0.106), ALT and AST data analysis

demonstrated significant differences between two groups (Pvalue<0.01), also ALP level was significantly different

between two intervention groups (P value= 0.006).

Conclusion: This study demonstrated there is no difference between sertraline and Rifampin in pruritus

improvement, but sertraline has less adverse effects and less effects on hepatobiliary enzymes levels, so it seems to

be safer than Rifampin to be used in management of cholestasis-associated pruritus.

Keywords: cholestasis, pruritus, Sertraline, Rifampin.



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15th IPSC Proceeding

QSAR and Molecular Docking Studies of 3-Hydroxy Pyrimidine-2, 4-Diones

Derivatives as Selective Inhibitors of HIV Reverse Transcriptase-Associated

Rnase H in The Treatment of AIDS

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Abstract

Introduction: HIV encodes three enzymes crucial for viral replicaton: Reverse Transcriptase (RT), IN, and protease. RT has two different activites including DNA polymerase and ribonuclease H (RNase H) activity. All of

marketed RT inhibitors target only the DNA polymerase activity. Therefore, ribonuclease H activity may serve as a

new target for drug discovery.

Methods: In this study, a series 3-Hydroxypyrimidine-2,4-dione as Selective Active Site Inhibitors of HIV Reverse

Transcriptase-Associated RNase H were applied to quantitative structure-activity relationship (QSAR) analysis.

Three methods include, MLR, FA-MLR and GA-PLS were applied to make relations between structural

characteristics of these compounds and HIV Reverse Transcriptase-Associated RNase H inhibitory effect. molecular

docking study was also carried out by AutoDock 4.2 on the compounds to found out the molecular binding

interaction of these compounds with the active site of target (PDB ID: 1HRH).

Results: The best multiple linear regression equation was generated by GA-PLS method. Based on the results a

combination 2D autocorrelations, topological and geometrical descriptors have been selected by GA-PLS that had

more effect on HIV Reverse Transcriptase-Associated RNase H inhibitory activity. Based on docking studies, the

ΔG bind values of the best docked poses of all compounds were ranged from -5.03 to -7.39 Kcal.mol-1 and

compound 20 had the highest binding energy. The important amino acids inside the active site of the enzyme

responsible for essential interactions are Gln475, Asp549, Tyr501, Ser515, Trp534, Asp493, Tyr472 and Gln480

which take part in hydrogen bond formation.

Conclusion: Three method of QSAR, MLR, FA-MLR and GA-PLS, were employed to obtain the Quantitative

relationships between molecular feathers of 3-Hydroxypyrimidine-2,4-dione derivatives and HIV Reverse

Transcriptase-Associated RNase H inhibitory activity. GA-PLS method was the best method can be used for

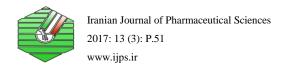
prediction of the HIV Reverse Transcriptase-Associated RNase H inhibitory activity. The results obtained from

molecular docking studies gave some insight into molecular binding mode and importance of amino acids in the

active site of enzyme that have significant roles in the inhibitory activity.

Keywords: QSAR, Molecular Docking, Reverse transcriptase, AIDS

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Potential Drug-Drug Interactions at a Referral Hematology-Oncology Ward in Iran: A Cross-Sectional Study

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Abstract

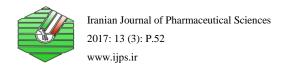
Introduction: To assess the pattern and probable risk factors for moderate and major drug-drug interactions in a referral hematology-oncology ward in Iran.

Methods: All patients admitted to hematology-oncology ward of Dr. Shariati Hospital during a 6-month period and received at least two anti-cancer or non-anti-cancer medications simultaneously were included. All being scheduled anti-cancer and non-anti-cancer medications both prescribed and administered during ward stay were considered for drug-drug interaction screening by Lexi-Interact On-Desktop software.

Results: One hundred and eighty-five drug-drug interactions with moderate or major severity were detected from 83 patients. Most of drug-drug interactions (69.73 %) were classified as pharmacokinetics. Fluconazole (25.95 %) was the most commonly offending medication in drug-drug interactions. Interaction of sulfamethoxazole-trimethoprim with fluconazole was the most common drug-drug interaction (27.27 %). Vincristine with imatinib was the only identified interaction between two anti-cancer agents. The number of administered medications during ward stay was considered as an independent risk factor for developing a drug-drug interaction.

Conclusions: Potential moderate or major drug-drug interactions occur frequently in patients with hematological malignancies or related diseases. Performing larger standard studies are required to assess the real clinical and economical effects of drug-drug interactions on patients with hematological and non-hematological malignancies.

Keywords: Drug-drug interactions Hematology-oncology ward Hematological malignancies Iran



Evaluation of the Effect of Coenzyme Q10 in Depression Phase of Bipolar Disorder as Adjuvant Therapy

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Abstract

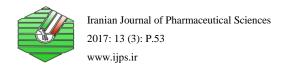
Introduction: Bipolar disorder is a severe, life threatening and prevalent psychiatric disorder that is mostly misdiagnosed. The exact mechanism of bipolar disorder is still unclear. Some studies demonstrated mitochondrial dysfunction and oxidative stress are contributed in bipolar disorder pathophysiologic mechanisms. In this study we evaluate the effects of Coenzyme Q10 (CoQ10), an essential cofactor in mitochondrial electron transport pathway and potent antioxidant agent as an adjuvant therapy in depression phase of bipolar disorder.

Methods: A total of 81 patients with diagnostic bipolar disorder based on DSM-5 (Diagnostic and statistical Manual of Mental Disorders-Fifth edition) and Montgomery Asberg Depression Rating Scale (MADRS) with current depressed episode were recruited in this study. Patients as a part of a randomized double blind study were divided into two groups with simple randomization method. Beside the standard treatment of bipolar disorder 41 patients in intervention group were treated by CoQ10 200 mg/day for 8 weeks and 40 patients in placebo group received Placebo for 8 weeks. MADRS score of patients was recorded at baseline, fourth week and eighth week of study

Results: Depression severity was analyzed after 8 weeks of study. Only 51 patients completed the course of study (26 patients in intervention group, 25 patients in placebo group. The difference of MADRS score at baseline and week 8 was significantly (P value =0.001) higher in intervention group that demonstrated CoQ10 is significantly effective in depression improvement.

Conclusion: This study demonstrated CoQ10 as an antioxidant agent and mitochondrial essential cofactor is effective in depression severity reduction in bipolar patients with depressed episode. Further studies with high doses of CoQ10 and larger sample size are needed to confirm antidepressant activity of CoQ10.

Keywords: Bipolar disorder, Depression severity, Coenzyme Q10, mitochondrial dysfunction.



Preparation and *in vitro* evaluation of an Oral Colon Specific Formulation of Aqueous Extract of *Malva Sylvestris* for Treatment of Inflammatory Bowel Disease (IBD)

Azadeh Hamedi*^a, Fatemeh Ahmadi^b, Ebrahim Salimi Sabour^a

Abstract

Intoduction: Ulcerative Colitis (UC) is one of the common types of Inflammatory Bowel Disease (IBD) which mostly affects the distal colon and rectum. Many new cases of IBD are diagnosed each year and the current drug choices for this disease present many adverse effects.

The Common Mallow is a well known medicinal plant that presents anti inflammatory effects and shows regulation of immune system. In a previous study, this plant showed anti inflammatory effect in animal model of Ulcerative Colitis. This research aims at preparation and *in vitro* evaluation of an oral colon specific formulation of aqueous extract of *Malva sylvestris* for treatment of Ulcerative Colitis treatment.

Methods: Aqueous extract of this plant which was standardized based on poly phenolic compounds was used to prepare colon specific tablet formulations.

Tablets were divided into two groups. In first group, release controlling polymer such as ethyl cellulose, hydroxyl propyl cellulose and hydroxyl propyl methyl cellulose were used and the tablets were prepared by wet granulation and direct compression methods. In the second group, after direct compression of the core, cellulose acetate phetalate solution (10%) and Eudragite S_{100} (1, 2%) were used as coating materials. Hardness, weigh variation, content uniformity and release tests were performed on tablets.

Result: Hardness, weight variation and content uniformity of the tablets were in the acceptable range recommended by references. Disintegration time of tablets of the first group was not in optimum level. Release behavior of CAP coated tablets for 2 hours in HCl 0.1 N and 2 hours in pH 7.4 showed 92.49% release which was not suitable. Tablets coated with Eudragit 1% solution did not provide regular release profile and showed highly variable drug release during study period.

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Tablets coated with Eudragit 2% solution exhibited 7.3% release after 2 hours, 42.33% after 6 hours and 96.21% after 10 hours.

Conclusion: tablets prepared by direct compression method and coated with Eudragit 2% solution, showed the most suitable results for clinical trials in ulcerative colitis cases.

Key words: Ulcerative Colitis, Malva sylvestris, Aqueous extract, Colon specific formulation, Euderagit S₁₀₀



15th IPSC Proceeding

Gallic Acid for Cardiovascular Diseases: A Systematic Review of Preclinical Studies

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Abstract

Introduction: Cardiovascular disorders are the first leading cause of mortality all over the world (1). Since not all patients are fully satisfied with conventional pharmacotherapy, they seek for complementary and alternative medicine (2). Gallic acid (GA) is a nutraceutical with phenolic structure present in foods and vegetables of human diet and has several health promoting effects. Here we systematically reviewed evidence regarding the effects of this phytochemical in cardiovascular diseases.

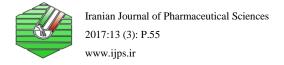
Methods: Databases including PubMed, Scopus, and Science direct were searched with the keywords "gallic acid" and "heart", "cardiovascular disease", "hypertension" or "dyslipidemia" from the date of inception until January

2017. Inclusion criteria were animal or cellular studies with English full-texts assessing the effect of GA or its derivatives in cardiovascular disorders. Primary results were screened by two independent investigators. Final included article were reviewed for type of animal model/cell line and GA mechanisms of action.

Results: Total of 12 papers was finally included. GA could successfully decrease total cholesterol, triglyceride, low-density lipoprotein and very low-density lipoprotein in rats; whereas increased high-density lipoprotein. It also reduced the myocardial damage which was evident from decreased levels of creatine kinase, lactate dehydrogenase and aspartate transaminase. Due to antioxidant properties, GA significantly reduced malondialdehyde and increased catalase, glutathione peroxidase, Heme oxygenase-1 gene expression, and superoxide dismutase. GA increased the activities of Na+/K+ ATPase, Ca2+ ATPase, and Mg2+ ATPase. GA enhanced the stability of lysosomes via inhibition of lysosomal enzymes release and decrease in the activity of the total lysosomal hydrolases. GA significantly decreased blood pressure in hypertensive rats. Furthermore, GA reduced biomarkers of cardiac fibrosis and hypertrophy. No toxicity was reported during the evaluations.

Conclusion: GA demonstrated positive effects in pre-clinical models of cardiovascular diseases; however, future studies are essential to confirm the safety and efficacy of this compound in human.

Keywords: Gallic acid, Cardiovascular Diseases, phenolic compound, Antioxidants



15th IPSC Proceeding

Investigation of the Production, Purification, and Binding Ability of J_{43} Scfv Antibody to TNF- α Identified by Phage Display Technique

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Abstract

Introduction: TNF- α is a cytokine responsible for regulating immune responses and different physiological processes. However, in higher levels, TNF- α participates in inflammatory conditions (1). Therefore, inhibition of TNF- α adverse effects is a useful strategy for treatment of various inflammatory diseases like rheumatoid arthritis, Crohn's disease and Septic shock. Using direct TNF- α binders is a method to neutralize TNF- α activity (2). In this

study, we aimed to investigate the production, purification and binding ability of single chain fragment variable anti-TNF- α antibody (i.e., J_{43}) to TNF- α identified by phage display technique.

Methods: The DNA sequence of J_{43} antibody identified by phage display method was modified to change stop codon present in CDR2 region to tyrosine codon with site directed mutagenesis and then the corrected sequence was cloned into pET28a expression vector. The constructed vector was transformed into *E.coli Bl21 plysS* and the protein of interest was expressed and subsequently purified using Ni-Sepharose affinity column. The produced scFv antibody was analyzed by SDS-PAGE and western blotting techniques. To assess the binding ability of the produced scFv antibody to TNF- α , ELISA experiment was performed, in which mouse anti-His and Goat anti-mouse IgG – HRP conjugated antibodies were used as primary and secondary antibodies.

Results: The J_{43} antibody was produced and purified in bacterial expression system. The protein band at about 25 kDa on SDS-PAGE was attributed to scFv of interest. In western blotting technique using anti-His antibody the production of scFv antibody was confirmed. In ELISA experiment, the produced antibody showed appropriate affinity towards TNF- α .

Conclusion: In the current work, anti-TNF- α scFv J_{43} antibody was expressed in a prokaryotic system and the affinity of the purified protein to TNF- α was elucidated. The findings in the current study can pave the way for developing and designing of new TNF- α inhibitors.

Keywords: TNF-α, Affinity Chromatography, Site directed mutagenesis, Stop codon



15th IPSC Proceeding

Identification and Quantification of the Caffeic Acid of Mullein (Verbascum Songaricum) Ecotypes from Southwest Iran by High-Performance Liquid Chromatography (HPLC)

Fatemeh Jamshidi Kia^a, Karamatollah Saeidi^a, Zahra Lorigooini ^b*

Abstract

Introduction: The mullein genus is the largest genus of Scrophulariaceae family which has extensive natural habitat in Southwest of Iran. Phenolic acid is one of the most important chemical compounds that have biological activity as

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diverse as is anti-inflammatory, antibacterial, antiviral, anti-tumor and antioxidant. Caffeic acid is one of these compounds. Therefore, this study aims to Identification and quantification of the Caffeic acid of *Verbascum songaricum* ecotypes from Southwest Iran.

Methods: In this study, 15 ecotypes of the species V. songaricum flower organs were collected from the South West of Iran. Identification and quantification Caffeic acid using reversed-phase high performance liquid chromatography (RP HPLC) detector (UV PDA 2800), C18 column with dimensions of 250×4.6 mm and the particle size was 5 micro liters.

Results: The results showed Mullein containing Caffeic acid composition and there was difference among ecotypes. the highest and lowest content of Caffeic acid obtained from the ecotype Sepidan 11.62 (μ g / 2.5 mg extract) and ecotype Farokhshahr 1.34 (μ g / 2.5 mg extract), respectively. To sum up, our results revealed a high level of variation in Caffeic acid among *V. songaricum* collected from different regions in southwest Iran and was affected by habitat climatic.

Conclusion: The results showed Mullein contain the caffeic acid, which can be combined as the source of the plant. Also, the pattern of habitats is suitable ecotypes superior in terms of composition to be selected and used for breeding and cropping Mullein.

Keywords: Mullein, Caffeic acid, HPLC, Southwest Iran.



15th IPSC Proceeding

Analysis and Detection Samples of *Cichorium Intybus* Aromatic Water from Iran Local Market

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Abstract

Introduction: Using plants for treating diseases was an old way in many countries such as Iran. Meymand in Fars and kashan are the most important local sources of product medical plants in our country and many of local producers are in this region. At present, using plants solo hydration is a simple and popular way for people. Solo hydration form of *Cichorium intybus* earns from water distillation of its stem, by distillation the aqueous phase include aromatic water and solo hydration was formed. *Cichorium intybus* products are one of the best sellers in

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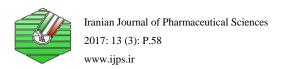
market Because of its effect on treatment of infection, poisoning, diabetes and allergy. It's complete study about *Cichorium intybus* phytochemical compounds and the aim of this study is define a method to recognize the original product. It is necessary to define acceptable standard to prevent of cheeping and should define the common compounds with exact range of percent.

Methods: We bought samples of *Cichorium intybus* aromatic water from local market, and we transferred them to laboratory. The sample compounds were extracted by liquid – liquid methods and evaluated by GC/MS and compared with the referenced book like Adams 2007. Obtained phytochemical data were analysis with SPSS and classified them by dendrogram method and was compared with our data earned from the standard sample that collected and prepared with ourselves.

Results: 41 compounds were detected. And, Carvacrol was the compound that was available in all samples from 1.14 percent to 39.34 percent. Also, Thymol was the compound that was available in most of samples from 1.24 percent to 69.32 percent. Moreover, we understood that some compounds like: Pulegone, Carvone, Carvacrol and Piperitenone were in all samples mostly with different percent. Also some linear hydrocarbon was detected in this method and some other unexpected compounds like cinnamaldehyde were detected.

Conclusion: Existence of some unusual hydrocarbons in trade samples showed that the used temperature for producing aromatic in local companies was high. Therefore, it disturbed original and useful components. Existence of some impure compounds like: Pulegone, Carvone, Piperitenone and cinnamaldehyde in trade samples showed cleaning of container not as well as need. Carvacrol and Thymol with exact range of percent are the common compounds to define acceptable standard for *Cichorium intybus* aromatic water.

Keywords: Cichorium intybus, GC/MS, Phytochemical compounds, Aromatic water.



15th IPSC Proceeding

Net Analyte Signal Standard Addition Method for Simulantaneous Quantitation of Tadalafil in Presence of Methyl Paraben: Application to Cocrystal Solubility Studies

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Abstract

Introduction: Net analyte signal standard addition method (NASSAM) is a novel tool to quantify two components simultaneously using spectroscopy methods. It can be used when two materials have overlapped spectra. It is fast, inexpensive and has simple steps in compared with other separation based methods like HPLC. Proposed method no needs for a prior separation or special condition to overcome the analytes overlapping problem and it is used for physicochemical properties evaluation of pharmaceutical cocrystals which they are composed of two crystalline

compounds via noncovalent interactions.

Methods: Fifteen mixtures of tadalafil and methylparaben were prepared and determined with UV spectrophotometric used to obtain NAS via Matlab software. Then the NAS curve versus concentration of the added analyte standards to determine the analyte concentration. Some mixtures of tadalfil and methyparaben with

known concentration were prepared to ensure accuracy and validity of the proposed method.

Results: The results showed that NAS of analyte (tadalafil) is not dependent on interferent (methylparaben) and there is good correlation between the norms of the NAS versus standard concentrations of analyte. The method provided a linear range between 2-10 mg/L with a correlation coefficient (R²) of 0.99 in presence of different concentrations of methyl paraben (up to 40 mg/L). The accuracy and precision of established method for

quantification of tadalafil were 6.97% and 1.15%, respectively.

Conclusion: Results showed NASSAM is an applicable method to determination of tadalafil (as an analyte) in presence of methylparaben (as an interferent) and it could be applied to determination of tadalafil solubility in

cocrystal form.

Keywords: Cocrystal, Net analyte signal standard addition method, Solubility, Tadalafil



15th IPSC Proceeding

Evaluation the Effect of Chronic Administration of Ethanolic Extract of Ocimum Basilicum on Morphine Withdrawal Syndrome in Rat

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Abstract

Introduction: Opioid analgesics are one of the most important drugs that have been widely used in attenuating moderate to severe pain. Unfortunately, the problems of long term use of opioids are tolerance, dependence, and ultimately addiction to mentioned drugs (1). It has been demonstrated that *Ocimum basilicum* extract has antinociceptive and anti-inflammatory properties (2). In this study the effect of total ethanolic extract of aerial parts of *Ocimum basilicum* on withdrawal syndrome of morphine in male rats has been evaluated.

Methods: Adult male Wistar rats were rendered morphine-dependent by injection of additive doses of morphine subcutaneously twice daily for 9 days. To determine effect of the extract on morphine withdrawal syndrome, 30 minutes after the injection of morphine (s.c), different doses of the extract (10, 20, 40 mg/kg, i.p) dissolved in %25 DMSO were injected for 8 days and on the ninth day 2hours after s.c injection of morphine, naloxone (4 mg/kg, i.p) was injected and withdrawal signs were recorded for 60 minutes. To sum up signs and to obtain an indication of registered trademarks and determine the severity of withdrawal points, total withdrawal syndrome (TWS) was calculated.

Results: The results showed that i.p injection of O.basilicum could significantly reduce the morphine withdrawal syndrome and total withdrawal score (TWS) in two doses (20 mg/kg with p<0.01 and 40 mg/kg with p<0.0\$\ddos\$) in comparison the morphine group. It seems that chronic administration of O.basilicum ethanolic total extract probably suppresses NMDA receptor activation and prevents morphine withdrawal signs by its inhibitory effects on immune system and pro-inflammatory cytokines.

Conclusion: The results showed that chronic use of ethanolic extract of *Ocimum bacilicum* could reduce the morphine withdrawal syndrome in a dose independent manner.

Keywords: Morphine, Dependence, Ocimum basilicum, Withdrawal syndrome.



15th IPSC Proceeding

Survey in Cellular and Molecular Mechanisms of Propylthiouracil Hepatotoxicity in Isolated Rat Hepatocytes

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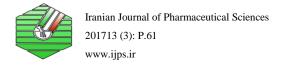
Abstract

Introduction: Propylthiouracil (PTU) is an anti-thyroid drug used in the treatment of hyperthyroidism, especially in pregnancy, because of the forbiddance of methimazol consumption. In 2009, the FDA confirmed the risk of liver failure in consumers of PTU. In this study we wished to investigate mechanism of hepatotoxic effects of PTU on isolated rat hepatocytes. Methods: Hepatocytes were obtained by collagenase perfusion of the liver and their viability was assessed by the trypan blue (0.2% w/v) exclusion test. Cytotoxicity was associated with reactive oxygen species (ROS) formation, lipid peroxidation and loss of mitochondrial membrane potential which were prevented by antioxidants and ROS scavengers (DMSO, mannitol), mitochondrial permeability transition (MPT) pore sealing agent (carnitine) and the ATP generator (L-glutamine), Lysosomal protective agent and glutathione discharge.

Results: According to the results, the concentration of PTU, which can cause death of 50% of cells, is equivalent to 180 μ M, that could significantly increase cell death, ROS production, lipid peroxidation induction and mitochondrial membrane slump compared to the control group (p <0.05). Antioxidants and ROS scavengers (DMSO, mannitol), mitochondrial permeability transition (MPT) pore sealing agent (carnitine) and the ATP generator (L-glutamine) could significantly decrease produce ROS, lipid peroxide and loss of mitochondrial membrane potential compared to the PTU group.

Conclusion: It may be that PTU leads to increased ROS production in a cell. Accordingly, if the produced ROS exceeds the defense capability of antioxidants, besides the cellular lipid peroxidation, multiple areas of a cell such as its membranes become exposed to damage. In addition, the produced ROS can inflict further damage to the cellular membranes like the mitochondrial membrane. Finally, mitochondrial damage can set the grounds for occurrence of liver failure due to PTU and cellular death.

Keywords: PTU, Hepatotoxicity, hyperthyroidism, oxidative stress, ROS



15th IPSC Proceeding

Phytochemicals in type II diabetes: a systematic review of clinical trials

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Abstract

Introduction: Type II Diabetes Mellitus (DM) is a multifactorial metabolic disease with a global increasing rate which significantly affects patient's quality of life (1). Glycated hemoglobin (HbA1c) as a long-term glycemic index is the gold standard method to evaluate the effectiveness of antihyperglycemic drugs (2). Plant-derived secondary

metabolites have long been used to manage several chronic disorders including DM. Here we systematically

reviewed phytochemicals for the treatment of DM in regard to their effect on HbA1c.

Methods: Electronic databases including PubMed, Scopus and Cochrane were searched using the keywords

"phytochemical", "extract", "herb", "plant", and "HbA1c" or "glycosylated hemoglobin" until October 2016.

Inclusion criteria were clinical studies with English full-text in which purified phytochemicals or fractions enriched with a specific phytochemical were assessed in type II DM. Animal and cellular studies, and reports on total extracts

were excluded. Primary results were screened by two independent investigators. Final included papers were

reviewed in regard to phytochemical name and dosage, study design and duration, sample size, and outcomes.

Results: Of 2059 studies, 31 relevant trials were finally included. Berberine and silymarin were the only

phytochemicals with enough evidence supporting their efficacy to control HbA1c in DM. Other phytocomponents

including curcumin, resveratrol, pycnogenol, isoflavones, lignan, catechin, pinitol, isohumulone, sterols and

saponins were also assessed; however, the available data is controversial. Small sample size, short follow-up period,

and heterogeneous baseline HbA1c level of included patients were limitation which caused conflicting results. Most

phytochemicals act as antioxidant and prevent lipid peroxidation, dyslipidemia, and improve endogenous

antioxidant defense mechanisms. Side effects were limited to mild gastrointestinal symptoms.

Conclusion: In conclusion, there are several phytochemicals potentially able to improve glycemic control of DM

patients; however, future clinical trials with larger samples size and longer follow-up periods are essential to confirm

the safety and efficacy of these agents in DM.

Keywords: Diabetes, HbA1c, glycosylated hemoglobin, Phytochemical



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15th IPSC Proceeding

Effect of Octreotide in Control of Non-Variceal Upper GI Bleeding: Randomized, Double-Blind, Placebo-Controlled Trial

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Payam Peymani^a

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Abstract

Introduction: Non-variceal upper gastrointestinal bleeding is a common medical emergency that resulted in high morbidity and high cost of medical care. Octreotide, an effective treatment in variceal upper GI bleeding, is theoretically effective in other bleeding ulcers. In this study, the effect of Octreotide was evaluated in non-variceal

hemorrhage (1,2).

Methods: In this randomized clinical trial, 116 patients with non-variceal gastrointestinal bleeding were randomly divided to group A (58 recipient of Octreotide) and group B (58 control). Patients in both groups received pantoprazole 40 mg initial dose, then 40 mg every 12 hours intravenously. In addition to pantoprazole, Octreotide at a dose of 100 mg subcutaneously every 8 hours was given to group A and placebo with the same dose to group B. After endoscopy, according to the results of endoscopy, regimens were continued for three days or until discharge. Mortality and rebleeding, as well as length of hospital stay, need for blood transfusion and surgery were compared

Results: After medical treatment, No significant differences were revealed between octreotide and placebo groups in term of mortality (5.17% vs 0, PV=0.21) and rebleeding rate (5.17% vs 1.72%, PV=0.5). Also, the statistical test showed no significant association between blood transfusion requirement (1.65 \pm 0.47 vs 1.7 \pm 0.25, PV =0.45), admission days (1.96 \pm 1 vs 1.64 \pm 0.84, PV = 0.44) and surgery (1.72% vs 1.72%, PV = 0.7) in two groups.

Multivariate analysis showed that mortality has a significant correlation with Rockall score as well as AIMS65

score. Notably rebleeding had a significant correlation with Rockall score as well as Blatchford score.

Conclusion: Based on the results obtained in this study, it is unlikely that the use of octreotide as an adjunctive treatment result in more effects in treatment of non-variceal upper gastrointestinal bleeding. It seems that other therapeutic methods should be evaluated to achieve better treatment outcomes.

Keywords: non-variceal upper gastrointestinal bleeding, octreotide, pantoprazole.

in two groups. Data was compiled and analyzed in SPSS V.21 statistical software.



15th IPSC Proceeding

Influence of Process Parameters on Physicochemical Properties of Nanoparticles Prepared by Thin Film Hydration Method

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Abstract

Introduction: TFH method is a simple method which is used widely to prepare nanoparticles such as liposomes and

niosomes. In this method lipophilic materials are dissolved in an organic solvent and thin film is prepared by

evaporating the solvent using rotary evaporator. Then to produce the particles, this dry film would be hydrated by a

hydrophilic phase usually distilled water or phosphate buffer solution. This method usually produces particles with

high polydispersed sizes. So some methods such as sonication, extrusion or high pressure homogenizer are used to

reduce the polydispersity and size of the particles (1, 2). The purpose of this study is to evaluate the effect of

different process parameters on the physiochemical properties of the particles.

Methods: Different particles were prepared by using different process parameters including: 1) Different hydration

time (15-30-60 minutes) 2)30 minutes hydration with and without seven glass beads 3) 30 minutes hydration with

and without glass beads plus Bath or probe sonicator 4) Different sonication duration (6 or 12 minutes). Span 60,

tween 80, cholesterol, quercetin, curcunin and distilled water were used to prepare the particles. The temperature was

constant (60°c). Size, polydispersity index and size of the zeta were evaluated by DLS method and zetasizer

respectively.

Results: Results showed that 30 minutes hydration formed better particles. This result is compatible with some

studies. Results also showed that particles prepared by glass beads had smaller size and lower polydispersity index

compared to particles prepared without glass beads. Type of the sonicators also had influences on particle sizes and

polydispersity index. Ruckmani and Sankar also studied the effect of process-related variables like hydration time,

sonication time, charge-inducing agent, centrifugation and rotational speed of evaporation flask on zidovudine

entrapment and release from niosomes. Their results showed that increased hydration time from 20 to 45 minutes

resulted higher drug entrapment. Their study also indicated that 2 min sonication produced uniform particles while

more sonication time destroyed the niosome structure (3).

Conclusion: Process parameters highly influence on the formation and physicochemical properties of the

nanoparticles.

Keywords: Process parameters, thin film hydration method, nanoparticles, size.



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15th IPSC Proceeding

Antihypertensive and Antioxidant Effects Of Protocatechuic Acid in Glucocorticoid-Induced Hypertensive Rats

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Abstract

Introduction: Oxidative stress is one of the important mechanisms involved in dexamethasone-induced

hypertension. Protocatechuic acid (PCA) is a natural compound with high antioxidant capacity and beneficial

cardiovascular activities. In this investigation, the effect of pretreatment with PCA was studied in dexamethasone-

induced hypertensive male Wistar rats.

Methods: For induction of hypertension, dexamethasone (30 µg/kg) was injected subcutaneously for 14 days. PCA

(50, 100 and 200 mg/kg, orally) was started from 4 days before dexamethasone administration and continued during

the test period. The antihypertensive positive control group received daily oral administration of captopril (40

mg/kg) and the antioxidant positive control group received daily oral administration of vitamin C (750 mg/kg). The

negative control group received daily subcutaneous injection of saline (1 ml/kg). Systolic blood pressure (SBP) was

recorded using tail-cuff method. Measurement of thymus weight was done as a marker of glucocorticoid activity.

The hydrogen peroxide (H₂O₂) concentration and ferric reducing antioxidant power (FRAP) were determined in

plasma samples.

Results: Significant increase in SBP and plasma H₂O₂ concentration and decrease in FRAP value and in the body

and thymus weights were observed in dexamethasone-induced hypertensive rats (P<0.001). Pretreatment with

captopril and PCA (200 mg/kg) significantly prevented dexamethasone-induced hypertension in rats (P<0.001 and

P<0.01, respectively). Vitamin C had no effect on prevention of hypertension. PCA also improved weight gaining

and reduced plasma H₂O₂ concentration and increased FRAP values at all doses (P<0.001).

Conclusion: These findings suggest that supplementation with PCA as a natural compound with health promoting

actions might be helpful for the prevention of hypertension through attenuation of blood pressure and improvement

of oxidative status.

Keywords: Protocatechuic acid; Hypertension; Dexamethason



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15th IPSC Proceeding

Investigation Antimicrobial Effect and MIC Determination of Pistacia Atlantica

and Humulus Lupus Abstracts on Some Bacteria And Fungi

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Abstract

Introduction: Because of synthetic antibiotic's side effects, researches focused on finding natural antibiotics. For decades Humulus Lupus used as sedative and treatment of Syphilis. Homolon and Lopolon are two essential compounds of Humulus Lupus with bactericide effect in foods. Flavonoid and glycoside flavonoids compounds in Pistacia atlantica have wide antimicrobial effects. Probably antimicrobial effects of this compound are because of making complex with protein and bacterial cell wall materials. Also phenolic and triterpenoic compounds in Pistacia atlantica have bacteriostatic effect. This research was done about antimicrobial effect of Humulus Lupus and Pistacia atlantica.

Methods: Humulus Lupus and Pistacia atlantica recognized in faculty of pharmacy. Extraction was done with maceration method. Well diffusion agar method and disk method used for determination of antibacterial and antifungal effect of extracts.

Results: After extraction, 9.5 mg extract taken from 100g Pistacia atlantica and 10.5 mg extract from 100g Humulus Lupus. Hydro alcoholic extract of Humulus Lupus have most effect on Candida Albicans, Aspergillus Fomigatus, Bacillus Sereus, Eshershia Coli (MIC=125) in well diffusion agar method. Hydro alcoholic extract of Pistacia atlantica have most effect on Aspergillus Fomigatus and Eshershia Coli (MIC=125) in well diffusion agar method. In the disk method, Humulus Lupus have most effect on Bacillus Sereus (MIC=150). Pistacia atlantica have most effect on Eshershia Coli (MIC=150) in disk method.

Conclusion: Results show powerful antibacterial and antifungal effect for Pistacia atlantica but have no powerful effect on psuodomonase aeruginosa. Humulus Lupus's extract have not powerful effect on it. Effectiveness of Humulus Lupus's extract on Candida Albicans and Aspergillus Fomigatus show good antifungal effect of it.

Keywords: Pistacia atlantica, Humulus Lupus, Hydro alcoholic extract, bacteria, fungi

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Investigating the Effects of Applied Dose on Stability and Behavior of Topical Gels

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Abstract

Introduction: In clinical use, only small amount of a topical gel is applied on large areas of the skin and the formulation is completely exposed to the air. Subsequently the vehicle evaporation of applied gel can change the concentration and physicochemical properties of drug such as dissolution, precipitation or crystallization (1). Hence an understanding of the extent of vehicle evaporation is important both in drug delivery and cosmetics, as the changed film of the topical formulation on the skin must act effectively over time (2, 3). This study aims to investigate the influence of applied amount of a topical gel on the remaining water of the formulation over time using thermogarvimetric analysis (TGA) to simulate the clinical use of topical preparations.

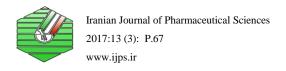
Methods: Water based 1% carbomer gel was prepared by dispersing carbomer 934P in water using mechanical stirrer and neutralizing with triethanolamine. To perform isothermal TGA (TGA-50, Shimadzu, Japan), the samples were heated from ambient temperature to 32°C at a rate of 10°Cmin⁻¹ and then kept at 32°C until a plateau in evaporation was observed. Samples were placed into aluminum pans in three different weights of about 3, 8 and 14 mg that called low, medium and high weights here respectively.

Results: Our results showed that evaporation rate, after an initial burst, continued by zero order kinetics until reached a plateau. The plateau time increased by increasing the weight. The remaining amount of formulation over 23 minutes was observed to be 23, 63 and 79 percent for low, medium and high weights respectively.

Our results show that the lower the amount applied, the more will be the change in the formulation and, therefore its properties.

Conclusion: The amount of applied formulation is crucial in properties and behavior of topical preparations and very important in drug delivery and cosmetics.

Keywords: Topical; Applied amounts; Evaporation; Thermogravimetry; Water; Vehicle



Evaluation and Comprarison of Antioxidant and Anti Lipid Peroxidation Activity Methanolic and Hydrolyzed Extract of Cuttle Fish (*Sepia Pharaonix*) Of Persian Gulf

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Abstract

Introduction: Cuttlefish belong to the class cephalopoda and their muscle tissue, skin and ink showed different therapeutide effects such as signifant antioxidative ones. Given that free radicals are the cause of several degenerative diseases such as cardiovascular diseases, cancer, Alzheimer, etc. this study was designed and conducted to evaluation and comparison of antioxidant activity of aqueous, methanolic extract of cuttle fish.

Methods: blue swimming crab fished and kept on freezing condition until extracting aqueous, methanolic, and hydrolyzed by pepsin extractions were done with maceration method to evaluated the antioxidant activity method of TEAC, FRAP, DPPH, hydroxyl radical seavenging were used and pro-oxidant effect was determined by bleomycin method inhabition of lipid peroxidation in the brain, liver, kidney and lungs of rats was performed in a laboratory setting.

Results: in DPPH,FRAP and ABTS tests the antioxidant activity of aqueous extract was more than other extrat.also aqueous extract have a greater impact on inhabit lipid peroxidation in the brain,liver and lungs.by comparing hydroxyl radical scavenging with and with out the presence of EDTA was observed that this extrat can directly inhibit the hydroxyl radical.bleomycin assay results showed that pro-oxidant effect increases with increasing concentration.

Conclusion: the result showed that all extract have acceptable antioxidant power.better effects of aqueous extract could be due to proteins copounds and water-slouble vitamins in it.

Key words: cuttle fish (Sepia pharaonis), DPPH, FRAP, ABTS, hydroxyl radical scavenging, antioxidant capacity

Investigation of the Binding Ability of Anti-Tnf α Scfv J₄₈ Antibody by Using ELISA and Estimating Possible Interactions by Docking Studies

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Abstract

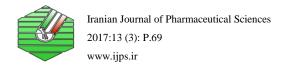
Introduction: TNF α is an inflammatory cytokine, which have different physiological and pathological functions. In this context, using antibodies with smaller size and stronger binding affinity is one of the common strategies to inhibit TNF α activity in chronic disease (1). In past works, we produced and purified the ScFv J₄₈ antibody which had been identified by Phage display technique (2). Now we aimed to examine binding ability of J₄₈ to TNF α by ELISA and evaluate the possible interactions among them by docking studies.

Methods: The purified ScFv antibody (i.e.J₄₈) in various concentrations from $0.012\mu M$ to $1\mu M$ was prepared and added to the TNFα coated wells. Then anti-6His and HRP conjugated goat anti mouse antibodies were used for ScFv J₄₈ detection. For docking studies, the Tree-dimensional structure of J₄₈ antibody was modeled in Swiss model website. Next, the modeled structure was docked to TNFα by using Z dock. To estimate the possible interactions between J₄₈ and TNFα, the docked complex was analyzed in PIC website.

Results: Analyzing of ELISA results showed that J_{48} has a relatively high binding affinity to TNF α . And docking results revealed that the hydrogen bond, hydrophobic bond, π -cation interactions were involved in the interactions between TNF α and J_{48} .

Conclusion: According to the results of the ELISA and docking studies, J_{48} has a good inhibition activity on TNF α . Therefore, J_{48} can be a suitable candidate for clinical trials or may be used for designing a new stronger anti- TNF α medications.

Keywords: TNF-α, ScFv, ELISA, Docking studies



Protective Effect of Testosterone on Haloperidol Induced Parkinsonism in Male Rats

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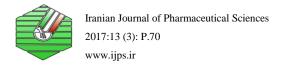
Abstract

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by a progressive loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc). Neuroleptic drugs such as haloperidol induce Parkinson-like syndrome through blocking brain D2 receptors in multiple pathways in the brain. Many of non-motor symptoms of PD such as depression, sleep disorders and sexual inability are correlated with testosterone deficiency. However, it is still opaque whether testosterone therapy can be influent directly on motor symptoms of PD or not. **Methods:** The experiments were performed on 24 male Wistar rats (200 -240 g). Animals were randomly divided into 4 groups (6 animals in each group). Rats pretreated with saline or testosterone (1 mg/kg, i.p.) or flutamaide (10mg/kg, i.p.) for 1 day or 7 consecutive days before haloperidol injection. Catalepsy and motor-imbalance were induced by an intraperitoneal (i.p) injection of haloperidol (1 mg/kg) at the end of drugs treatment. In animal models, haloperidol induces a behavioral state known as catalepsy in which the animals are unable to correct externally imposed postures. The effects of testosterone and flutamaide on haloperidol -induced catalepsy and motor impairment were assessed by the bar test and rotarod, respectively.

Results: Haloperidol 1 mg/kg, i.p, was able to induce catalepsy and motor imbalance. Testosterone pretreatment for 7 days prevented from halopridol induced catalepsy and could restore motor balance about to the level of normal animals, while concurrent administration of flutamide prevented from improving effect of testosterone.

Conclusion: Pretreatment by testosterone can significantly be effective in catalepsy remission, meanwhile administration of flutamaide as an androgen receptor blocker prevented from protective effect of testosterone. It seems that the anti-cataleptic effects of testosterone are exerted through affecting on androgenic receptors.

Keywords: Parkinson's disease, Testosterone, Flutamaide, Haloperidol, Catalepsy, Bar test, Rotarod



Predicting Passive Intestinal Absorption of Drug Compounds by CLFR

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Abstract

Introduction: The present study is a comparative study of three equations namely the Clausius-Clapeyron, Van'tHoff and Hildebrand (to calculate Crystal-liquid fugacity ratio (CLFR) of drug compounds) to select the best model in predicting the intestinal absorption and develop a new classification system based on dose number (D_O) and CLFR.

Methods: The required thermodynamic parameters (melting point, enthalpy of fusion (ΔH_m) and the differential molar heat capacity (ΔC_{pm}))were experimentally obtained by differential scanning calorimetry (DSC). Pharmacokinetic data (the human intestinal absorption (F_a) and apparent permeability of Caco-2 (P_{app} _Caco-2)) and D_O were obtained from the literature.

Results: Statistical comparison with Wilcoxon signed rank test showed that the CLFR values calculated by three equations are different. CLFR values of more than 1 mole percent correspond to the complete intestinal absorption (F_a) . There was a sigmoidal dependency between CLFR and F_a , similar to the dependency between P_{app} _Caco-2 and F_a . In these modelling, the excellent correlations were obtained in all three models as evidenced by a good coefficient of determination (r^2) without significant difference in the average absolute error. A new classification system from Hildebrand model based on D_o and CLFR was developed and was in agreement with the Biopharmaceutics Classification System (BCS) (70.5%) and the Biopharmaceutical Drug Disposition System (BDDCS) (65.6%).

Conclusion: This modelling approach can be a valuable tool for scientists as an alternative for intestinal permeability in the biopharmaceutical classification system to develop new oral drugs. The *CLFR* obtained from Hildebrand model is also more convenient than the Clausius Clapeyron model, because the former does not need to calculate ΔC_{pm} (difficult step in calculating *CLFR*) for drug compounds. This new classification can help to develop the new drug product in industrial and academic research, without necessary *in vivo* experiments.

Keywords: Thermodynamic, Crystal-Liquid fugacity ratio, BCS, BDDCS



15th IPSC Proceeding

In virto cytotoxic activity of a *Lactococcus lactis* antimicrobial peptide against breast cancer cells

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Abstract

Introduction: Nisin, an effective natural food preservative, is an antimicrobial peptide produced by *Lactococcus lactis*. Although it has been mainly studied and developed as potential alternatives for antibiotics, other pharmacological effects of nisin including cytotoxic and anti-tumor activity have been attracted many attentions. Here, we aimed to evaluate *in vitro* cytotoxic activity of nisin against breast cancer cells.

Methods: The effect of temperature, pH and chemical composition of medium on the yield of nisin production by *L. lactis* was evaluated. The anti-proliferative effect of nisin against a breast cancer cell line (MCF7) and a non-cancerous cell line (HUVEC) was determined using MTT assay. Furthermore, potential synergistic effect of nisin on doxorubicin cytotoxicity was evaluated.

Results: The survival of MCF-7 cells was significantly inhibited by nisin and the IC50 value of 17 μ g/ml was found. Nisin exhibited lower level of cytotoxicity for a normal cell line, HUVEC, with an IC50 value of 64 μ g/ml. This four-fold difference in nisin cytotoxicity against MCF-7 over HUVEC cells was showed to be statistically significant in MTT assay (P < 0.05). It was showed that co-incubation of nisin, increased cytotoxicity of doxorubicin. This synergic effect was more significant in lower concentration of doxorubicin and against MCF-7. Approximately, three-fold higher cytotoxicity was observed when MCF-7 cells were incubated with combination of nisin (10 μ g/ml) and doxorubicin (6 μ g/ml) compared with doxorubicin alone (P < 0.01).

Conclusion: In conclusion, our study reported effective cytotoxic effects of nisin against MCF-7, a breast cancer cell line. Furthermore, nisin exhibited a selective toxicity against cancerous cells in comparison to HUVEC, a normal cell line. Most importantly, combination of nisin with doxorubicin led to synergetic anticancer effect. It could be suggested that nisin either alone or in combination with other chemotherapeutic agents can be a potential treatment for breast cancer.

Keywords: nisin, breast cancer, cytotoxicity, Lactococcus lactis, antimicrobial peptide



15th IPSC Proceeding

Selective Toxicity of Chrysin on Isolated Mitochondria Obtained from Liver Hepatocytes of Hepatocellular Carcinoma Induced Rat

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Abstract

Introduction: Chrysin is a natural flavonoid currently under investigation due to its important biological anti-cancer properties. Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death. In patients with HCC current treatments show poor tolerance and low efficacy. So, alternative therapies with good efficacy are urgently needed. The aim of this research was to evaluate the selective apoptotic effects of chrysin on mitochondria obtained from the liver of HCC rats.

Methods: In this study, HCC induced by diethyl nitrosamine (DEN), as an initiator, and 2-acetylaminofluorene (2-AAF), as a promoter. After confirmation of liver cancer, rat liver mitochondria for evaluation of the selective

cytotoxic effects of chrysin were isolated, and mitochondrial parameters related to apoptosis signaling were then determined.

Results: Our results showed that chrysin was able to induce increased in reactive oxygen species (ROS) level, mitochondrial swelling, mitochondrial membrane permeabilization (MMP) and cytochrome c release only in cancerous but not in untreated normal hepatocyte mitochondria.

Conclusion: Finally, our finding underlines chrysin as a promising therapeutic candidate against HCC and recommends the compound for further studies.

Keywords: Hepatocellular Carcinoma; Chrysin; Mitochondrial Targeting; Apoptosis



15th IPSC Proceeding

A Survey of Effects of Nanoceria for Potentiation of Anticancer Effect of Doxorubicin and Inhibition of Doxorubicin-Induced Cardiotoxicity in Human Ovarian Cancer in Nude Mice

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Introduction: Nowadays combination therapy by different mechanism and synergetic effect is one of the main

procedures in cancer treatment [1]. Doxorubicin is an anthracycline antibiotic that it's usage is limited due to its

cardiotoxicity [2]. Nanoceria (Nano particle of cerium oxide) showed anti-oxidant effects [3] and in this study we

evaluated effect of nanoceria for potentiation of anticancer effect of doxorubicin and also attenuation of doxorubicin

cardiotoxicity.

Methods: In first step, we growth SKOV3 cell line in RPMI medium and then injected it to Nude mice for tumor

growth. After 2 month and rising of tumor we began drug and Nano ceria injection to inhibit tumor growth. We had

four group that first group just get doxorubicin 2mg/kg (G1), second group just get Nano ceria 100mg/kg (G2),

third group get both of them (G3) and control group that didn't get anything (G4). After 14 days tumor had been

exit, its size and apoptosis markers had been study. Hearts tissue had been exit too and oxidative stress markers such

as Lipid peroxidation and Glutathione were measured. Also, pathological changes in both tumor and heart tissue was

done

Results: Tumor growth during of 14 days especially in last days had been stabilize. For example tumor size in one

mouse in G3 after rising from 0.7 to 1 mm, in last day was 0.9 mm. Pathology samples showed wide and focal

necrosis especially in G3. Evaluation of oxidative stress markers showed nanoceria inhibited doxorubicin induced

oxidative stress in heart tissue.

Conclusion: Our data showed that synergic anticancer effect of doxorubicin and nanoceria and protection effect of

nanoceria against doxorubicin induced cardiotoxicity.

Keywords: Nano ceria, Doxorubicin, Ovarian cancer, Nude mice, Cardiotoxicity.



15th IPSC Proceeding

The Relation between Ghrelin Secretion and Lipid Profile in Long-Term **Exposures of Diazinon in Wistar Rat**

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Introduction: Metabolic disruption is one of the most complications following exposure to organophosphate compounds (OPCs) in worldwide. Ghrelin is an effective hormone in obesity that it has various physiological functions, such as the stimulation of growth hormone release and of appetite, and fat accumulation. The aim of this study was to evaluate the role of OPCs in ghrelin serum level and lipid profile following long-term exposure with Diazinon (DZN) in wistar rats.

Methods: 48 rats were randomly divided into 6 groups and treated orally for 30 days. The control group and second group were treated by normal saline and corn oil respectively. The 3-6 groups were received the doses of DZN 1/5, 1/10, 1/20 and 1/40 LD50, respectively. Finally, the serum samples were collected for biochemical analysis.

Results: Using DZN showed an increased in ghrelin levels in the dose-dependent manner. Additionally, triglyceride serum levels were increased and serum acetylcholine esterase (AChE) activity decreased in comparison with control. However, the significant changes were not observed in cholesterol, glucose serum levels. Our results showed that there is a correlation between ghrelin secretion and cholinesterase activity.

Conclusion: In conclusion, our findings show that OPCs can directly influence ghrelin secretion by inhibition of AChE activity. We suggest that ghrelin secretion may be regulated by cholinergic neurons and acetylcholine alterations in peripheral tissue.

Keywords: Diazinon, Ghrelin, Organophosphate



15th IPSC Proceeding

Adverse Drug Reactions Reported to Isfahan Food and Drug Administration in Spring and Summer of 2016: A Cross-Sectional Study in Isfahan, Iran

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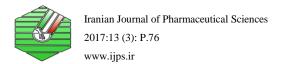
Introduction: Adverse drug reactions (ADRs) create costs and problems for health care system and seem as important outcomes of patient care. So identification and assessment of ADRs to predict and prevent of them are necessary (1, 2). In this study, we aimed to analysis the ADRs which reported to food and drug administration of Isfahan University of Medical Sciences in spring and summer of 2016.

Methods: In this cross-sectional study, 197 sheets of ADR reported to Isfahan food and drug administration from 20 March to 21 September of 2016 were evaluate. We excluded errors in drug administration, not completed sheets, and therapeutic failures. Results were statistically evaluated by SPSS20.0.

Results: The results of 197 reports showed the most complication were dermatologic (53.3%) then respiratory reactions (10.7%). The most ADRs was made by the injectable forms of drugs (71.6%). And antibiotics were at the top of list of drugs which caused problem (ceftriaxone=15.2%, vancomycin=13.2% & ciprofloxacin=6.1%). Women were affected more than men (52.3%). The most group show ADR were between ages of 1-5 which was 18.3% of patients. These ADRs were usually reported by nurses (76.1%) then physicians (10.2%), and just 3.6% of reporters by pharmacists.

Conclusion: The injectable antibiotics were the biggest problem. Regarding the irrational prescribing in our country which may lead to extra ADRs, more educational, managerial and regulatory strategies can help to reduce number of these problems. This study also suggests that pharmacists should challenge more than past in reporting ADR.

Keywords: Adverse Drug Reaction, Toxicity, Drug Administration Routes, dosage form



15th IPSC Proceeding

Differences of Satisfaction between Care Quality among Patients and Health Care Providers: A Cross-Sectional Study in Isfahan, Iran

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Abstract

Introduction: Patient satisfaction is very important in health care system while there is a paucity of data in order.

There is often a wide difference between perception of quality among patients and health care providers (1, 2). This

study aimed to compare the satisfaction level between the patients and the health care providers from one of the

main referral and university affiliated hospitals in Isfahan. The feedback would provide information that can be

forwarded to the hospital administration to take necessary steps.

Methods: In this cross-sectional study a valid and reliable 16-item questionnaire in the form of Likert scale

addressing various aspects of patient care was prepared. Data were collected from 40 patients and 35 staff of

Seyedoshohada hospital during May 2016. Results were statistically evaluated using SPSS 20.0. The means and

standard deviations were used to describe the overall assessment score of satisfaction. To compare the satisfaction

score between two groups Mann-Whitney test was used (p<0.05).

Results: The alpha Chronbach coefficient was calculated 0.95, which is an acceptable reliability. According to

patients' view, the most satisfying features of the hospital were willing of staff to help and quality of nursing

services. The least satisfying features were inconvenience during scheduling of appointments, status of changing

rooms and general cleanliness. Result of Mann-Whitney test showed significant difference between Patients and

staff's opinions. In fact, staff overall satisfaction scores were not as good as the patient's opinions (43.49±9.99 versus

56.6±16.71).

Conclusion: The measurement of satisfaction is a key tool used to identify problems and this study highlighted

some problems which should focus on the management of the hospital in order to improve the quality of service. By

training the service providers and criticizing them according to customer's expectation, we can achieve to high level

of satisfaction.

Keywords: Delivery of health care, Perception, Quality of health care, Personal satisfaction



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15th IPSC Proceeding

Acute, Subchronic, and Genotoxic Effects of Oral *Ulmus Minor Mill* 'S Gall:

A Phytochemical and Toxicological Study

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Abstract

genotoxicity tests of present work.

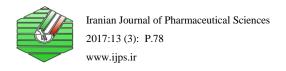
Introduction: Ulmus minor Mill 's gall produces due to effects of Eriosoma lanuginosum Hartig but its phytochemical and toxic properties have not determined yet. This study aimed to identify the phytochemical composition and quantification of its main components, as well as it's acute and repeated dose oral toxicity in mice to determine its possible safe dose (NOAEL) for further applications as an anti-mutagenic agent on the basis of

Methods: Phytochemical analysis was performed via pre phytochemical tests(1) to determine the tannins, and sterol levels. *In vivo* studies performed on both genders of mice according to OECD 423 and OECD 407 guidelines(2). Ames mutagenicity assessment was performed, on TA100 and YG1029 strains of Salmonella Typhymorium for anti-mutagenic test.

Results: Due to Phytochemical study on hydro alcoholic extract, the levels of condensed tannin and sterol were determined noticeable in comparison all previous studies. Although in acute toxicity study, LD₅₀ was determined in levels upper than 2000 mg/kg in both genders and this extract was classified as a practical non toxic agent according to GHS classification. In repeated dose ,28 days, oral toxicity study in doses of 125 mg/kg, different organ toxicities were observed including significant hypokalemia , hyperuremia and hyperglycemia, in female animals. Mutagenicity assessments by Ames method on different strains didn't show sufficient evidence for its animutagenic potentials.

Conclusion: This study clarified for the first time that *Ulmus minor's* galls contains noticeable amounts of condensed tannin according to the quantification tests. Histopathological evidences including ischemic injuries in neural tissues and several necrosis in essential organs have emphasized the necessity of further studies on its possible mechanisms of toxicity .We don't recommend this gall for any clinical applications according to present toxic effects.

Key words: Ulmus, phytochemistry, oral toxicity, Mutagenicity



None small Cell Lung Tumor Targeting with Radiolabeled D4 Peptide Conjugate as a SPECT Radiotracer

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Abstract

Introduction: None small cell lung cancer is one of the most leading causes of cancer death in the world. Early detection of cancerous mass plays an important role in cancer treatment. Molecular imaging is one of the diagnostic tools for tumor detection. Since, EGFR overexpression has been observed in many of human cancers, it has been selected as a suitable candidate for specific tumor targeting. D4 peptide (Leu-Ala-Arg-Leu-Leu-Thr) was selected as a good candidate for specific targeting of EGFR. In this study, new D4 peptide conjugate has been evaluated as a SPECT radiotracer for tumor targeting in NSCLC.

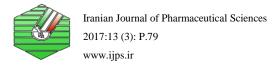
Methods: HYNIC conjugated peptide was labeled with ^{99m}Tc using tricine and mixture of EDDA/Tricine as coligand. Cellular EGFR-specific binding, affinity and cellular internalization as well as in-vivo tumor targeting were assessed.

Results: In each of the synthetic radiopeptides, radiochemical purity of them determined 98% without any purification. Specific binding experiment of 99m Tc-HYNIC-Ser-Ser-Ser-D4 peptide showed dissociation constant of $^{119} \pm 34$ nM. Biodistribution studies in normal mice and A-549 xenografted nude mice showed rapid clearance from blood and other non-target organs. In mice bearing A-549 xenografts, 99m Tc-HYNIC-Ser-Ser-Ser-D4 peptide showed rapid tumor targeting at 1 h after injection. Tumor uptake values (percentage of injection dose per gram of tissue) were $7.55 \pm 0.43\%$ and $6.82 \pm 0.32\%$ at 1 and 4 h after injection, respectively. *In vivo* blocking by presaturation of EGFR using an excess of non-labeled peptide reduced 36% tumor uptake of radioactivity at 1 h after injection and confirmed the specificity of radiopeptides tumor uptake. Finally, Gamma camera imaging was

performed at 1h after injection of radiopeptide by a dual-head e.cam gamma camera, equipped with a low-energy, high-resolution collimator.

Conclusion: Findings showed that modified radiolabeled peptide is a promising candidate for tumor targeting and molecular imaging in non-small cell lung cancer.

Keywords: Tumor Targeting, 99mTc, small peptide, EGFR, lung cancer.



15th IPSC Proceeding

Preparation and Physicochemical Characterization of Topical Chitosan-Based Film Containing Griseofulvin-Loaded Liposomes

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Abstract

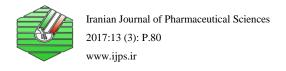
Introduction: Griseofulvin is an antifungal drug and is available as oral dosage forms. Development of topical treatment could be advantageous for superficial fungal infections of the skin.

Methods: In this study, films prepared from the incorporation of griseofulvin-loaded liposomes in chitosan film for topical drug delivery in superficial fungal infections. The properties of the films were characterized regarding mechanical properties, swelling, ability to transmit vapor, drug release, thermal behavior, and antifungal efficacy against *Microsporum gypseum* and *Epidermophyton floccosum*.

Results: The presence of liposomes led to decreased mechanical properties but lower swelling ratio. Higher amount of drug permeation and rate of flux were obtained by liposomes incorporated in films compared to liposomal formulations. Antifungal efficacy of formulations was confirmed against two species of dermatophytes *in vitro*.

Conclusion: Therefore, two concepts of using vesicular carrier systems and biopolymeric films have been combined and this topical novel composite film has the potential for griseofulvin delivery to superficial fungal infections.

Keywords: Antifungal effect, chitosan film, dermatophytes, griseofulvin, liposomes, skin permeation



Codon Optimization, Subcloning and Expression of Recombinant Human Microplasminogen

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Abstract

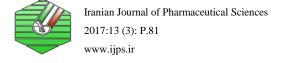
Introduction: Plasmin is a serine protease that can degrade extracellular matrix (ECM) components including fibrin, laminin, and fibronectin. Microplasminogen (μ Plg) is a truncated form of plasmin which can be used as a therapeutic agent such as inducing posterior vitreous detachment (PVD) in many vitreoretinal diseases and also in the dissolution of blood clots in thrombotic diseases.

Methods: The purpose of this study was to produce recombinant human microplasminogen in the methylotrophic Pichia pastoris .After codon optimization and synthesis of the gene, recombinant plasmid (pPICZα-μPlg) constructed and transformed into X-33 cells. The cells then were grown on a YPDS plate containing Zeocin antibiotic. For protein expression, the positive recombinant clones were transferred into YPM medium and were induced by methanol. μPlg was purified by Ni sepharose column, and the presence of the recombinant protein confirmed by SDS-PAGE.

Results: Our findings showed that the recombinant protein (28 kDa) has been successfully secreted into the supernatant of the induction medium without α -factor secretory signal. But further studies are needed to optimize the yeast cells culture conditions for increasing the concentration of secreted protein. Production of high purity μ Plg in Pichia pastoris implies that this system can be used to product variety of recombinant drugs.

Conclusion: In summary, μ Plg can be considered as a potentially valuable pharmaceutical agent for effective and less invasive treatment of traumatic and even prophylactic application in some disorders such as vitreoretinal and thrombotic diseases.

Keywords: Plasmin, Microplasminogen, Pichia pastoris, codon optimization



Development and Optimization of a Suitable Colloidal Lipid Formulation for the Curcuminoids and Physicochemical and *In Vitro* Characterization

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Abstract

Introduction: The curcuminoids molecules have poor bioactivity and instability in neutral and alkaline aqueous solutions and curcuminoids were subjected to light exposure there was 30% degradation. Besides the curcuminoids have low bioavailability. Lipid-based nanoparticle systems are prepared with solid structures at room temperature or at body temperature associated with surface-active agents and water lipids. The Major advantages of these systems are the high biocompatibility, the avoidance of organic solvents during production and the easy scale up of the fabrication. The major objective of this study was the development and optimization of a suitable colloidal lipid formulation for the curcuminoids and its substantial physicochemical and *in vitro* characterization.

Methods: Solid lipid nanoparticles incorporating curcuminoids were produced by the hot melt emulsion method employing a high-shear homogenizer. The particle size distribution and polydispersivity index were obtained by photon spectroscopy (PCS) employing a Zetasizer. The amount of incorporated drug was determined with UV/Vis spectroscopy. The stability of the incorporated curcuminoids was determined in SGF, and phosphate buffer pH 6.8. The drug release of the preparations was determined in SGF , and phosphate buffer pH 6.8.

Results: The values of mean sizes, polydispersivity and zeta potential for all nine experiments showed averaged particle size 151.4 ± 75.6 nm, The averaged zeta potential was -25.0 ± 2.2 mV. The curcuminoid loaded nanoparticles exhibited a good drug stability throughout the experiment. The encapsulation efficiency varied from

38 to 67% for total curcuminoids. All the samples of nanoparticles tested showed a sustained but not linear release. Approximately35% of curcumin was released after 2 h of experiment and within 24 h of release was around 84%. **Conclusion:** The application of factorial design to study the preparation process for nanoparticles showed to be a very important tool, allowing establishing the relationships among the factors and quality attributes.

Keywords: Solid lipid nanoparticles, curcuminoids, release profile



15th IPSC Proceeding

Preparation and Investigation of the *In Vitro* Release of Novel Bio-Composite Nanofibers Loaded Curcumin Nanoparticles

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Abstract

Introduction and Background: Curcumin is a powerful bioactive agent. Low water solubility of CUR leads to slow release profile. With reducing the size of CUR to nanometer, the bioavailability significantly improves. Here we used a novel hybrid nanofiber loaded with CUR nanoparticles to investigate the release behavior.

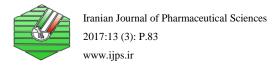
Methods: CUR loaded solid lipid nanoparticles (SLN) produced by melt-homogenization. The used lipid matrix was stearic acid. CUR nanoparticles used for the preparation of hybrid nanofiber. The morphology and physicochemical properties studied with (SEM), (FTIR), thermogravimetric analysis (TG-DTA). The surface area characterized by BET analysis. The *in vitro* release profile of hybrid nanofiber evaluated by dialysis bag and franz diffusion cell method.

Results: The optimized formulation showed an average size of 165.5 ± 5 and $91\% \pm 2.5$ drug entrapment efficiency. SEM micrographs showed a bead free, smooth and uniform morphology of nanofiber with an average diameter in

the range of 200–250 nm. FTIR analysis proved the existence of CUR in the fiber base where no undesirable chemical reaction between CUR and others composites fiber was indicated. TG-DTA analysis indicated that thermal stability improved significantly due to using SLN method for preparation of nanoparticles. BET analysis exhibited the surface areas about $6.03 \text{ m}^2\text{g}^{-1}$ thus the hybrid nanofiber is considered a semiporous material. The *in vitro* release demonstrated an initial burst release in the first 8 h with showing a cumulative release of 25% and released followed by controlled diffusion for a further 60 h. The R^2 values indicated the release profile of CUR fitted Higuchi model.

Conclusion: The novel composite nanofiber can be consider as a wound healing dressing due to improved thermal stability and surface area properties. The invitro release profile showed that novel nanofiber could be quickly dissolved in phosphate solution, while neglible dissolution was observed in pure CUR sample.

Keyword: nanofiber, electrospinning, Curcumin, SLN, Release profile.



15th IPSC Proceeding

Evaluation of the Effect of Education by Pharmacists in Hyperlipidemic Patients Treated with Statins on Patient's Adherence to Medications and Level of Blood Lipids

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Abstract

Introduction: Hyperlipidemia is one of the most common chronic diseases that millions people suffer it approximately. Studies show that many patients have suboptimal adherence to statin medication which leads to serious negative health consequences. This paper evaluated the effectiveness of educational intervention in hyperlipidemic patients treated with statins on adherence to statin medication and level of blood lipids.

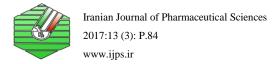
Methods: In this interventional clinical trial study the studied population was all patients with heart disease treated with statins that had been referred to the Hamadan Farshchian hospital from January 2016 to June 2016. The sample

size in this study was 50. The study data collection tools included a demographic and Morisky questionnaire and data of patient's lipid profile before and after 6 month after intervention. Data were analyzed in SPSS/19 using T-test, Mann-Withney and X2 tests. Significant level was considered less than 0.05.

Results: Data analysis reflects the homogeneity of medication adherence and levels of lipid profile in both groups before the intervention. Before intervention the medication adherence was not significantly different in both groups (p=0.49) but after intervention the medication adherence increased in the intervention group (p<0.001) and level of LDL significantly decreased (p=0.02) but after intervention there were no statistical difference in level of HDL, triglyceride and total cholesterol in both groups.

Conclusion: These findings suggest that educational counseling by pharmacists could have a positive role on patient's adherence to drugs and level of LDL.

Keywords: Hyperlipidemia, medication adherence, lipid profile



15th IPSC Proceeding

Evaluation of Antibiotic Resistance Pattern of Nosocomial Urinary Tract and Wound Infections in Hospitalized Patients in Al-Zahra Hospital of Isfahan

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Abstract

Introduction: Nosocomial infections are a serious threat to patients' health (1). Due to high mortality rates of nosocomial infections (2), the choice of appropriate antibiotics to treat these infections is very important requiring determination of antibiotic resistance pattern in the hospital. Urinary tract infections and wound infections are among the most common infections in hospitalized patients. The aim of this study was to determine antimicrobial resistance pattern of common pathogens from these two infections in Al-Zahra hospital of Isfahan.

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Methods: This cross-sectional study was conducted over a 6-month period. Clinical specimens including urine and wound secretions were obtained from patients with confirmed nosocomial infections and were cultured. The growing bacteria were identified and underwent antibiotic susceptibility test by Kirby-Bauer method (disk diffusion test) using standard antibiotic disks.

Results: 165 cases of infection including 118 UTI and 47 wound infection cases were recorded in this study. Escherichia coli was the most common pathogen of UTI that showed the highest sensitivity to Colistin (100%) as well as the highest resistance to ceftazidime (56%). Enterococcus spp. were the most common pathogens from wound infections with most susceptibility to linezolid (100%) and the highest resistance to levofloxacin (94.7%).

Conclusion: UTIs and wound infections in Al-Zahra hospital have high rate of resistance to different antibiotics representing the importance of improvement in antibiotic administration and infection control. In our hospital, colistin is the most effective antibiotic against E. coli causing UTIs and linezolid is the most effective antibiotic against Enterococcus spp. causing wound infections.

Keywords: Nosocomial infections; Urinary tract infection; Wound infections; Antimicrobial resistance pattern.



15th IPSC Proceeding

Quality Control of "Ustukhuddus" Prepared from Herbal Markets in Iran (Phase 1)

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Abstract

Introduction: Quality control of herbal medicines is necessary before usage, as well as awareness about the efficacy and safety. *Nepeta menthoides* is a species from Lamiaceae family (1) traditionally known as "Ustukhuddus" in Iranian herbal markets (2).

Ustukhuddus has a historical background in traditional medicine manuscripts for treatment of nervous ailments, rheumatic pains and high blood pressure (1, 2). The aim of this study was quality control of Ustukhuddus samples purchased from herbal markets.

Methods: 10 samples were purchased from herbal markets in Tehran, Karaj and Ardabil. In this study general methods of quality control for determining macroscopic characteristic, foreign matter, total ash, acid insoluble ash, water and volatile matter and thin layer chromatography were applied (3-5).

Results: In macroscopic assessments, the color of flowers were reddish- blue, violet and brown, leaf colors were light green and green. Thin layer chromatography of ethanolic extracts were showed 5 different fingerprints.

The amount of foreign matter and loss on drying was $\leq 4\%$ and 2-7.3%, respectively. The percentage of total ash and acid insoluble ash were found 7-13% and $\leq 2\%$, respectively. Among 10 samples, 5 different species recognized by general quality control methods.

Conclusion: According to available databases and best of our knowledge, quality control of *N. menthoides* have not been reported. This study will help in setting down pharmacopoeia standards in specifying the quality of Ustukhuddus samples. Evaluating the samples by other methods of quality control would be our further investigation.

Keywords: Nepeta menthoides, Quality Control, Ustukhuddus.



15th IPSC Proceeding

Nanofiber Based Drug Delivery System for Prevention of Local Cancer Recurrence Following Surgery

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Abstract

Introduction: Metastasis is the main problem in successful treatment of many types of cancer even after surgery of tumor because of cancerous cell which remain in site. The extracellular matrix (ECM) degradation also has a crucial role in the cancer metastasis. Nanofibers can provide a structure similar to ECM and limit the cancer cells migration if they are implanted in and around the tumors. Moreover, local delivery of anti-metastatic drugs which loaded in nanofiber can be useful.

Discussion: New therapeutic strategies are needed to decrease the risk of the metastasis and improve the patient survival. Nanofibers mimic the structure of the long chain proteins of ECM 1-3. Liu et al found that DOX loaded in PLA nanofibers which were applied on the cancer surface could effectively inhibit the growth of liver cancer in mice 4.Temozolomide (TMZ) was loaded in nanofibers to prevention of glioma recurrence and metastasis5. Zhang et al demonstrated a dual drug-loaded multilayered fiber mat, in which DCA and oxaliplatin were co-electrospun into the separate layer6. This system had synergistic effect on cancer cells after implantation on the resection margin of cervical carcinoma. Their system displayed enhanced anti-recurrence efficacy. Kaplan et al reported the fabrication nanofiber meshes loaded with cisplatin to conflict local lung cancer recurrence after resection7. These meshes exhibited sustain release of cisplatin over ~90 days. *In vivo* evaluation exhibited prevention of local cancer recurrence to >23 days. Metformin-Cellulose nanofibers (Met-Cel-NFs) for the prevention of human melanoma cancer metastasis were provided 8. Met-Cel-NFs meaningfully suppressed the migration of cancerous cells and block the migration of the melanoma cancer cells so can decrease melanoma cells invasion.

Conclusion: Nanofibers loaded by anticancer drugs that implanted in and around the tumors because of similarity to ECM and limit the cancer cells migration can prevention of metastasis after surgery of tumor.

Keywords: Metastasis, Nanofiber, ECM, Cancer recurrence.



15th IPSC Proceeding

Exploring the Interaction between Simvastatin and Its Active Metabolite with Human Serum Albumin: Application of Spectroscopic Methods

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Abstract

Introduction: The interaction between human serum albumin (HSA) and simvastatin (sv) and simvastatin hydroxy acid (sva) was studied using fluorescence quenching titration method at room temperature. HSA – drug interaction is one of the most important parameters of drug pharmacokinetic which can be affect both ADMET and pharmacodynamic characteristics of drug(1). Binding characteristics of simvastatin to HSA such as binding rate

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constant, binding constant and the number of binding site were obtained using stern-volmer equation. The results of this investigation could be helpful in improvement of pharmacokinetic of statins and also to creation of new drugs with lower side effects (2).

Methods: increased concentrations of sv and sva were added to the albumin solution in buffer with pH of 7.4 and the emission variation of HSA due to the sv and sva addition was studied. According to acidic nature of simvastatin hydroxy acid, NaOH was used to convert simvastatin to its active metabolite. Stern-volmer equation was used to correlate emission intensity with drug concentration.

Results: The fluorescence quenching titration results obtained by exciting of albumin and complex solutions in 278 nm, while the emission intensity recorded in 342 nm. The results showed that in physiologic condition (pH 7.4) the emission of HAS does not show significant change in present of sv, but in present of sva the emission of HAS is reduced by increasing the concentration of sva so it can be concluded that simvastatin could not bind to HAS but its active metabolite could bind to HAS tightly.

Conclusion: Simvastin convert immediately to its active metabolite (sva) in stomach and liver, so the acidic form of simvastatin enters the circulatory system and could bind tightly to HAS.

Keywords: fluorescence spectroscopy, fluorescence quenching, stern-volmer equation.



15th IPSC Proceeding

Herbal Medicines in Osteoarthritis and Rheumatoid Rrthritis: a Systematic Review

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Abstract

Introduction: Osteoarthritis and rheumatoid arthritis have different etiology, but both are chronic diseases that can affect joints, causing pain and joint stiffness (1). In spite of development of pharmacological agents for treating chronic diseases, there is a growing interest in medicinal plant practices (2). Therefore, this study aims to review the efficacy of medicinal plants in the treatment of these chronic diseases, systematically.

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Methods: The literature search spanned the time period between January 2003 up to November 2016 and included PubMed and Google Scholar databases. We included human clinical trials concerning the effect of herbal medicines on signs and symptoms of osteoarthritis or rheumatoid arthritis. The general structure of the search strategy was 'osteoarthritis' or 'rheumatoid arthritis' (or synonyms) and 'herbal' (or synonyms). We did not include non-English, unrelated and duplicate studies.

Results: Fourteen studies were included in the systematic review. Twelve clinical trials assessed the effect of different herbal medicines on osteoarthritis and two trials assessed their effect on rheumatoid arthritis. Five studies focused on efficacy and safety of *Curcuma*, two on avocado-soybean unsaponifiables, two on *Boswellia serrata*, and others assessed the efficacy of safety of other herbal medicines in patients with osteoarthritis or rheumatoid arthritis. The intervention less than three weeks and studies less than 15 participants in each group were excluded.

Conclusion: Our review suggests that avocado-soybean unsaponifiables have significant effects on patients with knee and hip osteoarthritis. *Curcuma longa* extracts and curcuminoids have also shown to be effective and safe in short-term therapy, but further studies with more patients and longer duration are needed to investigate their efficacy and safety. Further research is needed to support the efficacy and safety of other herbal medicines reviewed in this study.

Keywords: osteoarthritis, rheumatoid arthritis, herbal medicines, systematic review.



15th IPSC Proceeding

Antibiotic Prescription Evaluation in Al-Zahra Hospital

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Abstract

Introduction: Bacterial resistance to antibiotics is one of the most serious public health issues. There is ample evidence to show the relationship between irrational use of antibiotics and growing microbial resistance to antibiotics. This study concerns the antibiotic prescription patterns in Al-Zahra Hospital.

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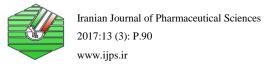
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Methods: The patients' records of this prospective, cross-sectional study was evaluated during a 2-month period. The medical records of 50 hospitalized patients in various wards were studied. Patients receiving at least one antibiotic were entered into the study. The data such as the name of the prescribed antibiotic, the number of antibiotics ordered for each patient, and the dosage regimen were extracted from the medical records. Furthermore, doctors' orders for iv antibiotics were monitored for containing: the type of IV solution, antibiotic's concentration and infusion rate. The data were analyzed using SPSS 23.

Results: Twenty-nine patients were men (58.00%) and 21 were women (42.0%). The average (+/-SD) age was 36.1 (+/-25.3) years. From the total 131 of prescribed antibiotics, the most commonly prescribed were ceftriaxone (13.0%), cefazolin (11.5%), vancomycin (10.7%) and meropenem (10.7%). Sixty-six percent of patients were receiving at least two antibiotics at the same time. More than eighty-four percent (84.7%) of prescribed antibiotics were to be administered intravenously. More than sixty-five percent (65.3%) of IV antibiotics ordered prescriptions did not include any of the following: the type of infusion solution, the needed concentration or the infusion rate. Forty percent of patients did not complete their antibiotic course. In 18.0% of them the type of antibiotic was changed.

Conclusion: Over-prescription of broad-spectrum antibiotics and vancomycin might play an important role in antibiotic resistance development. Lack of attention to antibiogram results may be one of the reasons of the frequent antibiotic change. Lack of complete information in doctor's antibiotic orders may contribute to medication errors threatening patient safety.

Keywords: Antibiotics, prescription pattern, rational use.



15th IPSC Proceeding

A Study on the Relationship between Blockade of Angiotensin Receptor 1 and NF-Kb Expression in Pulmonary Fibrosis Treatment

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Abstract

Introduction: Pulmonary fibrosis (PF) is a chronic, lethal lung disease with unidentified etiology. To date, no standard treatments have been introduced in clinical settings. There are a large number of reports that indicated the role of renin angiotensin aldosterone system (RAS) in pathogenesis of pulmonary fibrosis. Therefore, angiotensin

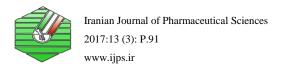
receptor blockers or angiotensin converting enzyme inhibitors could be effective on pulmonary fibrosis therapy (1). NF-κB is a transcription factors that play critical role in the progression of inflammatory diseases by regulation of many genes include pro-inflammatory and inflammatory cytokines .The aim of this study was to investigate the protective effect of valsartan as an angiotensin receptor blocker on NF-κB expression in bleomycin-induced pulmonary fibrosis.

Methods: Rats were given a single intratracheal administration of bleomycin (7.5 IU/kg); valsartan (20, 40, 80 mg/kg/day) was administrated to the rats orally, starting seven days before the induction of lung fibrosis and continuing for 3 weeks. The control group received a vehicle. The lung index and hydroxyprolin content were measured. Histopathological evaluation was studied by hematoxylin and eosin staining. NF-κB expression in lung tissue was investigated by Real time PCR.

Results: The hydroxyprolin content in lung tissue and lung index were decreased in rats that received valsartan. Patholigical examination indicated the protective effect of valsartan. Exposure to bleomycin elevated NF-κB expression and valsartan deceased the increased gene expression. Angiotensin II activated NF-κB via various mechanisms that leads to stimulate NADPH oxidase and increases reactive oxygen spices (ROS). Then ROS act as an important messenger in NF-κB activation and consequently increased cytokines expression (2). Valsartan by acting on angiotensin receptor1 on lung tissue, inhibited the effect of angiotensin II on NF-κB activation and inflammatory process.

Conclusion: Valsartan showed a significant protective effect against bleomycin-induced pulmonary fibrosis. Which were due to reduction of NF-κB expression.

Keywords: Valsartan, Pulmonary Fibrosis, NF-κB, Real time PCR.



15th IPSC Proceeding

Investigation of Heme Polymerization Inhibition of *Phlomis caucasica* Rech.f. as an Antimalarial Agent

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Introduction: Heme is a vulnerable criterion for the *Plasmodium* which catabolizes hemoglobin as a source of amino acids in an acidic, oxygen-rich lysosome-like digestive vacuole. Heme monomer, capable of generating oxygen radicals, transforms into a malarial pigment named haemozoin. Importantly, some antimalarial drugs inhibit haemozoin formation. Inhibition of the haemozoin formation will cause increasing the concentration of toxic free heme in the food vacuole which results in parasite death. The purpose of this study was to investigate antimalarial properties of *Phlomis* that have been traditionally used for antipyretic purposes.

Methods: Aerial part of *Phlomis caucasica* Rech.f. from Lamiaceae family was used for preparing methanol total extract and fractions including petroleum ether, chloroform, methanol, 70% methanol, and water by maceration method. Inhibition test of heme detoxification (ITHD) (1) as an spectrophotometric assay of inhibition of β-hematin formation was used for evaluation. Hemin Chloride, tween 20 and samples were added in each well of a 96-well plate, and incubated at 60° C. The plate was read with a micro-ELISA reader at 405 nm, and percentage of heme polymerization inhibition was calculated, subsequently.

Results: Aqueous fraction significantly demonstrated inhibition of β -hematin formation (100%).

The others including total extract (35%), petroleum ether (30%), chloroform (39%), Methanolic (4%), and hydroalcoholic (21%) fractions; didn't show any remarkable effect. Thus, the water-soluble compounds of the aerial part of this plant have been inhibited heme polymerization. Indeed, other studies were reported *in vitro* and *in vivo* antiplasmodial activity of this genus (2).

Conclusion: Based on our studies as well as other studies on antiplasmodial activity, this plant could be a proper candidate for further studies.

Keywords: Lamiaceae, heme detoxification, malaria, Phlomis caucasica



15th IPSC Proceeding

Evaluation and Comprarison of Antioxidant and Anti lipid Peroxidation Activity Methanolic and Hydrolyzed Extract of cuttle fish (*Sepia pharaonix*) of Persian Gulf

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Abstract

Introduction: Cuttlefish belong to the class cephalopoda and their muscle tissue, skin and ink showed different therapeutide effects such as signifiant antioxidative ones. Given that free radicals are the cause of several degenerative diseases such as cardiovascular diseases, cancer, Alzheimer, etc. this study was designed and conducted to evaluation and comparison of antioxidant activity of aqueous, methanolic extract of cuttle fish.

Methods: blue swimming crab fished and kept on freezing condition until extracting.aqueous,methanolic,and hydrolyzed by pepsin extractions were done with maceration method.to evaluated the antioxidant activity method of

TEAC,FRAP,DPPH,hydroxyl radical seavenging were used and pro-oxidant effect was determined by bleomycin

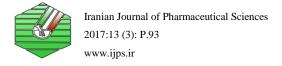
method.inhabition of lipid peroxidation in the brain, liver, kidney and lungs of rats was performed in a laboratory

setting.

Results: in DPPH,FRAP and ABTS tests the antioxidant activity of aqueous extract was more than other extrat.also aqueous extract have a greater impact on inhabit lipid peroxidation in the brain,liver and lungs.by comparing hydroxyl radical scavenging with and with out the presence of EDTA was observed that this extrat can directly inhibit the hydroxyl radical.bleomycin assay results showed that pro-oxidant effect increases with increasing concentration.

Conclusion: the result showed that all extract have acceptable antioxidant power.better effects of aqueous extract could be due to proteins copounds and water-slouble vitamins in it.

Key words: cuttle fish (Sepia pharaonis), DPPH, FRAP, ABTS, hydroxyl radical scavenging, antioxidant capacity.



15th IPSC Proceeding

Evaluating Glycerrhyzea Glabra Aqueous Extract against Acetaminopheninduced Liver Injury in Mice

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Abstract

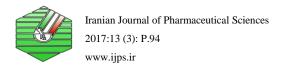
Introduction: Protective effects of *Glycerrhyzea glabra* (GG) aqueous extract against acetaminophen (APAP)-induced hepatotoxicity in swiss albino mice was examined.

Method: Animals received a single dose of APAP (1000 mg/kg, in normal saline, i.p) and different doses of GG (gavage).

Results: Acetaminophen treatment significantly depleted hepatic glutathione (GSH) content, increased hepatic malonyldialdehyde (MDA), and caused significant rise in serum LDH, AST, and ALT as biomarkers of liver injury. Liver histopathological changes endorsed acetaminophen-induced hepatotoxicity. Administration of different doses of GG extract (600 and 1200 mg/kg, gavage) effectively diminished acetaminophen-induced hepatic damage. Furthermore, glycyrrhizic acid as the major constituent of GG extract, showed hepatoprotective effect against acetaminophen-induced liver injury in mice.

Conclussion: These results suggest GG extract as a potential hepatoprotective agent against xenobiotics-inuced liver injury.

Key words: Acetaminophen, Glycerrhyzea glabra, Hepatotoxicity, Hepatoprotective.



15th IPSC Proceeding

Study of Antinociceptive Activity of the Hydroalcoholic Extract of *Potentilla*reptans L. in Male Mice

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Abstract

Introduction: Potentilla species (Rosaceae) are perennial and herbaceous plants. This genus traditionally have been used for various diseases such as diarrhea, wound healing and especially anti-inflammatory and analgesic agents in

Iran and other parts of the world. The aim of this study was investigation of antinociceptive effect and preliminary phytochemichal screening of *P. reptans* L. (popularly called creeping cinquefoil) which has a wide distribution in the North of Iran.

Methods: The present study investigated the antinociceptive activity of hydroalcoholic extract prepared from the aerial parts of *P. reptans* L. using the acetic acid-induced writhing, hot plate and rotarod test in male mice. Also we applied qualitative and quantitative assay for detection of phytochemicals such as terpenoids, saponins, alkaloids, flavonoids and phenolic compounds and determination of Total phenol, tannin and flavonoid contents in *P. reptans* L. aerial parts.

Results: Oral administration of the hydroalcoholic extract of *P. reptans* L. (100, 300, and 500 mg/kg) dosedependently reduced the number of writhings induced by acetic acid and increased reaction time in hot-plate test. The antinociceptive effects were significantly antagonized by naloxone (4 mg/kg; i.p.) in writhing test that be comparable with normal salin. In rotarod test none of the extract doses have affect locomotor activity. The phytochemical screening of the *P. reptans* L. aerial parts revealed the presence of high concentration of flavonoids, saponins, tannins and penta-cyclic triterpenoids. Content of total phenol and tannins was calculated 247.7 mg/g and 101.7mg/g expressed as tannic acid respectivly. Flavonoids content was 24 mg/g as quercetin equivalents in dry extract.

Conclusion: In this study suitable antinociceptive effect from hydroalcoholic extract of aerial part of *P. reptans* L. observed in hot plate and writhing test and didn't exhibit neurotoxicity in oral administration. Analgesic effect of the extract could be mediated via opioid receptors and inhibition of prostaglandins synthesis.

Keywords: antinociceptive, Potentilla reptans L., hot plate, writhing test, rotarod test.



15th IPSC Proceeding

Investigation of the Binding Ability of Anti-TNF α ScFv J₄₈ Antibody by Using ELISA and Estimating Possible Interactions by Docking Studies

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Introduction: TNF α is an inflammatory cytokine, which have different physiological and pathological functions. In

this context, using antibodies with smaller size and stronger binding affinity is one of the common strategies to

inhibit TNFa activity in chronic disease (1). In past works, we produced and purified the ScFv J48 antibody which

had been identified by Phage display technique (2). Now we aimed to examine binding ability of J_{48} to TNF α by

ELISA and evaluate the possible interactions among them by docking studies.

Methods: The purified ScFv antibody (i.e.J₄₈) in various concentrations from 0.012μM to 1μM was prepared and

added to the TNFα coated wells. Then anti-6His and HRP conjugated goat anti mouse antibodies were used for ScFv

 J_{48} detection. For docking studies, the Tree-dimensional structure of J_{48} antibody was modeled in Swiss model

website. Next, the modeled structure was docked to TNF α by using Z dock. To estimate the possible interactions

between J_{48} and TNF α , the docked complex was analyzed in PIC website.

Results: Analyzing of ELISA results showed that J_{48} has a relatively high binding affinity to TNF α . And docking

results revealed that the hydrogen bond, hydrophobic bond, π-cation interactions were involved in the interactions

between TNF α and J_{48} .

Conclusion: According to the results of the ELISA and docking studies, J₄₈ has a good inhibition activity on TNFα.

Therefore, J_{48} can be a suitable candidate for clinical trials or may be used for designing a new stronger anti- $TNF\alpha$

medication.

Keywords: TNF-α, ScFv, ELISA, Docking studies



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15th IPSC Proceeding

Protective Effect of Testosterone on Haloperidol Induced Parkinsonism in

Male Rats

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Abstract

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder characterized by a progressive loss of

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dopaminergic neurons in the substantia nigra pars compacta (SNpc). Neuroleptic drugs such as haloperidol induce Parkinson-like syndrome through blocking brain D2 receptors in multiple pathways in the brain. Many of non-motor symptoms of PD such as depression, sleep disorders and sexual inability are correlated with testosterone deficiency .However, it is still opaque whether testosterone therapy can be influent directly on motor symptoms of PD or not. **Methods:** The experiments were performed on 24 male Wistar rats (200 -240 g). Animals were randomly divided into 4 groups (6 animals in each group). Rats pretreated with saline or testosterone (1 mg/kg, i.p.) or flutamaide (10mg/kg, i.p.) for 1 day or 7 consecutive days before haloperidol injection. Catalepsy and motor-imbalance were induced by an intraperitoneal (i.p) injection of haloperidol (1 mg/kg) at the end of drugs treatment. In animal models, haloperidol induces a behavioral state known as catalepsy in which the animals are unable to correct externally imposed postures. The effects of testosterone and flutamaide on haloperidol -induced catalepsy and motor impairment were assessed by the bar test and rotarod, respectively.

Results: Haloperidol 1 mg/kg, i.p, was able to induce catalepsy and motor imbalance. Testosterone pretreatment for 7 days prevented from halopridol induced catalepsy and could restore motor balance about to the level of normal animals, while concurrent administration of flutamide prevented from improving effect of testosterone.

Conclusion: Pretreatment by testosterone can significantly be effective in catalepsy remission, meanwhile administration of flutamaide as an androgen receptor blocker prevented from protective effect of testosterone. It seems that the anti-cataleptic effects of testosterone are exerted through affecting on androgenic receptors.

Keywords: Parkinson's disease, Testosterone, Flutamaide, Haloperidol, Catalepsy, Bar test, Rotarod



15th IPSC Proceeding

In virto Cytotoxic Activity of a Lactococcus Lactis Antimicrobial Peptide against Breast Cancer Cells

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Abstract

Introduction: Nisin, an effective natural food preservative, is an antimicrobial peptide produced by *Lactococcus lactis*. Although it has been mainly studied and developed as potential alternatives for antibiotics, other

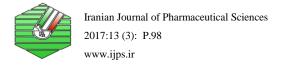
pharmacological effects of nisin including cytotoxic and anti-tumor activity have been attracted many attentions. Here, we aimed to evaluate *in vitro* cytotoxic activity of nisin against breast cancer cells.

Methods: The effect of temperature, pH and chemical composition of medium on the yield of nisin production by *L. lactis* was evaluated. The anti-proliferative effect of nisin against a breast cancer cell line (MCF7) and a non-cancerous cell line (HUVEC) was determined using MTT assay. Furthermore, potential synergistic effect of nisin on doxorubicin cytotoxicity was evaluated.

Results: The survival of MCF-7 cells was significantly inhibited by nisin and the IC50 value of 17 μ g/ml was found. Nisin exhibited lower level of cytotoxicity for a normal cell line, HUVEC, with an IC50 value of 64 μ g/ml. This four-fold difference in nisin cytotoxicity against MCF-7 over HUVEC cells was showed to be statistically significant in MTT assay (P < 0.05). It was showed that co-incubation of nisin, increased cytotoxicity of doxorubicin. This synergic effect was more significant in lower concentration of doxorubicin and against MCF-7. Approximately, three-fold higher cytotoxicity was observed when MCF-7 cells were incubated with combination of nisin (10 μ g/ml) and doxorubicin (6 μ g/ml) compared with doxorubicin alone (P < 0.01).

Conclusion: In conclusion, our study reported effective cytotoxic effects of nisin against MCF-7, a breast cancer cell line. Furthermore, nisin exhibited a selective toxicity against cancerous cells in comparison to HUVEC, a normal cell line. Most importantly, combination of nisin with doxorubicin led to synergetic anticancer effect. It could be suggested that nisin either alone or in combination with other chemotherapeutic agents can be a potential treatment for breast cancer.

Keywords: nisin, breast cancer, cytotoxicity, Lactococcus lactis, antimicrobial peptide



15th IPSC Proceeding

Selective Toxicity of Chrysin on Isolated Mitochondria Obtained from Liver Hepatocytes of Hepatocellular Carcinoma Induced Rat

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Abstract

Introduction: Chrysin is a natural flavonoid currently under investigation due to its important biological anti-cancer

properties. Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death. In patients

with HCC current treatments show poor tolerance and low efficacy. So, alternative therapies with good efficacy are

urgently needed. The aim of this research was to evaluate the selective apoptotic effects of chrysin on mitochondria

obtained from the liver of HCC rats.

Methods: In this study, HCC induced by diethyl nitrosamine (DEN), as an initiator, and 2-acetylaminofluorene (2-

AAF), as a promoter. After confirmation of liver cancer, rat liver mitochondria for evaluation of the selective

cytotoxic effects of chrysin were isolated, and mitochondrial parameters related to apoptosis signaling were then

determined.

Results: Our results showed that chrysin was able to induce increased in reactive oxygen species (ROS) level,

mitochondrial swelling, mitochondrial membrane permeabilization (MMP) and cytochrome c release only in

cancerous but not in untreated normal hepatocyte mitochondria.

Conclusion: Finally, our finding underlines chrysin as a promising therapeutic candidate against HCC and

recommends the compound for further studies.

Keywords: Hepatocellular Carcinoma; Chrysin; Mitochondrial Targeting; Apoptosis

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A Survey of Effects of Nanoceria for Potentiation of Anticancer Effect of

Doxorubicin and Inhibition of Doxorubicin-Induced Cardiotoxicity in Human

Ovarian Cancer in Nude Mice

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Abstract

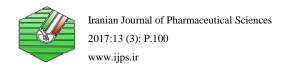
Introduction: Nowadays combination therapy by different mechanism and synergetic effect is one of the main procedures in cancer treatment [1]. Doxorubicin is an anthracycline antibiotic that it's usage is limited due to its cardiotoxicity [2]. Nanoceria (Nano particle of cerium oxide) showed anti-oxidant effects [3] and in this study we evaluated effect of nanoceria for potentiation of anticancer effect of doxorubicin and also attenuation of doxorubicin cardiotoxicity.

Methods: In first step, we growth SKOV3 cell line in RPMI medium and then injected it to Nude mice for tumor growth. After 2 month and rising of tumor we began drug and Nano ceria injection to inhibit tumor growth. We had four group that first group just get doxorubicin 2mg/kg (G1), second group just get Nano ceria 100mg/kg (G2), third group get both of them (G3) and control group that didn't get anything (G4). After 14 days tumor had been exit, its size and apoptosis markers had been study. Hearts tissue had been exit too and oxidative stress markers such as Lipid peroxidation and Glutathione were measured. Also, pathological changes in both tumor and heart tissue was done.

Results: Tumor growth during of 14 days especially in last days had been stabilized. For example tumor size in one mouse in G3 after rising from 0.7 to 1 mm, in last day was 0.9 mm. Pathology samples showed wide and focal necrosis especially in G3. Evaluation of oxidative stress markers showed nanoceria inhibited doxorubicin induced oxidative stress in heart tissue.

Conclusion: Our data showed that synergic anticancer effect of doxorubicin and nanoceria and protection effect of nanoceria against doxorubicin induced cardiotoxicity.

Keywords: Nano ceria, Doxorubicin, Ovarian cancer, Nude mice, Cardiotoxicity.



Effect of Astaxanthin and Melatonin on Cell Viability in Human Breast Cancer Cell Line

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Abstract

Introduction: Breast cancer is the second leading cancer among women. The estrogen dependent types (ER-rich), such as the T-47D cell-line, are responsive to chemotherapy [1]. Astaxanthin, a powerful antioxidant has great research prospects in cancer therapy [2], and also, Melatonin has repeatedly been shown to exert a negative growth-regulatory influence on the development and growth of hormone-responsive breast cancer [3]. In this study, we examined the effect of Astaxanthin and Melatonin on apoptosis in T-47D human breast cancer cell line.

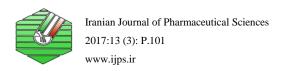
Methods: T-47D cell line were transferred to DMEM medium, supplemented with 10% FBS and antibiotics. Cells were seeded in 96-well plates, then cells were treated with various concentrations of Astaxanthin (1, 10, 50, 100 μ M) and Melatonin (1000, 8000, 14000, 28000 μ M) for 24 hours. Cell viability was assessed by MTT assay. Apoptosis was detected by Acridine Orange/Ethidium Bromide staining.

Results: Results showed that Astaxanthin and Melatonin decreased cell viability in T-47D cells in a dose dependent manner after 24 hr (p<0.05). The most significant effect of Astaxanthin is at a dose of 100 μ M but the most significant effect of Melatonin is at a dose of 28000 μ M. Available studies attributed induction of apoptosis by Astaxanthin in various cancer cell lines [4]. An increase in apoptotic cells were consistent with the decline in anti-apoptotic Bcl-2 following Astaxanthin treatment [5]. Melatonin at physiologic concentrations (10–9 M to 10–11 M), inhibits the viability of ER-positive cell lines, suggesting that the antitumoral effects of melatonin are mediated through the estrogen-response pathway. Our results showed that melatonin at pharmacological level (16000 μ M) induce apoptosis in T-47D cells significantly [6].

Conclusion: Our findings show that Astaxanthin can induce apoptosis in cancer cells at a lower dose than Melatonin and it could be considered as a therapeutic agent in breast cancer.

Keywords: Astaxanthin, Melatonin, T-47D, Apoptosis, MTT assay, carotenoid





Hepathoprotective Effects of *Allium Hirtifolium* against Cadmium-Induced Liver Injury in Wistar Rat

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Abstract

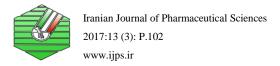
Introduction: Cadmium is a main environmental contaminant and is known for its wide toxic manifestations. *Allium Hirtifolium* (AH) which belongs to the same genus of garlic, naturally grows in various part of Iran. This study was undertaken to evaluate the effects of AH hydroalcoholic extract against cadmium hepatotoxicity in rats.

Material and Methods: Thirty-six male rats were divided into six groups: the first group received normal saline. The second and third groups received cadmium in drinking water (100 mg/l) and *AH* extract (200 mg/kg), respectively. The fourth, fifth and sixth groups were orally treated with 50, 100, and 200 mg/kg of *AH* extract as well as cadmium in drinking water (100 mg/l), respectively. After two weeks, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in serum samples and lipid peroxidation (LPO), total antioxidant capacity (TAC) and total thiol molecules (TTM) in liver tissue were determined.

Results: A significant increase was observed in ALT, AST levels in cadmium group when compared to control group. Following administration of *AH* extract, a remarkable decrease was seen in ALT and AST serum levels in comparison with cadmium group. In addition, hepatic oxidative damages in treated groups were improved by increasing of TAC and TTM and decreasing of LPO when compared to cadmium group.

Conclusion: The present study suggests that *AH* hydroalcoholic extract has protective effects against cadmium-induced hepatotoxicity.

Keywords: Allium Hirtifolium, Cadmium, Hepatotoxicity, Oxidative stress



15th IPSC Proceeding

Evaluation of the Effect of Chronic Administration of *Citrus Aurantium*Essential Oil on the Development of Morphine Withdrawal Syndrome in Male Rats

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Abstract

Introduction: Long-term exposure to opiates may lead to physical dependency and tolerance. Several mechanisms like serotonergic, dopaminergic and glutamatergic associated with morphine dependency have been identified (1). *Citrus aurantium* belongs to the Rutaceae family, containing linalool and linally acetat as major volatile components. Linalool administration produced anti-inflammatory and antinociceptive activities in several behavioral assays (2). In this study the effect of *Citrus aurantium* essential oil (CEO) on withdrawal syndrome of morphine has been evaluated in male rats.

Methods: Male Wistar rats (225-275g) were divided into seven groups (n=8) randomly, including: Morphine sulphate, CEO (20, 40 and 80 mg/kg) + Morphine, Kolliphor® HS15 30% in normal saline (vehicle of CEO) + Morphine. The rats were rendered morphine-dependent by injection of additive doses of morphine subcutaneously for 9 days. The procedure of the morphine administration was as followed: day1: 5 mg/kg/12h, day 2 and 3: 10mg/kg/12h, day 4 and 5: 15 mg/kg/12h, day 6 and 7: 20mg/kg/12h and day 8 and 9: 25 mg/kg/12h. On the 9th day, 2 hours after the last dose of morphine, naloxone (4mg/kg) was injected intraperitoneally. Some withdrawal behaviors was counted for 60 minutes. Data were analyzed with one way ANOVA and post-test Tukey, p values of less than 0.05 were considered as significant.

Results: The results showed that CEO could reduce the morphine withdrawal syndrome and total withdrawal score (TWS). Intraperitoneally injection of CEO in two doses (40 mg/kg with p<0.001 and 80 mg/kg with p<0.01)

significantly reduced the TWS in comparison the morphine- vehicle treated group. Reduce of TWS, probably due to anti-inflammatory effect of linalool.

Conclusion: Our results indicated that chronic administration of CEO had beneficial effects in reducing morphine withdrawal syndrome in standing on feet, head shakes, paw tremor, body grooming, face wiping and swallowing in a dose independently manner.

Keywords: Morphine, Withdrawal syndrome, Essential oil, Citrus aurantium, Dependency



15th IPSC Proceeding

Design, Molecular Modeling Study, and Synthesis of New Pyrimido [1, 2-A] Pyrimidin-4-One Derivatives as Anti- HIV Agents

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Abstract

Introduction: HIV-1 is the etiological cause of acquired immunodeficiency syndrome (AIDS). AIDS therapeutic targets principally consists of three key enzymes of HIV-1: reverse transcriptase (RT), protease (PR) and integrase (IN) (1,2). Integrase strand transfer inhibitors among the HIV inhibitors has the advantage of suitable safety profile and high potency (3). The chelating motif and coplanar hydrophobic aryl group are the common pharmacophores of an integrase strand transfer inhibitor (INSTI) (4). In this research, aimed at discovering new anti-HIV agents we designed a novel pyrimido [1, 2-a] pyrimidin-4-one derivatives based on HIV-1 IN inhibitors pharmacophores.

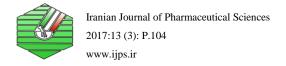
Methods: 2-amino-pyrimidine with methylethylene malonate-ethyl acetate was heated at 120 ° C with a mixture of Solvent deuterom under microwave radiation alternately. After cooling to room temperature, the solid thus formed, was washed with n-hexane. Then, this intermediate was dissolved in ethanol and hydrazine hydrate was gradually added to it. After completion of the reaction, the solvent was evaporated to dryness and the precipitated product was crystallized from absolute ethanol. In the next reaction step, the carbohydrazide intermediate was dissolved in absolute ethanol and carbon disulfide was added gradually to the basic reaction medium. After 8 hour reflux, the solvent was dried under vaccum and the residue crystallized from absolute ethanol. Final derivatives were synthesized by the reaction of 2-mercapto-1,3,4-oxadiazole intermediate with substituted benzyl

halide derivatives. Purification was performed with plate chromatography and spectroscopic techniques were applied to confirm the structures.

Results: Target compounds were synthesized and purified using different crystallization and chromatography methods. The structure of the synthesized compounds was confirmed by IR, LC-MS (ESI), 1H-NMR. A molecular modeling study using the later crystallographic data available for PFV (prototype foamy virus) integrase was performed to explain the probable mechanism of action of synthesized compounds.

Conclusion: We designed and synthesized a novel series of pyrimido[1,2-a]pyrimidin-4-one derivatives based on HIV-1 integrase inhibitors pharmacophores. According to HIV-1 integrase inhibitors structure activity relationship, carbonyl group and N atom of oxadiazole ring play as a chelator motif. The anti-HIV activity of novel compounds is under investigation.

Keywords: pyrimido [1, 2-a] pyrimidin-4-one, Anti-HIV-1 activity, Design, Synthesis, Molecular modeling, Integrase



15th IPSC Proceeding

Protective Effect of Cromolyn Sodium against Paraquat-induced Pulmonary Fibrosis Model in Rat

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Abstract

Introduction: The current study aimed to investigate the effects of Cromolyn Sodium (CS) on proinflammatory cytokines in Paraquat (PQ)-induced lung damage in rat.

Methods: Animals were randomly divided into 5 groups. Group 1 and 2 received nebulized vehicle and CS (8 mg/kg) for 3 consecutive weeks, respectively. Group 3 was treated with single oral dose of PQ (40 mg/kg). Groups 4 and 5 were PQ groups which received nebulized CS (6 and 8 mg/kg/day, respectively) from 1 week before to 2 weeks after PQ administration. Finally, the animals were scarified and the changes of hydroxyproline (HP) and histology were evaluated in lung tissue. In addition, IL-1 β , TNF- α and IL-8 levels were determined in serum samples.

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Results: The results showed that lung HP level as well as IL-1 β , TNF- α and IL-8 were significantly lower in the CS treated rats as compared to PQ group. The best response, however, was observed with the 8 mg/kg of CS as confirmed by histology findings.

Conclusion: This study suggests that CS may prevent progression of PQ-induced lung damage by decreasing of inflammatory cytokines.

Keywords: Cromolyn Sodium, Paraquat, Proinflammatory Cytokines



15th IPSC Proceeding

Effect of Cumin Seed Essential oil on Endocrine System and Vital Organs in Female Mice

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Abstract

Introduction: Cuminum cyminum L. seeds are active reservoirs of numerous bioactive compounds(1). This plant has been approved for several pharmacological activities and has been suggested for the treatment of many diseases(1). Although in rodent models, this essential oil showed antiepileptic and antihypertensive effects, its long term administration caused toxic effects in male mice and according to a study, Cuminum cyminum extract caused infertility in male rats(2). We aimed in the study to recognize the constitutes of Cuminum cyminum essential oil and effects in repeated dose models on endocrine effects in female mice.

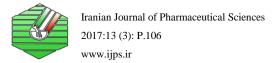
Methods: Essential oil of *Cuminum cyminum L*. was analyzed by GC_MS analysis. Doing acute study was to determine the range of LD50 by using OECD425 in female mice. Sub chronic studies were done according to OECD40. Following to daily administration of all doses in 28 days regimen, the daily variation of weight and clinical effects of toxicity reported in end of the study.

Results: Acute test didn't show any sign of toxicity in doses up to 2000 mg/kg also in repeated dose test there was Significant weight gains in all dose groups(p<0.001)which exposed to essential oil. Studies show no significant changes in T3andT4 levels by ANOVA test. Significant weight gains in the uterus (p=0.001),mild edema in endometrium, moderate edema in perimeter layers of animals which exposed to low and medium doses ,as its

hyperplastic effects in endometrial epithelium of high dose group suggested the endocrine disrupting effects which confirmed by marked estradiol elevation and antiprogesterone properties in all dose groups. hepatotoxic and nephrotoxic effects recorded by biochemical and histopathological evidence.

Conclusion: The study findings show this essential oil has effect on level of esteradiol and progestron but no significant effect on thyroidal hormons so, cause vital organ toxicity.

Keywords: Cuminum ciminum, Endocrine disruptors, Thyroid hormones



15th IPSC Proceeding

Investigation of the Effect of Addition of Gammaoryzanol on the Properties of the Nanoliposomes by Using Response Surface Methodology: Preparation, Characterization, and Optimization

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Abstract

Introduction: Nanoliposomes are one of the most important lipid-based nanocarriers which can be used for encapsulation of both hydrophilic and hydrophobic active compounds. Gammaoryzanol (GO), a phytosteryl ferulate mixture extracted from rice bran oil, has a wide spectrum of biological activities and specially used for its antioxidant activity. Purpose: The aim of this study was to investigate the effect of existence of GO in the lipid bilayer on the characteristics of nanoliposomal formulation prepared by a modified ethanol injection method.

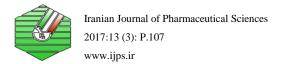
Method: GO bearing nanoliposomes were prepared with different phosphatidylcholine (PC): GO molar ratios, which was selected as the independent variables, and subsequently the particle size (PS), encapsulation efficiency percent (EE%) and drug release over 24 h (D24h), which were considered as dependent variables, were analyzed and optimized employing response surface methodology (RSM). Graphical response surface and contour plots were

also employed to understand the interaction of different variable. The optimum points for the variables were obtained from the optimization plot.

Results: The mean PS, EE% and D24h of Celecoxib nanoliposomes were 102.6 ± 9.5 nm, 67.6 ± 11.2 % and 36.62 ± 9.6 %, respectively. The results indicated that, PC: GO and PC: Drug ratio were the important contributing variables for PS, EE% and D24h of nanoliposomes. The optimum formulation of Celecoxib nanoliposomes, in which PC: GO and PC: Drug ratio were 4.6 and 3, had PS= 102 nm, EE% = 74.2 % and D24h = 59.9 %.

Conclusion: In conclusion using GO, ethanol injection method besides RSM techniques, are simple, rapid and beneficial approaches for preparation, optimization and investigation of the effect of GO in the bilayer structure on the properties of nanoliposomes.

Keywords: Gammaoryzanol, nanoliposomes, Response surface methodology, Ethanol injection method



15th IPSC Proceeding

Application of Translational Pharmacokinetic-Pharmacodynamic Models in Drug Discovery and Development: an Updated Review

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Abstract

Introduction: Lack of predictability of clinical efficacy and safety is an important problem facing pharmaceutical research today. Over the last decade the number of new medicines being launched has fallen sharply, due largely to the failure of drugs to progress beyond clinical phases (1). Translational science is a multidisciplinary form of science that bridges the recalcitrant gaps that sometimes exist between basic science and applied science, necessitating something in between to translate knowledge into applications (2). Translational PK–PD modeling is the integration of in silico, *in vitro*, and *in vivo* preclinical data with mechanism-based models to anticipate the effects of new drugs in humans (3).

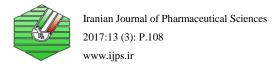
Methods: Related English electronic databases and technically published original articles and reviews were systematically searched for the purpose of this review. In this review, cases studies are presented, which outline successful implementation of the translational PK–PD methodology in the rational development of Active Pharmaceutical Agents across various stages of discovery and development.

Results: In this report, we present an inclusive review of literatures focusing on the Predicting side effects in humans from preclinical toxicity studies, translation of preclinical efficacy and safety information and using translational PK-PD modeling and simulation in children dosing.

Conclusion: Translational PK-PD analysis coupled with appropriate biological understanding serves as a useful tool both improving the predictive power of preclinical models and calibrating preclinical models using clinical data. Provides an understanding of pathway modulation vs efficacy relationships, allows quantitative assessment of similarities and differences between preclinical models and humans.

Incessant assessment of preclinical prediction with clinical results allows for calibration of preclinical models and increases confidence to translate across species.

Keywords: Translational Science, PKPD Models, Drug Discovery, Drug Development



15th IPSC Proceeding

Design and Synthesis of Novel N'-Arylidene-9-Methyl-4-Oxo-4H-Pyrido [1, 2-A] Pyrimidine-3-Carbohydrazide Derivative as Anti-HIV Agents

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Abstract

Introduction: The causative agent of acquired immune deficiency syndrome (AIDS) is the human immunodeficiency virus type 1 (HIV-1). During the past three decades, the combination of antiretroviral drugs in HAART (highly active antiretroviral therapy) regimens has transformed the management of HIV infection from a fatal disease to a manageable chronic condition. However, resistance to marketed anti-HIV drugs is increasing at an alarming rate. Thus, there is a need to improve existing agents and develop new agents which work by different mechanisms. HIV-1 integrase as one of the key enzymes for HIV-1 replication represents a crucial target for antiretroviral drugs, because it has no counterpart in mammalian cells. In this research, aimed at the discovery of new compounds as anti-HIV-1 agents, the HIV-1 integrase inhibitors were selected as a lead to design new analogues.

Methods: Preparation of novel compounds was started from the 2-amino-3-meyhylpyridine. The Gould–Jacob cyclization reaction was the main method to form the core structure. Condensation of 2-amino-3-meyhylpyridine

with ethoxymethylenemalonate diethyl ester (EMME) yielded methylene malonate intermediate. This compound was converted to ester intermediate in Ph_2O containing catalytic 2-chlorobenzoic acid. The ester was subsequently treated with hydrazine in DMF to form the corresponding hydrazide intermediate. Hydrazide intermediate was reacted with substituted benzaldehyde derivatives to give final products.

Results: Final compounds were synthesized and purified using different crystallization and chromatography methods. The structure of the synthesized compounds was confirmed by IR, LC-MS (ESI), ¹H-NMR and ¹³C-NMR. A molecular modeling study using the later crystallographic data available for PFV (prototype foamy virus) integrase was performed to explain the probable mechanism of action of synthesized compounds.

Discussion: We synthesized a novel series of N'-arylidene-9-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidine-3-carbohydrazide derivatives based on HIV-1 integrase inhibitors pharmacophores. The molecular modeling studies suggested that the anti-HIV activity of these compounds might involve a metal chelating mechanism. According to HIV-1 integrase inhibitors structure activity relationship, carbonyl groups play as a chelator motif. The anti-HIV activity of novel compounds is under investigation.

Keywords: Synthesis, anti-HIV activity, docking, N'-arylidene-9-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidine-3-carbohydrazide



15th IPSC Proceeding

Design and Synthesis of Novel Carbohydrazidebenzoquinolone Derivative as Anti-HIV Agents

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Abstract

Introduction: Resistance of human immunodeficiency virus (HIV) towards known drug regimens necessitates the discovery of novel antivirals with a diverse structure and mode of actions. HIV integrase (IN) which catalyzes the incorporation of viral DNA into the host chromatin plays critical roles in viral infection and the establishment of proviral latency. IN has been the subject of intense research for anti-HIV drug discovery, because it has no host

cellular counterpart and its inhibition should not interfere with cellular functions. So in this study we designed some novel derivatives based on HIV integrase inhibitors.

Methods: Preparation of novel compounds was started from the 1-naphthylamine. First of all, 1-naphthylamine was converted to ethyl 4-oxo-1, 4-dihydrobenzo[h]quinoline-3-carboxylate based on Gould-Jacob reaction. This compound was subsequently treated with hydrazine in DMF to form the corresponding hydrazide intermediate. Hydrazide intermediate reacted with substituted phenylisothiocyanate derivatives in DMF to give target derivatives.

Result: Final compounds were synthesized and purified using different crystallization and chromatography methods. The structure of the synthesized compounds was confirmed by IR, LC-MS (ESI), and ^{1H}-NMR. A molecular modeling study using the later crystallographic data available for PFV (prototype foamy virus) integrase was performed to explain the probable mechanism of action of synthesized compounds.

Conclusion: We synthesized a novel series of 2-(4-oxo-1, 4-dihydrobenzo[h]quinoline-3-carbonyl)-N-phenylhydrazine-1-carbothioamide derivative based on HIV-1 integrase inhibitors pharmacophores. The molecular modeling studies suggested that carbonyl groups play as a chelator motif. The anti-HIV activity of novel compounds is under investigation.

Keywords: Synthesis, Anti-HIV activity, Modeling, benzo[h]quinolin-4(1H)-one, benzoquinolone



15th IPSC Proceeding

A Cystatin C-Based Glomerular Filtration Rate Equation versus Cockcroft-Gault Serum Creatinine-Based Formula in Patients Receiving Amphotericin B

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Abstract

Introduction: Serum cystatin C (Cys C) has a number of advantages over serum creatinine for assessing kidney function. Apart from Cys C level itself, several formulas for estimating glomerular filtration rate (GFR) based upon its level have been also introduced in different clinical settings. The aim of the current survey was to compare a

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serum Cys C-based equation with the classic and prominent Cockcroft-Gault (CG) serum creatinine-based formula, both used for the calculation of GFR, in patients receiving amphotericin B.

Method: Fifty-four adult patients with no history of acute or chronic kidney injury planned to receive conventional amphotericin B for an anticipated duration of at least 1 week for any indication were recruited. At three-time points during amphotericin B treatment including days 0, 7, and 14, serum cystatin C as well as creatinine levels was measured. GFR at the above time points was estimated by both a creatinine-base (CG) and the serum Cys C-based equations (Gentian formulas). AmB nephrotoxicity was defined by either a 50 % or more decline in the estimated GFR according to the CG formula or the doubling of serum creatinine from the baseline values.

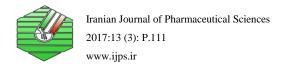
Results: There was significant correlation between creatinine-based and Cys C-based GFR values at days 0 (R = 0.606, P = 0.001) and 7 (R = 0.714, P < 0.001). The mean (95 % CI) decrease in creatinine-based GFR values at day 14 compared to day 0 (-50.457 [-89.477 to-11.437] ml/min/1.73 m2) as well as day 14 versus day 7 (-37.857 [-63.514 to-12.2] ml/min/1.73 m2), were statistically significant between individuals with and without AmB nephrotoxicity. In contrast to creatinine-based calculated GFR, the mean (95 % CI) Cys C-based GFR values at different studied time points were comparable within as well as between patients with and without AmB nephrotoxicity.

Conclusion: Our results suggested that Gentian Cys C-based GFR equation correlated significantly with CG formula at least early time period of amphotericin B treatment. However, the continuous decreasing trend in the mean (95 % CI) values of Cys C-based GFR at the studied time points was not statistically significant.

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Keywords: Serum cystatin C, Serum creatinine, Glomerular filtration rate, Amphotericin B



15th IPSC Proceeding

Preparation of Sustained-Release Hydroxy Ethylcellulose Films with Eudragit Nanoparticles Using Quasi-Emulsion Solvent Diffusion Method

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Abstract

Introduction: Frequent use of highly concentrated solutions may induce toxic side effects and cellular damage at the ocular surface. To enhance the amount of active substance reaching the target tissue or exerting a local effect in the cul-de-sac, the residence time of the drug in the tear film should be lengthened. In this paper, Eudragit nanoparticles were prepared and incorporated in hydroxy ethyl cellulose films to investigate the effect of nanoparticles on the ocular drug delivery.

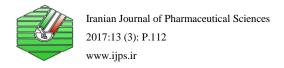
Methods: A Novel quasi-emulsion solvent diffusion method to prepare the controlled-release nanoparticles of drug model with eudragit polymers has been developed. FT-IR and scanning electron microscopy (SEM), loading analyses of the nanoparticles, mechanical properties, water vapor permeability, thermal stability of the films were analyzed.

Results: Technique was conveniently modified in order to produce

NPS-loaded film. These nanoparticles had a mean size of 293 nm, a zeta potential of -32 mV and high efficiency and loading (40 and 15%, respectively). *In vitro* release studies, performed under sink conditions, revealed a fast release during the first hour followed by a more gradual drug release during a 50-h period. The drug release rate from the NPs could be controlled by the type and the concentration of polymer formulated.

Conclusion: NSAID loaded Eudragit were successfully prepared by spontaneous emulsification technique. The obtained results showed that Eudragit could be a useful nanocarrier for non-steroidal anti-inflammatory drugs. The use of a water-soluble polymer enhanced the contact time and possibly also the penetration of the drug.

Keywords: Nanoparticles, Film, Ophtalmic drug delivery, ocular insert quasi-emulsion solvent diffusion



15th IPSC Proceeding

Design, Molecular Docking, and Cytotoxic Activity Evaluations of Novel Pyruvate Dehydrogenase Kinase Inhibitors as Anticancer Agents

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Abstract

Introduction: The Pyruvate dehydrogenase kinases (PDKs) are novel therapeutic targets in oncology. Dichloroacetate (DCA) is a pyruvate mimetic compound that stimulates the activity of the enzyme pyruvate dehydrogenase (PDH) through inhibition of the PDKs (PDK1-4). DCA works by turning on the apoptosis which is suppressed in tumor cells.

Methods: Here, a series of N-aryl-2,2-dichloroacetamide derivatives as PDKs inhibitors were synthesized and their cytotoxic activities against different cancer cell lines such as A549 (human lung cancer), KB (human oral epidermoid carcinoma) and MCF-7 (human breast cancer) were evaluated. Molecular docking of them were performed using AutoDock 4.2 to find their binding modes and the best direction on the base of their binding energy to their targets. The 3D crystal structures for four PDK isozymes, PDK1 (2Q8H), PDK2 (2BU8), PDK3 (1Y8O) and PDK4 (3D2R) were retrieved from protein data bank.

Results: The result of this study showed that these compounds had an acceptable anti-cancer activity. Among them, the best compound, 2, 2-dichloro-N-(9, 10-dioxo-9, 10-dihydroanthracen-1-yl) acetamide (1a), had an IC₅₀ of $2.5\mu\text{M}$, $6.5\mu\text{M}$ and $8.5\mu\text{M}$ against A549, KB and MCF-7 cancer cell lines, respectively. The docking binding energy values were in the order of PDK2>PDK1>PDK4>PDK3.

Conclusion: The docking study showed that, a π - π interaction between phenyl groups of the ligands with imidazole ring of His115 are involved in a ligand-receptor interaction with PDK2. It is also indicated that in compound 1a, a hydrogen bond acceptor interaction exists between Tyr80 in the PDK2 receptor with oxygen of benzoquinone group. The results revealed that these interactions are responsible for its PDK inhibitions. The docking binding sites with the other isozymes of PDK (1, 3 and 4) were also acquired. The validity of docking procedure was also explored by

means of high values of ROCAUC or EFmax factor. Therefore, this compound had a potential value for drug development.

Keywords: DCA, pyruvate dehydrogenase kinase, N-aryl-2,2-dichloroacetamide, Cytotoxic activity, Molecular docking



15th IPSC Proceeding

Evaluation of Medication Errors in Patients with Enteral Feeding Tubes in the Intensive Care Unit of Shahid Sadoughi Hospital in Yazd In A 3-Month Period

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Abstract

Introduction: Most patients admitted to intensive care units have problems in using oral medication or ingesting solid forms of drugs. Selecting the most suitable dosage form in such patients is a challenge. The current study was conducted to assess the frequency and the types of errors in oral drug administration to patients using enteral feeding tubes or having swallowing problems.

Methods: A cross-sectional study was performed in the ICU of Shahid Sadoughi Hospital, Yazd, Iran. Patients were assessed for the incidence and types of medication errors occurring in the process of preparation and administration of oral medicines.

Results: Ninety-four patients were involved in this study and 10,250 administrations were observed. Totally, 4753 errors occurred among the studied patients. The most commonly used drugs were pantoprazole tablet, piracetam syrup, and losartan tablet. A total of 128 different types of drugs and nine different oral pharmaceutical preparations were prescribed for the patients. Forty-one (35.34%) out of 116 different solid drugs (except effervescent tablets and powders) could be substituted by liquid or injectable forms. The most common error was the wrong time of administration. Errors of wrong dose preparation and administration accounted for 24.04% and 25.31% of all errors, respectively.

Conclusion: In this study, at least three-fourth of the patients experienced medication errors. The occurrence of these errors can greatly impair the quality of the patients' pharmacotherapy, and more attention should be paid to this issue.

Keywords: Intensive Care Unit, Medication errors, Pharmaceutical preparations, Enteral Feeding Tubes



15th IPSC Proceeding

Preparation and Antibacterial Activity of Antibiotic Nanofibers Using an Electrospinning Technique as ocular drug delivery: *In Vitro* and *In Vivo* Evaluation

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Abstract

Introduction: For the treatment of anterior eye segment infections using anti-infective agents, topical ocular application is the most convenient route of administration. Topical delivery of anti-infective agents is associated with challenges owing to the unique structure of the eye. Controlled delivery of poorly water-soluble drugs decreased toxicity and side effects, as well as patient compliance. Nanofibers are ultrafine solid fibers notable for their very small diameters. They have significantly large surface area to volume ratio, porosity, surface functionality, and superior mechanical properties. The aim of the present work was to develop azithromycin loaded ocular nanofibers composed of blends of PVA, PVP, chitosan and glutaraldehyde and evaluate their potential for sustained ophthalmic delivery.

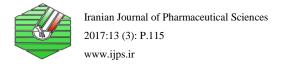
Methods: Nanofibers solutions were obtained upon the composition of 2% (w/v) chitosan to 3% PVA and 1%PVP with azithromycin Solved in ethanol under magnetic stirring at room temperatures. Preparation of the nanofibers was carried out using a customized electrospining system. The crosslinking process with glutaraldehyde was carried

out. The sterility testing of drug delivery systems were performed. Nanofibers were characterised by FT-IR, SEM. *in vivo* drug release tests in eyes rabbits were carried out.

Results: *In vivo* release studies in eye rabbits revealed a release during the 18 h followed. The overall results of the sterility test showed that ocular formulation prepared passes the sterility test as there was no evidence of the growth found in the negative control test tubes. SEM images reveal that nanofibers prepared have good uniformity with regular diameter of about 300 nm. FT-IR exhibited the existence of relevant functional groups of PVA, PVP and Chitosan in the nanofibers.

Conclusion: From these results, we can conclude that CS nanofibers may represent an interesting vehicle in order to enhance the therapeutic index of clinically challenging drugs with potential application at extraocular level.

Keywords: Nanofibers, ocular drug delivery, chitosan, Electrospinning, Azithromycin



15th IPSC Proceeding

Formulation and *In Vitro* Evaluation of Metoprolol Tartrate Carbopol Base Ophthalmic Gel

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Abstract

Introduction: eye drops are conventional ophthalmic delivery systems that often have poor bioavailability of drugs from ocular dosage forms and poor patient compliance because which cause rapid elimination of drug from the eye.

Although many methods of instilling drugs to the eye have been experimented with the use of drops has emerged and still remains the major method of administration for the topical route so that drop should be used frequently and it is not desirable. To solve these problems some new system were developed. One of them is in situ gel forming system. The drug chosen as a candidate for gel formulation in this study is Metoprolol Tartrate (MT) (1). It is a beta-1 selective adrenergic blocking agent and because of its ability to lower the elevated intraocular pressure, it is used clinically to treat patients with ocular hypertension or glaucoma (2). The purpose of the present work is our way and method to increase its contact to the cornea epithelium, giving a longer time of drug contact to the eye and slow possible release from the preparation.

Methods: In this study a trial was made to formulate MT in two concentrations, 0.5% and 1% (w/w). We were used Carbopol 934 in water base with some additive in different concentrations. All formulations were exposed to visual examinations, pH measurement, *in vitro* release and rheological study.

Results: Carbopol 934 gel formulations showed that this polymer extended the duration of pressure reducing effect of MT.

Conclusion: Showed that all formulations were clear, exhibited pseudo plastic flow behavior, and showed pH within the acceptable range suitable to be administered in the eye and it wasn't irritable. *In vitro* release results showed that the release rate of MT increased as the initial concentration increased.

Keywords: Metoprolol Tartrate, Carbopol 934, Ocular gel delivery, ocular hypertension



15th IPSC Proceeding

Evaluation of Anti-Malarial Activity of All Parts of *E*cballium Elaterium and Aerial Parts of *A*rtemisia Marschalliana

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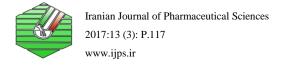
Introduction: The risk of drug resistance and the use of medicinal plants in malaria prevention and treatment have led to the search for new antimalarial compounds with natural origin. Artemisinin was one of the top list of these herbal medicinal products with an endoperoxide sesquiterpene lactone structure, which was derived from *Artemisia annua* and demonstrated potent anti-malarial effect. The objective of this study is evaluation of the anti-malarial effect of different extracts of all parts of *Ecballium elaterium* and aerial parts of *Artemisia marschalliana*.

Methods: dried powder plants was extracted (with n-hexane, dichloromethane (DCM) and methanol (MeOH)), and anti-malaria were investigated by Cell free β -Hematin formation method respectively.

Results: The MeOH extracts of Artemisia marschalliana ($IC_{50}=0.0105\pm\cdot\cdot\cdot^{9\xi}$) and The MeOH extracts of root of Ecballium elaterium ($IC_{50}=0.0293\pm\cdot\cdot^{77\xi}$) compared to positive control (chloroquine ($IC_{50}=0.014\pm\cdot\cdot\cdot^{7}$)) show significant inhibition of heme biocrystallization.

Conclusion: The MeOH extracts of *Artemisia marschalliana* and The MeOH extracts of root of *Ecballium elaterium* showed the significant potential antimalarial effects.

Keywords: Artemisia marschalliana, Ecballium elaterium, Antimalaria, IC50 inhibitory concentration



15th IPSC Proceeding

Synthesize Of Tio₂@Mzno-GO Hybrid Nanocomposites as a Ph-Responsive Nanocarrier for Colon Drug Delivery

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Introduction: In 2016, over one and half million new cancer cases are diagnosed and about six hundred thousand Americans were died of cancer the same year. Indeed colorectal cancer is the third leading reason of cancer death for both men and women (1).

Methods: In this work, we report the synthesis of a mesoporous titanium dioxide@ mesoporous zinc oxide-graphene oxide (TiO₂@mZnO–GO) and mesoporous titanium dioxide@ mesoporous zinc oxide (TiO₂@mZnO) by a facile sono-chemical (2) way to allow multifunctional properties to be imparted into such a nanostructure. CUR was loaded on NCs and the loading capacity and release behavior of CUR from NCs were tested. Also, structure, surface charge, morphology and Cell cytotoxicity of NCs were studied.

Results: The amounts of CUR incorporated in NCs are demonstrated. The release is faster in neutral pH than acidic pH which can be attributed to deprotonation of residual carboxyl groups in GO at higher pH, creating a repulsion force between the NCs and the drug. In addition in neutral medium, the breaking of hydrogen bonding between the NCs and CUR facilitated the release of the drug. Cell cytotoxicity results illustrated that the Curcumin loaded NCs showed significant toxicity due to which cell viability reduced to below 50% at 140 μg/ml concentration.

Conclusion: Novel TiO₂@mZnO-GO NCs were synthesized as a pH-sensitive carrier for colon-targeted drug delivery. The NCs showed pH-dependent drug release behavior due to the presence of large amount of carboxylic acid group in the GO network. MTT results showed that the Curcumin loaded NCs showed significant toxicity, thereby confirming its anticancer effects.

Keywords: Colon cancer, drug delivery, pH- responsive, sono-chemical method.



15th IPSC Proceeding

Design, Synthesis and Biological Evaluation of N'-Arylidene-Hydroxy-2-Methoxybenzohydrazide Derivatives as Tyrosinase Inhibitors

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Abstract

Introduction: Melanin is one of the most widely distributed pigments that is formed through a series of oxidative reactions involving the amino acid tyrosine in the presence of tyrosinase. Tyrosinase is a copper containing enzyme that catalyzes two distinct reaction of melanin synthesis: the hydroxylation of tyrosine and the oxidation of the resulting L-DOPA. Various dermatological disorders result in the accumulation of an excessive level of epidermal pigmentation among which is melanin. Various types of tyrosinase inhibitors have become increasingly important for medicinal and cosmetic product that may be used to prevent or treat this disorder. In present study, we designed, synthesized and biologically evaluated some novel N'-arylidene-hydroxy-2-methoxybenzohydrazide derivatives as

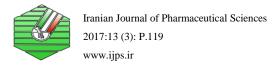
tyrosinase inhibitor.

Methods: The designed compounds were synthesized through two steps. The methyl 4-methoxy salicylate was treated with hydrazine hydrate in ethanol and the final products were obtained by reacting intermediate with different substituted aldehydin presence of catalytic amount of acetic acid in ethanol.the chemical structures of these compounds were confirmed by means of spectroscopic methods and elementalanalyzes. All synthesized compounds were evaluated for their inhibition activities on mushroom tyrosinase.

Results: All designed compounds were synthesized in excellent yield. The results showed that synthesized compounds were good inhibitors of tyrosinase (10-70% inhibition @50Mm). The structure activity and among them catechol derivative was found to be most active compound.

Conclusion: In coclusion, these compounds exhibited potent antityrosinase activities, taken together, these results suggested that such compounds coud serve as the promising candidates for the treatment of tyrosinase-related disorders and further development of such compounds might be of great interest.

Keywords: Melanoma, tyrosine inhibitors, dermatological disorders, hyperpigmentation



15th IPSC Proceeding

The Study of Silymarin (Livergol®) Effect as an Adjunctive Drug on Serum Levels of Neopterin and Catalase in Rheumatoid Arthritis Patients

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Abstract

Introduction: Rheumatoid Arthritis (RA) is a chronic debilitating autoimmune disease. Activation of complements will cause cytokines production and this will make the disease to start or to progress. Neopterin is a biomarker for activation of cellular immunity. Significantly higher Neopterin levels were found in patients with rheumatoid arthritis thus Neopterin determination might be useful in monitoring activity of RA. There is an imbalance between ROS production and the antioxidant defence system such as Catalase in inflammatory RA disease.

Silymarin has so strong antioxidant and anti-inflammatory effects that it made us to study its effect as an adjunct to DMARDs in treatment of patients with RA.

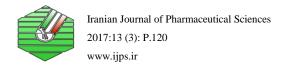
Methods: 42 RA patients with two years history of the disease participated in this clinical trial. They underwent a three month trial of treatment with Livergol, which contain Silymarin, 140 mg thrice a day, as an adjunct to DMARDs used by the patient. Fasting venous blood sample was obtained from all patients and collected serum was aliquoted and stored at -80 C until evaluation.

Serum level of Neopterin and Catalase were measured before and after adding Silymarin to routine drugs in RA patients by HPLC and Spectrophotometry. To analyze, we used Paired-Samples and Wilcoxon tests. (IRCT:2013121915870N1)

Results: There was a significant decrease in serum level of Neopterine and increase of Catalase in RA patients after 90 days administration of Livergol (p<0.05).

Conclusion: Oxidant stress plays a very important role in the pathogenesis of RA. Our findings show that silymarin can significantly reduce serum levels of Neopterin and increase Catalase in RA patients after 90 days administration of Livergol. The exact mechanism of therapeutic effects of Silymarin in RA patients is not clear but it can be result of its anti-inflammatory and anti-oxidative properties.

Keywords: RA, Neopterine, catalase, Silymarin



15th IPSC Proceeding

Evaluation of Antiviral Efficacy of Ribavirin on Crimean-Congo Hemorrhagic Fever from 2006 to 2017 in Zabol

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Abstract

Introduction: Crimean-Congo hemorrhagic fever (CCHF) is a fatal disease, widely distributed in different regions of the world(.1)

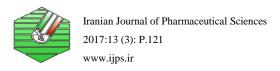
The fever is caused by the CCHF virus, which belongs to the *Nairovirus* genus and *Bunyaviridae* family. There is no proven antiviral treatment for CCHF infection. Ribavirin is an antiviral drug used for severe RSV infections. In this report we have evaluated the efficacy of ribavirin for the treatment of CCHF infection (.2)

Methods: We conducted a cross sectional study which consisted Crime Congo patients from Amir almomenin hospital Zabol, between 2006 and 2017. The data collected from medical records. We used descriptive statistic for our analysis.

Results: Ribavirin was used in 97% of patients. The findings showed that 99% of ribavirin-treated patients have survived from CCHF disease.

Conclusion: In comparison with other studies ribavirin can significantly reduce mortality of patients and we conclude that ribavirin is the first drug to offer a potentially effective treatment for CCHF.

Keywords: Crimean-congo hemorrhagic fever; ribavirin; infection; antiviral



15th IPSC Proceeding

Influence of Buffer, Ph and Preparation Method on Physicochemical Properties of Solid Lipid Nanoparticles (Slns) Negar Namini*, Seyedeh Maryam Mortazavi, Hamid Reza Moghimi

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Abstract

Introduction: Solid lipid nanoparticles (SLN) attract increasing attention as novel drug delivery systems (1). The lipid nanoparticles are well-tolerated carriers (2). It is obvious that the application of buffers in preparation of SLNs may be crucial, especially for SLNs containing pH-sensitive drugs. In spite of this, the effects of buffers on preparation method are not well investigated. This study aims to evaluate the effect of buffer type and order of

mixing on phospholipid-stearic acid SLNs.

Methods: SLNs were prepared by the solvent injection method (3). Stearic acid and lecithin were dissolved in acetone, mixed with the aqueous solution of drug, and then added drop wise to the water containing Tween 80. In order to determine buffer effect on size and zeta potential of SLN, three different buffers (citrate pH=6, citrate-phosphate buffer pH=8, and borate pH=8) were added in two different methods, method I: on the start and method II at the time of dispersing microemulsion into Tween aqueous solution. The particle size and zeta potential were

measured by Malvern Mastersizer 2000 and nano-zetesizer, respectively.

Results: Addition of buffer in method one, led to an increase in particle size (\leq 6000 nm) except from citrate buffer that remains \leq 250 nm, but when buffer was added in the second method the particle size of SLNs was reduced drastically to about \leq 250 nm, in all systems. The order of mixing did not affect the zeta potential of particles, possibly indicates that the particle surface and the electrolyte system properly remain the same in spite of size changes. However, by changing the buffer type the zeta potential changed (citrate -20 mV, borate -33.5 mV, citrate-

phosphate -45 mV).

Conclusion: Based on the present results, order of mixing and type of buffer are two important factors in the preparation of SLNs and should be taken into account.

Keywords: Solid lipid nanoparticle; Buffer; Zeta potential; particle Size



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15th IPSC Proceeding

Titanium Dioxide Nanoparticles as Carrier for Anticancer Drugs

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Introduction: Many chemotherapeutics used for cancer treatments show systemic toxicity during distribution to the normal tissues. Using nanoparticles improves drug delivery efficiency and decreases the side effects of anticancer drugs. Studies have shown that titanium dioxide (TiO₂) nanoparticles induce cytotoxicity in cancer cells, but not in normal cells. In our previous study, the anticancer activity of TiO₂ nanoparticles in combination with photo thermal therapy (PTT) technique completely destroys the melanoma tumor *in vivo*. The aim of this study was to load doxorubicin on multifunctional TiO₂ nanoparticles for its potential role in enhancing the anticancer efficacy of doxorubicin while reducing its side effects. Using these nanoparticles in combination with PTT technique enhances the treatment efficacy.

Methods: At first, for improving the dispersibility of TiO₂ nanoparticles in water, the polyethylene glycol (PEG) with two MW (1000 and 4000kDa) was used for wrapping the surface of TiO₂ nanoparticles. Doxorubicin was loaded into TiO₂ nanoparticles by forming complexes with titanium, to construct doxorubicin-TiO₂-PEG (Dox-TiO₂-PEG) nanoparticles. The effects of various weight ratios of Dox to TiO₂ on the loading efficiencies of nanoparticles were assessed. The stability of these nanoparticles in 3 different pH values (7.4, 6.8 and 5) was evaluated.

Results: The formation of a thin layer of PEG around the TiO_2 nanoparticles was confirmed through thermogravimetric analysis and transmission electron microscopy techniques. Fluorescence scanning results showed the complex formation between Dox and TiO_2 -PEG. The loading efficiency of Dox in TiO_2 -PEG₁₀₀₀ was 74% and in TiO_2 -PEG₄₀₀₀ was up to 85%. These complexes were stable at different pH values for long time (one month).

Conclusion: The characteristics of Dox-TiO₂-PEG show that this drug delivery system based on TiO₂ nanoparticles complexes with doxorubicin is a promising strategy for future clinical practice.

Keywords: Titanium dioxide, doxorubicin, drug delivery, nanoparticle



15th IPSC Proceeding

Medicinal Plants for Atherosclerosis: a Review of Clinical Studies

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Abstract

Introduction: Atherosclerosis is a highly prevalent cardiovascular disorder which is defined as the inflammation within the blood vessels. Elevated low-density lipoprotein, diabetes or hypertension results in endothelial dysfunction, vascular stiffness, and finally, atherosclerosis (1). Medicinal plants have long been used for the treatment of several cardiovascular disorders including atherosclerosis (2). Current study aims to review medicinal plants with clinically established therapeutic activity for the primary and secondary prevention of atherosclerosis.

Methods: Electronic databases including PubMed, Scopus and Cochrane library were searched with the keywords "atherosclerosis", "hypertension", "dyslipidemia", "hyperlipidemia" or "endothelial dysfunction" and "plant", "extract", or "herb" from the date of inception until February 2017 for clinical studies investigated the efficacy of medicinal plants in the prevention or treatment of atherosclerosis. Only papers with English full-text were included in our study. References of the finally included articles were also checked for more relevant studies.

Results: Garlic bulb, different types of tea, guar gum, soybean, black cumin, virgin olive oil, amla fruit, psyllium husk, pomegranate, cacao, cranberry, and grape are the most evident plants which represent beneficial effects for the prevention and treatment of atherosclerosis. The underlying mechanisms of action include the modulation of lipid profile and metabolic complications, improvement of endogenous antioxidant defense mechanisms, anti-inflammatory activities, antihypertensive effects, and also decrease in vascular muscle stiffness, reduction of insulin resistance and diabetes complications, as well as anticoagulant activity. Most of the treatments showed an acceptable safety profile and also no severe adverse effect was reported.

Conclusion: Current study supports the positive role of several dietary and supplementary administrations of medicinal plants for atherosclerosis; however, some of these plants have been assessed in trials with small sample size and short follow-up period. Future well-designed clinical trials as well as meta-analyses are essential to confirm the effectiveness of medicinal plants in atherosclerosis.

Keywords: Atherosclerosis, medicinal plant, herbal medicine, antioxidant, anti-inflammatory



15th IPSC Proceeding

Feasibility of Electrospray Technique for Continuous, One Step Production of Pharmaceutical Nano-cocrystals

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Abstract

Introduction: Cocrystals are a promising approach to improve unfavorable physicochemical properties of drugs such as dissolution and physical stability. Exploring new methods for efficient and rapid production of

pharmaceutical cocrystal with desired particle properties is an essential demand. This study investigated the utility

of electrospray for cocrystals synthesis of poorly water soluble drugs.

Methods: Four previously reported cocrystal forming systems, indomethacin-saccharin, indomethacin-nicotinamide,

naproxen- nicotinamide, and naproxen- isonicotinamide, were selected for the study. For these systems, the

possibility of cocrystal formation were examined by electrospray and conventional methods (solvent evaporation,

grinding). The phase purity, crystallinity, size and morphology of products were evaluated by powder x ray

diffraction, thermal analysis, infrared spectroscopy and scanning electron microscopy (SEM). The effects of

stoichiometric ratio, concentration and solvent type on cocrystal formation were investigated. Physical stability in

accelerated condition and dissolution properties of electrosprayed cocrystals were compared with reference

cocrystals.

Results: Electrospray was found to be an efficient and rapid method to produce high quality cocrystals for all

studied systems other than indomethacin-nicotinamide. It was showed that pure cocrystals only formed at specific

drug; coformer ratio. Solvent type has a weak effect on cocrystal formation and morphology of products by

electrospray. More ever electrosprayed cocrystal demonstrated comparable physical stability with reference

cocrystals. SEM analysis revealed that electrosprayed cocrystals exhibited distinct size and morphology. For

indomethacin-saccharin system electrosprayed cocrystals were in nanometer size ranges (mean size 230 nm) and

displayed superior dissolution rates in compare with solvent evaporated cocrystals.

Conclusion: Electrospray successfully was utilized to produce pure cocrystals with different morphologies and sizes

(nano-to-micron) in one step for poorly water soluble drugs. This study highlights the possible superiority of

electrospray cocrystallization for simultaneous rapid preparation and particle engineering of pharmaceutical

cocrystals in comparison to conventional cocrystallization methods.

Keywords: Electrospray, Cocrystal, Screening, Particle engineering, Nanoparticle, Dissolution



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15th IPSC Proceeding

Synthesis and Antiplatelet Aggregation Activity of Novel N-Alkylatedindolehydrazones

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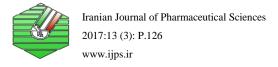
Introduction: Platelets have an important role in cardiovascular integrity and regulating the bleeding process by blood-clot formation (1). Arachidonic acid(AA) and ADP are endogenous mediators that play a role on platelet aggregation. It has been shown that aggregation of platelets plays significant role in pathogenesis of atherothrombosis (2). In our previous studies, hydrazone derivatives exhibited a promising inhibition of AA-induced platelet aggregation with IC_{50} values comparable to that of indomethacin. With this background, in this study we synthesized a new series of N-1 substituted indoles possess various phenylhydrazine derivatives.

Methods: To prepare the derivatives, there were two steps of synthesis. First, Indole 3-carboxaldehyde was reacted with different Alkyl halides (CH₃I, C₂H₅I, C₃H₇Cl) to access the intermediates. Second,the intermediates was reacted with substituted phenylhydrazines to obtain final derivatives. Structure of the synthesized compounds were confirmed by different spectral methods such as MASS, H-NMR, and IR spectroscopy and their antiplatelet aggregation activity were evaluated on human platelet aggregation induced by arachidonic acid and ADP using light transmission aggregometry.

Results: Most Compounds exhibited remarkable activity against AA-induced platelet aggregation with IC₅₀ values comparable to that of Indomethacin and no activity against ADP-induced platelet aggregation.

Conclusion: Analysis of structure–activity relationship shows that with increased bulk of the substituents at indole N–1, larger than ethyl, the antiplatelet activity is reduced, hence suggesting that steric hindrance at this position plays a major role in the activity of the tested compounds.

Keywords: Synthesis, Indole, Hydrazone, Antiplatelet aggregation activity



15th IPSC Proceeding

Spiro-2-Aminopyrimidinone Derivatives as Novel Dipeptidyl Peptidase-4 Inhibitors; Molecular Modeling, Design and Synthesis

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Abstract

Introduction: Dipeptidyl peptidase-4 is involved in degradation of insulin-sensitive hormone named GLP-1 which

is a potent stimulator of insulin release and inhibitor of glucagon release from pancreatic cells after food intake,

Therefore DPP-4 inhibitors has emerged as a new therapeutic agent to the treatment of type 2 diabetes. Sitagliptin is

a drug of this group which was approved by FDA for treatment of type 2 diabetes. We designed and synthesized a

series of spiro-2-amino pyrimidinone derivatives that inhibit DPP-4 with acceptable docking results.

Methods: Preparation of compounds was started from 4-benzylpiperidinone, Ethyl cyanoacetate and Sodium

hydride stirred in room temperature with absolute Ethanol as solvent for 15 minutes then Guanidine carbonate was

added and stirred in room temperature for 4 hours to form the spiro-aminopyrimidinone structure as an intermediate,

in another pot, Benzyl derivatives (such as benzylamine) in dichloromethane was treated with dropwise addition of

Chloroacetyl chloride and stirred for 30 minutes to form another reagent, after its completion and work up, the solid

product was added to the intermediate solution after its completion, and was stirred in room temperature for 4 more

hours to give final products.

Results: The designed compounds were synthesized and structurally confirmed by IR, NMR and Mass spectra.

These structures were designed based on the SAR of the selective DPP₄ inhibitor and results of docking study show

favorable affinity for active site.

Conclusion: Docking results of these novel series of spiro-2-aminopyrimidinone compounds showed excellent

binding with active site of DPP-4 enzyme followed by high potency of these compounds. Molecular modeling

showed that mostly heterocycle rings are needed for enzyme binding and cyano group helps the molecule to bond

with the hydroxyl group of serine in catalytic site of enzyme and improves its potency.

Keywords: Synthesis, Anti-diabetes activity, DPP-4 inhibitors, Spiro-2-aminopyrimidinone.



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15th IPSC Proceeding

Pluronic Gels for Otic Drug Delivery of Benzocaine

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Abstract

Introduction: Benzocaine is a local anesthetic. Benzocaine relieve pressure, reduce inflammation and congestion,

and to alleviate pain and discomfort in acute otitis media.

The objective of the present work was to formulate and evaluate mucoadhesive in situ otic gels of benzocaine.

Benzocaine relieve pressure, reduce inflammation and congestion, and to alleviate pain and discomfort in acute otitis

media.

Methods: A total of 15 formulations of in situ nasal gels were prepared using different polymeric concentrations of

poloxamer 407.

Results: All formulations had a clear appearance in the sol form, with gelling temperature of the otic gels ranging

 32.1 ± 1.67 . The gelling time of all the formulations varied from 2.0 ± 0.21 to 5 ± 0.22 min; the drug content was

>80-90%. The pH of the formulations ranged between 5.6 \pm 0.04 and 6.0 \pm 0.03, i.e. no mucosal irritation is

expected as the pH was in the acceptable range. Mucoadhesive strength was adequate (17-35 g/cm2) to provide

prolonged adhesion. In vitro drug release studies showed that the prepared formulations could release the drug for

up to 24 h with all of them following peppas kinetics. The DSC analysis revealed that there was no drug-polymer

interaction.

Conclusion: From these findings it can be concluded that in situ otic gels may be potential drug delivery systems for

benzocaine to overcome first-pass metabolism and thereby to improve the bioavailability.

Keywords: In situ nasal gel, benzocaine, poloxamer 407, Gelling temperature.



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15th IPSC Proceeding

Taste Masking and Characterization of Guaifenisen by Emulsion Technique

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Introduction: Guaifenesin is an expectorant. It helps loosen congestion in your chest and throat, making it easier to cough out through your mouth but it is very bitter and as yet no mouth dissolving/disintegrating taste-masked preparation that might be useful in pediatric and geriatric patients is available in the market. In the present investigation, bitter taste of guaifenesin is masked by preparing microparticles of drug with certain hydrophilic polymers such as Eudragit E and polyvinyl alcohol by using emulsion solvent diffusion method.

Methods: Microparticles of guaifenesin and polymer were prepared in ratios of 1:5, 1:7.5 and 1:10 by emulsification technique. At first, the drug and polymer were co-dissolved in an organic solvent mixture that was composed of ethanol, acetone (goodsolvent) and dichloromethane (bridging liquid). The drug solution was slowly injected into the external water phase (poor solvent) under agitating. Morphology and physicochemical characterization of the prepared guaifenesin microparticles was studied by drug loading, loading efficiency, yield, particle size, X-ray Diffraction (XRD), Fourier Transform Infrared Spectroscopy (FTIR) and differential scanning calorimetry (DSC). The *in vitro* release studies were performed in pH 1.2.

Results: The percentage yield of microparticles was found to be 25-50%. The encapsulation efficiency was found to be 40-72%. The *in vitro* drug release was found to be 60-90% in 0.1N HCL solution. The bitter threshold of guaifenesin recognized by the volunteers (Four male and four female) was between 25-35 μ g/ml drug.

Conclusions: The results indicate that the microsphere formulation can be a promising drug carrier for masking the bitter taste of guaifenesin.

Key words: guaifenesin, emulsion, diffusion, masking, bitter.



15th IPSC Proceeding

Gastroretentive Hydrodynamically Balanced Systems of Diazepam: *In Vitro*Evaluation

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Introduction: The objective of the present study was to develop a hydrodynamically balanced system of diazepam as a bilayer floating tablet. Various grades of low-density polymers were used for the formulation of this system. They were prepared by physical blending of diazepam and the polymers in varying ratios. The formulation was optimized on the basis of *in vitro* buoyancy and *in vitro* release in simulated fed state gastric fluid (pH 1.2). Effect of various release modifiers was studied to ensure the delivery of drug from the HBS capsules over a prolonged period. Tablets prepared with HPMC K4M and ethyl cellulose gave the best *in vitro* percentage release and were taken as the optimized formulation. Gastroretentive floating systems as hydrodynamically balanced systems (HBSs) are able to improve absorption of drugs especially those that are absorbed from stomach and small intestine. HBSs contain drug with gel-forming hydrocolloids meant to remain buoyant in the stomach content.

Methods: Hydrodynamically balanced systems (HBSs) of diazepam were prepared using lactose, HPMC K4M, PVP K 30, and avicel, which may increase the mean residence time in the gastrointestinal tract, and may be able to provide maximum drug at the site of absorption to improve oral bioavailability. Various grades of low-density polymers were used for the formulation of this system.

Results: All these formulated HBS were floated well over 6 h with no floating lag time. They also showed sustained drug release over 8 h. Time for 50% release of diazepam was within the range, 0.5-1 h. The *in vitro* drug release from these HBS capsules was dependent on HPMC K4M, PVP K 30, and avicel content.

Conclusions: the combination of two buoyancy mechanisms and gas-generating systems with swellable polymers would be beneficial for obtaining an appropriate floating lag time and duration of buoyancy, which in turn guarantees optimum efficiency of the pharmaceutical dosage form.

Keywords: buoyancy, drug release, hydrodynamically balanced systems, diazepam.



15th IPSC Proceeding

Preparation and *In Vitro* Evaluation of Bilayered Floating Tablets of Diazepam

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Abstract

Introduction: Celecoxib a non-steroidal anti-inflammatory drug (NSAID), is the first selective cyclooxygenase-2

inhibitor used in the treatment of osteoarthritis and rheumatoid arthritis in adult patients. This study was performed

to design bilayer floating tablets of celecoxib to give immediate and sustained release. Bilayer floating tablets

comprised two layers, i.e immediate release and controlled release layers.

Methods: The immediate release layer comprised sodium starch glycollate as a super disintegrant and the sustained

release layer comprised HPMC K100M and microcrystalline cellulose as the release retarding polymers which may

increase the mean residence time in the gastrointestinal tract, and may be able to provide maximum drug at the site

of absorption to improve oral bioavailability. Sodium bicarbonate was used as a gas generating agent. Direct

compression method was used for formulation of the bilayer tablets. Bilayer floating tablets was carried out to study

the in vitro buoyancy of the optimized formulation.

Results: All formulations floated for more than 8 h. More than 50% of celecoxib was released within 30 min.

HPMC K100M and microcrystalline cellulose sustained retarded the release of drug from the controlled release

layer for 8 h. The optimized formulation was found to be buoyant for 8 h in stomach. Therefore, biphasic drug

release pattern was successfully achieved through the formulation of floating bilayer tablets in this study.

Conclusion: Bilayer floating tablets (gastroretentive) oral drug delivery system of celecoxib prepared may be an

effective alternative to conventional oral tablets.

Key words: bilayer, floating, tablets, gasteroretentive, celecoxib.



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15th IPSC Proceeding

Effect of Lyophilized Technique on the Physicochemical Characterizations and Release Orally Disintegrating Tablets of Isosorbid Dinitrate

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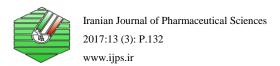
Introduction: Isosorbid dinitrate is a nitrate that is used as a vasodilator in the patients with angina. It is used in treatment of angina, prevention of heart pain and heart attack. Orally disintegrating tablets (ODTs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take it water. Drug dissolution and absorption as well as onset of clinical effect and drug bioavailability may be significantly greater than those observed from conventional dosage forms (25%).

Methods: The orally disintegrating tablets (ODTs) were prepared by freeze-drying an aqueous dispersion of isosorbide dinitrate containing a matrix former (gelatin), a sugar alcohol (mannitol), and a collapse protectant (glycerin). In addition, different disintegration accelerators were tested (sodium lauryl sulfate, tween and polyethylen glycol).

Results: Results obtained from disintegration and dissolution studies showed that lyophilized ODTs disintegrated within few seconds (3-21 sec) and showed significantly faster dissolution rate of isosorbide dinitrate compared to the plain powder drug and isosorbide dinitrate in commercially available immediate release tablet.

Conclusion: Isosorbide dinitrate ODT as a drug delivery system ensures less irritation of the GI tract and probably reduced hepatic side effects that may result either from the reduction of the required dose due to increased bioavailability or from the reduction of the dose reaching the liver due to bypassing the liver especially with increased exposure. Because ODT need not be swallowed, it could be convenient of pediatric and geriatric patients and may replace.

Key Words: Isosorbide dinitrate, Orally, Disintegrating, Lyophilized, Tablet.



15th IPSC Proceeding

Preparation and Physicochemical Characterization of Crystalline Tadalafil Nanoparticles through the Anti-Solvent Precipitation-Ultrasonication Technique: Optimization by Experimental Design

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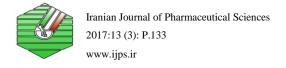
Introduction: Nanocrystals of Tadalafil, a poorly water-soluble drug, were successfully prepared by antisolvent precipitation-ultrasonication method for improving the solubility and dissolution rate.

Methods: The effective hydrophilic polymers and surfactants were screened for their abilities to produce nano particle size. Central Composite Design was utilized to evaluate the formulation factors that affect the size of nanosuspensions. After achieving the optimum condition for preparation, Tadalafil nanoparticles were characterized through SEM, FTIR, XRPD, DSC, HPLC and dissolution testing.

Results: Tween® 80 was chosen as an efficient surfactant in inhibition of aggregation. The optimum conditions were as follows: the drug concentration of 10 mg/ml, stabilizer concentration of 0.236 %w/v and antisolvent/solvent volume ratio of 15:1. Under optimum conditions, Tadalafil nanocrystals with a mean particle size of 358.47 nm were obtained. The analysis indicated that no substantial crystalline change was found in nanocrystals and their dissolution properties were significantly enhanced (3.46 fold) as compared to raw Tadalafil.

Conclusion: It was concluded that the antisolvent precipitation-ultrasonication technique could be a simple and useful technique to prepare poorly water-soluble drug particles with reduction in particle size, a narrow particle size distribution and enhanced dissolution properties.

Keywords: Tadalafil, antisolvent precipitation-ultrasonication method, nanocrystals, dissolution enhancement.



15th IPSC Proceeding

The Formulation of Anti-Candida Vaginal Suppository Containing *Trachyspermumammi* Essentialoil**

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Introduction: Nowadays antibiotical resistance is going to be an important concern of medical science, so it is essential to looking for suitable replacements such as natural products. In this study we focused on the yeast *Candida albicans* that is known as the most common vaginal pathogen in women.

Regarding the significant antimicrobial effect of *Trachyspermumammi* essential oil against *Candida albicans*, we were encouraged to formulate vaginal suppository containing *T. ammi* essential oil and invitro evaluate the physicochemical properties of the final formulation.

Methods: GC-MS was used to identify the potentially responsible oil compounds for observed property.

Six formulations of the suppositories were prepared by the molding method. Formulation series A (including A_1,A_2,A_3 and A_4) contained glycerinated gelatin and formulation series B (including B_1 and B_2) contained PEG 1000 and 4000 bases. The prepared suppositories were characterized for physicochemical properties.

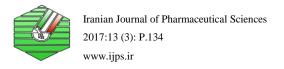
Disc diffusion method was used to evaluate antimicrobial effects of the essential oil and the selected formulation.

Result: According to physicochemical characteristics; suppositories of formulation B_2 containing T. *ammi* essential oil with the base of PEG 1000 (95% w/w), PEG 4000 (4% w/w) and tween 20 (1% w/w); were found to be satisfactory. T. *ammi* essential oil was found to be effective against C. *albicans* by the MIC value of 4 mg/ml while the formulation B_2 showed such effect by the MIC value of 25 mg/ml.

It was suggested that antimicrobial activities were caused by Thymol, ρ -Cymene and γ -Terpinene; which were identified as the major components of the studied oil.

Conclusion: According to the results, the most acceptable formulation of vaginal suppository containing T. *ammi*essential oil that provided the best antimicrobial effect against C.albicans was formulation B_2 .

Keywords: Trachyspermumammi - essential oil - vaginal suppository - antimicrobial - Candida albicans



15th IPSC Proceeding

Influence of the Modification of Mesoporous Silica

For Analysis of Repaglinide as Hydrophobic Model Drug by HPLC

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Introduction: Mesoporous silica particles (MSPs), such as MCM-41 (Mobil Catalytic Material Number 41), and SBA-15 (Santa Barbara Amorphous-15), are solid materials, which are comprised of a honeycomb-like porous structure with hundreds of empty channels (mesopores) that are able to absorb/encapsulate relatively large amounts of bioactive molecules. Their unique properties, such as high surface area, large pore volume, tunable pore size with a narrow distribution, and good chemical and thermal stability of these materials, make them potentially suitable for various applications in many fields of technology such as chemical and pharmaceutical sciences. In general, the surface area of a porous material is higher than the surface of an analogous non-porous material. Thereby the internal surface area is usually much higher than the one contributed by the external surface. The ease of introducing various organic functional groups, either through covalent bonding or electrostatic interactions, provides high level of versatility and many mechanized features to the mesoporous silica materials.

Methods: SBA-15 was prepared according to a known procedure with TEOS (tetraethyl orthosilicate) and pluronic P123 as silicon and surfactant sources, respectively. The surface modification of SBA-15 with methyl group (SBA-Me) was performed by methyltriethoxysilane in toluene reflux. The loading assays was implemented in ethanol solution of repaglinide (100ng/mL, 3mL) with 3 mg of the MSPs as carrier at ambient temperature.

Results: To investigate the enrichment efficiency of the microspheres, extraction conditions were optimized in the following work.

Under optimom conditions, our loading studies indicated that there was 27 and 71% loading efficiency in the presence of SBA-15 and SBA-Me as carrier. Therefore, the findings clearly showed the substitution of silanol groups with methyl groups had a positive effect on the loading efficiency (LE). This improvement in LE may be attributed to the hydrophobic interaction between the lipophilic drug repaglinide and the hydrophobic channels of SBA-15.

Conclusion: In summary, our present study confirmed that the surface functionalization of SBA-15 with menyl group caused to an improvement in LE of repaglinide as model hydrophobic drug.

Keywords: Loading efficiency, mesoporous silica materials, repaglinide, surface properties.



15th IPSC Proceeding

Reduction of Autophagy Markers Mediated Protective Effects of JNK Inhibitor and Bucladesine on Memory Deficit Induced By $A\beta$ in Rats

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Abstract

Introduction: Autophagy, the process of self-degradation of cellular components, has an important role in

neurodegenerative diseases, such as Alzheimer's disease. In this study, we investigated the effects of SP600125 as c-

Jun N-terminal kinase (JNK) inhibitor and bucladesine as a cyclic adenosine 3',5'-monophosphate (cAMP) analog

on spatial memory and expression of autophagic factors in Aβ-injected rats.

Methods: Male Wistar rats were used. Rats were randomly allocated into five groups as following: amyloid beta

(A β)-only group, A β + SP600125 (30 μ g/1 μ /side, n = 7) and/or bucladesine (100 μ M/1 μ l/side, n = 7), and the

normal control (vehicle only) group. The treatments were administered bilaterally to the CA1 sub-region of the

hippocampus stereotaxically. Spatial reference memory was performed using Morris Water Maze 21 days later. The

expression of authophagy markers (beclin1, Atg7, Atg12, and LC3 II/LC3 I) in the hippocampus was evaluated

using western blotting.

Results: Compared to the vehicle group, A β administration reduced spatial reference learning (P < 0.001) and

memory (P < 0.01) and upregulated the expression of beclin1, Atg7, Atg12, and LC3 II/I (P < 0.0001). Compare to

 $A\beta$ -only group, the administration of SP600125 and/or bucladesine improved spatial reference learning (P < 0.001)

and memory (P < 0.01). Compared to the A β -only group, the treatment with SP600125 and/or bucladesine also

reduced beclin1, Atg7, Atg12, and LC3 II/I (P < 0.0001) which was similar to amount of normal rats.

Conclusion: In summary, it seems that the improvement of spatial memory by SP600125 and/or bucladesine in Aβ-

injected rats is in relation with normalizing of autophagy to the physiologic level, possibly through neuroprotection

and/or neuroplasticity.

Keywords: Alzheimer disease; Amyloid beta (Aβ); Autophagy; Bucladesine; SP600125

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15th IPSC Proceeding

Evaluation of Pectin and Chitosan as Substituents for Excipients in the

Formulation of Dimenhydrinate Pellets

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Introduction: Pellets have advantages such as high absorption, high bioavailability and preventing dose dumping

(1, 2). Pectin and chitosan are polysaccharides which can be effective as substituents for excipients in the pellet

formulation regarding their natural and biodegradable characteristics and lower cost compared to the other excipients. The aim of this study was using pectin and chitosan in pellet formulation, and also to evaluate the

probable interactions of these polysaccharides with each other and also with drug in the pellet formulation.

Methods: Different formulations containing dimenhydrinate, microcrystalline cellulose (MCC), and various ratios of

chitosan: pectin were designed (Table 1). The pellets were prepared by extrusion-spheronization method.

Dissolution studies were carried out in HCl 0.1N and phosphate buffer (pH=6.8) using basket method (50rpm) at

37°C at 2 and 8 hrs, respectively. SEM¹, DSC² and FTIR³ analysis, porosity and density measurements and

MDT⁴calculations were also performed.

Results: All prepared formulations had acceptable sphericity. According to release test, the slowest release in acid

belonged to F1, having no pectin and chitosan, while F5, containing the most amount of chitosan with ammonium

groups that ionize in acid, had faster drug release than other formulations. Dissolution profiles in buffer showed that

formulation F1 exhibited the slowest drug release while F2, having the most amount of pectin with anionic groups

which dissociate in buffer, showed faster drug release compared to other formulations.

DSC and FTIR analysis presented no interactions between carboxyl group of pectin and ammonium group of

chitosan was observed.

Conclusion: Generally, formulations containing pectin and chitosan had faster release profiles compared to pellets

having only MCC, as excipients. Pectin and chitosan, as natural, biocompatible, low price and available

polysaccharides (3), can be suitable substituents for MCC in the formulation of dimenhydrinate pellets, while having

no interactions that effect drug release profiles.

Keywords: Dimenhydrinate- pectin- chitosan- pellet.



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Adverse Drug Reactions Reported to Isfahan Food and Drug Administration

in Spring and Summer of 2016: A Cross-Sectional Study in Isfahan, Iran

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Abstract

Introduction: Adverse drug reactions (ADRs) create costs and problems for health care system and seem as

important outcomes of patient care. So identification and assessment of ADRs to predict and prevent of them are

necessary (1, 2). In this study, we aimed to analysis the ADRs which reported to food and drug administration of

Isfahan University of Medical Sciences in spring and summer of 2016.

Methods: In this cross-sectional study, 197 sheets of ADR reported to Isfahan food and drug administration from 20

March to 21 September of 2016 were evaluate. We excluded errors in drug administration, not completed sheets,

and therapeutic failures. Results were statistically evaluated by SPSS20.0.

Results: The results of 197 reports showed the most complication were dermatologic (53.3%) then respiratory

reactions (10.7%). The most ADRs was made by the injectable forms of drugs (71.6%). And antibiotics were at the

top of list of drugs which caused problem (ceftriaxone=15.2%, vancomycin=13.2% & ciprofloxacin=6.1%). Women

were affected more than men (52.3%). The most group show ADR was between ages of 1-5 which was 18.3% of

patients. These ADRs were usually reported by nurses (76.1%) then physicians (10.2%), and just 3.6% of reporters

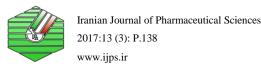
by pharmacists.

Conclusion: The injectable antibiotics were the biggest problem. Regarding the irrational prescribing in our country

which may lead to extra ADRs, more educational, managerial and regulatory strategies can help to reduce number of

these problems. This study also suggests that pharmacists should challenge more than past in reporting ADR.

Keywords: Adverse Drug Reaction, Toxicity, Drug Administration Routes, dosage form



15th IPSC Proceeding

Differences of Satisfaction between Care Quality among Patients and Health
Care Providers: A Cross-Sectional Study in Isfahan, Iran

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Abstract

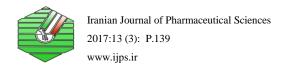
Introduction: Patient satisfaction is very important in health care system while there is a paucity of data in order. There is often a wide difference between perception of quality among patients and health care providers (1, 2). This study aimed to compare the satisfaction level between the patients and the health care providers from one of the main referral and university affiliated hospitals in Isfahan. The feedback would provide information that can be forwarded to the hospital administration to take necessary steps.

Methods: In this cross-sectional study a valid and reliable 16-item questionnaire in the form of Likert scale addressing various aspects of patient care was prepared. Data were collected from 40 patients and 35 staff of Seyedoshohada hospital during May 2016.Results were statistically evaluated using SPSS 20.0.The means and standard deviations were used to describe the overall assessment score of satisfaction. To compare the satisfaction score between two groups Mann-Whitney test was used (p<0.05).

Results: The alpha Chronbach coefficient was calculated 0.95, which is an acceptable reliability. According to patients' view, the most satisfying features of the hospital were willing of staff to help and quality of nursing services. The least satisfying features were inconvenience during scheduling of appointments, status of changing rooms and general cleanliness. Result of Mann-Whitney test showed significant difference between Patients and staff's opinions. In fact, staff overall satisfaction scores were not as good as the patient's opinions $(43.49\pm9.99 \text{ versus} 56.6\pm16.71)$.

Conclusion: The measurement of satisfaction is a key tool used to identify problems and this study highlighted some problems which should focus on the management of the hospital in order to improve the quality of service. By training the service providers and criticizing them according to customer's expectation, we can achieve to high level of satisfaction.

Keywords: Delivery of health care, Perception, Quality of health care, Personal satisfaction



15th IPSC Proceeding

Acute, Subchronic and Genotoxic Effects of Oral Ulmus *Minor Mill* 'S Gall: A Phytochemical and Toxicological Study

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Abstract

Introduction: *Ulmus minor Mill's* gall produces due to effects of *Eriosoma lanuginosum* Hartig but its phytochemical and toxic properties have not determined yet. This study aimed to identify the phytochemical composition and quantification of its main components, as well as it's acute and repeated dose oral toxicity in mice to determine its possible safe dose (NOAEL) for further applications as an anti-mutagenic agent on the basis of genotoxicity tests of present work.

Methods: Phytochemical analysis was performed via pre phytochemical tests(1) to determine the tannins, and sterol levels. *In vivo* studies performed on both genders of mice according to OECD 423 and OECD 407 guidelines(2). Ames mutagenicity assessment was performed, on TA100 and YG1029 strains of Salmonella Typhymorium for anti-mutagenic test.

Results: Due to Phytochemical study on hydro alcoholic extract, the levels of condensed tannin and sterol were determined noticeable in comparison all previous studies. Although in acute toxicity study, LD₅₀ was determined in levels upper than 2000 mg/kg in both genders and this extract was classified as a practical non toxic agent according to GHS classification. In repeated dose, 28 days, oral toxicity study in doses of 125 mg/kg, different organ toxicities were observed including significant hypokalemia, hyperuremia and hyperglycemia, in female animals. Mutagenicity assessments by Ames method on different strains didn't show sufficient evidence for its animutagenic potentials.

Conclusion: This study clarified for the first time that *Ulmus minor's* galls contains noticeable amounts of condensed tannin according to the quantification tests. Histopathological evidences including ischemic injuries in neural tissues and several necrosis in essential organs have emphasized the necessity of further studies on its possible mechanisms of toxicity .We don't recommend this gall for any clinical applications according to present toxic effects.

Keywords: Ulmus - phytochemistry - oral toxicity - Mutagenicity

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