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# The Abstract Book of

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# Oral Peresentation

O1

## Development and characterization of bilayered tablets of diazepam for oral drug delivery: design, optimization, and *in vitro* evaluation

*Mitra Alami-Milani[1,2], Sara Salatin[1,2], Mitra Jelvehgari[2,3]*

[1]Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran.
[2]Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.
[3]Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

corresponding author: Mitra Jelvehgari

Corresponding author Email: mjelvehgari@gmail.com, jelvehgri@tbzmed.ac.ir

Introduction: Oral bioavailability of drugs can be limited by short residence time of the pharmaceutical formulations in the upper part of the gastrointestinal tract (GIT) (1). The rate of gastric emptying plays a critical role in the dynamics of drug absorption and may lead to unpredictable bioavailability. One of the novel methods to extend the residence time of drugs in the upper part of the GIT is the use of floating bilayered tablets. This study was performed to design floating bilayered tablets of diazepam comprising two layers, i.e immediate and controlled release layers. Material and methods: Immediate and controlled release tablets were prepared by a direct compression method using sodium starch glycolate (SSG), polyvinyl pyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC), and microcrystalline cellulose (MCC). The tablets were evaluated for their thickness, hardness, erosion, weight, drug content, floating capacity, and in vitro release pattern. Optimized formulations of the immediate and controlled release tablets were used to develop the immediate and controlled release layers of the floating bilayered tablets.Results: All the prepared tablets exhibited desirable physicochemical properties. The weight, thickness, hardness, erosion, and drug content of the immediate release tablets were found to be 146.9-150.1 mg, 2.86-3.04 mm, 4.48-8.37 kg/cm², 0.93-1.43%, and 85.73-109.83%, respectively. The tablets showed a low disintegration time between 5-186 seconds. The weight, thickness, hardness, erosion, and drug content of the controlled release tablets were observed to be 296.4-299.3 mg, 2.75-2.84 mm, 5.43-7.93 kg/cm², 0.26-1.17%, and 91.84-122.85%, respectively. The weight, thickness, hardness, erosion, and drug content of the optimized bilayered formulation were determined to be 448.1 mg, 4.23 mm, 9.57 kg/cm², 0.43%, and 72%, respectively. This formulation was found to be buoyant for 8 h on the simulated gastric fluid. More than 90% of diazepam was released from the immediate release layer within 30 min. On the other hand, HPMC and MCC sustained the release of diazepam from the controlled release layer for 8 h. Discussion: The variation observed in the thickness values was related to different composition of the tablets. Marginal variation in the hardness values could be related to the random causes. The immediate release tablets, containing the highest amount of SSG, showed shorter disintegration time. SSG, as a disintegrant, causes a rapid break-up of solid dosage forms. Therefore, the disintegration time is decreased with increasing in the amount of SSG (2). Better swelling and floating capacities were found in the tablets containing higher amounts of HPMC. Higher concentration of HPMC probably limits the access of ways towards the tablet matrix (3) . Due to having an immediate release layer in their composition, the bilayered tablets exhibited faster release than the commercial tablet. On the other hand, existence of the controlled release layer caused slower release of the drug from the bilayered tablets than the commercial tablet.Conclusion: It can be concluded that floating bilayered tablets of diazepam may be able to extend the residence time of drug at the site of absorption to improve its oral bioavailability.

O2

## Antihyperlipidemic and Antioxidant Effects of Ethanol Extract of Sargassum angustifolium in Dexamethasone-Induced Dyslipidemic Rats

*Saeed Bazvand[1], Leila Safaeian[1*], Afsaneh Yegdaneh[2], Mahnaz Halvaei-Varnousfaderani[1]*

[1]Department of Pharmacology and Toxicology, Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Department of Pharmacognosy, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: Leila Safaeian.
Corresponding author Email: leila_safaeian@pharm.mui.ac.ir

Introduction: Recent data propose the beneficial antihyperlipidemic effects of several marine brown alga belonging to the genus *Sargassum*. In the current study, the effects of ethanol extract of *Sargassum angustifolium* were assessed on dexamethasone-induced dyslipidemia in rats.Material and Methods: The extract was prepared by maceration method and evaluated for total phenolic content using Folin-Ciocalteu method[1]. Dexamethasone as a potent member of glucocorticoids was used for induction of dyslipidemia in rats. It was injected subcutaneously (s.c.) at a dose of 10 mg/kg/day for 7 days [2]. Seven experimental groups of 6 rats were used as the following: Group 1 (normal control) received vehicle for 1 week; group 2 (extract control) treated only with 80 mg/kg *S. angustifolium* extract for 1 week; group 3 (dyslipidemic control) received dexamethasone (10 mg/kg/day, subcutaneously) for 1 week; groups 4-6 (test groups) received dexamethasone and simultaneously treated orally with 20, 40 or 80 mg/kg *S. angustifolium* extract[3] and group 7 (reference) received dexamethasone and atorvastatin (40 mg/kg, orally) for 1 week[4]. At the end of experiment, fasting blood glucose, lipid markers and malondialdehyde (MDA) levels were evaluated in serum specimens. Livers were weighed and processed for histopathological inspection. Results: The content of total phenolic was $87.21 \pm 2.4$ mg/g as gallic acid equivalent in dried ethanol extract. In the present study, dexamethasone-induced dyslipidemia was used as an animal model for estimation of potential effects of *S. angustifolium* ethanol extract on glucose and lipid profile. After 1 week exposure of rats to dexamethasone (10 mg/kg, s.c.), significant increase in serum fasting blood glucose ($p<0.05$), triglyceride ($p<0.001$), total cholesterol ($p<0.01$), LDL ($p<0.001$) and VLDL ($p<0.05$) levels and a notable decrease in HDL ($p<0.01$) level was observed compared to the normal control group. Treatment with *S. angustifolium* extract significantly reduced fasting blood sugar and atherogenic lipid markers. There was a reduction of 30.7% in blood glucose, 30.9% in triglycerides, 50.2% in total cholesterol and 59.5% in LDL level after 1 week administration of *S. angustifolium* extract at the dose of 80 mg/kg in rats. However, no significant effect was observed on HDL and VLDL levels.Discussion: Recent investigations has shown that some species of the genus *Sargassum* have beneficial cardiovascular properties, including lipid-lowering effects[5,6]. Our results also showed that treatment with *S. angustifolium* extract significantly decreased serum blood sugar,

triglycerides, total cholesterol, low-density lipoprotein-cholesterol (LDL) and MDA levels and also alleviated steatotic changes in liver tissues compared to the dexamethasone-induced dyslipidemic control group.Conclusion: Findings of the current study revealed anti-hyperglycemic, hypolipidemic and anti-lipid proxidative properties of *S. angustifolium* extract in an animal model of dyslipidemia.

## O3

## Preparation of *Hyssopus officinalis* mouthwash formulation and its effect on periodontal indexes in comparison with chlorhexidine mouthwash: a double-blind, randomized clinical trial

*Faezeh Bodaghabadi*[1], *Mohammad Hossein Hosseinzadeh*[1], *Emran Habibi*[2], *Hodis Ehsani*[3], and *Jafar Akbari*[4]

[1]Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[2]Assistant Professor of Pharmacognosy, Department of Pharmacognosy, School of Pharmacy, Pharmaceutical Sciences Research Center, Hemoglobinopathy Institute, Mazandaran University of Medical Sciences Research, Sari, Iran

[3]Assistant Professor of Periodontology, Department of Periodontics, School of Dentistry, Mazandaran University of Medical Sciences, Sari, Iran

[4]Professor of Pharmaceutics, Department of Pharmaceutics, School of Pharmacy, Traditional and Complementary Medicine Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: Faezeh Bodaghabadi

Corresponding author Email: fazibodaghabady@gmail.com

Introduction: Gingivitis means inflammation of the gums. The disease is characterized by symptoms such as increased volume, discoloration, and bleeding during probing. Microbial plaque is the main etiological factor in causing gingivitis. Chlorhexidine is one of the most effective mouthwashes available to treat this disease. Due to the negative effects of chemical mouthwashes and the history of using medicinal plants in dental treatments, attention is paid to the manufacture of herbal mouthwashes. Hyssopus (*Hyssopus officinalis*) from the mint family. Today, the antibacterial, antifungal, antioxidant, anti-diabetic, and anti-cancer effects of this plant have been studied. In this study, we aimed to evaluate the effectiveness of mouthwash containing *Hyssopus officinalis* on periodontal indices.Material and methods: the aerial parts of the *Hyssopus officinalis* plant were extracted by the maceration method. Also, the amount of total phenolic, total flavonoids, and tannin content. Also, the antioxidant properties were measured. In the study, 45 patients referred to Sari Dental School with gingivitis were treated with 2.5% herbal, chlorhexidine, and placebo mouthwashes. 2 weeks later, the plaque index, gingival index, bleeding on probing index, and stain index were examined.Results: The total phenolic, total flavonoid, tannin content, and antioxidant properties in *H. officinalis* hydroalcoholic extract is equal to 119.09±2.28 mg of gallic acid/g of extract, 45.71±3.25 mg of quercetin/g of extract, 65.63±4.54 mg of gallic acid/g of extract, and 18.64±0.05 µg/ml, respectively. At the beginning of the study, the amount of plaque index, gingivitis index, gingival bleeding index, and stain index were 1.59±0.34, 1.92±0.51, 0.69±0.22, and 1.91±1.02, respectively. Two weeks after using the mouthwash of *Hyssopus officinalis* extract, the amount of changes in plaque index, gingivitis, gingival bleeding, and staining were 1.11±0.40, 1.29±0.59, 0.29±0.25, and 1.55±0.68, respectively.Discussion: Many studies have been published on the effects of plant compounds in improving gingivitis indices, and it seems that these effects are due to the presence of phenolic and flavonoid compounds and their antioxidant properties. The results showed that *H. officinalis* extract has good antioxidant properties and phenolic and flavonoid compounds. After two weeks of treatment, a mouthwash of hydroalcoholic extract of *H. officinalis* reduced the plaque index, gingival index, bleeding on probing index, and stain index significantly (P <0.05). However, the improvement of these factors during two weeks of treatment was not significant compared to the placebo group (P> 0.05).Conclusions: Despite the richness of *H. officinalis* extract from phenolic, flavonoid compounds, and its appropriate antioxidant properties, *H. officinalis* mouthwash could not significantly reduce gingivitis indexes compared to the control group.

## O4

## Identification of new drug targets in glioblastoma through a systems biology approach

*Mohammad Javad Taghipour [1,2], Mohammad Kashkooli [3], Younes Ghasemi [1,2], and Manica Negahdaripour [1,2]*

[1]Department of Pharmaceutical Biotechnology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Manica Negahdaripour

Corresponding author Email: negahdaripour@sums.ac.ir

Introduction: Glioblastoma multiform (GBM) is a type of brain tumor and the most malignant form of glioma and a rare disease. GBM could invade to nearby tissues, and because of its location in brain, it causes symptoms such as vomiting, loss of memory, and seizures. Patients' survival rate is about 14-15 months. Currently, the gold standard for GBM treatment is surgery, radiotherapy, and temozolomide. Some new small molecules are also suggested including vorniostat, chaetocinchaetocin, choloroquine, and zebularine. However, better understanding of this disease is necessary to find the most important pathways for drug targeting [1]. Systems biology is a way to understand and analyze complex systems, which could produce valuable results by analyzing the data obtained via high-throughput technologies [2].The aim of this study is to Identify new drug targets in GBM using a systems biology approach.Methods: Glioblastoma gene expression dataset, GSE108474 (n=190 glioblastoma, n=7 normal) was downloaded from Gene Expression Omnibus (GEO). Network of protein-protein interaction was constructed and visualized using online tools, and its parameters were determined. Modularity of network was calculated by Gephi v0.9.2. Gene enrichment analysis was done on hub genes and modules using ENRICHR, and hub pathways were discovered. Survival analysis was also done, and hub genes with significant effect on survival rate were chosen. Non-coding RNAs were identified. Long non-coding RNAs interaction with coding RNAs were found using RNA interactome database. Coding- and non-coding interaction network was constructed by Gephi v0.92. Finally, the antagonist compounds of hub genes were downloaded from DrugBank using TargetMine modules.Results: P53 (tumor protein p53), MYC (MYC proto-oncogene), EGFR (epidermal growth factor receptor), CTNNB1 (catenin beta1), CCND1 (cyclin D1), and CASP3 (caspase3) were found as hub genes. Pathways in cancer, ribosome, spliceosome, proteasome, protein processing in endoplasmic reticulum, and nucleotide excision repair were found as hub pathways.

The survival rate analysis showed effectiveness of targeting the over-expressed hub genes. Minocycline, dalteparin, fostamatinib, captopril, and carfilzomib were found as effective antagonists against the target hub genes.Discussion: In this study, the genome-scale metabolic model of pathways in glioblastoma cancer was reconstructed and hypergraph clustering algorithms were then investigated based on stoichiometric matrix scattering. Finally, the effect of drugs on the metabolism was found to determine the change in the tumor biomass. Several small molecules were predicted to help in antagonizing the hub genes with pathogenic over-expression. Dalteparin was previously reported to inhibit angiogenesis in GBM, which is accordance with our finding about VEGFA (vascular endothelial growth factor A) targeting by dalteparin [3]. Captopril was also found effective in GBM treatment by inhibition of tumor cell migration [4]. It is highly recommended to investigate the effect of fostamatinib and other repurposed medications on glioblastoma.Conclusions: Here, relations of GBM patients' survival rates with over- or under-expression of some hub genes were detected, which could help in drug repositioning and designing. Validating the anti-tumor effects of the discovered small molecules and their mechanism of action in glioblastoma tumor cells through future studies is recommended.

## O5

## Decreasing the immunogenicity of streptokinase via point mutation, an in-silico approach

*Mohammad Hadidi[1], Sorush Hajizadeh[1], Mohammad Javad Raee[1]*

[1]Center for Nanotechnology in Drug Delivery, Shiraz University of Medical Sciences, Shiraz, Iran.

Corresponding Author: M.J. Raee

Corresponding author Email: raeem@sums.ac.ir

Introduction: Immunogenicity of therapeutic proteins is one of the main challenges in disease treatments. Streptokinase is an important enzyme for breaking down clots in some cases of myocardial infarction, pulmonary embolism, and arterial thromboembolism. Using this medication sometimes leads to undesirable side effects such as immunogenic or allergic responses. As Streptokinase is a bacterial product, the body has the ability to build up an immunity to it. Therefore, it is recommended that this medication should not be used again after four days from the first administration, as it can cause an allergic reaction. (1) Many attempts have been done by researchers to optimize this enzyme. In recent years, bioinformatics studies had become routine to modify or generate new molecules for better characteristics. (2,3) In the current study we have used bioinformatics tools to modify the streptokinase enzyme with higher stability and lower antigenicity.Materials & Methods: The present study was aimed at modification of streptokinase to achieve a convenient enzyme for clinical purposes. We have conducted several in-silico mutations in enzyme sequence and made a library of mutated sequences conducted several in-silico mutations in enzyme sequence, then various analyses were conducted to choose the best candidate of minimum immunogenicity. We have evaluated several properties of mutated sequences using bioinformatics tools such as Primary sequence analysis Secondary and tertiary structure prediction and validation, Localizing and quantifying the energetic frustration and Immunoinformatics assays.Results: According to homology modeling, simulation and several validation results, modified streptokinase with mutation at Asp268Val and Glu272Phe was chosen as the best candidate of lower antigenicity. Discussion: In this study, mutants of streptokinase were designed to decrease the immunogenicity. The mutations were selected based on preserving functional moieties and conformational stability. The results suggested that the strategy of mutating surface residues reduced protein immunogenicity while maintaining the structure and function of it.Conclusion: In-silico approaches and can significantly accelerate the drug discovery and modification processes. This approach can be used to screen suitable mutants via point mutation for reducing immunogenicity of therapeutic proteins.

## O6

## Protective effect of aspirin and gentisic acid on the acrylamide-induced neurotoxicity by inhibiting apoptosis and autophagy

*Yasaman Hosseinzadeh[1], Mahboobeh Ghasemzadeh Rahbardar[2], Soghra Mehri[2,3], Bibi Marjan Razavi [4,3*], Hossein Hosseinzadeh [2,3]*

[1]School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[2]Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

[3]Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[4]Targeted Drug Delivery Research Center, Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Correspondence Author:Bibi Marjan Razavi, Hossein Hosseinzadeh

Corresponding author Email: razavimr@mums.ac.ir , hosseinzadehh@mums.ac.ir

Objective: Acrylamide (ACR) is one of the most toxic agents in humans and animals, and has several industrial applications. Gentisic acid, an aspirin metabolite, has antioxidant activity. Therefore, the present study investigated the probable protective effect of aspirin and gentisic acid on ACR-induced neurotoxicity in PC12 cells and rats.Materials and methods: The MTT test was used to assess the effects of aspirin and gentisic acid on ACR toxicity. Male Wistar rats were randomly divided into 11 groups: 1. Control group, 2. ACR (50 mg/kg, 11 days, i.p.), 3-5. ACR+aspirin (25, 50, 75 mg/kg, 11 days, p.o.), 6-8. ACR+gentisic acid (25, 50, 75 mg/kg, 11 days, p.o.) 9. ACR+vitamin E (200 mg/kg, every other day, i.p.) 10. Aspirin (100 mg/kg, 11 days, p.o.) 11. Gentisic acid (100 mg/kg, 11 days, p.o.). Behavioral tests were assessed on the final day of the study. In brain tissue, malondialdehyde (MDA), glutathione (GSH), cleaved-caspase-3, and microtubule-associated protein 1A/1B-light chain 3 (LC3) protein levels were evaluated.Results: When compared to the ACR group, *in vitro* experiments revealed that aspirin (2.5, 5 µM) and gentisic acid (2.5 µM) significantly enhanced cell viability. In comparison to the control group, ACR induced severe motor impairment, elevated MDA, cleaved-caspase-3, LC3 II/I ratio, and decreased GSH levels in brain tissue. ACR-induced changes were significantly reversed by aspirin and gentisic acid (25 mg/kg).Conclusion: Oxidative stress, apoptosis, and autophagy have important roles in the neurotoxicity of ACR. Aspirin and gentisic acid significantly reduced ACR-induced toxicity by the inhibition of mentioned mechanisms.

## O7

## A simple, fast, sensitive and validated method for determination of plasma concentrations of amiodarone for in vivo studies

*Farnaz Khaleseh[1,2,3],Mohammad Barzegar-Jalali[4], Parvin Zakeri-Milani[5], Zahra Karami[6,7], Mohammad Reza Saghatchi Zanjani[6,7], Hadi Valizadeh [8]*

[1]Student Research Committee, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Department of Pharmaceutics, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

[3]Pharmaceutical sciences research center, Health Institute and School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

[4]Drug Applied Research Center and Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.

[5]Liver and Gastrointestinal Diseases Research Center and Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

[6]Department of Pharmaceutical Nanotechnology, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

[7]Pharmaceutical Nanotechnology Research Center, Zanjan University of Medical Sciences, Zanjan, Iran

[8]Research Center for Pharmaceutical Nanotechnology, and Department of Pharmaceutics, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.

Corresponding author: Hadi Valizadeh

Corresponding author Email: valizadehh@gmail.com

Introduction: Amiodarone is an antiarrhythmic drug which is administered for ventricular and supraventricular arrhythmias with a wide range of administered doses. When the dose is 3mg/kg, plasma concentration of drug is very low at final hours of drug detection follow up. So validation of a sensitive method with low LOD and LOQ is important for pharmacokinetic studies. A validated and rapid method for quantification of plasma concentrations of amiodarone in rats is reported in the present study.Methods: The method is HPLC combined with UV detection. Different plasma sample preparation methods have been evaluated and the one with higher recovery ratio was selected for the rest of study. The plasma sample preparation is simple protein precipitation by acetonitrile and zinc sulfate. The chromatographic separation is conducted on RP-chromolith speed rod endcapped column and mobile phase consisted of acetonitrile:distilled water adjusted to pH 4 by formic acid (60:40). The method was evaluated for in vivo pharmacokinetic studies in rat after iv administration of amiodarone.Results: The method is validated in the range of 10-5000 ng/ml plasma concentrations and the linearity was acceptable with the $r^2$, mean slope and intercept of 0.99, 630.62, 16.03, respectively. Different method validation parameters including precision, accuracy and system suitability were in the acceptable range. The pharmacokinetic parameters consisted of AUC0-∞, t1/2, Vd and clearance after 6 mg/kg iv bolus injection were 9868.059 (ng.h/ml), 74.011 (hr), 1615.737 (ml) and 0.022 (L/hr), respectively.Discussion: The method sensitivity is comparable to those by LC/MS/MS detection which the sensitivity is much higher than HPLC/UV methods routinely. Also the least volume of plasma (100µl) is enough for evaluation although previous studies were conducted by higher plasma volumes as 1 ml. The advantageous of lower volume sampling is that the number of serial sampling can be increased so the follow up can be during the longer period of time especially for invivo studies in animals with low total blood volume.Conclusions: According to the results, the present method is a useful, fast, simple, time and money saving HPLC/UV method for quantification of low concentrations of amiodarone in rat plasma and can be applied for pharmacokinetic studies.

O8

## Role of pentoxifylline in patients with primary hypertension: A randomized clinical trial

*Elnaz Khani[1], Taher Entezari-Maleki[2]*

[1]Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Department of Clinical Pharmacy, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

Corresponding author: Taher Entezari-Maleki

Corresponding author Email: tentezari@gmail.com

Introduction: Hypertension (HTN) is a common disease that affects approximately 1 billion individuals worldwide and causes 7.1 million deaths annually. Considering the crucial role of blood viscosity (BV) in the regulation of blood pressure (BP) and hemorheological effects of pentoxifylline (PTX), we assessed the PTX role in patients with stage 1 hypertension.Material and methods: In this randomized clinical trial, 62 patients with stage 1 hypertension were entered. The intervention group (n=30) received 1200 mg PTX in three divided doses plus 25 mg captopril three times a day whereas, the control group (n=32) received only 75 mg captopril in three divided doses. Measurements of BP were done at baseline, first and second month after entering the study. Results: Comparison of the systolic BP in the intervention and the control groups showed no significant differences at baseline (150.4±6.03 vs.150.4±6.2, p=0.98), first (138.4 ±9.4 vs. 142.3 ±5.6, p=0.08) and second (134.6 ±8.9 vs. 137.4±6.0, P=0.20) months. Also, no significant difference was observed in the diastolic BP at baseline (91.7±3.9 vs. 92.0 ±3.7, p=0.84), first (85.5±5.1 vs. 86.9 ±3.8, p=0.27) and second (82.6 ±5.7 vs. 84.0 ±3.5, p=0.31) months.Discussion: Previously, several studies evaluated PTX on vascular disease and inflammation; for example, in 59 patients with type 2 diabetes and nephropathy, the effects of adding PTX to losartan on urine and serum parameters were evaluated during three months. It has been shown that in the losartan group, blood pressure was decreased more than in the PTX group. Of note, patients were normotensive in this research. (BP less than 140/90). Another study assessed the protective effects of PTX on retinopathy in 56 children with type 1 diabetes during six months, and it indicated that PTX did not have a significant effect on BP. The study population in this research had normal blood pressure. In a study by Plotnikov et al., it has been shown that in spontaneously hypertensive rats at the early stages of HTN, adding PTX to captopril could significantly improve the anti-hypertensive activity of captopril due to PTX effects in reducing BV.Our study has several strong points in evaluating the effect of PTX on HTN; first, unlike previous studies, it assessed the efficacy of PTX on the early stage of HTN (between 140/90 to 159/99). Second, patients in this study received just one type of anti-hypertensive agent so that analyzing the effect of PTX on BP became more reliable. Third, patients with secondary HTN did not enter this study. Fourth, this study directly evaluated the PTX effect on HTN after one and two months. Lastly, in the current study, all blood pressure measurements were according to AHA guidelines; however, the previous studies didn't mention the blood pressure measurement method. The results of the present study were in accordance with previous research; however, more studies are required.Conclusions: According to the results of our study, adding PTX

to captopril was not associated with BP reduction in patients with stage 1 hypertension.

## O9

## Evaluation of effect of *Satureja Khuzestanica Jamzad* essential oil on spleen toxicity induced by chlorpyrifos and diazinon in male Wistar rats

*Arefeh Khani[1,2,3], Zahra Haghighatian[4], Marzieh Rashidipour[4], Fatemeh Dehghan[1,2,3], Javad Ghasemian Yadegari[2] , Javad Khalili Fard[1,4]*

[1]Department of Pharmacology and Toxicology , Faculty of Pharmacy, Lorestan University of Medical Sciences, Khorramabad , Iran

[2]Department of Pharmacognosy, Faculty of Pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran

[3]Student Research Committee, Faculty of Pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran

[4]Razi Herbal Medicines Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran

Corresponding authors: Javad Khalili Fard, Javad Ghasemian Yadegari

Corresponding author Email: javad.khalilifard@gmail.com, jvd.ghasemian@gmail.com

Introduction: Organophosphates like chlorpyrifos and diazinon arepesticides inhibiting acetylcholine esterase enzyme. Despite their widespread use, chlorpyrifos and diazinon that, can increase oxidative stress and therefore cause damage to certain tissues such as spleen. *Satureja khuzestanica Jamzad* has antioxidant property and is effective against oxidative stress. Consequently, in this study, the effects of concurrent administration of *Satureja khuzestanica Jamzad* essential oil and these two toxicants on spleen injury induced by these compounds, were evaluated in male Wistar rats. Material and methods: Forty-two Wistar rats (weight: 180-220 Kg) was randomly divided into 6 groups. Group 1: control, group 2: *Satureja Khuzestanika Jamzad* essential oil, group 3: Dazinon (0.0002 mg/kg/day i.p.), group 4: Chlorpyrifos (0.01 mg/kg/day i.p.), group 5: Chlorpyrifos (0.01 kg/mg/day i.p.) and 1 hour later *Satureja Khuzestanika Jamzad* essential oil, group 6: Diazinon (0.0002 kg/mg/day i.p.) and 1 hour later *Satureja Khuzestanika Jamzad* essential oil. *Satureja Khuzestanika Jamzad* essential oil was administered equal to 25 mg/kg/day carvacrol i.p. After 10 consecutive days of treatment, rats were anesthetized and spleens were isolated. Then tissue slides were provided using hematoxylin-eosin. After histopathological studies, results were statistically analyzed and compared ($p < 0.05$).Results: Diazinon had no toxic effect on spleen and concurrent administration of diazinon and *Satureja Khuzestanika Jamzad* essential oil did not cause significant spleen damage in compare with control group. However, chlorpyrifos administration induced macrophages and pigments accumulation and splenic white pulp atrophy, which were decreased by co-administration of *Satureja Khuzestanika Jamzad* essential oil.Discussion: Spleen injury caused by organophosphates is usually determined by emerge of giant cells, white pulp atrophy and accumulation of macrophages and pigments. As most of these symptoms were observed in rats of group 4 but not in rats of group 5, *Satureja Khuzestanica Jamzad* was effective against splenic damage caused by chlorpyrifos. Furthermore, we also concluded that application of Diazinon in agriculture is less hazardous compared with chlorpyrifos.Conclusions: The use of organophosphates is accompanied by some toxic effects especially due to oxidative stress. *Satureja Khuzestanika Jamzad* found to be effective in prevention of tissue injury probably due to its antioxidant compounds such as carvacrol.

## O10

## Antileishmanial Activity of New Steroidal Saponin Isolated from the Flowers of Allium austroiranicum

*Zeinab Delazar[1], Mahrouz Ashrafi[2], Masoud Sadeghi dinani[3]*

[1] Ph.D Student of pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Iran.

[2] Pharmacy Student, Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Iran.

[3] Associate Professor, Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Iran.

Corresponding authors: Masoud Sadeghi dinani

Corresponding author Email: m_sadeghi@pharm.mui.ac.ir

Introduction: Alliums are rich sources of steroidal saponins, flavonoids, and sulphoric compounds of which steroidal saponins have recently received more attention due to their important pharmacological activities(1,2). Allium austroiranicum is a common edible vegetable in western regions of Iran, especially in "Chaharmahal and Bakhtiari" province, where it is named “Lopo” and considerably used as a raw vegetable, flavouring agent, and as a medicinal plant(3). Material and methods: The chloroform-methanolic extract was fractionated using MPLC, the appropriate fractions were then subjected to isolation and purification of the constituents by HPLC. Structure elucidation was done using comprehensive spectroscopic methods including 1D and 2D NMR. Antileishmanial effects of the isolated compound against the promastigotes of Leishmania major were evaluated using MTT method. Results: Phytochemical investigation of chloroform-methanol extract of the plant resulted in the isolation and identification of a Nicotianoside C related steroidal saponin and its chemical structure was determined as (25S)-5α-Spirostan-1β,3β-diol-3-O-{α-L-rhamnopyranosyl-(1→2)-{α-L-rhamnopyranosyl-(1→4)}-[β-D-glucopyranoside}. Investigation of in vitro antileishmanial activity of the isolated compound, in 10 and 50 and 100 µg/mL concentrations, exhibited significant leishmanicidal effects against the promastigotes of Leishmania major. Discussion: The isolated compound is structurally related to the steroidal saponins isolated from Allium tuberosum, Allium ampeloprasum and Nicotiana tabacum, in previous studies. This structure is a new spirostan steroidal saponin Which has not been reported before.Conclusions: The results established a valuable basis for further studies about A. austroiranicum and anti-parasitic activity of steroidal saponins.

## O11

## Evaluation of antihyperlipidemic effect of Spirulina algae concentrate powder grown in Iran in type 2 diabetic patients in Mashhad

*Sahar Rajabzadeh Karizi, Zhila Taherzadeh[1]*

[1] Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding authors: Sahar Rajabzadeh Karizi

Corresponding author Email: saaahaar.r169@gmail.com

Introduction: Cardiovascular disease (CVD) is the leading cause of death worldwide, killing 17.9 million people each year. Most people are prone to hyperlipidemia due to diabetes. Both of these factors increase the risk of cardiovascular disease.Although the use of common drugs is very effective in lowering blood lipids, but the severe side effects of these drugs are quite obvious and inevitable. Therefore, new research introduces the use of complementary medicine, especially herbal medicine, as a low-cost treatment with minimal side effects. due to the anti-lipid effects of spirulina, it is predicted that this compound will be useful in the treatment of hyperlipidemia in diabetic patients. The aim of this study was to evaluate the efficacy of spirulina in comparison with placebo in type 2 diabetic patients in Mashhad.Material and method: Sixty patients with type 2 diabetes who were treated for diabetes in the age range of 30-60 years and less than 5 years were studied in two groups: spirulina and control. Patients in the spirulina group received 2 grams of spirulina tablets daily in two divided doses and patients in the control group received 2 grams of placebo tablets daily in addition to their medications. This intervention lasted 90 days. Cholesterol , HDL, LDL, TG were examined on days 0, 30, 60 and 90.Result and discussion: Mean LDL in spirulina group significantly after three months from 111.87 ±49.58 to 73.47 ±37.40 ($P < 0.05$) and mean TG in spirulina group from 183.77 ±70.92 to 113.63 .± 5 40.56($P < 0.01$) and mean cholesterol decreased from 190.43 ±48.14 to 149.07 . ± 40.02 ($P < 0.05$) and HDL decreased from 42.10±7.09 to 45.10 ±6.83 ($P < 0.05$) during 90 days. The results of statistical analysis comparing the difference between the mean of the studied factors between the two groups showed that this difference was significant after 90 days from the start of the study between the two groups, which indicates the effectiveness of spirulina in the treatment of hyperlipidemia in diabetic patients compared with placebo. ($P < 0.001$) Also, daily consumption of 2 grams of spirulina tablets can significantly reduce liver enzymes ($P < 0.009$) in addition no serious side effects observed during the study in both spirulina and placebo groups.Conclusions: According to the results of the present study, taking spirulina capsules at a rate of 2 grams per day can be effective in reducing blood lipids in patients with type 2 diabetes and resulting in a significant reduction in LDL, TG, and cholesterol.

## O12

# Evaluation of Interaction between nitrogen-containing polycyclic heterocyclic compounds and c-Met receptors and their cytotoxic effects on pancreatic cancer cells

*Elahe Raoufi[a,b], Omidreza Firuzi[a], Mehdi Khoshneviszadeh[a,b], Najmeh Edraki[a], Somaye Pirhadi[a]*

[a]Medicinal and Natural Products Chemistry Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[b]Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Iran

Corresponding authors: Elahe Raoufi

Corresponding author Email: elaheh.raoufy1373@gmail.com

Cancer is the second leading cause of death in the world after cardiovascular diseases. Cancer develops when normal cells in a particular part of the body begin to grow out of control. Despite considerable advancements in cancer biology, it is still one of the most lethal diseases, mainly due to the resistance of cancer cells to existing drugs. For this reason, targeted therapies have received much attention in the recent years. One of the pathways that play an important role in proliferation and invasion of cancer cells is the HGF/c-MET pathway. Aberrant HGF/c-MET signaling has been reported in a variety of cancers, pointing out the importance of development of c-MET inhibitors as anticancer agents.In this study, the interaction of phenanthro (e-9,10) (1,2 ,4) triazine derivatives, poly aromatic acenaphtho[1,2-e]-1,2,4-triazine derivatives and amino naphthoquinone (1,2,3) triazole with c-MET receptor was evaluated via docking and Gold Score software. Antiproliferative and apoptosis induction effects of these compounds were evaluated by sulforhodamine-B (SRB) and Hoechst staining assays, respectively, in four pancreatic cancer cell lines including AsPc-1, SUIT-2, PANC-1, MIAPaCa-2 with dissimilar expressions of c-MET receptor.Some of these compounds, such as p4-10 with the structure of 3-(2-(3-nitrobenzylidene) hydrazinyl) phenanthrene [9,10-e] [1, 2, 4], showed good cancer cell growth inhibitory effects. The major interactions observed for this compound included a pi-pi stacking bond with Tyr1159 with 1,2,4-triazine ring and a hydrogen bond between Tyr1230 with the carbonyl group as well as a hydrogen bond between Met1160 with the N atom in triazine ring. These bonds contribute to better binding of this derivative to the receptor's active site and enhance the growth inhibitory effect. This compound showed a considerable antiproliferative effect against AsPC-1 cells with high c-MET expression with an $IC_{50}$ value of 5.1 µM. The data from the Hoechst staining assay also revealed that some of these compounds can induce apoptosis in cancer cells, thus more specific tests are needed to evaluate other aspects of the anticancer effect of these compounds.According to the findings of this study, some of these compounds, especially p4-10 may have c-Met inhibitory effects and could be considered as promising targeted anti-cancer agents.

## O13

# Evaluating antioxidant activity of some of the traditional anti-Alzheimer's herbs via DPPH assay

*Zhiwan Zomorodi[1], Zahra Noormohammadi[1] , Mohammad Mahdi Ahmadian-Attari[2], Nafiseh Khosravi Dehaghi[3]*

[1]Pharmacy Student, Pharmacy Students Research Committee, School of Pharmacy, Alborz University of Medical Sciences, Karaj, Iran

[2]Department of Traditional Pharmacy, School of Pharmacy, Alborz University of Medical Sciences, Karaj, Iran

[3]Department of Pharmacognosy, School of Pharmacy, Alborz University of Medical Sciences, Karaj, Iran

Corresponding author: Zhiwan Zomorodi

Corresponding author Email: zhivan_zomorodi@yahoo.com

Introduction: Reactive oxygen and nitrogen species (RONS) are produced by several endogenous and exogenous processes, and their negative effects are neutralized by antioxidant defenses. Oxidative stress occurs from the imbalance between RONS production and these antioxidant defenses. Today, many conditions and diseases including aging, cancer, cardiovascular and neurodegenerative diseases have been supposed to be related with oxidative stress (1). In Iranian traditional medicine, there are several plants prescribed for prevention and treatment of neurodegenerative diseases like Alzheimer's disease(2). In this study, we tried to evaluate radical scavenging activity of these herbs via DPPH assay.Material and methods: Nepeta menthoides(3), Terminalia chebula(4), Phylanthus emblica (5), Melissa officinalis (6), and peganum harmala (7) were obtained from Tehran botanical market, authenticated in Herbarium of Faculty of Pharmacy, Alborz University of Medical Sciences, and extracted by methanol. The extracts were then concentrated via rotary evaporator and left to dry under laboratory fume hood. TLC plates of each herb was developed on TLC Silica gel $60F_{254}$ aluminium plates (Merck Millipore). 10 micL of each extract was separately loaded on the plate. The optimal mobile phases were selected from references 3 and 4. After running the solvent systems, several spots were separated on the chromatograms each of them represented one or a few chemical compounds. To evaluate the antioxidant capacity, the purple DPPH solution (0.2% in methanol) was sprayed on the plates. If each spot covert purple color to yellow, it means that that spot contains compound(s) with antioxidant activity.Results: the results showed that Terminalia chebula, Phylanthus emblica, and Peganum harmala have more antioxidant compounds than the other herbs. The intensity of yellow color showed that these compounds probably have stronger antioxidant activities than othersDiscussion: Terminalia chebula, Phylanthus emblica, and Peganum harmala contain strong antioxidant compounds. Identification of these compounds as well as studying anti-inflammatory activities of them may help finding new active compounds for prevention and treatment of diseases with the background of oxidative stress.Conclusions: The herbs studied in this research can be used in prevention and/or treatment of Alzheimer's disease.

## O14

## Preparation and characterization of an injectable methylcellulose based hydrogels for bone regeneration

*Zahra Sadat Sajadi-Javan[1], Jaleh Varshosaz[2], and Mina Mirian[3]*

[1]Student's Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Department of Pharmaceutics, School of Pharmacy and Novel Drug Delivery Systems Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

[3]Department of Pharmaceutical Biotechnology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: Jaleh Varshosaz

Corresponding author Email: varshosaz@pharm.mui.ac.ir

Introduction: Methylcellulose (MC) has been extensively studied for biomedical applications due to nontoxicity, biodegradability, and good biocompatibility (1). However, its high gelling temperature, relatively low mechanical properties and inadequate cell proliferation restrict its application as an injectable hydrogel for regeneration of hard tissues (2). This study aimed to prepare a novel thermosensitive injectable hydrogel based on MC and Bassorin (Ba) to improve the rheological properties and gel-formation ability of MC hydrogel. Meanwhile, halloysite nanotubes (HNTs) were incorporated into the hydrogel to enhance the mechanical properties and osteogenic activity of the hydrogel. Moreover, tubular morphology of HNTs enables them to be used as carrier for drugs which makes this system a desirable in situ forming hydrogel for bone tissue engineering (3,4).Material and methods: In this experimental study, Ba isolated from the ribbon type of Gum Tragacanth was blended with MC hydrogel with a concentration of 0.25-1.5 w/v%. The best MC/Ba gel was chosen based on the results of injectability, rheological and mechanical tests. Then HNTs (1-7%) were added to this formulation and tested for the mechanical, rheological, and biological properties of the developed MC-based hydrogels. *In vitro* biological evaluations including cell proliferation (by MTT assay), cell attachment (by SEM), osteogenic activity (by Alizarin Red staining and alkaline phosphatase assay), and osteogenic gene expression (by quantitative real-time polymerase chain reaction) were done using MG-63 cells.Results: Blending Ba with MC hydrogel decreased the gelling temperature and time and enhanced mechanical properties. For example, increasing the Ba concentration from 0 to 1% reduced the gelling time and temperature from 300 s to 90 s and 37-39 °C to 26-37 °C, respectively. Hydrogels containing Ba in concentrations greater than 0.5 w/v% were not practically injectable ($F_{MAX}$> 30N), so MC/Ba 0.5% was selected as an optimum formulation for HNTs incorporation. Gel strength was notably increased by 3 w/v% HNTs, while it was reduced by incorporating 5 and 7w/v% HNTs. The presence of HNTs and bassorin affected the degradation rate and swelling degree of MC-based hydrogel. MG-63 cells were shown to proliferate, differentiate, mineralize better and expressed a higher level of the specific gene when cultured on MC/Ba/HNTs 3% compared to MC/Ba 0.5% and MC. Discussion: Ba provided additional binding sites for ionic crosslinking, and this effect resulted in the improved gel formation ability of MC/Ba hydrogels. HNTs incorporation was further enhanced the MC/Ba gel strength due to the reinforcing effect of HNTs through increasing crosslinking sites which is useful for application in bone repair. However, the aggregation of nanotubes at 5 and 7 w/v% resulted in the reduced gel strength of MC/Ba/HNTs. HNTs as aluminosilicate-based materials had a positive effect on cell growth and attachment due to the presence of Si ions but overloading of HNTs resulted in decreasing cell viability. Also, synergistic effects of Ba and HNTs on the enhancement of cell response were interesting.Conclusions: A novel injectable hydrogel based on MC/Ba incorporated with HNTs was developed which could be potentially applied for bone tissue engineering.

## O15

## Evaluation of the effect of Boswellia serrata extract in the treatment of oral aphthous ulcers: a randomized placebo-controlled clinical trial

*Sara saeidi[1], Amir Entezar Hojjat[1], Mustafa Ghanadian[2], Zahra Saberi[3], Rasool Soltani[4*]*

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of medical Sciences, Isfahan, Iran

[2]Department of Pharmacognosy and Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[3]Dental Research Center, Department of Oral Medicine, Dental Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

[4]Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran*

Corresponding author: Rasool Soltani

Corresponding author Email: soltani@pharm.mui.ac.ir

Introduction: Recurrent aphthous stomatitis (RAS) is the most common oral mucosal disease. Frankincense (Boswellia serrata) is an oleo-gum resin from the Burseraceae family which its anti-inflammatory, analgesic, and antimicrobial effects have been shown in many studies. This study aimed to evaluate the clinical effectiveness of frankincense extract in the treatment of oral aphthous ulcers.Material and methods: Patients with aphthous ulcers who met the inclusion criteria were randomly assigned to either drug (Boswellia serrata) or placebo groups. The two groups were asked to place the orally disintegrating tablets on their ulcers four times a day for three days. The intensity of the pain and the size of aphthous ulcers were measured and recorded for each patient before the intervention (day 0), as well as on the second and fourth (end of intervention) days. The criterion for assessing the intensity of the pain was the Visual Analog Scale (VAS), which evaluated the intensity of pain from 1 (no pain) to 10 (worst pain imaginable) by patients. The criterion for assessing the size of aphthous ulcers was the largest diameter of the white area of the ulcer which was measured in millimeters.Results: The application of oral disintegrating tablets of Boswellia serrata significantly reduced the size of the ulcer on the second day (2.48 ± 1.87% vs. 4.88 ± 1.01; P<0.001) and fourth day (2.16 ± 1.57 vs. 4.88 ± 1.05; P<0.001) of the study compared to the placebo group. The application of oral disintegrating tablets of Boswellia serrata significantly reduced the pain score on the second day (4.44 ± 3.52 vs. 7.52 ± 1.93; P=0.002) and the fourth day (2.84 ± 3.27 vs. 6.88 ± 2.02; P<0.001) of the intervention. Furthermore, the number of patients with complete ulcer healing and complete pain relief in the drug group was significantly more than the control group (5 vs. 0 and 11 vs. 0).Discussion: The use of oral disintegrating tablets of Boswellia serrata results in the reduction of the size of the aphthous ulcer as well as reducing the pain score in patients with aphthous lesions.Conclusions: Boswellia serrata could be effective in the treatment of oral aphthous ulcers. However, more studies with larger sample size and longer duration are required to confirm this effect.

O16

## *In vivo* evaluation of miR-219 effects through imaging, PET scan, LFB staining, fluorescent microscopy, TEM, and rt-PCR

*Nahal Shamaeizadeh[1], Jaleh Varshosaz[1] , Mina Mirian[2], Mehdi Aliomrani[3]*

[1]Department of Pharmaceutics, Faculty of Pharmacy and Novel Drug Delivery Systems

[2]Research Centre, Isfahan University of Medical Sciences, Isfahan, Iran

[3]Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

[4]Department of Pharmacology, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: Jaleh Varshosaz1

Corresponding author Email: varshosaz@pharm.mui.ac.ir

Introduction: Multiple sclerosis (MS) is a chronic neurodegenerative demyelinating disease, so that stimulating remyelination could diminish patients' symptoms. MicroRNA-219a-5P (miR-219) enhances remyelination through oligodendrocyte progenitor cells (OPCs) differentiation, suppresses unwanted neurogenic factors that bring OPCs to inappropriate pathways, and maintains myelin homeostasis make it a proper strategy to recover the damages. Thus, we appraised a novel non-viral targeted vector to bring the miR-219 to the central nervous system (CNS) through the blood-brain barrier. The vector enhanced CNS specific targeting, stability against the nucleases, serum anions, and boosting their payload nucleic acids amount (1-2).Material and methods: The physicochemical properties of nanoparticles, including particle size, zeta potential, morphology, encapsulation capacity, stability against nucleases, and polyanions were studied. The optimized formulation was injected into the cuprizone induced MS model in C57BL⁄ 6 mice to interrogate the *in vivo* features of nanoplexes (approved ethical ID: IR.MUI.RESEARCH.REC.1398.217). To evaluate the miR-219 effects, in vivo imaging, Positron Emission Tomography (PET) scan, Luxol fast blue-cresyl violet staining (LFB), fluorescent microscopy, Transmission electron microscopy (TEM), and real-time PCR were carried out.Results: LFB staining, TEM microscopy, and proteolipid protein 1 overexpression following the targeted miR-219 delivery confirmed the remyelination; meanwhile, PET scan demonstrated the inflammation decrease in the treated group. In addition, fluorescence microscopy and *in vivo* imaging showed the miR-219 accumulation pattern in mice bodies. Finally, we demonstrated the probable relation between miR-219 and crystalline alpha B, apolipoprotein E genes.Discussion: The primary gene therapy challenge for CNS-related diseases is delivering the therapeutic nucleic acids to the CNS across the BBB. For this purpose, we designed a novel carrier to maximize the miR-219 accretion in the brain and improve its bioavailability. The targeted miR-219 plasmid was administered intravenously to evaluate the BBB permeability of the polyplex, and *in vivo* imaging demonstrated the highest green fluorescent protein (GFP) expression in the brain. The significant difference between targeted delivery (TD) and non-targeted delivery (NTD) groups represented the absolute capability of NPs to protect and deliver the pDNA to the CNS through BBB. Remyelination evaluation by LFB staining determined that the myelin percentage of phase II represented about half of the healthy group. Meanwhile, the NTD group showed half of the TD myelin percentage. TEM microscopy as a complementary experiment depicted a significant difference between myelin sheaths of TD and NTD. PET scan showed a non-significant difference in Fludeoxyglucose F−18 （18−FDG ）uptake between phase II and the healthy group as the inflammation increased FDG uptake and neutralized cell death (3). We gave the impression that the ApoE and CRYAB, the potential miR-219 targets, were affected by miR-219 during different stages of the cuprizone MS model in mice. It depicts that Plp1 is expressed nine-fold more than in the NTD group. Remyelination was authenticated through this observation (4-5).Conclusions: The results of this study implicated the efficiency of the vehicle for miR-219 specific

targeting and accumulation in the brain, miR-219 overexpression, inflammation abatement, and promote remyelination in MS patients.

## O17

# Ultra-high ciprofloxacin adsorption using synthesized graphene oxide/Fe-Mg layered double hydroxides nanocomposite

*Farzaneh Sadeghi* [1], *Gholamreza Dehghan Nodeh* [2], *Maryam Dolatabadi* [3], and *Saeid Ahmadzadeh* [*2, 4]

[1]Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

[2]Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.

[3]Environmental Science and Technology Research Center, Department of Environmental Health Engineering, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

[4]Pharmaceutical Sciences and Cosmetic Products Research Center, Kerman University of Medical Sciences, Kerman, Iran.

Corresponding author: Saeid Ahmadzadeh

Corresponding author Email: chem_ahmadzadeh@yahoo.com, saeid.ahmadzadeh@kmu.ac.ir

Introduction: Ciprofloxacin (CIP) as a synthetic antibiotic has been widely used for treatment of bacterial infectious disease in humans and animals. It is noteworthy to mention that drug manufacturers and hospitals are the most important sources of wastewaters containing pharmaceutical contaminants such as CIP (1, 2). Moreover, inappropriate disposal of unused or expired CIP and incomplete metabolization of it in humans severely result in increasing the CIP contamination of surface water in the last decade. It is reported that the presence of CIP in daily drinking water may cause nervousness, nausea, vomiting, headaches, diarrhea and tremors. Higher concentrations may cause serious adverse effects including thrombocytopenia, acute renal failure, elevation of liver enzymes, eosinophilia and leucopenia. On the other hand, the presence of antibiotics in water sources result in the development of bacteria resistant (2, 3). Since the long term exposure to antibiotic cause chronic effects on human, organisms as well as ecological systems, the effective removal of them from water sources has become an increasingly important subject.Material and methods: Graphene oxide-Mg-Fe layered double hydroxides (GO/Mg-Fe LDHs) was prepared through a modified Wang's and Li's methods (3, 4). Fourier transforms infrared spectroscopy (FTIR), and field emission scanning electron microscopy (FE-SEM) was investigated to determine the characteristics of the GO/Mg-Fe LDHs. Response surface methodology (RSM) under central composite design (CCD) category of Design Expert 11 software was used to achieve efficient removal of CIP. The main objective of the CCD method is to optimize the response surface and quantifies the relationship between the controllable input parameters and the obtained response surfaces. The effect of various variables including; pH solution (4-10), adsorbent dosage (100-400 mg $L^{-1}$), initial CIP concentration (1-25 mg $L^{-1}$), and reaction time (5-60 min) investigated to achieve the best removal condition. The First and second-order kinetic models and Freundlich and Langmuir isotherm models were studied.Results: GO/Mg-Fe LDHs was synthesized via a facile procedure for the removal of CIP from hospital wastewater. The optimal experimental parameters for CIP removal efficiency were studied using central composite design (CCD). Experimental results were fitted with quadratic model which indicated that obtained regression equation can describe the influence of effective parameters properly. The most influencing factors among the main terms were found to be initial CIP concentration, followed by adsorbent dosage, reaction time, and pH, respectively. The obtained experimental results are in good accordance with the Langmuir isotherm model for CIP adsorption on GO/Mg-Fe LDHs nanocomposite. The kinetic studies showed that the CIP adsorption was best described using the second order kinetic model. Discussion: The experimental removal efficiency was in satisfactory agreement with the predicted removal efficiency. The normal plot of residuals demonstrated revealed that the linear curve of normal probability versus the internal residuals was reasonably close to a straight line with the $R^2$ of 0.987. Chemical adsorption was suggested for the mechanism of CIP adsorption onto the surface binding sites of the adsorbent (4, 5).Conclusions: Based on the obtained results, GO/Mg-Fe LDHs nanocomposite could be an efficient, environmentally friendly, economical, and low-cost adsorbent for the removal of CIP from hospital wastewater.

## O18

# Exploring pH dependent delivery of 5-fluorouracil from functionalized multi-walled carbon nanotubes

*Aida Solhjoo* [1], *Zahra Sobhani* [2], *Amirhossein Sakhteman* [1], *Zahra Rezaei* [1], *Soghra Khabnadideh* [1] *and Ali Sufali* [3]

[1]Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Department of Quality Control of Drug Products, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Department of Chemical Engineering, School of Chemical and Petroleum Engineering, University of Tehran, Tehran, Iran

Corresponding author: Aida Solhjoo

Corresponding author Email: aida.solhjoo86@gmail.com

Introduction: Multi-walled carbon nanotubes (MWCNT), as a typical carbon structure based nanocarrier are being widely used in drug delivery [1]. In the current study, we investigated pH effects on the loading, and release of 5-FU, from the functionalized MWCNT by means of atomic molecular dynamic simulation (MD) and wet lab experiments. Material and methods: Modification of oxidized MWCNTs was done by mixing OCNT with Poly(ethylene glycol) diamine [2]. Amounts of 5-FU were loaded onto the carrier in PBS medium at three pH levels. After 24 h of stirring at 37℃, optimum drug loading was calculated by HPLC method. The pattern of drug release from carrier was studied with PBS as the release medium at pH 5.0, 7.4 and 9.0. MD simulations were carried out for all systems using the GROMACS package and the OPLS-AA force field for 30 ns [3]. Since, on a microscopic scale, the graphene sheets can be used to mimic the MWCNT surface with an average radius of about 12.5 nm, these sheets were used in MD simulation studies for more simplicity.Results: The 5-FU loading on OCNT-PEG at three pH were analyzed. The loading efficiency was found to be 41.26 % at pH = 7.4 and 30.20 % at pH = 5. However, no significant drug loading occurred at the pH = 9.0. The amount of drug release was at pH=5.0 was higher than pH=7.4. MD analysis were confirmed with the experimental results at three pH levels. MM_PBSA results showed that the interaction energy between the 5-FU and the GO-PEG at pH = 7.4 was higher than pH = 5.0 and 9.0. The average of hydrogen bonds in three pH level 5.0, 7.4 and 9.0 were 1.73, 2.39 and 0.95. The diffusion coefficient for 5-FU molecules was lowest at neutral pH. According to the gyration radius analysis, the decrease in the gyration radius of 5-FU at acidic pH was lower compared to other pH levels.Discussion: Since 5-FU has an aromatic ring, the results showed that the maximum adsorption of 5-FU on the surface of OCNT-PEG at pH=7.4 took place through more-polar interactions and π–π interactions. The more tendency of the 5-FU molecules towards the GO-

PEG surface at neutral pH can be explained by the more negative energy terms of vdW, elec, and binding energies. The RDF plot of the drug molecule in pH = 7.4, 5.0 and 9.0 with GO exhibited peaks related to the type of interaction between 5-FU and GO surface. From the MSD results, increasing the pH from neutral pH to basic levels led to higher diffusion coefficients for the 5-FU molecules, which announced a low drug loading in the basic system.Conclusions: The present study has provided theoretical and molecular insight into the factors that affect the pH-responsive binding which enable the prediction of pH-dependent behavior of previously unknown nanomaterials/drugs. This information prepared the way for the development of a pH-controlled intracellular drug delivery method using functionalized OCNT-PEG carriers, which is anticipated to be useful for the improvement of tumor-targeting cancer therapy.

## O19

# Fabrication of modified nanostructured electrochemical sensor based on carbon paste electrodes for the quantitative determination of norepinephrine using voltammetric techniques

*Sara Samadi*[1], *Alieh Ameri* [2], and *Saeid Ahmadzadeh* [3, 4*]

Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Department of Medicinal Chemistry, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran

Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.

Pharmaceutical Sciences and Cosmetic Products Research Center, Kerman University of Medical Sciences, Kerman, Iran.

Corresponding author: Saeid Ahmadzadeh

Corresponding author Email: chem_ahmadzadeh@yahoo.com, saeid.ahmadzadeh@kmu.ac.ir

Introduction: The electrochemical determination of norepinephrine (NE) as a biomolecule has been investigated in the current work. NE is one of the derivatives of cathecholamines secreted in the adrenal medulla and plays important physiological roles in the central nervous. Hence, it is very necessary to develop sensitive, selective and practically reliable method for the direct determination of the NE dosage for monitoring physiological activities and diagnosing diseases (1-3). In order to discriminate the NE, numerous instrumental procedures employed. Most of them are time-consuming, costly; require complicated sample preparation and expert operator which is not suitable for routine analysis. In contrast, the electrochemical techniques received extraordinary attention due to their low cost, rapid response, easy operation, low detection limit, and relatively short analysis time. Recently, carbon paste electrodes (CPEs) received extraordinary attention due to the advantages of easy preparation and renewability, generous surface chemistry, stable response, wide potential window and low ohmic resistance. In addition to all the benefits mentioned, the use of modifiers that effectively accelerate and facilitates the electron transport between the analyte and the electrode has made the modified carbon paste electrodes a suitable candidate for quantitative determination of the analytes by reducing the overpotential required for the electrode reactions (4, 5).Material and methods: The applied electrochemical compartment consisted of a conventional three-electrode system including NiO/NPs/1E3MITFB/CPE, platinum wire, and Ag/AgCl (3 M KCl) as working, counter, and the reference electrode, respectively. To prepare the high sensitive modified carbon paste electrode (NiO/NPs/1E3MITFB/CPE), NiO nanoparticles and 1-ethyl-3-methylimidazolium tetrafluoroborate (1E3MITFB) employed. Cyclic voltammetry (CV) and square wave voltammetry (SWV) techniques applied for determination of trace amount of NE. The synthesized NiO nanoparticles were characterized with different methods such as SEM and XRD.Results: After optimization of analytical conditions at pH 7.0 phosphate buffer (0.1 M), the oxidation peak current was found to vary linearly with NE concentration in the range of 20.0-300 µM with satisfactory lower detection limit of 5.0 µM. The NiO/NPs/1E3MITFB/CPE showed several advantages such as good reproducibility, low limit of detection (LOD) and simple preparation. By investigating the relationship between the anodic peak current intensity ($I_p$) vs. potential scan rate (ν) and the square root of potential scan rate ($\nu^{1/2}$), it was found that a satisfactory linear relationship between $I_p$ and $\nu^{1/2}$ with a correlation coefficient of 0.9981 observed which confirmed that the electrode process of NE oxidation controlled by diffusion mechanism at the surface of working electrode. The diffusion coefficient (D) of NE and the electron transfer coefficient (α) at the surface of NiO/NPs/1E3MITFB/CPE estimated to be $1.02\times10^{-4}$ cm $s^{-1}$ and 0.81.Discussion: A significant enhancement in the peak current and sensitivity of the proposed sensor observed by using modifiers in the composition of working electrode compared to bare CPE which is in accordance with the results obtained from electrochemical impedance spectroscopy investigations.Conclusions: The proposed sensor as a promising and low-cost method successfully applied for the determination of NE in commercial pharmaceutical formulations available in the market.

## O20

# Pharmacophore modeling and virtual screening studies to identify new c-Met inhibitors from natural compounds

*Elham Ziaei*[1]

[1]Department of Pharmaceutics, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, I.R. Iran.

Corresponding author: Elham Ziaei

Corresponding author Email: ziaei.elham@yahoo.com

Introduction: Overexpression of human c-Met tyrosine kinase induces tumor proliferation and migration. There are still no commercial drugs that can be used to suppress this goal (1, 2). Therefore, the main goal of this research is to find effective natural compounds to prevent the overexpression of c-Met tyrosine kinase.Material and methods: The pharmacophore model was generated using Phase (Schrödinger 11.5). Twelve potent c-MET inhibitors reported in literature used to construct a common feature pharmacophore model (3, 4). Compounds from Afro DB Natural Products using the ZINC 15 database were obtained and subjected to energy minimization and chemically correction using LigPrep (Schrödinger 11.5) with OPLS 2005 force field. Only compounds whose adsorption, distribution, metabolism, excretion, and toxicity (ADMET) descriptor followed Lipinski's rule of five (QikProp, Schrödinger 11.5) were selected for ligand-based virtual screening. The alignment was measured using a survival score. The X-ray crystallographic structure of the tyrosine kinase domain of the c-Met was downloaded from the PDB database (PDB ID: 1R0P) and UCSF Chimera version 1.15 with AMBER ff14sb force field was used for energy minimization. Hydrogen atoms were added to the protein to correct ionization and tautomeric states of amino acid residues. The Auto-Dock Vina (PyRx 0.8 - Virtual Screening Tool) was used to dock

and to score the lead-like compounds to identify potential ligands. A 2D-QSAR was performed using the Binding DB database. The statistical parameter $R^2$ was calculated to evaluate the overall significance of the model. Compounds with the highest Dock Score value were subjected to $IC_{50}$ prediction. Compounds with lowest $IC_{50}$ value subjected for further molecular dynamics simulation analysis using Gromacs 4.6.5 and visualized using VMD 1.9.2.Results: Through 440 molecules of Afro DB Natural Products, 302 molecules followed Lipinski's rule of five and screened using AHHRR hypothesis obtained from pharmacophore modeling with survival score of 5.226 (hydrogen bond receptor (A), hydrophobic group (H), and aromatic ring (R)). Eight molecules with a fitness score>0.6 were selected and subjected to docking analysis. Five molecules with binding affinity<-8 and Root Mean Square Deviation (RMSD)=0 were selected for $IC_{50}$ prediction using QSAR modeling with R2=0.9102. Only molecule 18 (ZINC ID: ZINC000005854604), Fitness score: 0.723256, Binding affinity: -10.1 (kcal/mol) and $IC_{50}$: 0.2177 nM identified as the novel natural product capable of c-MET. It makes two hydrogen bonds with ARG1227 and ALA1226 residues and occupancy of 32.67% and 1.98% respectively. After the 1ns simulation, their average h-bond distance was 1.202 nm and 0.869 nm, and the average RMSD has obtained 0.164 nm and 0.134 nm, respectively.Discussion: All the twelve compounds used for pharmacophore modeling showed a five feature pharmacophore model with high survival score. Though molecules used for pharmacophore modeling and QSAR were different, compound 18 which has highest fitness score also showed desirable binding affinity and $IC_{50}$.Conclusions: In the current study a five feature pharmacophore model using potent c-MET inhibitors along with docking and 2D-QSAR was performed and h-bonds between ligand and target was analyzed. Compound 18 could serve as novel scaffold for further refining and optimizing.

## O21

## A photothermally active injectable hydrogel containing bismuth nanoparticles for enhanced tumor-targeting and photo-chemo-immumotherapy

*Samin Abbaszadeh [1], Vahideh Nosrati Siahmazgi [2], Mohammad Reza Eskandari [3], Aziz Maleki [4], and Mohammad-Ali Shahbazi [4,5]*

[1]Department of Pharmacology, School of medicine, Zanjan University of Medical Sciences, Zanjan, Iran

[2]Department of Pharmaceutical Biomaterials, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

[3]Department of Pharmacology and Toxicology, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

[4]Department of Pharmaceutics, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

[5]Department of Biomedical Engineering, University Medical Center Groningen, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, Netherlands

Corresponding author: Mohammad-Ali Shahbazi

Corresponding author Email: m.a.shahbazi@umcg.nl

Introduction: Photothermal therapy (PTT) is a rapidly growing field and offers opportunities to achieve desirable cancer ablation. Bismuth sulfide ($Bi_2S_3$) nanoparticles (NPs) are emerging as promising photothermal agents for cancer therapy due to their light-to-heat conversion ability for the apoptosis induction on the tumor cells. These agents can be incorporated within injectable hydrogels with chemo-immunotherapy potential to increase the chance of cancer eradication without metastasis to other vital organs. In this work, cancer cell membrane and sorafenib were loaded into a photoactive injectable hydrogel to render tumor-specific immunotherapeutic function and chemotherapy to the developed hydrogel. In addition, the incorporation of these agents within injectable hydrogels can increase their localization within the cancer tissue for better therapeutic responses.Material and methods: $Bi_2S_3$ NPs were prepared using a simple chemical reaction and coated with hyaluronic acid to form BiH NPs. An injectable hydrogel of poly methyl vinyl ether-maleic acid (PMVE-MA) and gelatin was prepared via chemical crosslinking. BiH NPs, cancer cell membrane (CCM) and sorafenib, were loaded within the hydrogel for chemo-photo-immuno cancer therapy. The morphology, elemental analysis, porosity, and surface area of the NPs were examined and photothermal ability of the NPs and hydrogel were assessed both in vitro and in vivo. Afterwards, in vivo toxicity, hemocompatibility and both in vitro and in vivo antibacterial activity of prepared hydrogels were evaluated. The photothermal efficiency and therapeutic effects of the prepared hydrogels were assessed in 4T1 tumor bearing mouse model.Results: BiH NPs showed spherical structure and desirable concentration-dependent photothermal response during a 10-min near infrared (NIR) irradiation (1.5 $W/cm^2$). The in vivo photothermal performance of the hydrogel containing 200 µg/ml of BiH NPs showed that with the power of 1 $W/cm^2$, the temperature elevated to around 59˚C within 5 min, which is sufficient to kill cancer cells. The in vitro hemolysis assay confirmed the hemocompability of the hydrogel. In addition, the hematoxylin and eosin staining of main organs of treated rats showed no significant histopathological changes in the main organs. Furthermore, the BiH loaded hydrogel showed very potent antibacterial activity with and without NIR irradiation. The combined intratumoral photo-chemo-immunotherapy using the hydrogel containing BiH NPs, sorafenib and CCM demonstrated better anticancer effect than the individual photothermal therapy, chemotherapy or immunotherapy alone.Discussion: In this study, an injectable hydrogel containing BiH NPs, CCM and sorafenib for photothermal therapy against cancer was reported, which shows excellent photo-heat conversion ability of BiH NPs and the synergistic effect of chemotherapy, photothermal therapy and immunotherapy. In addition, the injectable hydrogel had the capability to load drugs for sustained release at the cancer tissues over a long period.Conclusions: This new design platform displays synergistic photo-chemo-immunotherapy, which ultimately enhances the cancer therapeutic performance.

## O22

## Design and Construction of a Bispecific Aptamer and in-vitro Study of its Potential for Her2 Positive Breast Cancer Treatment

*Mohammed Hussain Alimardani , Meysam Soleimani Badia*

Corresponding author: Mohammed Hussain Alimardani

Corresponding author Email: mhalimardani9747@gmail.com

Introduction: HER2 positive breast cancer (BC) is a type of breast cancer with HER2 protein overexpression which promotes the growth of cancer cells and poor prognosis. Also, presence of cancer stem cells can cause tumor heterogeneity that leads to the lack of appropriate treatment. In contrast to conventional therapies, dual targeted therapeutic approaches have emerged as an efficient treatment for HER2 positive BC. The aim of this study was construction of a HER2/CD44 aptamer and investigation of the mechanisms and different anti-cancer properties them.Material and Methods: The bispecific aptamer was constructed through in vitro transcription. MTT assays was used for assessment the

cytotoxic activities of CD44 aptamer, HER2 aptamer and the bispecific molecule against MDA-MB-361 cancer cell line. Cell death mechanism also was determined with Annexin V/propidium iodide (PI) assay.Results: The bispecific aptamer treatment for 48 hrs demonstrated a significant cytotoxicity on the MDA-MB-361 breast cancer cell line in a dose-dependent manner, while the bispecific aptamer was significantly more effective than individual aptamers. The flow cytometry results revealed that the early ($p<0.05$) and total ($p<0.001$) apoptotic cells were increased in treated group compared to control cells. Conclusion: Our study suggests that bispecific HER2-CD44 aptamer has provide a potent addition to receptor-targeting therapeutics for HER2 and CD44-expressing BC cells which can potentially suppress cellular proliferation and induce apoptosis.

## O23

## Preparation and Assessment of Usnic acid-Loaded Nanoparticles in Treatment of Breast Cancer

*Jaleh Varshosaz[1], Mehrnaz Farzan[2], Mina Mirian[3], Mohsen Minayian[4]*

[1] Novel Drug Delivery Systems Research Center, Department of Pharmaceutics, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2] Pharmacy Student, Pharmacy student's Research Committee, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

[3] Department of Biotechnology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[4] Department of Pharmacology and Toxicology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: Mehrnaz Farzan

Corresponding author Email: Mehrnaz.Farzan@gmail.com

Introduction: Usnic acid (UA) has been used in research as an antitumor drug (1), however, its hepatotoxicity has been a burden to its therapeutic use (2). The purpose of the present study was to prepare a targeted delivery system of usnic acid for targeting CD44 overexpressed receptors on breast cancer cell lines.Material and methods: Usnic acid loaded Gliadin nanoparticles targeted with Hyaluronic acid (HA-UA-GNPs) were prepared using desolvation method and their physicochemical characteristics were determined. Cytotoxicity and drug uptake assays were studied on 4T1 cell line.Results: HA-UA-GNPs showed a significantly more cytotoxic effect compared to UA-GNPs and free UA on 4T1 cells and HA-UA-GNPs on CD44-saturated 4T1 cells. Targeted GNPs were significantly more uptaken by 4T1 cells compared to non-targeted GNPs. Discussion: The higher cytotoxic effect and cellular uptake of HA-UA-GNPs compared to the equal dosage of UA-GNPs and free drug shows a successful CD44 targeting.Conclusions: Targeting usnic acid loaded gliadin nanoparticles with hyaluronic acid could potentially be an effective strategy for using UA in treatment of breast cancer.

## O24

## Screening test on halophile or halotolerant Streptomyces strains isolated from diverse environments of Iran to discover the antimicrobial agent producers

*Soheil Forootan [1], Abolghasem Danesh[2], and Zeinab Hadiyan[1]*

[1]School of Pharmacy, Mashhad University of Medical Science, Mashhad, Iran

[2]Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran.

Corresponding author: *Abolghasem Danesh*

Corresponding author Email: danesha@mums.ac.ir

Introduction: Streptomyces are gram-positive, filamentous, and non-motile bacteria. They are used widely as the major source of manufactured secondary metabolites and industrial antibiotics. The main goal of this project is to identify halophile or halotolerant actinobacteria that produce active antibacterial substances.Material and methods: An initial screening test was applied on Streptomyces strains that had been reviewed before by Dr. Amoozegar and his colleagues at Tehran University, using two agar layers assay consists of base layer inoculated, before, with actinobacteria containing different concentrations of calcium carbonate and seed layer containing indicator bacteria, *Bacillus subtilis* (ATCC:6633) and *Escherichia coli* (PTCC:1330). To evaluate the effect of agar concentration on the production and release of active antibacterial secondary metabolites, 5 different concentrations of agar (0.6%, 0.9%, 1.2%, 1.5%, and 1.8%) were used on one strain. In addition, the effect of 8 different time courses was tested. The secondary screening was performed using sub-merged liquid fermentation followed by the Disk Diffusion method as an antibacterial assay.Results: Indicator strains in the seed layer grew well when the different calcium carbonate concentrations were added to the base layer. Among 32 Streptomyces strains, about 25% and 22% of strains showed antibacterial activity against *B. subtilis* and *E. coli*, respectively. The most antibacterial activity against both indicators was seen in a 1.8% concentration of agar. The zone of inhibition diameter against the *B. subtilis* was observed more after 3 days of incubation, while a period of 2 days was the best to form the widest zone of inhibition against the *E. coli* indicator. Unfortunately, no acceptable result was found during the secondary screening.Discussion: In 2001, Pandey and his colleagues report that 21% of the 106 isolated Actinomycetes strains show antibacterial activity against *B. Subtilis*. Hayakawa and his colleagues found that *Streptomyces Violaceusniger* strains produce substances that can inhibit the growth of 43% of isolated gram-negative bacteria. They also report 100% inhibition in the growth of isolated gram-positive bacteria. In research in Saudi Arabia, 73.68% and 52.63% of isolated strains showed antibacterial activity against *B. subtilis* and *E. coli*, respectively. Ramazani and his colleagues found that just 8.7% of isolated Streptomyces strains from Zanjan Province, Iran, showed antibacterial activity against *E. coli*. As we found the best period for growth inhibition by active Streptomyces strains is different between gram-positive and gram-negative bacterial indicators, and according to the differences between gram-positive and gram-negative bacteria, especially the existence of lipopolysaccharides in gram-negative bacteria, we can hypothesize that two different kinds of antibacterial metabolites exist and they can inhibit the growth of special kinds of bacteria. Conclusions: Native halophile and halotolerant Streptomyces of different Iran environments have the potential to produce active antibacterial agents.

## O25

## Expression and biological evaluation of a tandem diabody target CTLA-4 and PD-1 receptors

*Mohammad Ghoreishi*[1], *Vajihe Akbari* [2], *Nafiseh Esmaeil* [3]

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Department of Pharmaceutical Biotechnology and Isfahan Pharmaceutical Research Center, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

[3]Department of Immunology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: *Mohammad Ghoreishi*

Corresponding author Email: ghoreishi75@gmail.com

Introduction: Immune checkpoint blockade (ICB) for cancer describes using antibodies that disrupt negative immune regulatory checkpoints. Cancer cells use these checkpoints to remain safe from immune attacks. Clinical studies showed us using two different ICBs nivolumab (anti-PD-1) and ipilimumab (anti-CTLA-4) simultaneously; is significantly more efficient than using them individually. Other forms of bispecific antibodies binding to CTLA-4 and PD-1 have been developed and, some of them are in clinical trials. However, there is no report on the production and biological evaluation of single-chain tandem diabody. This study aims to express and purify diabody. Furthermore, we will evaluate the biologic activity of diabody based on its affinity to PD-1 and CTLA-4 and T cell activation and proliferation.Material and methods: The diabody plasmid was transformed into the *E.coli* BL21(DE3) by heat shock. After protein expression, cell disruption was performed; inclusion bodies were extracted and purified. PBMCs were isolated by density centrifugation and were simulated with 2.5 µg/ml ConA and incubated with different concentrations of diabody for 96 hours. Then the supernatant was collected and evaluated for IFN-γ production using an IFN-γ ELISA Kit.Results: SDS-PAGE and western blot analysis confirmed the expression of protein weighing about 55 kDa. The soluble protein with a purity of over %90 was obtained (208µg/ml). ELISA results showed that diabody enhanced IFN-γ production by PBMCs in response to ConA stimulation in a dose-dependent manner.Discussion: Optimization of expression, isolation, and purification conditions can significantly increase the yield of soluble protein production. *In vitro* assays demonstrated the ability of diabody; that potently enhances cytokine production of PBMCs.Conclusions: We performed functional expression and purification of a diabody derived from nivolumab and ipilimumab. The diabody enhances PBMCs responses *in vitro*. Further development of bispecific PD-1/CTLA-4 diabody is in progress.

O26

## SAMET: A machine- learning web based platform for management, interpretation and analysis of IR spectral data

*Maryam Kabiri, Mina Zarei , Ali Khodabandehlou, Amirhossein Sakhteman*

Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Maryam Kabiri

Corresponding author Email: kabiriyasaman8@gmail.com

Introduction: Versatile supervised and unsupervised machine learning techniques are widely used in different branches of pharmaceutical sciences. Application of supervised techniques including hierarchical cluster analysis (HCA), k-means and kohonen neural network in clustering of different spectral data such as infra-red (IR) spectroscopy can lead to better interpretation as well as investigation of batch to batch variations in chemicals (1). To integrate different unsupervised learning methods as well as providing a suitable management platform in an easy to use interface, we designed and developed a web based software in django frame work by means of python and JS programming (2). SAMET (Spectral Analysis via Machine Learning Estimation of Trained models) can be hosted in both windows and linux operating systems for management and analysis of IR spectral data. This software can visualize, present descriptive interpretation for IR spectroscopy and perform unsupervised learning methods on dpt files resulting from IR spectroscopy. This platform can be utilized in different branches of pharmaceutical industry such as quality control labs.Material and Methods: SAMET was developped as a web based platform in backend running on python 3.6 and in front end runing on HTML and javascripts. For visualization of dpt files, we used both matplotlib in Python and amcharts in java script to provide facile and interactive visualization platform for analysis of IR data. Different clustering methods including HCA and kmeans were implemented in the backend of SAMET as python scripts using scikit learn libraries in order to provide a comprehensive machine learning analysis for batch to batch variations in pharmaceutical preparations. Meanwhile, the user can select normalization methods like SNV (standard normal variate) for baseline corrections before clustering analysis of data. In the interactive JS panel, the user can select different peaks and subsequently presence of different functional groups will be displayed in the selected regions. Different modules of SAMET were tested using dpt files resulting from an IR vertex 70 spectrometer at Shiraz University of Medical Sciences.Results: The applicability of SAMET was verified in a case study with different batches of montelukast using ATR-IR data. The results revealed that by using a normalization method before data analysis and performing HCA, different batches of monetlukast can be recognized using SAMET as separate clusters. Discussion: Due to different management and analysis methods implemented in SAMET, in can be presented as a novel product for visualization and investigation of batch effects in pharmaceutical industry(3). Since different clustering methods can provide results with minor changes, SAMET benefits from two different analysis methods including HCA and k-means to allow users for a better comparison and results of unsupervised methods. Conclusion: A web based platform was developed to investigate batch to batch variation as well as interpretation of spectral data. This platform incorporates different machine learning methods in the background and can be considered as a management and analysis application in quality control and batch to batch variation.

O27

## Searching for alternative toxicology testing systems: The response of isolated mitochondria from Saccharomyces cerevisiae, potato tuber, and mouse liver to a toxic insult

*Farkhonde Karimi* [a], Pouria Mobasher [b,c], Mohammad Mehdi Ommati [b,d], Asma Najibi [b,e], Amin Reza Akbarizadeh [f], Younes Ghasemi [b,c], Reza Heidari [b,*]

[a] Student Research Committee, *School of Pharmacy*, Shiraz University of Medical Sciences, Shiraz, Iran

[b] Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz Iran

[c] Department of Pharmaceutical Biotechnology, Shiraz University of Medical Sciences, Shiraz Iran

[d] College of Life Sciences, Shanxi Agricultural University, Taigu, Shanxi 030801, China

[e] Department of Toxicology and Pharmacology, Shiraz University of Medical Sciences, Shiraz Iran

[f] Department of Quality Control, Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Correspondence: Reza Heidari and Younes Ghasemi; e-mails: rheidari@sums.ac.ir; ghasemiy@sums.ac.ir

Introduction: Mitochondria are cellular power plants known as essential organelles for energy (ATP) metabolism(1,2). However, today it is evident that various vital compounds are partially or exclusively synthesized in mitochondria. Moreover, this organelle plays a pivotal role in essential processes such as cell death. The isolated mitochondrion is an excellent experimental model for evaluating the role of mitochondria in the pathogenesis of diseases. Various *in vitro* and *in vivo* experimental models have been developed to study mitochondria. On the other hand, some alternative models could also help decrease the use of animal models. The obtained data could help in the development of alternative toxicology testing systems for future investigations.Material and methods: In the current study, we compared the response of mitochondria isolated from mouse liver, *saccharomyces cerevisiae* (*S.c*), and potato tuber to various concentrations of calcium ($Ca^{2+}$) as a robust mitochondrial disturbing agent.Results: The current study found that the addition of $Ca^{2+}$ to mitochondrial preparations from different species dose-dependently caused a significant decrease in mitochondrial ATP metabolism. Hence, this toxic insult impaired a fundamental feature of the mitochondrion. Like other measurements carried out in the current study, no significant difference in $Ca^{2+}$-induced ATP depletion was detected when various mitochondrial preparations were compared.Discussion: We are aware that mitochondria from different species have a huge structural and enzymatic variance. Hence, these models could just estimate the effect of xenobiotics in biological systems. However, the data derived from this study could finally help to decrease the use of experimental animals and provide new approaches for evaluating mitochondrial function.Conclusions: No significant difference between mouse liver, *S.c*, and potato tuber mitochondria were

## O28

# Antioxidant and genoprotective effects of osthole against cadmium-induced DNA damage in human umbilical vein endothelial cells

*Ehsan Vahidifar[1], Mahmoud Etebari[1*], Seyed Ebrahim Sajjadi[2]*

[1]Department of Pharmacology and Toxicology, Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2] Department of Pharmacognosy, Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: Mahmoud Etebari

Corresponding author E-mail: etebari@pharm.mui.ac.ir

Objective : Osthole, a plant-derived coumarin, has been shown numerous pharmacological effects. However, its genoprotective effects against cadmium-induced DNA damage have not been determined yet. Therefore, this study aimed to evaluate protective effects of osthole against genotoxicity caused by cadmium. Materials and methods: Human umbilical vein endothelial cells (HUVECs) were treated with different concentrations of osthole (40, 60, 80, and 120 µM) 24 h before cadmium chloride ($CdCl_2$) administration (40 µM) and then DNA damage was evaluated by comet assay. Furthermore, DPPH and also free thiol groups assays were used to determine reactive oxygen species (ROS) scavenger and antioxidant capacities of osthole. Results: All concentrations of osthole significantly ($p < 0.001$) decreased $CdCl_2$-induced DNA damage. The results of DPPH and free thiol groups assays indicated that osthole has appropriate antioxidant properties. Conclusion: Taken together, the findings of the present study revealed that osthole can ameliorate cadmium-induced genotoxicity, in part, by its antioxidant activity.

## O29

# Evaluation of the effectiveness of frankincense oily lotion containing boswellic acid enriched extract in the treatment of knee osteoarthritis: a randomized placebo-controlled clinical trial

*Afsaneh Mohsenzadeh[1], Rasool Soltani[2], Mansoor Karimifar[3], Valiollah Hajhashemi[4]*

[1]Pharmacy student, Student Research Committee, School of Pharmacy and Pharmaceutical Science, Isfahan University of Medical Sciences, Isfahan, Iran.

[2]Associate professor, Department of Clinical Pharmacy and Pharmacy Practice, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.

[3]Associate professor, Department of Rheumatology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

[4]Professor, Department of Pharmacology and Toxicology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.

Corresponding author: Afsaneh Mohsenzadeh

Corresponding author Email: afsaneh.mohsenzd@yahoo.com

Introduction: Osteoarthritis (OA) is a common inflammatory degenerative disease that involves 13% of women and 10% of men 60 years of age or older (1). Knee OA is the most common type that results in negative effects on the patient life due to joint pain and function problems (2). Pharmacological and non-pharmacological treatments of osteoarthritis have some side effects including gastrointestinal complications and renal failure due to the NSAID consumption (3). *Boswellia serrata* is rich in boswellic acids that have antioxidant and anti-inflammatory effects (4). Topical drug delivery is suitable for boswellic acid enriched extract because of its low bioavailability by oral consumption (5). The aim of this study was evaluation of the clinical effectiveness of *Boswellia serrata* extract in the treatment of knee OA.Material and methods: This was a randomized double-blind placebo-controlled clinical trial. Eligible patients were randomly divided into two groups of Boswellic acid extract (33 patients) and control (37 patients), to use oily lotion of the extract or placebo, respectively, on the involved knee three times daily for 4 weeks. All patients received acetaminophen as the standard treatment. Pain score (measured by Visual Analog Scale [VAS]), Patient Global Assessment (PGA) and Western Ontario and

McMaster Universities Osteoarthritis Index (WOMAC) were determined and recorded for all patients. Results: The median [IQR] scores of VAS (9 [7-10] to 4 [2.5-5] for *Boswellia* and 9 [8-9.5] to 6 [3.5-9] for placebo), PGA (3 [2.5-4] to 1.8 [1-2.5] for *Boswellia* and 3.5 [3-4] to 3 [1.9-3.5] for placebo) and WOMAC (67 [58-79] to 24 [15-36.5] for *Boswellia* and 70 [54-83.5] to 52 [25-74] for placebo) decreased significantly in both groups ($P < 0.001$ for all). However, the reduction was significantly higher in *Boswellia* group compared to placebo one at the end of study ($P = 0.005$, 0.004, and 0.002, respectively). Also the median scores of pain, flexibility, and function in WOMAC index of *Boswellia* group was significantly lower in *Boswellia* group compared to placebo ($P = 0.014$, 0.001, and 0.001, respectively). Discussion: In this study, *Boswellia serrata* extract showed more pain decrease and function improvement in knee OA patients versus placebo. This efficacy may be related to the inhibition of 5-lipoxygenase enzyme and nuclear factor kappa B transcription in the inflammatory pathways causing a reduction in metalloproteinase level of synovial fluid and improvement of joint function.Conclusions: The use of topical oily lotion of boswellic acid enriched extract could be effective in joint pain reduction and improvement of flexibility and function in knee osteoarthritis patients.

## O30

## Hyaluronic acid coated MIL-101-NH2 nanoparticles boosting delivery of Pt-cucuminate complex to triple negative breast cancer cell line

*Mohammadmahdi Moradi*[1], *Fatemeh Emami*[1], *Shahram Tangestaninejad*[2], *Mehdi Aliomrani*[3], *Jaleh Varshosaz*[4], *Hossein Kazemian*[5] *and Mahboubeh Rostami*[*1]

[1]Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical science, Isfahan University of Medical Science, Isfahan, Iran

[2]Department of Chemistry, Isfahan University, Isfahan, Iran

[3]Department of Pharmacology and Toxicology, Faculty of Pharmacy and Pharmaceutical science, Isfahan University of Medical Science, Isfahan, Iran

[4]Department of Pharmaceutics, Faculty of Pharmacy and Pharmaceutical science, Isfahan University of Medical Science, Isfahan, Iran

[5]Northern Soil and Groundwater Remediation Research Laboratory, University of Northern British Columbia, Prince George, V2N 4Z9, Canada

Corresponding author: Mahboubeh Rostami

Corresponding author Email: m.rostami@pharm.mui.ac.ir

Introduction: Platinum-based drugs such as cisplatin can damage DNA, stop the cell cycle and cause apoptosis in cancer cells. In this group, due to the side effects and resistance of cancer cells, structural changes by modifying the leaving groups may contribute to the synthesis of new cytotoxic platinum agents. The use of organic-metallic frameworks (MOFs) as porous carriers has attracted much attention in drug delivery. In this study, for the first time, hyaluronic acid (HA)-targeted MOF (NH2-MIL-101 (Fe)) nanoparticles were used to deliver platinum-curcumin (Pt-CUR) prodrug to the MDA-MB-231 triple-negative breast cancer cell line, and the cytotoxicity and cellular uptake of these nanoparticles have been studied. Methods: Solvo-thermal method was used for the synthesis of NH2-MIL-101 nanoparticles (MIL NPs). The curcumin-platinum complex was synthesized from the reaction of cisplatin with the solution of deprotonated curcumin, and then the complex was loaded into MIL NPs, and finally, the NPs were coated with HA. Chemical structures were identified and confirmed by FT-IR, UV-vis, BET, XRD, CHNS, ICP-MS, and TGA analysis. Cytotoxicity test was performed on the MDA-MB-231 cancer cell line and HUVEC normal cell line. In addition, the DCFDA test was used to measure ROS production. Cellular uptake was determined by flow-cytometry and ICP-Mass technique. Results: The prepared NPs have a uniform morphology and the hydrodynamic size of the optimized loaded and uncoated particles increased to about 252 nm with a zeta of +26.9 and after coating with HA the size increased to 310 nm and the zeta potential changed to -28. Based on TGA results and atomic absorption (ICP-Mass), the drug loading percent was determined to be about 30-35%. Release of the drug from the coated system in the neutral condition is slow and continuous and after 36 hours a maximum of 60% of the drug is released, but in acidic conditions, the release is increased and by 18 hours, the release is about 20% more than neutral. The toxicity of MOF NPs containing Pt-CUR is greater than that of the free drug, and HA targeted has resulted in more cellular uptake compared to the NPs without hyaluronic acid coating. Discussion and Conclusion: Cellular studies show that the final optimized system has better toxicity effects than the free complex and the concentration of 50% growth inhibition in these NPs is reduced by 8 micrograms per milliliter. On the other hand, in coated systems, the effects of toxicity are obvious at higher concentrations, which is due to the low loading percent of the drug in this system. Prepared NPs showed fewer toxicity effects on normal cells and this lack of toxicity is very significant for targeted systems. In HA targeted systems, the cellular uptake percent based on ICP results is about 25% higher than non-targeted NPs. Therefore, coating nanoparticles is a good strategy to reduce the cytotoxic effects on normal cells. In general, these new MOF-based HA-coated NPs can be introduced to pre-clinical researches after completing in vitro and in vivo studies.

## O31

## Investigation of the protective effects of Mito-Tempo on cadmiumexposed mesenchymal stem cells (MSC)

*Sadaf Ab hayat*[1], Eftekhar Morabbi[2], and *Fatemeh Tavakoli*[3]*

[1]Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi, University of Medical Sciences, Yazd , Iran

[2] Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi, University of Medical Sciences, Yazd , Iran

[3] Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi, University of Medical Sciences, Yazd , Iran*

Corresponding author: Fatemeh Tavakoli

Corresponding author Email: f.tavakoli@ssu.ac.ir

Introduction: Cadmium is one of nature's most toxic metals. Prolonged exposure to cadmium due to its accumulation in the body causes various toxic effects in tissues such as the heart, kidneys, liver and central and peripheral nervous system. MitoTEMPO is a mitochondrial antioxidant with superoxidase activity and radical scavenger. Due to the fact that cadmium induces oxidative stress reactions and can cause oxidative damage, this study investigated the protective effect of Mito-TEMPO against oxidative damage caused by cadmium in the rat mesenchymal cell line extracted from bone marrow.

Material and methods: In the present study, the toxicity of cadmium

chloride on the induction of oxidative stress in rat bone marrow mesenchymal stem cells was investigated. To evaluate the effect of concentrations of 1, 10 and 100 µg / ml Mito-Tempo on toxicity of cellular cadmium chloride, malondialdehyde (MDA) and lactate dehydrogenase (LDH) in cadmium-exposed MSC cells by two methods of pre-treatment and co-treatment Evaluated. Results: With increasing concentration of Mito-Tempo, the amount of lactate dehydrogenase in MSC cells decreased and this reduction was significant. In concomitant treatment, Mito-Tempo at concentrations of 1 and 10 ($P < 0.01$) and 100 µg/ml ($P < 0.05$) had a statistically significant decrease compared to the cadmium chloride group. In concomitant treatment, the amount of malondialdehyde in the groups of concentrations of 1, 10 and 100 µg / ml Mito-Tempo with cadmium was significantly different from the group of cadmium chloride ($P < 0.01$) But it was not significantly different from the positive control group treated with Mito-Tempo. The lowest rate of lipid peroxidation and also the highest improvement of MSC cells was observed at a concentration of 100 µg/ml Mito-Tempo. Discussion: When the mitochondria are exposed to cadmium for a long time, the mitochondria produce less energy and more ROS, which can be involved in the carcinogenic oxidative stress of cadmium. Measurements of MDA caused by oxygen free radicals indicate the level of damage to the biological membrane. The LDH enzyme can act as a sensitive marker in tissue damage. During cell damage, this enzyme passes through the cell membrane and is released And its activity can directly indicate cytotoxicity. As a result, measurements of this enzyme can indicate the extent of cell damage and mortality. Mito-Tempo is a mitochondrial antioxidant with superoxidase activity and radical scavenger that we studied its protective effect against cadmium. In a study by Lin et al., The MDA and LDH levels were significantly reduced in the Mito-Tempo-treated group compared with placebo. In the study of Ying et al., It was also observed that Mito-Tempo has a concentration-dependent antioxidant effect and more positive effects can be seen with increasing concentration. A study by Wang et al. Also found that Mito-Tempo reduced doxorubicin-induced platelet apoptosis. Conclusions: Taking Mito-Tempo as an antioxidant, simultaneously or before exposure to cadmium, reduces cell damage; As the concentration of Mito-Tempo increases, the amount of damage decreases more, although confirmation of these findings requires further studies.

## O32

# Biological activities and phytochemical constituents of *Ferula assa-foetida* L. fruits

*Sina Maskokian [1], Anita Oyarhossein[1], Azadeh Manayi[2] and Mohammad-Reza Delnavazi[1]*

[1]Department of Pharmacognosy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[2]Medicinal Plant Research Center, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Sina Maskokian

Corresponding author Email: sinamaskokian@gmail.com

Introduction: *Ferula assa-foetida* L. (Apiaceae) is a perennial plant distributed in Iran, Afghanistan and Pakistan (1). This species is mostly known for medicinal uses of its oleo-gumresin, however, its fruits have also been mentioned in Iranian traditional medicine as tonic, diuretic, aphrodisiac, memory enhancer, analgesic and wound healing agent (2, 3). In the present study some biological potential of *F. assa-foetida* fruits were assessed and phytochemical constituents of the most active extracts were investigated.Material and methods: Free radical-scavenging activity, general toxicity and acetylcholinesterase enzyme inhibitory activity of the *n*-hexane, dichloromethane and methanol extracts were assessed in DPPH, brine shrimp lethality test (BSLT) and ELLMAN methods, respectively. Phytochemical constituents of methanol and dichloromethane extracts were analyzed by chromatography on silica gel (normal and reversed phases) and Sephadex LH20 columns. Structures of the isolated compounds were elucidated using NMR (1D and 2D) and MS spectral analyses.Results: As the result of biological activity assay, methanol extract showed the highest free radical-scavenging activity with $IC_{50}$ value of 3.89 µg/ml. In BSLT test, dichloromethane extract was the most toxic extract with $LD_{50}$ value of 2.18 µg/ml. None of the extracts demonstrated considerable inhibitory activity on acetyl and butirylcholinesterase enzymes. Phytochemical study on methanol extract resulted in the isolation of eight compounds, namely, luteolin (1), quercetin-3-O-glucoside (2), luteolin-7-O-glucoside (3), chrysoeriol-7-O-rutinoside (4), luteolin-7-O-rutinoside (5), chrysoeriol-7-O-glucoside (6), 3,5-di-O-caffeoylquinic acid (7) and 3,5-di-O-caffeoylquinic acid methyl ester (8). Five compounds were also isolated from dichloromethane extract, namely, galbanic acid (9), farnesiferol B (10), farnesiferol C (11), lasidiol angelate (12) and a new compound, lasidiol tiglate (13). Discussion: The methanol extract of *F. assa-foetida* fruits was found rich in flavonoid and caffeoylquinic acid derivatives (1-8). Regarding to well-known free radical scavenging activity of natural polyphenols these compounds could be assumed as responsible for potent antioxidant activity observed from the methanol extract (4). Sesquiterpene coumarins and daucane-type sesquiterpene esters (9-13) were also identified as the main constituents of dichloromethane extract of *F. assa-foetida* fruits. These compounds may be contributed to toxicity of dichloromethane extract and can be tested for their cytotoxic potential on cancer cell lines in future studies.Conclusions: The results of present study introduce the fruits of *F. assa-foetida* as a source of potentially active flavonoid, caffeoylquinic acid, coumarin and sesquiterpene derivates and suggest it as an appropriate candidate for antioxidant and anticancer drug development researches.

## O33

# Anticonvulsant effects of Ivermectin on Pentylenetetrazole and maximal electroshock Induced Seizure in Mice: Role of GABAergic system and ATP sensitive potassium channels

*Mohammad Amin Manavi[1], Razieh Mohammad Jafari[2], Hamed Shafaroodi[2], Mohammad Sharifzadeh[1], Ahmad Reza Dehpour[2]*

[1]Department of Pharmacology and Toxicology, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[2]Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Mohammad Amin Manavi

Corresponding author Email: ma-manavi@student.tums.ac.ir

Introduction: Seizure is the clinical manifestation of an abnormal, excessive, hypersynchronous discharge of a population of cortical neurons. Ivermectin, 22,23-Dihydroavermectin B1, derived from avermectin B1, has been shown to be a highly effective drug for the treatment of a wide variety of metazoan parasitic diseases in animals. Ivermectin binds to glutamate-gated chloride channels and open it and effects by involvement of GABAergic system. The ATP-sensitive

potassium ($K_{ATP}$) channels are a group of potassium channels that are sensitive to alterations in the intracellular concentration of the ATP and the ATP/ADP ratio, linking the electrical activity of the cell to its metabolic state. Material and methods: We investigated the effect of three different doses of Ivermectin (0.05, 0.2, 0.5, 1, 5 mg/kg) on IV and IP pentylenetetrazol (PTZ)-induced seizures compared with the seizure threshold and protection against death of the control group, which had been given normal saline. Also, in separate groups of animals, glibenclamide and cromakalim injected prior to ivermectin for studying probable contribution of KATP, and also, diazepam and flumazenil has been used for investigating of role of GABAergic system in Anticonvulsant effects of Ivermectin. Data are expressed as mean ± S.E.M. of clonic seizure threshold and protection against death in each experimental group. differences were considered statistically significant in case the probability of type I error (P value) was less than 0.05.Results: Ivermectin affects PTZ-induced clonic seizure threshold. Our preliminary experiments revealed Ivermectin dose-dependent anticonvulsant effects on IV PTZ test. pre-treatment with glibenclamide (1 mg·kg-1) 30 min before administration of Ivermectin (5 mg·kg-1) and 60 min before determination of PTZ-induced seizure threshold reversed seizure threshold down to the saline-treated control group. Pre-treatment with Cromakalim (10 µg·kg-1) 15 min before administration of sub-effective dose of Ivermectin (0.2 mg·kg-1) significantly increased the anticonvulsant effects of sub-effective dose of Ivermectin. Likewise, diazepam (0.02 mg·kg-1) and flumazenil (0.25 mg·kg-1) was injected intraperitoneally before ivermectin by enhancing and preventing effects of ivermectin respectively. Furthermore, IP PTZ test and maximal electroshock was shown that Ivermectin (5 mg·kg-1) could protect mice against tonic clonic seizure and death. Discussion: The present study demonstrated the dose-dependent anticonvulsive effects of Ivermectin on PTZ-induced seizures in mice. Our data for the first time, to our knowledge, suggested a role for involvement of KATP channels in the anticonvulsive effects of ivermectin. Also, we confirm that GABAergic system has an important role on this effect. Pretreatment with the GABA receptor agonist diazepam and potassium channel opener cromokalim also enhanced the anticonvulsive effects of Ivermectin on seizure threshold. Conclusions: In summary, our present data demonstrated anticonvulsant effects of Ivermectin in the PTZ-induced seizure model in mice. We also found that both the GABAergic system and $K_{ATP}$ channels, alone or in combination with each other, could be involved in the anticonvulsant effects of ivermectin in three animal model, IV PTZ induced seizure, IP PTZ induced seizure and maximal electro shock.

## O34

# An evaluation of the in vitro cytotoxic activity of N-substituted piperazinyl dichloroethanone as potent antitproleferative agents

*Fatemeh Malekmakan[1,2], Zeinab Faghih[1*], Zahra Faghih[3], Zahra Rezaei[1,2], Fatemeh parsa[1;2].*

[1]Pharmaceutial Science Research Center, Shiraz University of Medical Sciences, Shiraz, I.R. Iran

[2]Department of Medicinal Chemistry, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Shiraz Institute for Cancer Research, Medical School, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Zeinab Faghih

Corresponding author Email: Faghihl@sums.ac.ir, Layafaghih@gmail.com

Introduction: Pyruvate dehydrogenase kinase (PDK) is a mitochondrial enzyme. It is activated in a variety of cancers and selectively inhibits pyruvate dehydrogenase which converts the cytosolic pyruvate to mitochondrial acetylcholine, substrate for the Krebs cycle. Inhibition of PDK by dichloroacetate reverses the suppression of mitochondrial apoptosis. This treatment, in addition to increasing the production of Krebs cycle mediators, can inhibit proliferation transcription factors.Material and methods: In this study, 10 alkyl and aryl piperazinyl 2, 2 dichloroethanone derivatives were prepared and synthesized using appropriate methods and raw materials. Then, the structure of these compounds was completely identified by spectroscopic methods (Mass, IR, $^{13}$C-NMR, $^{1}$H-NMR). To evaluate the anti-cancer properties, cytotoxicity of these compounds were evaluated on three human cancer cell lines: A549 (lung cancer), 5637 (bladder cancer) and MCF-7 (breast cancer) using MTT assay.Results: The results of cytotoxic evaluation showed that, compounds 3e, 3f and 8b with $IC_{50}$ values of 11.9, 10.3 and 14 µM against MCF-7 cell line, 18.4, 9.7 and 15.6 µM against A549 cell line and 15, 10.5 and 13.6 µM against 5637 cell line respectively, had the most toxicity effects compared to other compounds, even more than cisplatin as a positive control on cell lines.Discussion: Structure activity relationship (SAR) of investigated compounds revealed that among N-methyl and aryl piperazine derivatives of dichloroethanone (3a-f), compound 3a which contained the methyl substitution on N-4 position possessed the lowest toxicity compared to the aryl-substituted ones against all three cell lines. Among phenyl-substituted compounds, the electronegative groups at para-position in order of NO2>Cl, increased the anticancer activities whereas 3e and 3f had the highest cytotoxic effect. In investigated compounds, containing of benzyl group on both C-2 and N-4 position (5a-b and 8a-b), has resulted in better efficacy. Among them, the presence of bromine group on the phenyl ring in 5b and 8b, significantly increased the inhibitory effect compared to those which had methyl group instead (5a and 8a).Conclusions: Notably, it seems size, electronegativity and position of substitution, all together as well as Log p played crucial role in order to have better inhibitory activity among these investigated compounds. In summary, N-phenyl and N-benzyl derivatives with para-substituted halogen electron withdrawing groups showed higher activity against all investigated cell lines. These results indicate these piperazine-dichloroethanone derivatives may be effective in the development of novel anticancer therapies.

## O35

# Title 4-Hydroxyhalcone effects on Cisplatin induced genotoxicity model

*Melika Maleki[1], Mehdi Aliomrani[2]*

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.

[2]Department of Toxicology and Pharmacology and Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences and Health Services, Isfahan, Iran.

Corresponding author: Mehdi Aliomrani

Corresponding author Email: maliomrani@pharm.mui.ac.ir

Introduction: The genotoxicity of Cisplatin (CP) as a Platinium based antineoplastic agent due to its oxidative stress induction was well known. In this research, we examined 4-Hydroxychalcone (4-HCH) as a natural food presents flavonoid effects on reactive oxygen species (ROS) production and CP induced in vivo genotoxicity.Material and methods:

Cytotoxicity of CP and 4-HCH were measured on Human embryonic kidney 293 cells with MTT assay. Then, intracellular ROS content at IC50 concentration of CP was measured with 2',7'-dichlorofluorescein diacetate (DCFDA) dye. Finally, 4-HCH was administered intraperitoneally at 10 and 40mg/kg/BW doses as a pre and post-treatment schedule in mice model of CP genotoxicity (7mg/kg). Acridine orange stained bone marrow cells were quantified for micronucleus presence examination.Results: The calculated IC50 of CP and 4-HCH were reported around 19.4 and 133.6µM on HEK293 cells. Also, it was observed that 4-HCH at 0.2, 2 and 10 µM concentration did not show obvious cytotoxicity. The fluorimetry confirmed that pre-treatment with 10µM and co-treatment with 2µM of 4-HCH could attenuate the CP induced ROS production ($p<0.05$ and $p<0.01$, respectively). Also, the lowest micronucleated cells were seen in 10mg/kg 4-HCH treated group after CP exposure (39±7.9, $p<0.0001$).Discussion & Conclusions: Our results demonstrated the anti-genotoxic action of 4-HCH in CP treated mice bone marrow cells for the first time in both concentration of 10 and 40mg/kg especially in the form of co-treatment. Further studies required for clinical application of this compound in a combination of CP to attenuate the normal cells genotoxicity side effects.

## O36

## Fabrication and characterization of sunitinib loaded Dextran-PLGA copolymeric micelles

*Parisa Mahdavi*[1] *, Zahra Pourmanouchehri*[2]*, Mazdak Limoee*[3]*, Mohammad rasool Khazaei*[1] *, and Leila Behbood*[2]

[1]Students Research Committee, Kermanshah University of Medical Science, Kermanshah, Iran.

[2]Pharmaceutical sciences research center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran.

[3]Nano drug delivery research center, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran.

Corresponding author address: Leila Behbood

Corresponding author Email: leila_behbood@yahoo.com

Introduction: Sunitinib is one of the novel antineoplastic agents employed for the management of a variety of cancers. However, challenges like poor aqueous solubility and dose-dependent side-effects limit its clinical applications. Polymeric micelles using amphiphilic macromolecules are promising vehicles for antitumor targeting. In this study, we prepared sunitinib-incorporated polymeric micelles using novel block copolymer.Material and methods: We synthesized a block copolymer composed of dextran and poly (lactic-co-glycolic acid) (DEX-PLGA) via esterification reaction confirmed by FT-IR and NMR spectra. The critical micelle concentration (CMC) of micelle was determined using UV spectroscopy and iodine as hydrophobic probes. Sunitinib was incorporated into polymeric micelles by the nanoprecipitation-dialysis method. Sunitinib-incorporated DEX-PLGA micelle was observed by transmission electron microscopy and scanning electron microscopy. The drug release from micelle was determined using the dialysis bag technique. Furthermore, the cytotoxicity of drug-loaded micelles was examined by MTT assay.Results: In this study, we synthesized dextran/ poly (lactic-co-glycolic acid) block copolymers successfully. The CMC of prepared micelles was observed to be 9.997µg/ml respectively. The morphological studies showed that the nanoparticles were spherical and smaller than 300 nm, with a narrow size distribution. The particle size of sunitinib incorporated polymeric micelles increased with increasing drug content. Higher initial drug feeding also increased the drug content. At the polymer/drug weight ratio of 20:2.5, drug loading efficiency was 62.7%. Drug release profile had the most similarity to Higuchi kinetic model with a sustained release over 12 hours. Cytotoxicity evaluation of drug-loaded nanoparticles on different cancerous cell lines demonstrated that the sunitinib-loaded micelles had similar cytotoxicity on cancerous cells to that of free drug at equal drug concentrations. In addition, micelles without drugs showed no toxicity on normal HUVEC cell lines indicate that the drug delivery system is biocompatible.Discussion: negative zeta potentials of micelle indicated their stability in the bloodstream and lack of easy removal by the reticuloendothelial system. The high drug loading efficiency in the micelles proved that the micelles can deliver the drug at the required therapeutic dose to the target tissue, which reduces the need for frequent use. Extending the release time of the drug in micelle compared to the formulations on the market that are released explosively, showed that by using the formulation containing micelles, the patient's need to use the drug is reduced and in addition to preventing a large amount of drug wastage, it does not cause unwanted side effects for the patient. Due to the lack of cytotoxicity, this system has the ability to be used systematically. Also, the polymers resulting from the degradation of micelles are fully compatible with the body, decomposed in the body, and excreted by the kidneys. Conclusions: In the present study, loading of sunitinib in a polymeric micellar system led to an improvement of drug aqueous solubility, drug release prolongation, and dose-dependent side-effects reduction comparing to free drug application. However, more clinical studies are required to confirm the results.

## O37

## Synthesis And Cytotoxic Evaluation Of POMOF Hybrid Nano-Structure POM@ZIF-8/PEG On MDA-MB-231

*Zahra Moazeni Bistgani*[1], Fatemeh Shafiee [2], Jaleh Varshosaz[3], and Mahboubeh Rostami [4*]

[1]Student Research Committee, school of pharmacy and pharmaceutical science, Isfahan university of medical science, Isfahan, Iran

[2]Department of Pharmaceutical Biotechnology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[3]Department of Pharmaceutics, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[4*]Novel Drug Delivery Systems Research Center and Department of Medicinal Chemistry, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: Mahboubeh Rostami

Corresponding author Email: m.rostami@pharm.mui.ac.ir

Introduction: Some polyoxometalate (POM) clusters have confirmed attractive antineoplastic properties. Unfortunately, their cytotoxicity upon normal cells is one among the many side effects blocking their further clinic application as inorganic drugs. During this research, we report a new hybrid conjugate drug delivery system based on POM-Zeolitic imidazolate frameworks (ZIF) (POMZIF8) to beat this problem.Material and methods: Initially, the POM cluster, $K_6As_2W_{18}O_{62}$, were prepared by hydrothermal approach and entrapped by ZIF-8 to making a pH-sensitive hybrid carrier matrix. The obtained nanoparticles (NPs) were coated with poly (ethylene glycol) (PEG) to increase cell penetration. All the above steps were happened in one pot to create POM@ZIF-8/PEG. The final NPs were characterized by different instrumental analysis methods comprising UV-Vis, FTIR, XRD, TGA, SEM, and DLS. ICP-OES was used for quantifying the cellular uptake, loading percentage, and amount of releasing content. A breast cancer cell (MDA-MB-231) and non-cancerous human vena

umbilical endothelial cell (HUVEC) were used for the cytotoxicity studies.Results: The characteristic peaks and peaks shape for $K_6As_2W_{18}O_{62}$ and ZIF-8 were like those reported in other literature in FTIR, XRD, and TGA spectrum. loading percentage was 94% calculated by UV-Vis spectroscopy. At phosphate buffer saline (PBS) (pH =7.4) POM@ZIF-8/PEG released 98% of its POM contents after 24 hours, the similar releasing content happened around 1 hour in acetate buffer (pH = 5). The particle size of POM@ZIF-8/PEG was around 300 nm and +29.4 mV is the surface charge of the Nanocomposite obtained by Zeta potential. The IC50 of POM@ZIF-8/PEG on MDA-MB-231 and HUVEC were 252.5 and 530 ppm, respectively.Discussion: Prepared hybrid POMZIF8 cluster NPs with uniform morphologies and ideal characteristic features had better cytotoxicity profile than POM on MDA-MB-231 cell line with reduced toxicity on normal cells. Better cytotoxicity could be related to the better cellular uptake of final NPs. The cellular cytotoxicity results showed that ZIF-8/PEG carrier was successfully helped to extend $K_6As_2W_{18}O_{62}$ effect on cancerous cells.Conclusions: According to these initial results, it could be said that POMZIF8 NPs can impart enhanced antitumor activity and selectivity, thus representing a new concept to develop a unique drug delivery system with the potential synergistic effect: increased bioactivity and lower side effect.

## O38

## Impact of Educational Intervention by Community Pharmacists on Asthma Clinical Outcomes, Quality of Life, and Medication Adherence

*Hossein Mahdavi*[1], *Mehdi Mirheidari*[1],*Behrad Azadmehr*[2], *Hadi Esmaily*[3*]

[1]Student Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran , Iran

[2]Student Research Committee, Faculty of Pharmacy, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[3]Department of Clinical Pharmacy, Shahid Beheshti University of Medical Sciences , Tehran , Iran

Corresponding author: Hadi Esmaily

Corresponding author Email: Esmaily_hadi@sbmu.ac.ir

Introduction: Asthma is estimated to be involving more than 339 million people worldwide(1). Patient compliance ensured by communicating with the pharmacist is easy enough that could effectively contribute to lowering the burden. This study aims to evaluate the effects of pharmacists' educational interventions in the community pharmacy settings on asthma control and severity, quality of life (QOL), and medication adherence.Material and methods: Databases PubMed, Scopus, and Web of Science have been searched for evidence regarding asthma severity and control, QOL, and medication adherence after pharmacists' interventions in community pharmacy settings. Twenty-one studies were eligible for qualitative and quantitative analysis. Indices and questionnaires were used in the studies, such as Asthma-related quality of life (AQLQ), Asthma Control Test (ACT), Perceived Control of Asthma Questionnaire (PCAQ), inhaler technique (IT), Asthma Control Questionnaire (ACQ), 36-Item Short Form survey (SF-36), and peak expiratory flow rate (PEFR). The outcomes were extracted, pooled, and analyzed as percentages, means, standard deviations and errors, and 95% confidence intervals (CIs)(2–4).Results: Community pharmacists in all studies educated and followed up the asthmatic patients, addressing the outcome measures. Pharmacists underwent training courses of at least a day. Standardized mean differences for the indices were pooled as follows: IAQLQ -0.241 (95% CI, -0.362 to -0.121), ACT 0.14 (95% CI, 0.02 to 0.27), PCAQ -0.15 (95% CI, -0.28 to 0.01), IT 0.79 (95% CI, 0.05 to 1.54), ACQ -0.50 (95% CI, -0.69 to -0.30), SF-36 0.39 (95% CI, 0.16 to 0.62), PEFR 0.13 (95% CI, 0.01 to 0.26), and asthma symptoms score -0.34 (95% CI, -0.49 to -0.18).Discussion: The community pharmacists play their critical role in these interventions by educating the patients about the inhalers and drugs administration methods, improving the relief and control of the symptoms, and general health.Conclusions: This study shows that pharmacists' educational interventions in community pharmacy settings could significantly improve asthma severity and control, QOL, and medication adherence.

## O39

## Design, synthesis and biological evaluation of 1,2,3-triazole-1,2,3,4-tetrahydropyrimidine hybrids as anticancer and antimicrobial agents

*Sahar mirzayi*[1], *Saghi Sepehri*[2], *Mahmoud Ghazi Khansari*[3] ,*and Maryam Kakanj*[4]

[1]Student Research Committee, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[2]Department of Medicinal Chemistry, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[3]Department of Pharmacology, School of medicine, Tehran University of Medical Sciences, Tehran, Iran

[4]Food and Drug Laboratory Research Center, Food and Drug Administration, Tehran, Iran

Corresponding author: Dr. SaghiSepehri

Corresponding author Email: sepehri.saghi@yahoo.com

Introduction: Worldwide, 9.9 million cancer deaths occurred in 2020 (More than twice as many deaths from the COVID-19 pandemic) [1]. Multifactorial diseases such as cancer can be effectively treated by mainly attacking multiple targets, hybrid drugs seem to be the best solution to avoid cancer resistance which leads to therapeutic failures. Hybrid molecules are defined as chemical entities with two or more structural domains having different biological functions [2].In this study, designed and synthesized new 1,2,3,4-tetrahydropyrimidine and 1,2,3-triazole hybrid derivatives and their cytotoxicity activity was evaluated against MCF-7, Hep-G2 and A549 cell lines.Material and methods: In this study, a series of hybrid derivatives were designed and synthesized through Biginelli and Click reactions in three steps. After purification of the synthesized derivatives, their chemical structures were identified and confirmed by $^1$H-NMR, FT-IR and Mass spectroscopy techniques. Then, their cytotoxicity activity was evaluated against MCF-7, Hep-G2 and A549 cell lines and the results were compared with doxorubicin as a positive control.Results: According to the results, the best hybrid compounds having the thioxo group in the C2 position and the benzyl carboxylate group in the C5 position of the tetrahydropyrimidine ring, had the highest activity among other compounds against the two cell lines. In addition, screened compounds showed no activity against A549 cell line.Discussion: The investigation of the structure and activity relationship shows that the hybrid derivatives of 1,2,3-triazole-1,2,3,4-tetrahydropyrimidine with higher lipophilicity groups such as thioxo in the C2 position of tetrahydropyrimidine ring and also the bulk aromatic moieties in C5 position of this ring shows higher cytotoxic activity compared to other compounds with tested the cell lines.Conclusions: As a consequence, The emergence of drug-resistant especially multidrug-resistant cancers has already put a heavy burden on the world health system and hybrid drugs seem to be the best solution to avoid cancer

resistance. A series of 1,2,3-triazole–tetrahydropyrimidine hybrids have been designed and synthesized by Click chemistry and Biginelli reaction. The in vitro anti-cancer activity of all the synthesized compounds against three cancer cell lines MCF-7, Hep-G2 and A549 was evaluated and it is found that the compound $S_6$ have shown promising results in comparison with the marketed drug doxorubicin. Therefore, these compounds can serve as a promising lead candidate for further study.

## O40

## Synthesis and preparation of oral delivery systems based on folic acid-targeted resveratrol-loaded nanoparticles and investigating the efficacy in suppressing colonic inflammation

*Mahshid Naserifar[1], Mona Alibolandi[2]*

Corresponding author: Mona Alibolandi

Corresponding author Email: alibolandim@mums.ac.ir

Objective:Colonic inflammation is the most common inflammatory disease after rheumatoid arthritis and due to the side effects of chemical drugs, herbal remedies have been welcomed.Resveratrol (trans-3,5,4'-trihydroxystilbene), which is largely found in the skins of red grapes belongs to a class of polyphenolic compounds . Resveratrol demonstrated the ideal therapeutic effect while after oral administration it shows very short plasma half-life about 8 minutes. The aim of the current study was to prepare a PLGA-based resveratrol nanoparticles (NPs) which targeted with Folic Acid in order to protect resveratrol from fast degradation, modify its pharmacokinetics properties and increase the intestinal permeation and to evaluate the efficacy of the prepared drug system to suppress colon inflammation.Methods and Materials:First, the carboxylic acid group of folic acid was activated by EDC and NHS, then aminated by ethylene diamine and pyridin. At the next stage, PLGA was activated by EDC and NHS and reacted with aminated folic acid.
Resveratrol was encapsulated in PLGA and FA-conjugated PLGA in order to prepare targeted and non-targeted formulations.The amount of encapsulated resveratrol was analyzed through RP-HPLC at 310 nm. The size and morphology of the prepared nanoparticles was investigated using DLS and FE-SEM. The release profiles of the prepared formulation were evaluated at HCl 0.1 N for 2 h and PBS pH 7.4 for 144 h in order to mimic stomach and intestinal condition respectively. Caco-2 cells were used for trans-well permeability test. To evaluate the efficacy of *in vivo* drug delivery system, the effective concentration of TNBS was first determined to induce rectal inflammation in rats. Then the efficacy of synthesized drug delivery systems in suppressing colonic inflammation was investigated.Results: Obtained results demonstrated that the prepared formulations encapsulated the resveratol with high encapsulation efficiency of 90.67%±5.13% for PLGA, 59.05%±3.26% for PLGA-FA and loading content of 78% for PLGA, 42% for PLGA-FA. The sizes of nanoparticles were under 150 nm. *In vitro* release experiment showed that the prepared formulation was capable in retaining good amount of resveratrol in simulated gastric condition, while significant amount of resveratol was released in simulated intestinal condition.The permeability rates through Caco-2 monolayer was 4.45%, 60.96% and 99.03% for resveratrol, non-targeted and targeted formulations respectively during 180 minute.The effective concentration of TNBS to induce colonic inflammation in rats is 60kg/mg. According to the macroscopic results, improvement of colonic inflammation, folic acid targeted formulation shows better results than non-targeted formulation and Asacol as positive control. The pathological results of rat intestinal samples also show no effective treatment of inflammation by resveratrol solution form versus formulations in which resveratrol is encapsulated, and it is worth noting that, the microscopic studies also showed that the targeted formulation is well able to inhibit inflammation and reduce neutrophil and lymphocytes accumulation after one week's patrol.Conclusion:It could be concluded that the encapsulation of resveratrol into biodegradable PLGA nanoparticles increased the half-life of resveratrol, and the efficacy of the synthesized formulation in suppressing colonic inflammation. It is worth noting that targeted system demonstrated highest efficacy in suppressing colon inflammation.

## O41

## The prevalence of extended spectrum betalactamases (ESBLs) producing *Enterobacteriaceae* isolated from hospitalised patients in Shahid Rahimi hospital in khorramabad from june to September 2019

*Najibpour Nasim[1]*

[1]Department of pharmacotherapy, Faculty of pharmacy, Lorestan University of Medical Science, Khorramabad, Iran

[2]Student Research Committee, Faculty of pharmacy, Lorestan University of Medical Science, Khorramabad, Iran

[3]Research Center, Lorestan University of Medical Science, Khorramabad, Iran

Corresponding author: Kharazmkia Ali

Corresponding author Email: kharazmkia@gmail.com

Introduction: Beta-lactam antibiotics are one of the most widely used antibiotics in the treatment of bacterial infections. The production of beta-lactamases among gram-negative bacteria, especially Enterobacteriaceae, is one of the major causes of resistance to these antibiotics worldwide. The resistance in Enterobacteriaceae bacteria is increasing due to the presence of broad-spectrum beta-lactamases against antibiotics. Also their prevalence varies in different countries, regions and even hospitals. So our aim in this study was to investigate the frequency of this enzyme in clinical samples. Our data are obtained from patients admitted to Shahid Rahimi Hospital in Khorramabad.Material and methods: In this descriptive cross-sectional study, 215 *Enterobacteriaceae* isolates were collected from clinical specimens of patients admitted to Shahid Rahimi Hospital in Khorramabad and identified by standard biochemical tests. After initial screening by Kirby-Bauer method, *Enterobacteriaceae* isolates producing ESBLs were identified by confirmatory combination disk test. Then our collecting data were entered into SPSS26 software and analyzed. Chi-square test was used to investigate the relationship between qualitative variables.Results: In this study, 215 *Enterobacteriaceae* isolates were examined. (69.3%) 149 samples of all isolates were generators of ESBLs. The prevalence of *Enterobacteriaceae* isolates producing ESBLs was in urine (61.4%), blood (5.1%) and fecal (2.8%) samples, respectively. The highest prevalence of ESBLs generating isolates was obtained in inpatient emergency wards (24.1%) and inpatient Internal intensive care units (8.8%), respectively. The highest frequency of ESBLs was among the identified bacteria in Escherichia coli (51.2%). From the samples obtained, (36.7%) were female and (32.6%) were male ESBLs producers. The highest frequency of ESBLs isolates was in the age group over 65 years (32.6%).Discussion: In our study, 215 Enterobacteriaceae isolates were collected from hospitalized patients during the period from June to September 2019, of which 149 isolates (69.3%) were positive for ESBLs. This suggests that in our study the role of ESBLs in resistance to cephalosporins was more important than other resistance mechanisms such as the efflux pump.The differences in the results of our study with other studies may be due to various reasons, including the pattern of antibiotic use, especially cephalosporins, the amount of antibiotics used,

and the difference in the collection time of Enterobacteriaceae isolates.Conclusions: Statistical studies showed the highest frequency of ESBLs in Escherichia coli. The highest frequency of ESBLs-producing isolates was in the age group over 65 years. The inpatient emergency department and internal ICU had the highest prevalence of ESBLs, respectively. There was no relationship between gender and the presence of ESBLs as well as the type of sample and the presence of ESBLs.

## O42

## Preparation and characterization of a novel crown ether based vesicular carrier for topical ocular drug delivery

*Mohammad Norouzi[1], Nooshin Tasharrofi[1]*

[1]Department of Pharmaceutics, faculty of pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran

Corresponding author: Mohammad Norouzi

Corresponding author Email: m.norouzi.pharmacist@gmail.com

Introduction: One of the main challenges with ocular drug delivery is the low penetration of the drug from the surface of the eye (1). The use of safe penetration enhancers could be a solution in this regard. Crown ethers are molecules that have shown promising effects in ocular drug delivery. These molecules can increase membrane permeability due to the chelating effect of calcium ions which in turn can weaken the binding of tight junctions (2). The use of drug delivery systems such as liposomes for topical drug delivery to the eye has also received considerable attention (3). In the present study, a new 18-crown-6-based amphibian compound was synthesized and used as a component of liposomes to make them flexible and facilitate their passage through the biological membrane as well as increasing their penetration.Material and methods: A novel amphiphile molecule was synthesized from coupling oleic acid and 2-aminomethyl-18-crown-6 and the molecule formation was confirmed by FTIR. The molecule was placed in the liposome structure along with other components, namely soybean phosphatidylcholine, and cholesterol. A model hydrophilic drug was exploited for loading in the liposome. Using the design expert statistical program, I-optimal surface response model was used to optimize the liposome components; the entrapment efficacy (EE) and stability (after 30 days at different temperatures) were considered as the responses. Then the release profile of the optimal formulation was verified. Morphology, size, and zeta potential were also assessed using SEM and zetasizer, respectively. Finally, the passage through the excised bovine cornea was examined through ex-vivo studies.Results: In optimal formulation, Cholesterol, drug and amphiphile molecules were used in weight ratios of 6.8%, 69%, 58% to phosphatidylcholine with 13 cycle of freeze-thaw and was shown to have the maximum % EE (85± 7.4%). By increasing amphiphile molecule ratio and cycle of freeze-thaw, EE% will increase. Using more cholesterol in formulation will decrease EE%. Optimized formulations for long term preservation:For long term stability in 25℃ temperature, Cholesterol, drug and amphiphile molecules were used in weight ratios of 11%, 46%, 47% to phosphatidylcholine with 5 cycle of freeze-thaw and was shown to have the maximum stability at 25℃ after 30 daysFor long term stability in 4℃ temperature, drug and amphiphile molecules were used in weight ratios of 11%, 46%, 47% to phosphatidylcholine with 5 cycle of freeze-thaw and was shown to have the maximum stability at 4℃ after 30 days.For long term stability in -8℃ temperature, Cholesterol, drug and amphiphile molecules were used in weight ratios of 11%, 24%, 51% to phosphatidylcholine with 9 cycle of freeze-thaw and was shown to have the maximum stability at -8℃ after 30 daysThe calculated size of the carrier was 100 ± 5 nm with a spherical appearance and zeta potential was -20. Analysis of the release data demonstrated that the optimal formula follows the first-order release profile. The ex-vivo experiments are not accomplished by now and their data will be reported then.Discussion: In this study, an optimal formulation was obtained that was able to show appropriate pharmaceutical properties. If this formulation can also show good results in clinical studies, we can hope for a bright future for non-invasive ocular drug delivery systems which can pave the way for new treatments for various eye problems.Conclusions: In this study a novel liposomal formulation containing a penetration enhancer, in the form of an amphiphile molecule, has been made and optimized. Using design expert program, optimized formulation with 85± 7.4%EE were made and tested for release profile which followed the first-order release profile. this drug delivery system showed us promising results and could be an optimal solution for long term drug delivery to posterior segment of the eye after more complete in-vivo studies.

## O43

## Neuroprotective Effect of Naringenin Loaded Solid Lipid Nanoparticles against STZ-Induced Neurotoxicity through Autophagy Blockage

*Zeinab Nouri[1], Soraya Sajadimajd[2], Mohammad Hosein Farzaei[2]*

[1]Student Research Committee, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah Iran

[2]Pharmaceutical Sciences Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

Corresponding author: Mohammad Hosein Farzaei

Corresponding author Email: mh.farzaei@gmail.com

Introduction: Naringenin (Nar) has been identified as a neuroprotective compound with displayed beneficial effects in Alzheimer's disease (1). However, low bioavailability and solubility are the major concerns pertaining to the use of Nar (2). Autophagy has been described as a cell-quality control that possesses the ability to maintain cellular homeostasis and normal function by removing damaged macromolecules and organelles (3). Aberrant function of autophagy has been found as a well-established participant in the pathogenesis of neuronal degeneration (4). In the present study, Nar and Nar-loaded solid lipid nanoparticles (Nar-SLNs) were used to protect rat PC12 cells against streptozotocin (STZ)-induced neurotoxicityMaterial and methods: Nar-SLNs were fabricated by a solvent evaporation-ultrasonic method (5). Nar-SLNs characterized for particles size, size distribution, and polydispersity index (PDI), zeta potential, scanning electron microscope (SEM), and Fourier transform infrared spectroscopy (FT-IR). The drug loading and encapsulation efficiency were calculated indirectly by measuring the amount of non-capsulated Nar. Depending on the experimental patterns including pre-treatment, co-treatment, and post-treatment, PC12 cells were exposed to STZ and desired doses of the SLN, Nar, and Nar-SLNs. The viability of the cells, the mitochondrial membrane potential (MMP) and the expression of miR-21, miR-22, Akt, ATG5, Beclin1, and LC3 were evaluated by using MTT assay, rhodamine 123 fluorescent dye, and qRT-PCR, respectively.Results: SLNs and Nar-SLNs possess the smooth surface with an average size of 108 and 180 nm, respectively, with a negative zeta potential. The encapsulation efficiency and loading capacity of Nar in SLNs were 90.32%, and 40.1%, respectively. The nanoformulation revealed a sustained drug release *in vitro* up to 72 h and followed Higuchi kinetics. Nar-SLNs displayed neuroprotective effect

by augmenting the viability of PC12 cells and increasing MMP. In addition, Nar-SLNs suppressed autophagy which was stimulated by STZ whereas, the free Nar demonstrated lower effect. Discussion: In our study, Nar-SLNs demonstrated an initial burst release within 2 h, followed by a sustained release pattern up to 72 h. This initial burst release could be attributed to the rapid dissolution of Nar that are incorporated in the shell of SLNs. To overcome this drawback the surface modification of the SLNs has been developed. Our study suggested that the mechanism of neuroprotective activity of Nar and its nanoformulation against STZ-induced neurotoxicity might be attributed to autophagy blockage and MMP promotion. In the present experiment, pre-treatment of PC12 cells with either Nar or Nar-SLN alleviated neurotoxicity induced by STZ but Nar-SLN indicated a stronger efficacy. This is may be due to low particle size of Nar-SLN, which can facilitate accessibility and permeability through the membrane lipid bilayer. Conclusions: Taken together, these results clearly indicated that Nar-SLNs could be a good candidate for the prevention of neurodegenerative diseases. Further preclinical and clinical investigations are necessary to confirm the efficacy of Nar and its nanoformulation therapy in patients with neurodegeneration. Additionally, future investigations should be focused on engineered methods to design surface modified nanostructures of the SLNs to access optimized drug delivery systems.

## O44

## Design and optimization of Niosomes for topical delivery of Allantoin: Application of Box–Behnken design and in-vitro evaluation

*Mohammadreza Niavand[1], Mozhgan Rostaei[1] and Seyed Yaser Vafaei[1]*

[1]Department of Pharmaceutics, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran

Corresponding author: Seyed Yaser Vafaei1

Corresponding author Email: y.vafaei@umsha.ac.ir

Introduction: Allantoin is a chemical substance with proved anti-inflammatory effects and several uses in cosmetic and medicinal products. This compound has poor penetration from the stratum corneum as the result of its low Distribution coefficient (Log p ≈ 3.14), and this is the biggest limitation in topical uses of Allantoin. In recent studies for improving allantoin pharmacokinetics, various drugs carrier is used and evaluated. Novel drug nanocarriers like niosome can improve skin penetration, alter the release profile of drugs and ameliorate drugs Physico-chemical specification, and lastly can enhance the effectiveness of allantoin. This study aims to evolve and optimize the Allantoin-loaded niosome.Material and methods: Box-Behnken (BB) was applied to optimize formulation to reach higher Entrapment efficiency (EE%) and adequate particle size. A total of 15 experiments were operated, three independent variables were evaluated, drug amount, Span 60: Tween 80 weights ratio, and Surfactant: Cholesterol molar ratio. Particle size, polydispersity index (PDI), and EE% were selected as dependent variables. Niosome were produced by the thin-film hydration method.Particle size (z-average), PDI, and zeta potential of noisome suspension were measured by dynamic light scattering (Zetasizer Nano Series, Malvern instrument Ltd., Malvern, UK)The EE% was evaluated indirectly. Exerting Amicon Ultra-15-membrane (MWCO 15,000 Da). By measuring the difference between the absolute amount of Allantoin in the formulation and the amount of Allantoin that passed through the filter membrane. The concentration of the drug was calculated by UV-Visible spectroscopy.The optimized formula was acquired using design expert software to reach maximum EE% and Sufficient particle size. The optimized formula was then prepared and appraised to investigate the validity of the calculated optimal formulation.Results: The preliminary studies were carried out to choose the best Surfactants for preparing Allantoin-loaded niosome, Different surfactants tested and tween 80: span 60 were chosen as they performed the highest EE% and optimal particle size.The size of the Allantoin-loaded niosome is ranged between 135 and 256 nm, the range of PDI is between 0.412 to 0.683 and finally, a range of EE% is between 75.3-88.1 %Discussion: The key target of the Box-Behnken design is achieving maximum EE% and adequate particle size, independent variables play a pivotal role in particle size and EE%. An increase in the amount of cholesterol can enlarge niosomes. A mixture of Span 60 and Tween 80 is produced the smallest particle size and PDI.Design expert software calculates an optimal formula to be prepared whose overall desirability was 0.671. The design expert optimum formula prepared and evaluated, the difference between predicted and observed responses were insignificant, demonstrating the optimization processes validity.Conclusions: In this study, Allantoin-loaded Niosome were investigated, Box-Behnken design was applied to statistically optimize the formulation variable, the optimum formulation showed reasonable drug EE% and optimum particle size. This selected formula can improve the pharmacokinetics of Allantoin and possible promising way of Allantoin topical delivery, further in vitro and in vivo study is required to confirm the advantages and safety of developed niosomes.

## O45

## Optimization of Ultrasound-Assisted Acidic-Solvent Extraction of Colchicine from Colchicum kurdicum (Bornm.) Stef. Using Response Surface Methodology

*Faezeh Vahidi Motlagh[1], Ali Davoodi[2], Maryam Khaki[3]*

[1]Department of Pharmacognosy, School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[2]Department of Pharmacognosy and Biotechnology, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[3]Pharmacy Faculty, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran

Corresponding author: Faezeh Vahidi Motlagh

Corresponding author Email: Faezehvhdi1997@gmail.com

Introduction: Colchicum kurdicum (Bornm.) Stef. is a flowering perennial monocotyledon plant that has many important bioactive compounds especially colchicine and colchicine derivatives. In this study, the ultrasound-assisted acidic-solvent extraction method coupled with response-surface method was presented as the successful method for large scale extraction of colchicine as an alkaloid compound. Moreover, Colchicum kurdicum was introduced as an important endemic plant for extraction of colchicine.Material and methods: According to the literatures, methanol/deionized water (70:30) solvent system was selected for the extraction. In addition, the response-surface method was used for analysis and optimization of colchicine extraction by ultrasonic-assisted acidic-solvent extraction method. Subsequently, colchicine was extracted using this method and the effects of solvent pH, extraction time, solvent/plant ratio, power, and temperature were evaluated.Results: After all analysis procedures, 0.99 mg colchicine/g dried corms was achieved with the following conditions: solvent pH 4, Extraction time 120 minutes, solvent/plant ratio 20 mL/g, power 100 W,

and temperature 60 ºC.Discussion: Studies such as the present study can be helpful to increase the extraction of important bioactive compounds with low cost and high facility as the main efficacies of this method. In addition, this method has several advantages for the extraction of all compounds especially high yield, low extraction time and being held in lower temperatures.Conclusions: According to this study, ultrasonic-assisted acidic-solvent extraction was found an effective method for extraction of colchicine from Colchicum kurdicum (Bornm.) Stef. compared to other extraction methods.

# Poster presentations

## P1

## Anti-HPV activity prediction and identification of novel HPV type 16 inhibitors by protein-based virtual screening

*Sahar mirzayi[1], Saghi Sepehri[2], Nima Razzaghi-Asl[2] , and Karim Mahnam[3]*

[1]Student Research Committee, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[2]Department of Medicinal Chemistry, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[3]Department of Biology, Faculty of Basic Science, Shahrekord University, Shahrekord, Iran

Corresponding author: Dr. SaghiSepehri
Corresponding author Email: sepehri.saghi@yahoo.com

Introduction: Human papillomavirus (HPV) is the most common sexually transmitted infection. It is estimated that HPV-related cancers involving various anatomical sites account for 4.5% of all human cancers.[1]. Two HPV types (16 and 18) cause 70% of cervical cancers and precancerous cervical lesions [2].In this study, we introduce novel small molecular hits to inhibit HPV type 16 using a structure-based virtual screening technique.Material and methods: Candidate compounds were collected from Pubchem and DrugBank databases and subjected to some filtering processes in subsequent steps.The filtering criteria included pharmacokinetic properties as well as molecular docking and molecular dynamics simulation. This study was carried out in two stages. A library of more than 8 thousand compounds was established based on structural similarity with jaceosidin and cidofovir. At the second step, the following criteria were considered to choose the best compounds: The highest scoring obtained by PyRx software, pharmacokinetic properties based on the drug-likeness criteria using Molinspiration web server, ADMET properties for analysis of the disposition of these compounds within an organism using a proper server, the highest binding energy and the best interactions with the active site residues performed for the last filtered compounds using the Autodock software, and further analysis of the interactions of these compounds with the HPV active site residues by molecular dynamic simulation.Results: Among all compounds of the library, 100 compounds were able to pass successfully all filtrations. Molecular docking of approved compounds was performed. In the next step, compounds were investigated based on the best free binding energy and different interactions with active site residues. Finally, MD simulations on three top-ranked structures were carried out. Furthermore, RMSD, RMSF, hydrogen binds, Rg and energy analysis during MD simulation certainly indicated the stable binding of selected compounds with HPV structure.Discussion: Docking and MD results revealed that hydrophobic contacts and optimum hydrogen bonds were determinant factors in the interactions of in silico hits and HPV. Furthermore, the presence of some residues seemed was essential for interaction with compounds in the active site.Conclusions: Molecular docking simulation was carried out to identify interactions of the filtered molecules. Molecular dynamics confirmed the superior inhibitory ability of selected compounds over the jaceosidin and cidofovir. Analyses of the molecular docking and dynamic simulation results showed that the selected hits are more stable and potent than jaceosidin and cidofovir in the HPV type 16 binding site.

## P2

## Insight into Structure Activity Relationship of Privileged Azoles as Antifungal Agents

*Ata Ahmadi Beiraq[1], Elahe Mohammadnezhadi[2], Nima razzaghi Asl[3], Pari Karami[4]*

[1] Student Research Committee, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[2] Student Research Committee, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[3] Department of Medicinal Chemistry, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[4]Biosensors and Bioelectronics Research Center, Ardabil University of Medical Sciences, Ardabil, Iran

Corresponding author: Ata Ahmadi Beiraq
Corresponding author Email: Ataahb99@gmail.com

Introduction: The prevalence of fungal infections has increased dramatically during past decades and the situation is regarded as a severe threat to human health and life [1]. Fungal infection ranges from non-fatal skin and mucous membrane disease to systemic life-threatening infections involving many organs. Increased incidence of life-threatening fungal infections (mycosis) occurs mainly in immunosuppressed hosts, patients subjected to cancer chemotherapy or organ transplantation and patients with acquired immunodeficiency syndrome (AIDS) [2]. Diverse natural and synthetic antifungal compounds hitting different fungal targets have been proposed up to now and careful inspection of the literature reveals that significant number of the reported antifungal structures belong to the 5-membered azole heterocycles i.e., triazoles, pyrazoles, imidazoles, tetrazoles, or relevant bio isosteric compounds. In continuation to our interest in medicinal chemistry of antimicrobial agents and with the aim of providing a forum for extending the scope of privileged azole-based antifungals, it was attempted to retrieve a structure-based classification along with structure activity relationship (SAR) of respective small molecules. Material and methods: Reviewed structures included azole-based antifungal molecules that were reported throughout 2016-2020 without considering anti-phytopathogenic fungal agents. Major source of information was the validated ScienceDirect and PubMed articles including azole based antifungal agents.Results: In overall 237 azole derivatives were taken into consideration. To explain more, 43 triazoles, 57 imidazoles, 60 pyrazoles, 12 tetrazoles and 65 bio isosteres including thiazole, isoxazole, oxathiadiazole and oxadiazole were evaluated in term of structure activity relationships (SAR).Discussion: Although, the arsenal of antifungal drugs has been used against different fungi species, currently available chemotherapeutic agents do not meet the growing requirements for infection management. Drug induced toxicity, drug resistance and lack of desired drug potency in some cases calls an urgent need to explore and develop novel antifungal agents as a constant necessity in the clinical therapy. Accordingly, following strategies may extend the scope of privileged medicinal scaffolds as antifungal agents: (1) Developing new chemical entities (NCEs) that hit selectively a vital fungal target, (2) Repositioning (repurposing) of available drugs as antifungal agents, (3) Combination therapy and (4) Developing

hybrid/chimeric antifungal agents hitting two or more fungal targets.Conclusions: The importance of attaining non-resistant, selective and cost-effective treatment has encouraged the design and development of new antifungal agents. A great deal of relevant effort has been focused on the synthesis and biological assessments of nitrogen containing heterocycles and in particular azole derivatives. In this regard, SAR studies conferred applicable concepts about substituent effects and enclosed structural potentials of candidate molecules toward developing potent and selective antifungal agents.

P3

## Insight into Structure Activity Relationship of Privileged Azoles as Antifungal Agents

*Ata Ahmadi[1], Elaheh Mohamadnejadi[1], Pari Karami[2], Nima Razzaghi-Asl[3, *]*

[1]Student Research Committee, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[2]Biosensors and Bioelectronics Research Center, Ardabil University of Medical Sciences, Ardabil, Iran

[3]Department of Medicinal Chemistry, School of Pharmacy, Ardabil University of Medical Sciences,

Corresponding author: Nima Razzaghi

Corresponding author Email: n.razzaghi@pharmacy.arums.ac.ir

Introduction: The prevalence of fungal infections has increased dramatically during past decades and the situation is regarded as a severe threat to human health and life [1]. Fungal infection ranges from non-fatal skin and mucous membrane disease to systemic life-threatening infections involving many organs. Increased incidence of life-threatening fungal infections (mycosis) occurs mainly in immunosuppressed hosts, patients subjected to cancer chemotherapy or organ transplantation and patients with acquired immunodeficiency syndrome (AIDS) [2]. Diverse natural and synthetic antifungal compounds hitting different fungal targets have been proposed up to now and careful inspection of the literature reveals that significant number of the reported antifungal structures belong to the 5-membered azole heterocycles i.e., triazoles, pyrazoles, imidazoles, tetrazoles, or relevant bio isosteric compounds. In continuation to our interest in medicinal chemistry of antimicrobial agents and with the aim of providing a forum for extending the scope of privileged azole-based antifungals, it was attempted to retrieve a structure-based classification along with structure activity relationship (SAR) of respective small molecules. Material and methods: Reviewed structures included azole-based antifungal molecules that were reported throughout 2016-2020 without considering anti-phytopathogenic fungal agents. Major source of information was the validated ScienceDirect and PubMed articles including azole based antifungal agents.Results: In overall 237 azole derivatives were taken into consideration. To explain more, 43 triazoles, 57 imidazoles, 60 pyrazoles, 12 tetrazoles and 65 bio isosteres including thiazole, isoxazole, oxathiadiazole and oxadiazole were evaluated in term of structure activity relationships (SAR).Discussion: Although, the arsenal of antifungal drugs has been used against different fungi species, currently available chemotherapeutic agents do not meet the growing requirements for infection management. Drug induced toxicity, drug resistance and lack of desired drug potency in some cases calls an urgent need to explore and develop novel antifungal agents as a constant necessity in the clinical therapy. Accordingly, following strategies may extend the scope of privileged medicinal scaffolds as antifungal agents: (1) Developing new chemical entities (NCEs) that hit selectively a vital fungal target, (2) Repositioning (repurposing) of available drugs as antifungal agents, (3) Combination therapy and (4) Developing hybrid/chimeric antifungal agents hitting two or more fungal targets.Conclusions: The importance of attaining non-resistant, selective and cost-effective treatment has encouraged the design and development of new antifungal agents. A great deal of relevant effort has been focused on the synthesis and biological assessments of nitrogen containing heterocycles and in particular azole derivatives. In this regard, SAR studies conferred applicable concepts about substituent effects and enclosed structural potentials of candidate molecules toward developing potent and selective antifungal agents.

P4

## In silico Saturation Analysis of Mtb KatG Variants via Molecular Docking and DFT Methods: Protein Stability, Functionality and Intermolecular Interactions

*Nasrin Panahi[1], Nima Razzaghi-Asl[2]*

[1] Student Research Committee, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

[2] Department of Medicinal Chemistry, School of Pharmacy, Ardabil University of Medical Sciences,

Corresponding Author: Nima Razzaghi-Asl

Corresponding author Email: n.razzaghi@pharmacy.arums.ac.ir

Introduction: Tuberculosis (TB), usually caused by *Mycobacterium Tuberculosis* (Mtb), is a common infectious disease in current century. Despite the high efficacy of isoniazid (INH) as an important first-line TB drug, resistance toward INH is one of the serious challenges. In association with INH resistance, the spontaneous mutation in the *KatG* gene is widely reported. Missense mutations that reduce or eliminate the activity of KatG, a heme-dependent enzyme, lead to increased resistance to INH.Material and methods: Protein stability variations were estimated through Gibbs free energies of folding and moreover; flexibility fluctuations of the enzyme were obtained via changes in vibrational entropies were predicted via elastic network contact model (ENCoM) by DynaMut server. To determine the functionality of the enzyme, more stringent cutoff was applied for deriving PROVEAN scores. Subsequently, combined molecular docking (AutoDock4.2) and density functional theory (DFT) (ORCA software) were used to explore the intermolecular interaction of INH to wild type KatG (D137, M255 & S315) and all mutant variants. Binding contribution of interacted residues within target active site were all estimated through amino acid decomposition analysis in B3LYP level of theory with Def2-TZVPP split basis set.Results: Our calculation level indicated protein stability changes upon saturated Mtb KatG mutagenesis between -2.412 (M255G, the most destabilizing) to 2.476 kcal/mol (D137W, the most stabilizing). All of the SPMs on Ser315 exhibited stabilizing effect on enzyme structure whereas, in the case of Asp137, most of the mutations (%85) were classified as stabilizing and for Met255, destabilizing effects (%85) were dominant. D137I, D137F, D137W and M255G showed high stabilizing/destabilizing effect ($\Delta\Delta G \geq |2|$ kcal/mol) on KatG structure. Substitution of Asp137 with valine represented a mere conformation with no flexibility change in KatG structure. The Gibbs binding free energy between INH and wild type Mtb KatG was estimated to be -7.03 kcal/mol. Although estimated affinity changes to heme were subtle but in the case of M255C, $\Delta\Delta E_{mutation}$ was found to be -6.43 kcal/mol. Accordingly, Arg104 ($\Delta\Delta E_{mutation}$ 0.491 kcal/mol) and Ile228 ($\Delta\Delta E_{mutation}$ 0.057 kcal/mol) were the only destabilizing residues and it seemed plausible to design INH derivatives with reinforced interactions to Arg104 and Ile228.Discussion: observed trends revealed that almost stabilizing effects of mutations were occurred with rigidification of structure and vice versa. Obtained results were in accordance with the

previous reports since no H-bond interaction could be observed for secondary amine of INH and moreover Ser315 did not contribute to any hydrogen bonds. It was revealed that INH participated in significant H-bonds interface compromising polar residues Asp137, His108, Trp107 and Tyr229. Primary amine participated in H-bond interaction with Asp137 side chain carboxyl whereas, carbonyl oxygen and pyridine nitrogen each emerged as bidentate hydrogen bond acceptors (HBA). Appropriate spatial orientation of INH provided a parallel π-stacking contact between pyridine aromatic ring and one of the heme porphyrin pyrroles. Conclusions: Besides experimental mutations collected from the literature, several new mutations that may disrupt the interaction of INH with the enzyme and cause deleterious effects were also identified. Various pathogenic SPMs persuade the design and discovery of new bioactive agents to overcome drug-resistance.

P5

## Efficacy of Iranian traditional medicine in the treatment of hair loss

*Milad Saadatkish[1], Mehrdad Zeinalian[2], Mohammad Ansaripour[3]*

[1] School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences.

[2] Department of Genetics and Molecular biology, School of Medicine, Isfahan University of Medical sciences, Isfahan, Iran

[3] Department of Persian Medicine, Faculty of Medicine, Isfahan University of medical sciences, Isfahan, Iran.

Corresponding author: Mohammad Ansaripour

Corresponding author Email: moansaripour@yahoo.com

Introduction: Every year, millions of people around the world suffer from different hair loss disorders. Iranian traditional medicine (ITM) refers to a wide range of knowledge, skills, and training. Due to its low side effects, simplicity, and availability, it has long been used to treat various diseases. The available documents for the treatment of various diseases, including hair loss disorder, have been recorded in the references of Iranian traditional medicine. However, few papers studied the scientific evidence supporting the beneficial effects of these compounds for various diseases. In this paper, we evaluated the claims of ITM about anti-hair loss products using scientific evidence. To shed light on the possibility of using ITM remedies for new medical strategies in the health care system.methods: First, intrinsic and extrinsic factors controlling the hair growth cycle were evaluated. The most important factors were selected.Next, three main ITM texts including Tohfat-ulmomenin (Mo'men tonekaboni), Makhzan-ul-Adviah (Aghili Shirazi), and al-Qanun fi al-Tibb (Avicenna) have been examined. Efforts were also made to find the best scientific name of the traditional herbs. Then the electronic resources, including Google Scholar, and PubMed, were reviewed to find available articles about this topic. All papers that studied the effect of herbs on the selected factors were examined. In addition, all related In-vitro, In-vivo, and clinical trials, were evaluated. Only original articles published in English and Persian were taken into consideration.Results: The initial studies illustrated that the main factors and bio-markers controlling the hair growth cycle include: IGF-1, VEGF, EGF, eNOS, FGF, DHT, and TGF-β. In such a way that the last two activate the genes responsible for hair follicle regression, but others stimulate hair follicle development. Eight compounds were selected among the mentioned anti-hair loss products based on the number of repetitions in the texts and availability. These compounds include; myrtus communis, Lawsonia inermis (Henna), Phyllanthus emblica (Amla), Terminalia chebula (myrobalan), Aloe spp, Adiantum capillus veneris (fern), Ziziphus spina-christi (Cedar), and Trigonella.Examination of the effects of herbal extracts on biomarkers showed that Amla has 6 of the 7 factors needed to prevent hair loss. After that, Aloe, Henna, Terminalia, Trigonella (5 items), and Myrtus, Fern, and Cedar (3 items) are the most reliable herbs to prevent hair loss regarding these data. It should note that Amla significantly inhibited the DHT level, the most important biomarker responsible for hair follicle regression.Discussion and conclusion:According to the In-Vitro and In-Vivo tests and also few clinical trials, acceptable results were showed for 6 compounds. This can suggest that the claims of ITM are mostly true about the mentioned hair loss products. It should note that more clinical trials are needed to prove these findings.

P6

## Efficacy of Zagros medicinal plants as a wound-healing agent: a comparative review

*Milad Saadatkish[1], Mohammad Ansaripour[2]*

[1] School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences.

[2] Department of Persian Medicine, Faculty of Medicine, Isfahan University of medical sciences, Isfahan, Iran.

Corresponding author: Mohammad Ansaripour

Corresponding author Email: moansaripour@yahoo.com

Introduction: Traditional medicine is related to the studies and experiences of the past thousands of years, and ethnobotany and ethnomedicine are related to the knowledge of native plants and local therapies of a region. Traditional and ethnobotanical medicine are closely related. According to World Health Organization (WHO), about 80% of primary treatments in developing countries are performed using traditional medicine. In addition, people living far from the city generally do not have access to conventional medical treatments. The Zagros Mountains are a long mountain range in Iran, southeastern Turkey and northern Iraq. The zagros is home to a wide variety of herbal plants. Acute and chronic wounds are one of the most important problems in the healthcare system, which millions of people suffer from it annually.In the present paper, we studied the claims of ethnomedicine about wound healing products using scientific evidence to clarify the efficacy of these home remedies for new medical strategies in the wound care system.methods: We searched google scholar and Pubmed with the following search terms "zagros ethnomedicine" and "zagros ethnobotanical" and "zagros traditional medicine". Moreover, the main keywords were also searched for the provinces in which the Zagros Mountains are located, including Ilam, kordestan and lorestan.All claimed wound healing product were investigated. Then electronic databases were used to study their safety and efficacy in wound healing. All in-Vitro, In-vivo and possible clinical trials were investigated.Results: 24 compounds with the wound healing claim were found in the ethnobotanical papers. The efficacy of 6 compounds on wound healing was proven via a pharmacologic model. These compounds include: Myrtus communis /Nerium oleander /Scrophularia striata /Sesamum indicum L./ Tragopogon graminifolius /Citrullus colocynthis.Moreover, 10 compounds had the potential of wound healing effect. In such a way that they have shown good anti-oxidant and anti-microbial effects. These compounds include:Calendula persica/ Scrophularia deserti/ Sesamum indicum L./ Seidlitzia rosmarinus/ Ferulago angulate/ Aristolochia clematitis L. /Echium italicum L. /Achillea wilhelmsii K.Koch /Calendula arvensis /Solanum americanum Mill.Discussion and conclusion:The studies in this article show that ethnomedicine's claims about wound healing of more than 60% were consistent with existing scientific literature. It should note that all 24 compounds can have amazing wound-healing effects, but until now a few studies have considered their effects. Hence, studies are needed to prove their specific effectiveness.

P7

## BR2, a Novel Cancer Specific Cell Penetrating Peptide for Targeted Cancer Therapy: a Review Article

*Fatemeh Sadeghi*[1], *Marziyeh Kajbaf*[1], *Fatemeh Shafiee*[2 *]

[1]Department of Pharmaceutical Biotechnology, school of pharmacy and pharmaceutical sciences, Isfahan University of Medical Sciences, Isfahan, Iran.

[2*] School of Pharmacy and Pharmaceutical Sciences. Isfahan University of Medical Sciences, Hezar Jarib Ave. Isfahan, Iran.
Corresponding author: Fatemeh Shafiee
Corresponding author Email: f_shafiee@pharm.mui.ac.i

Introduction: Conventional chemotherapeutic agents for the cancer treatment mainly focus on mass cell killing without high specificity, thus often cause severe toxicities (He & Shi, 2014). The concept of targeted cancer therapy is an important mean to improve the therapeutic potential of anticancer agents (Y Ahmed et al., 2010). using of cell penetrating peptides for drug delivery is a good approach for this concept (Ansari et al., 2014). However, there is a strong need for the development of cancer-specific and non-toxic CPPs drug delivery vehicles for effective and specific cancer treatments (Ansari et al., 2014). Buforin II (BF2) is an antimicrobial peptide with cell penetrating ability especially for cancer cells (H.-C. Wu, Chang, & Huang, 2006). This review focuses on the studies used buforin and its derivatives as the targeting moiety for the production of immunotoxins with cancer specifity for eradication of various tumor cells.Material and methods: Key words including BF2, buforin II, Buforin IIb, BR2, Buforin derivatives, anti-microbial peptide, AMPs, cell penetrating peptides, CPPs, targeted therapy and drug delivery was searched in Medline, google scholar, ScienceDirect, and Scopus data bases. All related articles were analyzed for their results. Results: About 84 Articles, only in four articles, buforin or its derivatives has been used for the targeted delivery of various chemotherapeutic agents against different cancer cell lines including: BR2-scfv-kRAS (Lim et al., 2013), DT386-BR2 (Shafiee, Rabbani, & Jahanian-Najafabadi, 2016), cysplatin-bufIIb (D. Wu et al., 2014), and cTPP-Buf (Ducry & Stump, 2009) , Buf-II-PEA-magnetite(Perez et al., 2019), IL24-BR2 (Pourhadi, Jamalzade, Jahanian-Najafabadi, & Shafiee, 2019), VEGF siRNA-BR2(Y. W. Lee et al., 2018), BR2-SOX17(Yang et al., 2020)Discussion: buforin and its derivatives caused effective targeting in delivery of various anti-cancer agents for different cells.Conclusions: it is concluded that those buforin derivatives with the lower cytotoxicity against normal cells but with ability to penetrate to cancer cells has the potency for acting as a targeted delivery vehicle.

P8

## Designing and expression of a novel immunotoxin containing anti-HER2 single chain variable fragment and modified form of *Pseudomonas aeruginosa* exotoxin.

*Zahra Shariaty*[1]*Vajihe Akbari*[* 2], *and Fateme Shafiee*[2]

[1]Student of Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Department of Pharmaceutical Biotechnology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
Corresponding author:Vajihe Akbari
Corresponding author Email: **v_akbari@pharm.mui.ac.ir**

Introduction: The most prevalent cancer around the world as well as Iran among women is breast malignanceis. Many breast cancer cells express human epidermal growth factor receptor2 (HER2) on the cell surface Which correlate with poor prognosis and candidate patients to receive anti-HER treatments such as monoclonal antibodies trastuzumab and pertuzumab. However, drug resistance encourages scientists to design new drugs such as immunotoxins (ITs). ITs are proteins containing a targeting and toxic moiety. The mechanism of action of the ITs is binding to antigen on the surface of the targeted cell and enter the cell via endocytosis then the toxic domain induces cell toxicity. In this study we produced a novel IT targets HER2 on the surface of breast cancer cells by a scFv derived from pertuzumab and a modified form of Pseudomonads exotoxin.Material and methods: The fusion protein was designed by modeller software and the best linker between two parts was chosen. The designed sequence was chemically synthesized by BIOMATIK company in pET28a vector. the recombinant plasmid was

transformed to E. coli BL21(DE3) and the optimum temperature and IPTG concentration for protein expression was found. The protein was purified in different condition to find the best purification condition. The bioactivity of protein on MDA-MB- 231 and BT-474 cell lines was examined by MTT assay.Results: (EAAAK)2 sequence shows good function in preventing the interaction between two domains. The optimum condition of protein expression in E. coli BL21(DE3) was 37 ˚C and 0.5 mM IPTG and protein was purified in the denaturing condition. The protein was refolded by dialysis in Tris 10 mM. Finally, The IT showed cytotoxic effect on MDA-MB-231 and BT-474.Discussion: Discussion: In both cell lines cytotoxic effect was observed. this effect was significantly more than cytotoxic effect of alone scFv and toxic moiety.Conclusions: In this study we found that IT can effectively cause death in breast's tumor cells with HER2. The IT is more cytotoxic than scFv alone and it shows that the connection of modified form of PE with appropriate linker to scFv can increase effectiveness and potency of monoclonal antibodies.

P9

# Internalizing RGD, a Great Targeting Moiety for the Targeted Peptide and Protein Delivery: a Review Article

*Zeinabosadat Davoodi*[1], *Fatemeh Shafiee*[2*]

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Department of Pharmaceutical Biotechnology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: Fatemeh Shafiee
Corresponding author Email: f_shafiee@pharm.mui.ac.ir

Introduction: Low permeability of various therapeutic or diagnostic agents is a limiting factor for targeted cancer therapy. Internalizing RGD (iRGD) was introduced at the first time in 2009, is a modiefied form of RGD motif which is recognized by the integrin receptors on the cell surface. This peptide was used as an enhancer of drug penetration to the cancer cells over-expressed the integrin receptors when conjugated with various types of drugs. This review focuses on the studies used iRGD for the targeted delivery of various proteins in vitro or in vivo as the targeting moiety for the production of immunotoxins with cancer specifity for eradication of various tumor cells.Material and methods: Key words including: iRGD, internalizing RGD, targeted moiety, with protein, targeted drug delivery, integrin receptor, tumor targeting, Tumor-penetrating peptides, and Drug penetration, and expression was searched in Pubmed, Science Direct, Scopus and Google scholor databases. All related articles were analyzed for finding the related data.Results: About 127 articles, 36 of them were about iRGD conjugated with peptide or proteins used for tumor targeting delivery. The proteins and peptides was including: anti EGFR, HPRP-A1, IL24, sTRAIL, TP5, and so on that used for their cytotoxic effects against cancer cell with over-expressed αvβ3 receptors especially breast cancer cells.Discussion: iRGD conjugated with peptide and protein caused effective targeting in delivery of various anti-cancer agents for different cells as well as xenograft mouse models in some examples.Conclusions: Since 2009, after the designing of iRGD, there are increasing evidence in the usage of this short peptide as an efficient cell penetrating peptide specifically enter the cytotoxic agent to the cancer cells. So, this peptide is an attractive targeting moiety in the targeted therapy of special cancer. However, there is no evidence about iRGD derivate fusion protein enter the clinical phase and more information needs to be collected on the effectiveness of this peptide in clinical and pre-clinical studies in order to make a more accurate judgment about its future use as a targeted agent for the cancer treatment.

P10

# The efficacy and safety of probiotics in people with cancer who undergo chemotherapy or radiation therapy or surgery in the abdomen: a systematic review

*Negin Salehi*[1], *Melika Maleki*[1], *and Vajihe Akbari* [2]

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Pharmaceutical Biotechnology, Isfahan Pharmaceutical Research Center, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran
Corresponding author: *Vajihe Akbari*
Corresponding author Email: akbarivajihe@yahoo.com

Introduction: According to the World Health Organization (WHO), cancer is the second most common cause of death, affecting over 19.3 million people and 10 million deaths worldwide in 2020 and it is anticipated that the number of new cases will double by 2040. There are a variety of therapeutic strategies for reducing cell proliferation and disease progression, including surgery, chemotherapy, radiation therapy, and, most recently, immunotherapy. Those treatments have important side effects. chemotherapy- and radiation therapy alter the composition of the intestinal microbiota in a process called dysbiosis, which is often associated with biochemistry and immunological disorders in the gastro-intestinal tract. Several strategies are under development for amending them. Probiotics are one of them. probiotics, defined as living micro-organisms that are beneficial to the health of the host when given in sufficient amounts, However, because people with cancer tend to be immunocompromised, it is important to evaluate adverse events such as infection, which could result from the deliberate ingestion of live microorganisms. The purpose of this review was to assess the effectiveness and safety of probiotic supplements as a therapeutic strategy for treatment-related side effects in cancer patients.Material and methods: We searched the electronic databases including PubMed, Scopus, web of science, Cochrane Central Register of Controlled Trials, and clinical trial.gov up to August 2021. The prospective clinical trial registries and reference lists for the included studies were also searched. The general structure of the search was " cancer " (or synonyms) and " probiotics " (or synonyms) and we included studies that people with cancer undergo chemotherapy or radiation therapy or surgery in the abdomen received probiotics as an intervention.Results: A total of 2919 articles were retrieved from databases searching (PubMed (n = 311), Scopus (n = 1167), web of science (n = 1033), Cochrane Central Register of Controlled Trials (n = 353), and clinical trial.gov (n = 55)) of which 284 papers discarded by duplicity. Forty eight studies were included in this review. Included studies revealed that probiotics reduced the incidence of treatment-related side effects particularly diarrhea (grade ≥ 2 diarrhea). There was no evidence that Probiotics cause any severe adverse effects. Discussion: We found in this study that probiotic strains are capable of stabilizing the intestinal microbial environment and increase the permeability of the intestinal barrier, resulting in a reduction of the inflammatory response and the promotion of changes to the intestinal flora. Despite the main conclusions of these studies on the safety and effectiveness of probiotic supplements in treating or preventing these side effects, further research involving larger groups, specific strains, and length of treatment is required to conclude the beneficial effects for every side effect.Conclusions: Our results showed

the beneficial effects that probiotics can have in a range of treatment-related side effects that directly impact the quality of life of oncology patients.

P11

## Intracellular expression of interferon β-1-a in Pichia pastoris

*Diba Saeidi1, Sara Saeidi1, Fatemeh Moazen2,and Vajihe Akbari2**

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Pharmaceutical Biotechnology and Isfahan Pharmaceutical Research Center, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran*
Corresponding author: Diba Saeidi,Vajihe Akbari
Corresponding author Email: dibasaeidi17@gmail.com ,v_akbari@pharm.mui.ac.ir

Introduction: Interferon beta-1alpha (IFN β-1a) has antiviral, anti-proliferative, and immunomodulatory properties. Nowadays, interferon β (IFN β) is usually considered the most commonly used drug for Multiple sclerosis (MS). Based on the antitumor effect, the effectiveness of interferon beta 1 in cancer was considered by researchers. IFN-β-1a (glycosylated form produced by mammalian cells) has less side effects and an identical sequence to its human endogenous form. Although the production and purification of human recombinant proteins in that cell line is complex and expensive. *Pichia pastoris*, a methylotrophic yeast, can be overexpressed both intracellular and secreted proteins in it and has many advantages including posttranslational modifications, proper protein folding, reduced time, and cost of bioprocessing, high level of protein expression, and ease of application. The aim of this study was to optimize intracellular expression of IFN β-1a in *P. pastoris*. Purification and evaluation of in vitro biological activity of the expressed protein against cervical cancer cells will be conducted.Material and methods: IFN β-1a gene was designed based on the amino acid sequence of human interferon and optimized for expression in *P. pastoris*. The specific primers were used for flanking the gene with the *Eco*RI and *Xho*I restriction sites during PCR. Subsequently, the *Eco*RI/*Xho*I-digested fragment containing the IFN β-1a gene was subcloned into pPICZA expression vector.*P. pastoris* GS115 was used as a host to express that gene. Appropriate medium of protein conditions such as pH,temperature, and concentration of inducer (methanol) chose. Results: Sequencing and double digestion confirmed the accuracy of coloning.SDS-PAGE analysis confirmed the expression of interferon with a molecular weight of 22KDa using 2% methanol at pH 7.0 culture medium at 30 C.Discussion: Expression of IFN in the cytoplasm would lead to more stability of product than the extracellular method. Furthermore, protein glycosylation has not occurred in the form of hypermannosylation.Conclusions: Our findings show that the approach developed in this work is capable of large quantity expression of IFN β-1a in *P. pastoris* and could be contributing to improving the expression level of other therapeutic proteins with similar features.

P12

## Periplasmic expression of tandem diabody for simultaneous targeting of two immune system checkpoints in order to treat cancer

*Diba saeidi[1], Mahsa Behzadi[1]*, and *Vajihe Akbari[2]**

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Pharmaceutical Biotechnology and Isfahan Pharmaceutical Research Center, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran*
Corresponding author: Diba Saeidi ,Vajihe Akbari
Corresponding author Email: dibasaeidi17@gmail.com, v_akbari@pharm.mui.ac.ir

Introduction: Cancer immunotherapy is a new approach and includes various methods such as checkpoint inhibitors. Clinical studies have shown that concomitant use of two different checkpoint inhibitors, nivolumab, and ipilimumab, has significantly improved therapeutic efficacy compared to either alone. Bispecific antibodies are a combination of two antibodies that simultaneously can recognize two antigens. In comparison with synchronic administration of two antibodies, bispecific antibodies have better immunity, fewer side effects, and higher therapeutic efficacy. The present study aimed to produce a new tandem diabody antibody to target the two immune checkpoints PD-1(protein death cell programmed-1) and CTLA-4 (cytotoxic T-lymphocyte-associated protein 4) together.Material and methods: In this study, the tandem diabody ( bispecific antibody ) gene was designed and codon optimized for expression in the bacterial system.,The synthetic gene was subcloned into the pET-22b vector and expressed by E. coli BL21(DE3) this gene. The effect of temperature and concentration of inducer on protein expression were investigated. The soluble and insoluble portions of the protein were separated and purified by affinity chromatography.Results: SDS-PAGE and western blot results confirmed the expression of protein weighing about 55 kDa in E. coli BL21(DE3). The most amount of soluble protein was obtained at 23 ° C and a concentration of 1 mM Isopropyl ß-D-1-thiogalactopyranoside (IPTG). The soluble protein expressed was purified under native conditions by nickel column-based chromatography with a purity of over %91 and confirmed by SDS-PAGE gel and Western blotting.Discussion: Optimization of temperature and IPTG concentrations can moderately increase soluble expression of diabody in periplasm E. coli BL21(DE3).Conclusions: In future studies, the use of manipulated strains, such as *E. coli* Origami (DE3) or concomitant expression with chaperones, could be used to improve soluble protein production.

P13

## Cytotoxicity and Apoptosis Inducing Effects of Some Lathyrane and Tigliane Diterpenes against Breast Cancer Cell Lines

*Melika Maleki[1], Fatemeh Shafiee[2]*

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
[2]Department of Pharmaceutical Biotechnology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
Corresponding author: Fatemeh Shafiee
Corresponding author Email: fatemehshafiee85@gmail.com

Introduction: Natural compounds and specially herbal medicine are of great interest due to their various biological effects and their potential to act as a drug for the treatment of various neoplasms especially breast cancer that we are facing with its increasing prevalence around the world. The aim of this study was to evaluate the cytotoxic and cell death mechanism of some diterpenoids (Lathyrane or Tigliane) extracted from the Euphorbia sogdiana Popov against two breast cancer cell lines, MCF-7 and 4T1.Material and methods: Determination the cytotoxic effects of four various diterpenoids was performed using MTT assay against MCF-7, 4T1, and HUVEC cell lines. The IC50 of each compound against cell lines was determined by drawing the dose-response graph using graphPad prism software. Finally, the apoptotic effects of compound with the most cytotoxic effectswas determined by flow cytometery assay for 24 hrs of incubation in IC50 concentration.Results: Statistical analysis confirmed compound (3) with the most cytotoxicity against both cancer cell lines. The IC50 of compound (3) was determined as 10.1 ± 5, 28 ± 5, and 50 ± 3 µg/ml, for MCF-7, 4T1, and HUVEC cells, respectively. Furthermore, the cells treated with 5 and 10 µg/ml of compound (3) for 24 hrs, showed 49 and 57% of apoptosis.Discussion & Conclusions: These surveyed compounds have the potential to be considered as useful anti-breast cancer agents due to the great cytotoxicity and apoptotic effects against related cancer cell lines and safety profile according to their rational selectivity index.

P14

## Recombinant production of DFF-40-lyc-1 fusion protein in E. coli and evaluation its biological effects.

*Zahra Shafiee-ardestani*[1]

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
Corresponding author: *Zahra Shafiee-ardestani*[1]
Corresponding author Email: miss_shafiee@yahoo.com

Despite the fact that chemotherapy play a vital role in the treatment of various cancers, these agents affect all sub-types of cells including both healthy and cancerous tissues with a high proliferation rate. Apoptosis inducing molecules can prevent the development of cancer and be considered as a novel concept in the treatment of cancers. One type of the mentioned factors is DNA fragmentation factor (DFF). In this study, Lycosin-1, which is a peptide that was derived from spider venom, was utilized for targeted transmission of DFF-40 into cancerous cells. So, the aim of our study was to produce a fusion protein containing DFF-40 and lycosin-1 by recombinant DNA technology which can be used as a drug candidate for the targeted cancer therapy.

P15

## Recombinant production of DFF-40-lyc-1 fusion protein in *E. coli* and evaluation its biological effects.

*Zahra Shafiee-ardestani* [1], *Fatemeh Shafiee* [2]

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Pharmaceutical Biotechnology, School of Pharmacy and Harmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.
Corresponding author: *Fatemeh Shafiee*
Corresponding author Email: f_shafiee@pharm.mui.ac.ir

Introduction: Despite the fact that chemotherapy play a vital role in the treatment of various cancers, these agents affect all sub-types of cells including both healthy and cancerous tissues with a high proliferation rate. Apoptosis inducing molecules can prevent the development of cancer and be considered as a novel concept in the treatment of cancers. One type of the mentioned factors is DNA fragmentation factor (DFF). In this study, Lycosin-1, which is a peptide that was derived from spider venom, was utilized for targeted transmission of DFF-40 into cancerous cells. So, the aim of our study was to produce a fusion protein containing DFF-40 and lycosin-1 by recombinant DNA technology which can be used as a drug candidate for the targeted cancer therapy.Material and methods: The coding sequences of each native peptide and protein, and also the fusion protein (DFF-40, lyc-1, DFF40-lyc-1) separately were transformed in *E. coli* BL21 (DE3) strain expression system, as fusion to intein 1 and 2 of pTWIN-1 vector. The peptide or protein expression was induced by IPTG. Furthermore, to reach the maximum level of soluble protein, IPTG concentration, and temperature of incubation were optimized. For removing the intein 1, we altered pH (8.5 to 6.5) 24 hours as incubation time at room temperature and for intein 2 we used Dithiothreitol (DTT) for more three days incubation. In order to evaluate the biologic effects of produced novel molecule, the treatment of HeLa and HUVEC cell lines with recombinant proteins is on-going using MTT assay method.Results: Successful cloning established by restriction enzyme digestion and DNA sequencing of each recombinant constract. in the expression level, bands with approximately 58, 95 and 100 kDa for lycosin-1, DFF-40 and DFF-lyc1 was shown on 12% SDS-PAGE, respectively . In addition, bands with 3, 40 and 43 kDa indicated lycosin-1, DFF-40, DFF40-lyc1 purified molecules, respectively. Discussion and Conclusions: With regards to the previous studies, a novel fusion protein with targeted cancer therapy properties has been designed and produced for the first time. Moreover, it is expected that the observed cytotoxic effects of this fusion protein will be more in cancer cells in comparison to the normal cells due to its higher entrance rate to the cancer cell lines.

P16

## Bee Venom–Derived BBB Shuttle and its Correlation with Oligodendrocyte Proliferation Markers in Mice Model of Multiple Sclerosis

*Fatemeh Emami*[1], *Tannaz Danesh-seta*[2], *Mohammad Hossein Nasr Esfahani*[3], *Kamran Ghaedi*[4], *Mehdi Aliomrani*[5]

[1]Department of Toxicology and Pharmacology, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Toxicology and Pharmacology, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran
[3]Department of Animal Biotechnology, Cell Science Research Center, Royan Institute for Biotechnology, ACECR, Isfahan, Iran
[4]Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran
[5]Department of Toxicology and Pharmacology, Faculty of Pharmacy, Isfahan Pharmaceutical Science Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Multiple sclerosis is a chronic demyelinating disease with a functional disturbance in the immune system and axonal damages. It was shown that Apamin as a blood–brain barrier shuttle acts as a Ca2+ activated K+ channels (SK channels) blocker. In this study, the effects of Apamin on oligodendrocyte differentiation markers were evaluated on an induced model of MS. Briefly, C57BL/6 male mice (22 ± 5 g) except the control group were fed with 0.2% (w/w) cuprizone pellets for 6 weeks. After cuprizone withdrawal, mice were divided randomly into six groups. Apamin (100 µg/kg/BW) was administered intraperitoneally as a co-treatment during phase I (demyelination) or post-treatment phase II (remyelination) twice a week. Mice were anesthetized, perfused with phosphate-buffered saline, then fixed brains were coronally sectioned and the changes in oligodendrocytes markers such as Olig2, PDGFR-α, and BrdU incorporation were assessed by immunohistochemistry assay. Apamin administration increased Olig2+ cells in phase I as compared to the control group (p < 0.0001). Also, a decreasing trend in PDGFRa+ cells observed after cuprizone withdrawal (p < 0.001). 5-Bromo-2′-deoxyuridine (BrdU) incorporation test was confirmed stimulation of oligodendrocyte progenitor cell proliferation in phase I in the Apamin exposed group (p < 0.0001), especially at the subventricular zone. This study highlights the potential therapeutic effects of Apamin as a bee venom–derived peptide on oligodendrocyte precursor proliferation and elevation in myelin content in an oxidative induced multiple sclerosis model due to cuprizone exposure.

## P17

## L-Tryptophan and Ginger: A suggestive combination for the treatment of refractory nausea in COVID-19

*Milad Saadatkish[1], Mohammad Fakhrolmobasheri[2], Amir-Abbas Shiravi[3], Hossein Khanahmad[4], Elham Tabesh[5], Mehrdad zeinalian[6]*

[1] School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences.

[2] Department of Genetics and Molecular Biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

[3] Department of Genetics and Molecular biology, School of Medicine, Isfahan University of Medical sciences, Isfahan, Iran

[4]Department of Genetics and Molecular biology, School of Medicine, Isfahan University of Medical sciences, Isfahan, Iran

[5]Department of Internal Medicine, School of Medicine, Isfahan University of Medical sciences, Isfahan, Iran

[6]Department of Genetics and Molecular biology, School of Medicine, Isfahan University of Medical sciences, Isfahan, Iran

Corresponding author: Mehrdad zeinalian
Corresponding author Email: zeinalianmehrdad@gmail.com

Introduction: To date, a large number of studies have reported gastrointestinal symptoms in patients with COVID-19. In addition, patients with gastrointestinal involvement report nausea and vomiting as the most annoying gastrointestinal symptoms. However, the prevalence of nausea/vomiting varies and their role in COVID-19 is unclear. Tryptophan (TRP) is one of the essential amino acids that should be obtained from dietary proteins. Ginger is a popular spice that has proven effects on nausea through its bioactive components. In the present paper, we studied the synergic action of the L-tryptophan and ginger in adjusting brain serotonin levels. In such a way that prevents resistant nausea in COVID-19 patients.Methods: First, we studied the total serotonin synthesis mechanism. The Acute Tryptophan Depletion (ATD) method and its effects on the body were reviewed to investigate the Tryptophan roles in the body. Next, we evaluated the effects of the Sars Cov-2 on TRP absorption and 5-HT serum levels. Ginger, as a potent anti-emetic herb, and the roles of its bioactive components were investigated. Finally, we surveyed the possible synergic action of L-tryptophan and ginger in adjusting serotonin levels leading to anti-emetic effects.Results: Approximately 90 % of the total serotonin synthesis performs in the gastrointestinal epithelium. In the synthesis process, Troponin hydroxylase produces L-5-hydroxytryptophan (5-HTP) from L-tryptophan, which is the rate-limiting step of serotonin synthesis. So, TRP levels are tightly correlated to serotonin production. In the ATD method, serum Tryptophan (TRP) levels will be diminished through a diet consist of a TRP-free amino acid mixture. So troponin hydroxylase cannot produce 5-HTP from L-Tryptophan Which leads to a decrease in serotonin levels. A recent study showed that ATD can lead to nausea in thirty-eight healthy females when subjected to head movements and body rotation. Therefore, lowered serotonin levels in the brain as a result of tryptophan depletion, can lead to nausea and vomiting.On the other hand, serotonin plasma levels will be lowered significantly both in non-severe and severe COVID-19 patient. Since the absorption of TRP in the gut will be affected by angiotensin-converting enzyme 2 (ACE2), lowered levels of ACE2 in COVID-19 patients can decrease serotonin production through reduced TRP absorption. Hence, TRP supplementation can be considered a feasible intervention for preventing nausea in COVID-19 patients.Ginger is a popular spice that has proven effects on nausea through its bioactive components. Studies have shown that the main ginger polyphenols, inhibited the activation of 5-HT3 receptors up to 45%. 5-HT3 receptors are responsible for most of the nausea effects. It is shown that 5-HT3 antagonists, as well as ondansetron, are effective treatments against nausea and vomiting. Inhibition of 5-HT3 receptors both centrally and peripherally results in anti-emetic effects.Discussion and Conclusion: As part of a nausea-preventive diet in COVID-19 patients, L-tryptophan and ginger may act via synergic action of adjusting serotonin levels in the brain and 5-HT3 receptor inhibition.

## P18

## Magical scaffold of flavonoids, a gift from the nature, for the treatment of Parkinson's Disease

*Fatemeh Haddadi[1], Salime Lavian[2]*

Corresponding author: *Salime Lavian*
Corresponding author Email: lavian.gct@gmail.com

Parkinson's disease (PD) is a neurodegenerative disorder of the CNS which there is a progressive loss of dopamine level and imbalance of dopamine and acetylcholine in brain. There are two features of symptoms for PD disorder. Motor and non-motor symptoms which are include resting tremors, rigidity, bradykinesia or akinesia, disturbance, posture, freezing (motor block), sleep disorder and nightmares (non-

motor symptoms). Although the abnormal level of dopamine and acetyl choline in the brain is the main cause of these effects and can be treated by using of dopamine analogues or MAO and COMT inhibitors or anti-cholinergic products, but the disorders could be related to oxidative stress, abnormal apoptosis, immunological reactions, iron overload and protein malfunctions too. A number of herbal products contain active components which are known to possess MAO inhibitory action that can improve the level of dopamine in PD patients and in addition they can act as antioxidant, anti-apoptosis, iron chelating agents and etc. Hence, the potential role of herbal products in treating PD cannot be undermined. In this review, the main aim is to discuss the pathogenesis of PD, and evaluated the SAR of different potential herbal extracts as a choice for the treatment of PD and its symptoms.

## P19

## Copper-curcumin-bipyridine dicarboxylate complexes as anticancer candidates

*Fatemeh Emami[1], Mohammadmahdi Moradi[2], Shahram Tangestaninejad [3], Mehdi Aliomrani[4], Hossein Kazemian[5], Mahboubeh Rostami[6]*

[1] Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical science, Isfahan University of Medical Science, Isfahan, Iran
[2] Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical science, Isfahan University of Medical Science, Isfahan, Iran
[3] Department of Chemistry, Isfahan University, Isfahan, Iran
[4] Department of Pharmacology and Toxicology, Faculty of Pharmacy and Pharmaceutical science, Isfahan University of Medical Science, Isfahan, Iran
[5] Northern Soil and Groundwater Remediation Research Laboratory, University of Northern British Columbia, Prince George, V2N 4Z9, Canada
[6] Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical science, Isfahan University of Medical Science, Isfahan, Iran

Corresponding author: Mahboubeh Rostami
Corresponding author Email: m.rostami@pharm.mui.ac.ir

Copper (Cu) plays an important role in cell function as an enzyme cofactor that is crucial for most of the biological pathways. Recently, there is a growing attention on the different biological activities of copper complexes as antioxidant or cytotoxic activity. Curcumin, an active pharmaceutical ingredient of curcuma longa, has demonstrated various pharmacological activities such as antioxidant and cytotoxicity. Furthermore, different researches reported that metal-curcumin complexes can be able to interact with DNA that induce apoptosis in cancer cell lines. On the other hand, recently there are some different evidences that show bipyridine derivatives ligands in complex with transition metals like Ru2+, Pt2+, and Zn2+ can bind to DNA and induced cytotoxicity by activation of apoptosis signaling pathways. The aim of this study was synthesis, characterization and cytotoxicity evaluation of six novel complexes of copper (Cu), Curcumin (Cur) and, 2,2'-bipyridine- 5,5'-dicarboxylic acid (BPYD) on MDA-MB-231 cell line. Two different salts of Cu (acetate and nitrate) were used for synthesis of complexes. In this regard, copper salts were dissolved in water, and the ethanolic solution of curcumin and/or solution of BPYD in DMAC were added dropwise to copper aqueous solutions and stirred for 3 hours at 60-80°C. All of the complexes were characterized by FTIR, UV-Vis, CHNS, TGA, ICP-MS and Mass spectroscopy. The in-vitro cytotoxicity was studied on MDA-MB-231 cell line as cancerous cells and HUVEC cell line as normal cells. Furthermore, the DCFDA test were used to measure the amount of ROS production by different complexes in MDA-MB-231 cell line. Statistical analysis was done with GraphPad Prism 9. The structure of all complexes were confirmed via all of the characterization methods. The in-vitro assays demonstrated that all of the copper complexes have higher cytotoxicity effects on MDA-MB-231 cancerous cell line in compare with carboplatin as positive control (p-value<0.01). Moreover, all of the structures revealed less cytotoxicity on HUVEC cell line. It can be discussed that all of the synthesizes Cu complexes have much more cytotoxic effects on cancerous cell line meanwhile they are almost safe on normal cells. In addition, it was indicated that the Cu-Cur-BPYD from both Cu salts have the most cytotoxic effects (IC5= 3.5 and 1.7 µg/ml) among all of the complexes and also have less cytotoxic effects on normal cell line in compare with carboplatin. Furthermore, the DCFDA test showed the higher amount of ROS production by these two complexes in MDA-MB-231 cell line and this could be a promising result to further upcoming researches in this field. This study highlighted that Cu-Cur-BPYD complexes can be effective candidates for pre-clinical studies as anticancer agents.

## P20

## Administration of C29 derivative for treatment of rheumatoid arthritis

*Shiva nasresfahani[1], jaleh varshosaz[2], valiolah hajhashemi[3]*

[1]Novel Drug Delivery Systems Research Centre, Department of Pharmaceutics, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Novel Drug Delivery Systems Research Centre, Department of Pharmaceutics, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[3]Department of Pharmacology and Toxicology, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Corresponding author: Jaleh varshosaz
Corresponding author Email: varshosaz@pharm.mui.ac.ir

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease. The most commonly used drug for this disease is methotrexate (MTX) with some sever adverse effects. C29 derivative (o-vanillin) is an inhibitor of Toll like receptors (TLR), which can inhibit TLR-2/1 and TLR-2/6 signaling in macrophages and therefore, prevent inflammation . The glucan is a cereal fiber recognized by dectin-1 or β-glucan receptors of phagocytic macrophages. The hollow cavity of glucan particles (GPs) allows highly encapsulation of payload molecules and targets drug to macrophages. The purpose of the present study was preparation of β-glucan microspheres for targeted of vanillin to macrophages to reduce the inflammation of induced RA in animal model.Material and methods: β-glucan was extracted from baker's yeast (*Saccharomyces cerevisiae*) and identified by scanning electron microscopy (SEM). Dried glucan was mixed with gelatin solution at room temperature for loading vanillin. Then GPs were characterized for their particle size, drug loading and release efficiency of C29 derivative (o-vanillin). RA was induced by injection of Freund's adjuvant in paw of Wistar rats. After 24 hours the rats received normal saline (1 mg/kg, ip), MTX (2 mg/kg/week, ip), β-glucan suspension (1 mg/kg/week, ip), GPs-MTX suspension (2 mg/kg/week, i.p.), GPs-vanillin suspension (200 mg/kg/day, po) and the last group received vanillin suspension (200 mg/kg/day, po) for 14 days. After that TNF-α and IL-6 were evaluated in serum by ELISA method.Results: The results showed that the optimized GPs had the particle size of 3.5 µm. C29 derivative (o-vanillin) loading efficiency in glucan microspheres was 44.2%. The microspheres released 95.1% of C29 derivative (o-vanillin) over 24 hours. The results of *in vivo* studies

showed significant reduction in paw volume, TNF-α and IL-6 ($P<0.05$) in animals treated with glucan microspheres loaded with vanillin compared to the two drugs in free.Discussion: Encapsulation of C29 derivative (o-vanillin) nanoparticles and MTX in GPs caused to drug deliver more controlled and localized than free drugs. Importantly, the results of *in vivo* administration showed that treatment with GP-vanillin significantly reduced the progression of RA in adjuvant-induced arthritis rats. On the other hand, comparison of the administration of GP-vanillin with administration of free MTX and vanillin showed a beneficial approach which provides more anti-inflammatory efficacy at the inflammation site and decrease inflammatory mediators in blood and prevent disease progression than free drugs.Conclusions: Administration of C29 derivative (o-vanillin)-doped GPs may be more effective than free MTX in RA.

P21

## Design, synthesis, and biological evaluation of novel targeted nanoparticle for gene delivery to MCF-7 breast cancer cells

*Nazita Tavazohi[1], Mina Mirian[*]*

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Department of Pharmaceutical Biotechnology, Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Iran
Corresponding author: Mina Mirian
Corresponding author Email: mina.mirian@pharm.mui.ac.ir

Introduction: Gene therapy is an exciting new therapeutic option for different diseases. The selection of a suitable and successful gene delivery vector is a critical step in gene therapy. Non-viral gene delivery methods have been offered as safer alternatives to viral vectors since they may be delivered repeatedly with little human immunological reaction, are stable in storage, and can be easily mass-produced. Chitosan (CS) has several benefits as a non-viral vector for gene transfer, including non-toxicity, strong biocompatibility, biodegradability, high stability, and low cost. Combining CS with anionic polymers, such as hyaluronic acid (HA), can enhance the transfection effectiveness of CS vectors.Material and methods: In this study, we have used hybrid hyaluronic acid (HA)/chitosan (CS) nanoparticles, which are targeted with LHRH as novel non-viral gene delivery vectors for MCF-7 cell line. The complicated coacervation of the cationic polymers with pEGFP plasmid resulted in the formation of CS/HA /pDNA nanoparticles. Particle size and zeta potential were evaluated by (DLS). To evaluate the stability and efficiency of nanoparticles against DNase and heparin, agarose gel electrophoresis tests were done. Furthermore, nanoparticles with different N/P ratios were assessed by agarose gel electrophoresis test. Then, plasmid uptake into MCF-7 cells was determined by fluorescent microscopy and flow cytometric analysis of pEGFP positive cells and expressed as 54.3% of all living cells post-transfection. Moreover, the cytotoxicity of CS/HA-LHRH/plasmid nanoparticles was estimated using the MTT assay.Results: Particle size and zeta potential depended on weight ratio of CS:HA. Nanoparticles with N/P ratio of 6 were at the most stable state when the weight ratio of CS:HA was 4:1 at pH 5.5. The zeta potential and particle sizes were around $16.3 \pm 0.5$ mV and 152.5 nm respectively. Conjugating HA to LHRH was confirmed by FT-IR. Zeta potential and particle size of targeting nanoparticles were changed to 14.7 mV and 171.3 nm. Agarose gel electrophoresis test showed that nanoparticles with N/P ratio of 6 can completely entrap DNA and were resistant against DNase I and heparin. The transfection yield of targeting and non-targeting nanoparticles using flow cytometry represented the transfection efficiency of 54.3% and 23.2%, respectively. The average viability of cells transfected with HA-LHRH/CS-plasmid nanoparticles was over 82%. Discussion: In overall, referring to the FT-IR results the amide band among the carboxylic and amine of HA and LHRH, respectively, was formed via carbodiimide reaction. The size and zeta potential of the nanoparticles were changed due to the incorporation of negatively charged LHRH to the polypelex structure. Based on uptake results, LHRH as a targeting agent successfully enhanced internalization of the nanoparticles carrying plasmid in MCF-7 breast cancer cells.Conclusions: Taken together, our findings suggest that HA-LHRH/CS-plasmid nanoparticle with proper biocompatibility and high transfection efficiency could be considered as an effective non-viral vector for targeted gene delivery to MCF-7 breast cancer cells.

P22

## Optimized tolterodine taste-masked in orally disintegrating tablets

*homa talabakii[1], somayeh teymouryi [2], and sayed abolfazl mostafavi[3]*

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

[2]Department of Pharmaceutics, Faculty of Pharmacy and Isfahan Pharmaceutical Sciences Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

[3]Isfahan Pharmaceutical Sciences Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
Corresponding author: somayeh teymoury
Corresponding author Email: teymoury_s@yahoo.com

Introduction: montmorillonite is a smetic clay traps drugs with the ability to cation exchange capacity between its interlayers. Tolterodine tartrate, using as treating frequent urination, urinary incontinence, or urinary urgency, has an unusual taste(1,2).in present study, we developed ODT containing TT-MMT hybrid with taste-masking ability. TT-MMT hybrid were prepared by strong ionic interactions due to held within the layered space of MMT and end up preventing drug release in the buccal cavity. The disintegration time, hardness and friability for each formulation was design by computer, were analyzed by Design expert software to determine the importance of each studied factorMaterial and methods: TT was obtained as a gift sample from the Tehran darou Co. K10 Montmorillonite was purchased from Sigma Aldrich (US), Avicel, sodium Carmelose, mannitol, Talk, Mg stearate and saccharin were obtained from Merck (Germany). The TT–MMT hybrid was prepared by ion exchange reaction. In order to achieve maximum intercalation of TT within the interlayer region of MMT, effect of various parameters such as, initial concentration of TT, MMT, temperature and pH were investigated(3). D-optimal design with 2-factors and 3-levels was used for optimization study using Design-Expert software (version 11, USA). The Avicel and croscarmellose sodium (CS) amount were selected as independent variables. The disintegration time, hardness and friability were chosen as responses. The component of 16 formulations generated by Design Expert software Results: The effect of MMT concentration, drug amount, pH and temperature on drug intercalation capacity of MMT has been evaluated. The impact of different concentration of MMT, TT, pH and temperature on EE of TT in the MMT is examined by different methods like UV spectrophotometry Powder X-ray diffraction, DSC, FTIR, Zeta potential and size analysis(4,5). finally, the optimized formulation of TT-MMT-ODTs was predicted upon the Design-Expert.Discussion: The optimized formulation was selected based on the minimum disintegration time minimum frability and maximum hardness. . Computer optimization process and a desirability function

determined the effect of the levels of independent variables (croscarmellose and Avicel®) on the responses and amount of crosscarmelose and Avicel revealed a strong influence in the hardness and friability outputs.Conclusions: all data analysis show successfully drug loaded in to MMT and The results of the human taste panel revealed that all volunteers rated the designed formulations as pleasant or slightly pleasant tasting, with no reports of unpleasant or bitter taste so formulation has acceptable taste masking effect.

## P23

## Fennel Role in Premenstrual Syndrome: Clinical Trials Systematic Review

*Mohammad Razeghian[1], Ehsan Amiri Ardakani [2]*

[1] Isfahan University of Medical Sciences
[2] Shiraz university of medical sciences
Corresponding author: Ehsan Amiri Ardakani
Corresponding author Email: ehsanamiri@sums.ac.ir

Introduction: Premenstrual syndrome (PMS) with many physical and emotional symptoms occurs in young and middle-aged women. Common symptoms of PMS include irritability, mood swings, anxiety, depression, chest tenderness, bloating, and headache. The side effects of chemical drugs are relatively high, which is why adjuvants such as herbal supplements have recently become popular. Foeniculum vulgare Mill. (fennel) is a plant that has been considered due to various effects such as anti-inflammatory, anti-spasm, diuretic, and laxative This plant is also traditionally used for menstrual disorders. Due to this disease's medicinal importance, we systematically review all clinical trials evaluating fennel role in PMS management.Material and methods: We searched Science Direct, Pubmed, and Google Scholar databases for all English clinical trials published up to 2021 February. We searched for the following keywords for the following articles: [(Premenstrual syndrome) AND (Fennel)], [(Premenstrual syndrome) AND (Foeniculum vulgare)], [(PMS) AND (Fennel)], [(PMS) AND (Foeniculum vulgare)]. Reviews, case studies, animal studies, and articles evaluating other medicinal plants and diseases were excluded. The extracted information includes the number of participants, age, drug dose, duration of treatment (number of menstrual periods), and route of administration. Finally, based on included articles effect of this plant on different PMS indices was evaluated.Results and discussion: Totally 9 cases were included in this systematic review. Fennel plant has different effects on PMS, which can be divided into three parts. In the case of indicators related to PMS include pain, amount, and severity of bleeding, menstrual interval studies show that fennel has been shown to be beneficial for PMS pain. However, there is no significant difference between menstrual severity and menstrual interval. In Psychiatric symptoms of PMS include fatigue, anger, stress and anxiety, depression, emotional retention, and fluids studies show that fennel can reduce the symptoms of fatigue, anger, stress, and depression caused by PMS, but there has been no significant reduction in the symptoms of emotional retention and fluids. In addition, other symptoms of PMS that fennel can affect include nausea and weakness. Studies show that fennel can reduce nausea. Also, consuming fennel for one to three months can reduce weakness. In some studies, the symptoms of PMS have been studied in general, which shows that fennel improves the symptoms of PMS in general. Odor and bad taste and a case of vision problems were observed among the study group, which is one of the side effects of fennel.Conclusions: The results of this study show that fennel can have benefits in PMS. Fennel affects menstrual, physical, and mental symptoms and has reduced these symptoms, but in some studies, these symptoms have not been significantly reduced. However, this plant can reduce the effects of PMS such as fatigue, anxiety, depression. Studies show that exercise with fennel can have a better effect on PMS. It is recommended that the effect of fennel with exercise be further investigated in PMS.

## P24

## The Antibacterial Activity of Ethanolic Extract of *Berberis integerrima*

*Sara saeidi[1], Mustafa Ghanadian[2*]*

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of medical Sciences, Isfahan, Iran
[2]Department of Pharmacognosy and Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran*
Corresponding author: Mustafa Ghanadian
Corresponding author Email: ghannadian@gmail.com

Introduction: *Berberis integerrima* is a shrub widely distributed in the Middle East and central part of Asia. Recently, biological and pharmacological studies on different Berberis species showed their antimicrobial effect. They are also used in traditional medicine for many years for the treatment of infectious fevers, plagues, typhus, diarrhea. According to the increasing resistance of pathogenic bacteria against antibiotics, searching to find new alternatives to chemical drugs and antibiotics has recently become popular. This study aimed to investigate the Antibacterial effect of alcoholic extract of *Berberis integerrima*.Material and methods: Air-dried roots were powdered by using an electrical mill (mesh number 100) and extracted by percolation method with ethanol. The percolated extract was filtered and evaporated by a rotary evaporator at reduced pressure at 50°C.The antibacterial activity was tested at different concentrations of the extract by using the disc diffusion method. Paper discs loaded with different concentrations of the extract (0.2, 0.5, 1, 2, 5, 10 mg/disc). The sample discs were left overnight to dry their moisture. Clindamycin discs (0.2, 0.5 µg/disc) were used as positive control. *Staphylococcus aureus* inoculum (McFarland turbidity standard 0.5) was plated onto Mueller–Hinton agar by sterile swabs and then the discs were added. The plates were incubated at 37 °C for 24 h. The diameters of the inhibitory zones were measured in millimeters.Results: The inhibition zone diameters were 11, 12, 13, 14 and 17 mm at 0.5, 1, 2, 5, 10 mg/disc concentrations of the extract. The minimum inhibitory concentration of the *Berberis integerrima* ethanolic extract was 0.5 mg/disc against *Staphylococcus aureus*.The inhibition zone diameters were 10 and 20 mm at 0.2 and 0.5 µg/disc concentrations of the clindamycin.Discussion: The results showed that the *Berberis integerrima* ethanolic extract has an antibacterial effect against *Staphylococcus aureus*.Conclusions: *Berberis integerrima* can be a potential source of antibacterial drugs. Further studies are recommended to determine the mechanism responsible for the antibacterial effect and identify the therapeutic effects.

## P25

## Preparation and in vitro characterization of novel nanoparticles for carboplatin delivery

*Aliakbar Akbari[1], Jaleh Varshosaz[2]*

[1]Student's Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of medical Sciences, Isfahan , Iran
[2]Department of Pharmaceutics, Novel Drug Delivery Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan , Iran
Corresponding author: Jaleh Varshosaz

Corresponding author Email: varshosaz@pharm.mui.ac.ir

Introduction: Carboplatin is a platinum based chemotherapeutic agent, which has widely been used for different forms of cancer due to its excellent antineoplastic efficiency. However, high systemic side effects and drug resistance are major challenges in application of this drug. Poly(β-amino ester)s (PβAE)s are a class of synthetic polycationic polymers prepared by Michael addition reaction. While PβAEs are widely studied for gene delivery due to their good biocompatibility and biodegradability, pH responsive nature and easy production; limited research has been done for using them as drug delivery vehicles. In this study we prepared novel poly(β-amino ester)-alginate nanoparticles (NPs) and studied them for encapsulation of a chemotherapeutic drug, carboplatin.Material and methods: NPs were prepared by adding aqueous solutions of sodium alginate, containing different concentrations of sodium alginate and carboplatin, to aqueous solution of PβAE. Obtained NP dispersions were then ultrasonicated for 3 minutes to form NPs with appropriate size and low poly dispersity index. Different physicochemical properties of NPs including; particle size, zeta potential, encapsulation efficiency and drug release profiles were studied.Results: NPs were self-assembled by ionic interaction of positively charged PβAE and negatively charged sodium alginate. Resulted NPs had particle size range of 269.5 to 802.1 nm and zeta potential -1.24 to +5.5 mV. Drug encapsulation efficacy was measured 35.0-61.5% for different formulations. *In vitro* release profiles showed a prolonged drug release (more than 48 h) compared to pure drug solution (less than 4 h).Discussion: Our results showed that carboplatin loaded PβAE-alginate NPs had tunable particle size and surface potential, acceptable drug loading efficiency and sustained drug release profile.Conclusions: This study suggests that novel PβAE-sodium alginate NPs might be good candidates for drug delivery of carboplatin and presumably other chemotherapeutic agents. Further *in vitro* and *in vivo* studies are needed to show their potential in cancer therapy.

## P26

## Rebociclib loaded nanoparticles prepared from a derivative of gellan gum

*Sarvin Shirani 1, Jaleh Varshosaz2*

[1]Pharmacy student, Pharmacy Student's Research Committee, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran.
[2] Department of Pharmaceutics, School of Pharmacy and Pharmaceutical Sciences, Novel Drug Delivery Systems Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
Corresponding author: Jaleh Varshosaz
Corresponding author Email: varshosaz@pharm.mui.ac.ir

Introduction: Ribociclib (RIB) is a CDK4 and CDK6 (Cyclin-dependent kinases 4, 6) selective inhibitor that received FDA approval in March 2017 for the treatment of breast cancer metastases.Despite its excellent effectiveness, this medicine has several side effects like neutropenia, nausea, grade 3 neutropenia, fatigue, diarrhea, leukopenia, alopecia, and vomiting. On the other hand, because of RIB's limited solubility in water, drug delivery devices can improve its efficacy. Gellan gum (GG) is a natural
polysaccharide generated by *Pseudomonas elodea* and used as a hydrophilic component in the preparation of nanoparticles. GG is used in novel drug delivery systems like gel beads, micro-and nanoparticles, films, viscous liquid formulations for oral and topical delivery, etc. due to its non-toxic,biocompatible, and biodegradable properties, resistance to temperature, acidic environments, and enzymes in the GIT, high water holding capacity, and stability. Considering the proper characteristics of
this biomaterial, we used a GG derivative to form nanoparticles for intravenous delivery of RIB to breast cancer cells.Material and methods: Several ratios of RIB to GG derivative were dissolved in DMSO and added dropwise to deionized water while the mixture was sonicating with a probe sonicator. The particle size
and zeta potential of the nanoparticles were determined by the zeta sizer. RIB's loading efficiency and release rate were also studied by a spectrophotometric method.Results: The particle size and zeta potential of nanoparticles were between 131.53 to 181.13 nm and -16.96 to -22.83 mV, respectively. Increasing the drug to polymer ratios increased the absolute value of zeta potential and size of nanoparticles. The drug loading efficiency was in the range of 83.4 to 90.73 percent. Furthermore, RIB was released 63.21 to 78.47 percent from GG nanoparticles after 72 hours.Discussion: Although by increasing the drug to polymer ratio as a formulation variable the absolute value of zeta potential, size and release percent of nanoparticles increased, but there wasn't any special
relationship between the drug loading efficiency with this variable. RIB was released in a sustained release pattern from GG derivative nanoparticles.Conclusions: The results of this investigation suggest that the designed polymer from the derivative of GG may be used as a suitable carrier for RIB, which not only enhances its water-solubility but also extends its release profile.

## P27

## Efficiency of a Pharmacist-Developed Guideline for Drug Administration *via* Nasogastric Tube for Nurses in the Neurology ICU in Reducing Drug Delivery Errors

*Shamim Khabazi[1*], Leila Kouti[2], Maryam Nematifar[3], Nastaran Majdinasab[4], Mandana Izadpanah[5]*

[1]School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

[2]Clinical Pharmacy Department, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

[3]Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

[4] Neurology Department, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

[5]Clinical Pharmacy Department, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
Corresponding author: Leila Kouti
Corresponding author Email: kouti-l@ajums.ac.ir

Introduction: Special considerations should be observed for drug delivery *via* a nasogastric tube, inattention to which can result in negative outcomes for patients and hospitals. This study aimed at recognizing the errors of drusg administration *via* nasogastric tubes and evaluating the efficiency of a pharmacist-developed guideline.Material and methods: This quasi-experimental study was performed in the neurology ICU of Golestan Hospital in Ahvaz, Iran. A guideline was developed for oral medicines by a pharmacist and followed by nurses. The correct drug delivery indicators for drugs administered *via* the nasogastric tube were evaluated before and after development of the guideline and informing the nurses. The data were analyzed through descriptive, Kolmogorov-

Smirnov, and McNemar tests in SPSS 21.Results: A total of 1736 drugs were investigated in this study. The results showed a significant difference in the drug delivery errors before and after development of the guideline, so that the error rate of drug preparation was reduced from 100% to 12.17% ($p$<0.001), drug-drug interaction and drug-nutritional formula interaction from 17.26% to 5.52% ($p$<0.001), and drug-nasogastric tube interaction from 7.7% to 2.26% ($p$<0.001).Conclusions: Given the positive effect of developing a guideline for administrating drugs *via* nasogastric tubes particularly on the ward' drugs and the cooperation of pharmacists and nurses this method seems feasible and may improve drug delivery to patients.

## P28

## Evaluation the role of zingerone on oxidative stress and manic-like behavior induced by ketamine in rats

Mahsa Maleki [1], *Mohammad Javad Khodayar*[2], *leila zeidooni*[3] *and Mehrnoosh Moosavi*[4]

[1]Student, Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

[2]Department of Toxicology, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

[3]Department of Toxicology, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

[4]Department of Toxicology, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Corresponding author: Mahsa Maleki

Corresponding author Email: Dr.mm4676@gmail.com

Introduction: Bipolar disorder is a chronic and debilitating illness characterized by episodes of mania and depression. The aim of the present study was to investigate the effect of Zingerone on oxidative stress, behavioral parameters and inflammatory markers in a model of mania induced by ketamine administration in rats.Material and methods: Animals were pretreated with extract (150 mg/kg, once a day for 14 days), lithium chloride (45 mg/kg, twice a day for 14 days), or vehicle. Between the 8th and 14th days, the animals received injection of ketamine (25 mg/kg) or vehicle. On the 15th day, thirty minutes after ketamine administration, the animals' locomotion was assessed using open-field apparatus. After the experiments, the animals were euthanized and cerebral structures were removed for neurochemical analyses.Results: The results showed that ketamine treatment induced hyperlocomotion and oxidative damage in the cerebral cortex and hippocampus. In contrast, pretreatment with lithium and zingerone was able to prevent hyperlocomotion and oxidative damage in the cerebral cortex and hippocampus. In addition, IL-6 and IL-10 levels increased by ketamine, while zingerone prevented these effects in the cerebral cortex.Discussion: Ketamine increased open-field behaviours and nitric oxide levels. Administration of zingerone was associated with variable degrees of reversal of these effects.Conclusions: Our results show that zingerone may have the potential of a possible preventive intervention in BD, since this extract have demonstrated neuroprotective properties as well as antioxidant and anti-inflammatory effects in the ketamine-induced mania model.

## P29

## Introducing a mass hearing screening program in elders for prevention of Alzheimer's disease

*Ayeh Sabaghk Kashani*[1], *Sasan Dastaran*[2]

[1]Faculty of Pharmaceutical Sciences, Islamic Azad University of Medical Sciences, Tehran, Iran

[2]Department of Pharmacology, School of Medicine, Shahid Beheshti University, Tehran, Iran

Corresponding author: Sasan Dastaran

Corresponding author Email: sasan_dastaran@hotmail.com

The most prevalent form of dementia is Alzheimer's disease (AD) (1). The scientists believe the number of people with AD increases and tripled in a few decades (2). AD is the costliest disease to society, and in 2018 it costs 60 billion dollars (3). Unfortunately, AD is an incurable and neuronal degenerative disease. While AD is incurable, prevention is possible. Studies show there is a relationship between age-related hearing loss and Alzheimer's disease (1). One reason that leads to a reduction of cognition ability is loneliness; besides, feeling secluded and lonely are results of hearing loss (4). So as to prevent social isolation and cognition deficits, it is necessary to assess hearing status in adults to diagnose hearing dysfunction early and start using hearing aids as a non-invasive solution (5).We review the connection between hearing loss and AD because of reducing brain function and feeling secluded. We suggest a mass screening program among the elders to diagnose early symptoms of hearing loss to decrease the chance of dementia and cognitive decline. The screening program's age target is older than 65 years old and covers both genders without recognizing memory deficits. It divides into two stages. Firstly, with the aid of a mobile application, the hearing quality will be assessed. Second, the identified patients will be introduced to the nearest audiometry center. The hearing loss of more than 25 decibels is considered the threshold for recognizing a patient as a candidate to receive hearing aids. The result of our idea is that we can prevent one of the costliest diseases, Alzheimer's disease, with a low-cost, easy, and non-invasive screening method. When a person has vision obstacles, they see an optometrist immediately. Still, they may not notice soon if someone has a hearing problem, Because the path of hearing issues is chronic; however, the person's relatives realize this problem early, so that the possibility of communication for the person disappears; thus, the person becomes isolated and lonely, and this issue can lead to Alzheimer's disease. Our screening method's advantage is that even in the first stage, we can detect hearing loss without going to audiometry centers with audiometer application at home, resulting in faster detection of hearing loss. Using the audiometer applications on the phone eliminates the need for lots of audiometry centers and avoids congestion. If the person has a hearing problem, we refer the person to an audiometry center near where we liveThe objective of developing this program is to predict the probability of developing Alzheimer's in people several years before the onset of the disorder and then eliminate the underlying factors that are a risk factor for the condition to keep the person from developing Alzheimer's. Therefore, by performing this screening program, people are identified even before the onset of the early symptoms of Alzheimer's, thus preventing many economic, social, and emotional pressures in the future.

## P30

## Medication Adherence and Health Literacy in Psoriasis Patients: A National Survey in Iran

*Yasaman Avazeh*[1], *Soheila Rezaei*[2], *Peivand Bastani*[3], and *Gholamhossein Mehralian*[4,*]

[1]Department of Pharmacoeconomics and Pharmaceutical management, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad Tehran Medical Sciences University, Tehran, Iran

[2]Department of Pharmacoeconomics and Pharma management, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3Health Human Resources Research Center, Department of Health Service Management, School of Management and Information Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
*Department of Pharmacoeconomics and Pharma management, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Corresponding author: Gholamhossein Mehralian
Corresponding author Email: gmehralian@gmail.com

Introduction: Health literacy is recognized as one of the most basic components of ability to increases medication adherence to achieve better treatment results and reduce the health care system costs. Medication adherence among Psoriasis patients is often inadequate which has been identified as a significant problem in Psoriasis symptoms management. This study aimed to evaluate the medication adherence level of Iranian Psoriasis patients and its relationship with the patients' health literacy level and demographic conditions. To the best of our knowledge, the present study is the first of its kind to contribute new knowledge among Iranian psoriasis patients in this area.Material and methods: This is a cross-sectional study among Iranian psoriasis patients conducted through a web-based questionnaire survey between 26 July 2020 and 5 January 2021. The questionnaire consisted of 3 sections: First, demographic information and disease characteristics were evaluated. Second, the medication adherence was evaluated by using valid Morisky Medication Adherence Scale-8 (MMAS-8), and finally the health literacy was evaluated by using Health Literacy for Iranian Adults (HELIA). Data was analyzed using SPSS software, version 22 with descriptive statistics; Chi-square and Kruskal–Wallis tests. Stepwise multiple linear regression was also used to evaluate the impact of independent variables related on medication adherence score. Results: Results showed that the mean health literacy score in the study population was 74.3 ± 14.23, and the mean medication adherence score was 4.1 ± 2.18. Out of 575 subjects, the percentages of high, sufficient and insufficient health literacy were 28.8%, 67.1% and 4%, respectively. The majority of subjects (70.7%) reported low adherence, while 24.1% reported medium, and 5.2% reported high adherence. The results of Chi-square test showed a significant relationship between the age, comorbidities, type of treatment, satisfaction with treatment, experience of adverse effects and health literacy with medication adherence ($P<0.05$). The final constructed model of regression was highly statistically significant ($F=20.384$, $p<0.0001$). The highest beta coefficient in the final model belonged to the total health literacy score.Discussion: Recent studies have highlighted the low adherence rate in patients with chronic dermatological conditions such as psoriasis. The results of the current study also confirmed this. A study indicated that psoriasis patients with lower levels of health literacy might have difficulty adhering to complex treatment modalities. The results of current study also indicated that patients with higher overall health literacy had better medication adherence. In contrast to a study, which reported that a large number of psoriasis patients had shortcomings in health literacy, the majority of the participants in the present study had high and sufficient levels of health literacy, which could be attributed to the online nature of the survey. Conclusions: Based on the results, medication adherence among Iranian psoriasis patients is low. Of all five variables mentioned, health literacy is found the main predictor of medication adherence. Since the thoughtful consideration of factors associated with high adherence is important for optimal therapeutic outcomes, it is recommended to evaluate the impact of each of other factors associated with medication adherence on its level.

P31

# Scrutiny of The Ivermectin Effects on COVID-19 Treatment Processes

*Fateme Sadat Hosseinipour*[1], *Seyedeh Hannaneh Eshaghi Deravi*[1], *Zahra Arabzadeh*[1], *Arghavan Zarafshar*[1], *Sama Niakan*[1], *Saeede Esmaeili*[1], *Zahra Zahrian Esfahani*[1], *Shadi Sarahroodi*[2]*

[1]School of pharmacy and pharmaceutical sciences, Tehran Medical Sciences Islamic Azad University, Tehran, Iran
[2]Department of Pharmacology&Toxicology, School of Pharmacy, Tehran Medical sciences Islamic Azad University*
Corresponding author: Shadi Sarahroodi
Corresponding author Email: Sarahroodi@iautmu.ac.ir

Introduction: In December 2019, the first known case of Coronavirus disease (COVID-19) was identified in Wuhan, China. The disease has since spread worldwide, leading to an ongoing pandemic. COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and can cause fever, cough, headache, fatigue, and breathing difficulties although these signs may appear differently in different people. Ivermectin is one of the most important veterinary and human drugs. This medication is considered a potent treatment for parasitic, viral, and bacterial diseases. After December 2019 many drugs participated in studies and as a result, Ivermectin was observed as an effective drug for COVID-19 treatment processes.Material and methods: In this review, the authors searched three medical databases including Google Scholar, PubMed, and Scopus based on terms related to COVID-19 and Ivermectin and synonyms of them from 2019 until May 2021. Published articles, clinical trials, World Health Organization reports were collected, reviewed, interpreted, and summarized regarding Ivermectin's role in COVID-19.Results: According to reports, Ivermectin has been found to be docked between the viral spike and the ACE2 receptor and may affect COVID-19 as an antiviral. Molecular computing revealed high binding affinity to various SARS-CoV-2 viral proteins (including high binding affinity to viral S protein as well as the human cell surface receptors ACE-2 and TMPRSS2) and perform multidisciplinary actions. Many studies showed the possible efficacy of Ivermectin in reducing mortality, clinical recovery time, COVID-19 progression, and hospital admission duration in patients of all stages of clinical severity. Ivermectin can influence COVID-19 in combination with other drugs such as Hydroxychloroquine, Doxycycline, etc. A few studies showed the opposite results and expressed that Ivermectin combination with other official medications in COVID-19 can pose severe side effects comparing with the use of Ivermectin solely. Studies show the dosage is very important in these cases and we should use dosage with much Ivermectin effective material with inevitable more side effects.Discussion: According to most of the studies Ivermectin can be effective in the reduction of COVID-19 deaths, progression, and clinical recovery time. Conclusions: The results of the researches emphasize on benefits of Ivermectin as prophylaxis or treatment of COVID-19 Some clinical trials revealed that Ivermectin either solely or in combination with other medications could be effective for patients with COVID-19, it seems this effect is dose-related and according to results better effects can be with a higher dose. In this regard, our study expresses that Ivermectin is effective on COVID-19 but its proper dose and combinations need more studies, clinical trials, and pharmacokinetic corrections to reduce adverse effects and the better use, for these patients.

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## Study the effect of Viola odorata topical ointment on the Treatment of Patients with acute and subacute eczema

*Azin Mohammadkhah*[1]

[1]Department of Clinical Pharmacy,Pharmaceutical Sciences Branch,Islamic Azad university,Tehran,Iran
Corresponding author: Maryam ShiehMorteza
Corresponding author Email: mshi1973@yahoo.com

Introduction: Eczema is a chronic, pruritic, inflammatory disease that affects people of all ages. Eczema can be treated both topically and systemically. Eczema causes people to turn to chemical drugs because it interferes with their quality of life. On the other hand, the occurrence of complications such as skin atrophy and liver and kidney disorders, the plan to use other treatments has significantly increased the characteristics of medicinal plants. This study was performed to evaluate the effectiveness of ointment containing Viola Odorata oil in the treatment of acute and subacute eczema.Material and methods: Viola Odorata plant was prepared from Tehran medicinal plants market and was identified and approved in the herbarium of the Faculty of Pharmacy of Tehran Azad University of Medical Sciences. Sweet almond oil was purchased from Barij Essence Pharmaceutical Co. (Kashan, Iran). All other chemicals were provided as analytical grades or higher from different commercial suppliers and used as received without further purification. In the present single blinded clinical trial study, 30 patients were diagnosed with acute and subacute eczema. According to the TIS index, the severity of each individual's eczema was scored and for two weeks on one hand only the standard treatment, Topical corticosteroids and on the other hand, they used topical corticosteroids along with the ointment containing Viola Odorata oil, and after two weeks, the relevant results were collected.Results: Comparison between topical corticosteroids alone and ointment containing Viola Odorata oil with topical corticosteroids showed that the combination of topical corticosteroids and ointment containing Viola Odorata oil significantly improved the lesions caused by eczema ($p < 0.01$). Also, two factors, age and gender, had no effect on the results.Discussion: Family history in 36% of patients indicates that heredity plays an important role in the development of eczema. Proper drug formulation is one of the most basic steps in a successful treatment. In this study, sweet almond oil was used due to its higher moisturizing properties than sesame oil as well as lack of the side effects. Also, in order to comply with ethical standards, none of the patients were deprived of topical standard corticosteroid treatment. At the end of the study, patients were asked to rate their recovery on a scale. The majority of patients reported an acceptable improvement at the end of the treatment period. As it was observed, after one week of using topical corticosteroids with aromatic violet ointment, the scores are significantly lower than using topical corticosteroids alone ($P < 0.001$). Continuation of treatment after one week showed similar outcomes ($P < 0.001$). To further confirm the results, the absolute value of the reduction of scores before and at the end of the treatment was examined, which showed a meaningful reduction during the study.Conclusions: This study presents the effectiveness of using ointment containing Viola Odorata oil on reducing the symptoms of eczema, which due to low side effects and effectiveness of Viola Odorata is recommended to use more of this plant.

P33

## A new systematic review from evaluation of the place of DOACs in the treatment of patients with renal failure

*Maryam* Nikfarjam[1], Fatemeh Tahmasebi[1], and Amir Rezazadeh[2]

[1]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[2]Department of Clinical Pharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
Corresponding author: Amir Rezazadeh
Corresponding author Email: amirrezazadeh86@yahoo.com

Introduction: Direct oral anticoagulants (DOAC) are mostly prescribed to prevent cardioembolic stroke in patients with non-valvular atrial fibrillation (AF) and Treatment of venous thromboembolism (VTE). Drugs in this category include dabigatran, edoxaban, rivaroxaban, apixaban and betrixaban. A slight but significant reduction in the risk of all-cause mortality, stroke or systemic embolism, and major bleeding with DOAC compared with vitamin K antagonists (VKA), caused them to outperform warfarin and other VKA. Material and methods: In this systematic review which was done in 2021 June, three medical databases including PubMed, Google Scholar and Scopus were searched with keywords based on MeSh database. Search word were: "direct oral anticoagulants"," renal failure"," chronic kidney disease"," apixaban", "rivaroxaban"," dabigatran"," edoxaban". In this review 57 article were found in mentioned databases from 2021 to 2017. The articles were screened in three steps. In first step the title of articles screened, in second step the abstract of articles screened and in final step the full texts screened. In each step the irrelevant articles excluded and finally the qualified 15 articles were selected with according to several clinical professors. The main therapeutic strategies extracted from remained articles.Results: Renal clearance of DOACs varies; Most of them are dabigatran (%80) and the least rivaroxaban (%36) & apixaban (%27). The half-life of the drugs in this category is almost the same and is about 12 hours (Most betrixaban with 37h, which has recently been approved). The renal complications observed in DOACs are dose-dependent: dabigatran %4.6, rivaroxaban %3.5, apixaban %2 (It has also been observed that apixaban has anti-inflammatory and antioxidant effects that can improve kidney function.) and edoxaban %1.7, which has no special effect on the kidneys. In DOACs the most plasma protein binding belongs to rivaroxaban & apixaban and the lowest is related to dabigatran.Discussion: DOACs reduced the risk of mortality in patients with moderate-severe or severe CKD (chronic kidney disease) and the risk of major bleeding in patients with moderate-severe or moderate CKD. Among these categories rivaroxaban has a high efficacy, apixaban and edoxaban have a most safety and dabigatran has the lowest bioavailability. Multiple medication uses for treating superimposed co-morbidities is common in both elderly and CKD patients and drug interaction may cause accumulation of DOAC, thereby increasing the risk of bleeding.Conclusions: The safety profile of DOAC in patients with CKD has not been defined with any certainty, particularly in those with severely impaired renal function or end stage renal disease. DOAC have at least similar safety and efficacy profiles in patients with CKD stages G2 to G3b and in patients with normal renal function. In patients with CKD G4, DOAC should be used with caution because of lack of strong supporting evidence from RCTs. At present, there are not enough data available to recommend the use of DOAC in patients with CKD G5 or on long-term dialysis, but latest data has suggested that apixaban may be used with great caution in this stage.

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## Management of post COVID syndrome

*Mona Rastad* [1], *Parisa Niazmand*[1], and Amir R*ezazadeh*[2*]

[1]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[2]*Department of Clinical Pharmacy , Faculty of Pharmacy , Tehran University of Medical Sciences, Tehran,Iran

Corresponding author: Amir Rezazadeh

Corresponding author Email:Amirrezazadeh86@yahoo.com

Introduction: COVID- 19 pandemic has a broad spectrum of manifestations which may continue after acute phase of disease too. Theses persistent and/or long-term complications often occur beyond 4weeks from the onset of symptoms and often include symptoms like fatigue, weakness, cough, dyspnea, neuropsychological symptoms, arthritis, vascular and organ fibrosis and hair loss. Additionally, some patients may complain about loss of smell (anosmia) or taste (ageusia). These problems can affect the quality of life and they may also increase mortality in patients. A set of these symptoms is called post COVID syndrome.Material and methods: Scientific databases such as PubMed, ScienceDirect and Google Scholar were searched systematically with search terms"COVID-19","post COVID syndrome","cytokine", "interleukin","inflammatory phase","thromboembolic events"and " fatigue" based on Mesh database. After the screening, related articles were selected and data was extracted.Results: According to our research, immune system responses and an increase in the level of cytokines such as interleukins 1 and 6 and TGF beta may be identified to develop the symptoms. TGF beta could lead to development of the symptoms. Increased level of TGF beta may increase the risk of lung fibrosis. Chronic lethargy, sleep disturbances, depression symptoms and migraine-like headaches may occur due to increased cytokines. Tumor necrosis factor alpha causes modulating cardiomyocyte ion channel expression, as a result of this event, arrhythmias and tachycardia might occur in the patients. Immune reactions also cause hyperinflammatory state in patients, which increases the risk of thromboembolic events in patients.Discussion: Our systematic review evaluated studies which investigated the role of immune system and its hyperactivity in COVID-19 patients, so it seems the use of immunosuppressive drugs such as corticosteroids, tocilizumab etc., may decrease the severity of symptoms, in addition to these agents, anticoagulant therapy is a main intervention for hospitalized and severe COVID-19 patients to reduce the risk of thromboembolic event, which has a mutual correlation with inflammation.Conclusions: The result of this systematic review demonstrated complications of post COVID-19 syndrome can be fatal and may increase mortality after discharge. Careful selection and continuation of medication such as corticosteroids and anticoagulant after discharge may be a beneficial intervention particularly for high risk patients (severe disease, higher inflammatory marker, high D-Dimer etc.) for prevention of thromboembolic events and post COVID syndrome.

## P35

# A review on the role of biomarkers in prognosis and early detection of Alzheimer’s disease:

*Kowsar Sedghi[1], Niloofar Alizade[2]*

[1]Student Research Committee, Faculty of Pharmaceutical Science, Islamic Azad University of Medical Sciences, Tehran, Iran

[2]Student Research Committee, Faculty of Pharmaceutical Science, Islamic Azad University of Medical Sciences, Tehran, Iran

Corresponding author: Kowsar Sedghi

Corresponding author Email: kowsar.sedghi@gmail.com

Introduction: Alzheimer’s disease (AD), a neurodegenerative disease, is common among the elderly and its prevalence is spreading. The biggest concern about AD is its early diagnosis, before the disease progresses and neurons are degenerated. There are several measures used today to diagnose Alzheimer’s disease, including: neuroimaging tests such as MRI (Magnetic resonance imaging) or PET scan (positron emission tomography) which are expensive for patient, CSF analysis which is invasive and neuropsychological assessments which occurs in clinical stage. Despite all these diagnostic methods, we need a method to help in early diagnosis and easier treatment.Material and methods: In this review article, we collected data on biomarkers that can be used to diagnose AD in the preclinical stage. We focused on search terms “Alzheimer early detection” and “Alzheimer drugs” in PubMed, Science Direct, Google Scholar databases. After screening related articles, their data was extracted.Results: Prescribed drug regimen, which includes Galantamine, Donepezil, etc. only prevents the progression of Alzheimer, nevertheless taking drugs does not heal the damage. Of course oligopeptides composed of 42/40 amino acid residues appear in pre-clinical stages. Therefore, measuring Aβ 42/40 ratio is one of the methods of Alzheimer's diagnosis.Discussion: Different ways were offered for early detection, but the proposal to examine the level of biomarkers changed the process of diagnosing of Alzheimer’s. Total tau protein which is a product of MAPT gene, is a diagnostic biomarker for AD and in normal condition is soluble and unfolded. YKL-40 as CSF biomarker is useful in MCI in early stages of AD and found in inflammatory diseases which can be used to diagnose dementia and mild stage AD. Also hyper phosphorylated tau protein is a useful biomarker in the early detection of Alzheimer's. However, the most important biomarkers identified in CSF are amyloid peptides; which is a group of insoluble beta sheet proteins from filamentous structure that would refers to oligopeptides composed of 42/40 amino acid residues.Conclusions: By discovering of measure of brain amyloid plaques by amyloid PET scan, and its association with ratio of Aβ 42/40, we would be able to diagnose AD in pre-clinical stages. Measuring tau hyper phosphorylation (tau 217) as an acute predictor of β-amyloidosis at asymptomatic and symptomatic stages, has the key role in predicting future AD risk.

## P36

# Early treatment with corticosteroid in Covid-19

*Zahra Zahed[1] , Shadi Azghandi[2] , Fatemeh Tadayoni[3] , Amir Rezazadeh[4]*

[1]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[2]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[3]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[4]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Corresponding author: Amir Rezazadeh

Corresponding author Email: amirrezazadeh86@yahoo.com

Introduction: In December 2019 sars-cov-2 was first reported in Wuhan, China. Soon after it, covid 19 became a global issue that led WHO to declare a pandemic.So far, the ongoing pandemic has caused 92628 deaths and 4057758 identified cases in Iran.The immune system reacts to eliminate the virus but its inappropriate reaction may cause systemic hyper-inflammation and it may develop as acute respiratory distress syndrome (ARDS). Early onset of anti-inflammatory treatment, such as corticosteroids, may reduce rate of mortality in moderate to severe ARDS cases. And it’s necessary to be careful about use, timing and dose of these anti-inflammatory treatment.Material and methods: The goal of

this study is to summarize the data of various articles and case studies published in google scholar, PubMed and Cochrane that were published in 2021 and 2022. We used the following terms related to the subject: 'Covid-19', 'Coronavirus disease', 'SARS-CoV-2', 'Corticosteroid', 'pneumonia', Critically ill patient', Outcomes, 'Mortality', 'Virus shedding', Ventilator free daysResults: Analyzing multiple articles demonstrated that early corticosteroid treatment resulted in lower ICU mortality, higher number of ventilator-free days, shorter length of ICU stay, less secondary infections than the patients who received the treatment late in the course of disease. Whether to use high or low dose of corticosteroids are controversial.Discussion: These articles discuss corticosteroids treatment and its benefits. According to WHO criteria about receiving corticosteroids, patients who developed severe disease and require oxygen without mechanical ventilation, are candidates to receive corticosteroid treatment. But in patients who don't receive a respiratory support, treatment with corticosteroids have negative effects.Patients with severe infection may need a wide range of oxygen therapy (1 to 10 L/min) and different types, dosing and duration of corticosteroids administration depending on the sickness severity; which seems to need more study and investigation.Conclusions: In conclusion, corticosteroids may be one of the main treatments in patients with severe Covid-19. Early treatment with corticosteroids (first 48h of ICU admission) was closely related to reduction in the length of hospital stay and reduction in ICU mortality. It's also in relationship between positive effect on organ dysfunction However more researches about optimal drug, onset, dose and duration of treatment with corticosteroids is needed.

## P37

# Article Title: Can Diuretics slow down Alzheimer's disease from Progressing?

*Arghavan zarafshar*[1], *Saeede esmaeili*[2], *Rozhin solhjoei*[3] , *Nastaran fahiminiya*[4], *Farnaz vosough*[5], *Pariya khodabakhsh*[6*]

[1]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[2]Department of Pharmacology, School of Medicine, Shahid Beheshti University of Medical Science, Tehran, Iran

Corresponding author: Pariya Khodabakhsh

Corresponding author Email: p.khodabakhsh@sbmu.ac.ir

Introduction: Alzheimer's disease (AD) is a progressive memory-relate neurodegenerative disease, which is characterized by two principal pathological features, including the aberrant extraneuronal accumulation of amyloid-beta plaques, as well as the formation of intraneuronal neurofibrillary tangles (1). The etiopathogenesis of AD is still unknown. A huge number of studies have so far been carried out worldwide to better understand the risk factors for AD. However, it still warrants further studies in order to define optimal preventive strategies. Several longitudinal studies have been shown that AD is one of the most important complications in people with cardiovascular disorders, especially high blood pressure (2). Besides, there are numerous studies that focused on the link between the use of antihypertensives and the risk of developing AD or dementia (3, 4). In the present article, we aim to review studies that investigated the possible link between the chronic use of several classes of diuretics, as the main antihypertensive therapies and the future risk of AD development.Material and methods: In this narrative review, we search four medical databases including Google Scholar, PubMed, MEDLINE, and Science Direct based on terms related to Alzheimer's disease, dementia, antihypertensive agents, diuretics, and synonyms. The search for eligible literature was conducted up to 3 August 2021. Furthermore, specific drug names were used as search items in the databases to identify related articles. Both clinical and pre-clinical studies were included. Only articles published in English were reviewed.Results: The main results were initially obtained by Chuang YF et al in a prospective population-based cohort study, which have shown that diuretics significantly reduce the risk of AD development (adjusted hazard ratio [aHR],0.61, 95% confidence interval [CI], 0.37-0.98). There is also evidence that the use of combining the two diuretics was associated with a significantly decreased risk of AD (aHR 0.63, 95% CI 0.42-0.94) (5).Discussion: Despite one of the main causes of AD is high blood pressure, it cannot be said with certainty that long-term use of diuretics is associated with a lower risk of AD development because different factors can affect the association. Nevertheless, a number of studies have reported that some classes of these antihypertensives, such as thiazide and potassium-sparing diuretics, especially when used in combination, may reduce the progression of the disease and the important point is that no negative impact has been observed in the studies from diuretics (3). Several mechanisms can be considered for this relationship. For example, in the case of potassium-sparing diuretics, raising potassium levels may play a crucial role, as it has been shown to reduce the formation rate of reactive oxygen species in endothelial cells (3).Conclusion: So far, several clinical studies have suggested an inverse relationship between the use of diuretics and the incident rate of AD. We can hope to achieve more reliable results with further long-term studies.

## P38

# Therapeutic potential of topiramate against metabolic syndrome

*Fatemeh Rostamian*[1], *Narges Abbasi Aval*[1], *Sanam Soltani*[1], *Melika Kokabidana*[1], *Hedieh Sadat Shamsnia*[1], *and Samaneh Olapour*[*]

[1]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

*. Department of Pharmacology, Faculty of Medicine, Islamic Azad University, Tehran Medical Branch, Tehran, Iran

Corresponding author: Samaneh Olapour

Corresponding author Email: olapour.s@gmail.com

Introduction: Metabolic syndrome (MetS) is a combination of medical conditions including obesity, insulin resistance, hypertension, and dyslipidemia, and is strongly associated with an increased risk for developing diabetes and cardiovascular disease. Environmental and genetic factors lead to obesity and insulin resistance, which contribute to metabolic abnormalities. MetS has gained significant importance recently due to the exponential increase in obesity worldwide. Topiramate is a fructose derivative, currently indicated for the treatment of epilepsy. It appears to have multiple actions including inhibition of neuronal voltage-dependent sodium channel, enhancement of activity of γaminobutyric acid, and inhibition of activity of glutamate at its receptors. This drug is approved for marketing worldwide as an adjunctive anti-seizure therapy in patients with partial onset seizures and generalized tonic-clonic seizures. Its usage has been extended to other disorders including migraine, essential tremor, obesity, and alcohol addiction. The aim of this review is to summarize the more recent evidence concerning benefits of topiramate in the treatment of the major components of MetS. Experimental studies have shown that topiramate significantly induces weight loss and decreases hyperglycemia, insulin resistance, and hypertriglyceridemia, while increases adiponectin plasma levels in diet-induced obesity rats. In addition, weight loss, with a reduction in visceral body fat, has been observed with topiramate treatment among patients with seizure disorders and migraines. The weight loss is typically minimal in individuals of normal body weight but significant in overweight or obese individuals. In 2012, topiramate in combination with phentermine is approved in the United States for the treatment of obesity. Of all the currently approved antiobesity drugs, phentermine/topiramate has the most robust efficacy, with a placebo-subtracted 1-year weight loss of 8.6% to 9.3% at the 15/92 mg dose in 2 large randomized controlled trials. Various studies suggest that topiramate-induced weight loss results from increased energy expenditure, decreased energetic efficiency, and decreased caloric intake

as an appetite suppressant.Material and methods: For our research we reviewed 5 Pubmed published articles from 2011 to 2020. Results: Topiramate has been reported to improve glycaemic control and promote a moderate weight loss in obese patients. Discussion: Topiramate has drawn much attention in recent years due to its newly recognized beneficial effects. Topiramate has diverse effects through its action on different tissues including, but not limited to, liver, adipose, brown fat, and pancreas. Topiramate inhibits lipid synthesis and promotes fatty acid oxidation. In addition, it is a potent inhibitor of carbonic anhydrase isoenzymes, thereby impeding lipogenesis. Decreased calorie intake appears to be a significant factor associated with topiramate induced weight loss in humans. It may also influence body weight via its effects on hypothalamic corticotropin-releasing hormone and galanin. Moreover, topiramate is capable of preventing glucotoxicity-induced pancreatic β-cell dysfunction via reduction of reactive oxygen species. Conclusions: Topiramate may enhance insulin action and glucose transport, as well as increase adiponectin secretion in the adipose tissue, thus potentially reducing metabolic disease. Although the weight loss benefits with topiramate are clearly demonstrated in several studies, the efficacy of topipamate in reducing comorbidities associated with the MetS remains inconclusive.

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## Targeting TMPRSS2 and ACE2 anti-inflammatory receptors as therapeutic pathway for COVID-19 / IBD overlap

*Naser-Aldin Lashgari[1], Nazanin Momeni Roudsari[1], Saeideh Momtaz[2] and Amirhossein Abdolghaffari[3]*

[1]Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran Medical Sciences, Islamic Azad University, Tehran 1941933111, Iran.Student Research Committee, Faculty, University, City, Country

[2]Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Tehran 31375369, Iran; Toxicology and Diseases Group, the Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences, Tehran 1417614411, Iran; Gastrointestinal Pharmacology Interest Group (GPIG), Universal Scientific Education and Research Network (USERN), Tehran 1417614411, Iran.

[3]Department of Toxicology & Pharmacology, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University (IAUPS), Tehran 1941933111, Iran; Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Tehran 1941933111, Iran; Toxicology and Diseases Group (TDG), Pharmaceutical Sciences Research Center (PSRC), The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences, Tehran 1941933111, Iran; Department of Toxicology and Pharmacology, Faculty of Pharmacy, Tehran University of Medical Sciences Tehran 1941933111, Iran; Gastrointestinal Pharmacology Interest Group (GPIG), Universal Scientific Education and Research Network (USERN), Tehran 1941933111, Iran.Research Center, University, City , Country

Corresponding author: Dr. Amir Hossein Abdolghaffari
Corresponding author Email: amirhosein172@hotmail.com

Introduction: Inflammatory bowel diseases (IBD) refer to a subgroup of chronic, progressive, long-term, and relapsing inflammatory disorders. IBD may spontaneously grow in the colon, and in case of severity may result in tumor lesions such as invasive carcinoma, in inflamed regions of the intestine. The ongoing coronavirus disease (COVID-19) pandemic caused serious morbidity and mortality worldwide. Epidemiological reports indicate that old age and underlying diseases such as IBD contribute to severity of these diseases and increase mortality in patients with COVID-19. Similarly, it has been shown that the Transmembrane Serine Protease 2 (TMPRSS2) protease and angiotensin-converting enzyme 2 (ACE2) are an essential factor for viral activation, thereby promoting viral engulfment. Generally, viral entry causes 'cytokine storm' involving excessive generation of pro-inflammatory cytokines/chemokines including interleukin (IL)-6, IL-2, IL-7, Tumor necrosis factor (TNF)-α, and interferon (IFN)-γ(1). Material and methods: Data from clinical, *in vitro* and *in vivo* studies were collected in English, From PubMed, Google Scholar, Scopus, and the Cochrane library, until May 2021. Search terms included “corona virus” OR “COVID-19” AND “Inflammatory bowel disease” OR “IBD” OR “Inflammation” AND “TMPRSS2” OR “ACE2” AND “TMPRSS2 inhibitors” OR “ACE2 inhibitors”.Results: the TMPRSS2 and ACE2 signaling pathways mediate inflammation, and also introduce the synthetic or natural TMPRSS2 and ACE2 inhibitors as probable approaches for IBD treatment in COVID-19 situation. Synthetic (Salicylates, Corticosteroids, Cyclosporin, Azathioprine, methotrexate, Vedolizumab and Ustekinumab) or natural (hesperidin, chrysin, emodin, kaempferol, quercetin, fisetin, quercetin, absinthin, glabridin, gallic acid, fangchinoline, tetrandrine, carvacrol, geraniol, anethole, L-4-terpineol, cinnamyl acidic, thymol, pulegone, limonin, obacunone and ursolic) compounds could improve COVID/IBD due to inhibition of inflammatory and oxidative process through TMPRSS2 and ACE2 pathways(2, 3).Discussion: Information on the physiologic and pathophysiologic functions of ACE2/TMPRSS2 is still scant. Also, the relationship between ACE2/TMPRSS2 and IBD merits further consideration for better understanding of unhealthiness in patients with IBD. Taking everything into account, investigating the multifunctional nature of ACE2/TMPRSS2 in COVID/IBD will develop the knowledge on the pathophysiology of this illness. Future research could concentrate on developing these inflammatory immunological responses, efficient to encounter COVID-19. This analysis elucidates the role of inflammation and immune responses during IBD infection with COVID-19 and provides a list of possible targets for IBD-regulated therapies in particular(4). Conclusions: This article provides clinical based evidences that introduce the synthetic or natural based TMPRSS2 and Angiotensin-converting enzyme 2 (ACE2) inhibitors, that are able to reduce covid-19-induced inflammation and cytokine storms in IBD patients. Hence targeting the TMPRSS2 and ACE2 could be noticed as a novel approach for IBD treatment(5).

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## High dosage prenatal folic acid usage effects on Autism

*Fatemeh Safari[1], Negar Amirkardoust[1], Zahra Mousavi[1], Farangis Marboutian[2], Parvaneh Najafizadeh[3]*

1 Pharmacology and toxicology department, faculty of pharmacy and pharmaceutical sciences Tehran medical sciences Islamic Azad university

2 Iranian Society of Emergency Medicine

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

Corresponding author: Parvaneh Najafizadeh

Corresponding author Email: najafizadeh.p@iums.ac.ir

Introduction: Autism spectrum disorders (ASD) includes a collection of neuro-developmental conditions known as Autism. It has some behavioral symptoms such as communication impairments and social interaction, repetitive behaviors, stereotypies, and a limited selection of interests and activities. ASD certainly has an underlying genetic basis, however, the role of the environmental factors could not be ignored. The incidence of ASD is increased in recent decades remarkably which is parallel by the increase of prenatal supplement usage by pregnant women. Maternal exposure to dietary factors during pregnancy can affect embryonic development and may modulate the phenotype of offspring through epigenetic programming. Folate is a water-soluble B

vitamin that is essential for nucleic acid synthesis, DNA methylation, and repair. Preconception intake of dietary folic acid (FA) is credited with reduced neural tube defects in infants. However, abnormal folate level and related pathways have been identified in children with ASD (1). The aim of this study was to investigate the relationship between high folate level and autism disorder incidence in children.Material and methods: Two medical database were used for finding the related studies in the field including PubMed and Google Scholar using keywords based on the MeSh database (May 2021). This systematic review was based on standards of PRISMA guideline.Results: In this review 172 article were found in the aforementioned databases. After reading the abstract of the articles, 10 relevant papers were extracted. There were contradictory reports between the reported results. Surén et al, and Schmidt et al. were reported FA near the time of conception was associated with a significant reduction autism development risk (2). On the other hand, some other studies reported that the ASD was positively related to self-report of folic acid supplementation usage during pregnancy. For instance, one of the studies was shown that the high folate level reported from a blood sample 72 h negative neurodevelopmental outcomes in offspring ours before delivery was associated with a doubling in risk for ASD (3).Another study, in 2017, reported both low and high folate level were associated with increased risk for ASD. Also, very high maternal blood levels of folate and B12 at the time of birth both increased the risk of ASD 2.5 times (4).Discussion: Optimum dosage of supplementary folic acid in early pregnancy may be associated with enhanced vocabulary development, communicational skills, and verbal comprehension at 18 months of age. Conversely several recent studies of ASD and other psychiatric disorders have revealed associations with metabolic abnormalities related to folate metabolism. These associations have been categorized into five groups: immune dysregulation, inflammation, oxidative stress, mitochondrial dysfunction, and environmental toxicant exposure.Children who develop ASD may receive a massive dose of folic acid in utero. Also, excessive usage of maternal vitamin B12 (>600 pmol/L) in pregnancy was shown to be related to greater ASD risk in offspring. The risk of ASD was the highest if the mother had both excess prenatal folate and vitamin B12 levels (5).Conclusions: At least three studies were reported association between negative neurodevelopmental outcomes in offspring and high dosage of supplement usage during pregnancy. To conclude, caution regarding taking supplement during pregnancy is warranted.

## P41

# Novel therapeutic targets and comparison effect of approved drugs for patients with irritable bowel syndrome

*Dorsa Mohammadzadeh*[1]

[1]Pharmacy student,Isalamic azad university,Tehran,Iran
Corresponding author:Dr Sassan Dastaran
Corresponding author Email : Dastaran@sbmu.ac.ir

IBS( Irritable bowel syndrome) is a functional disease of the gastrointestinal tract and the exact mechanism of this disease is not known, so comparing the effect of new and current therapeutic targets can be used to discover a drug with the least side effects in improving the quality of life of patients have an important role and also IBS is more common in women. Clinical symptoms such as abdominal pain, diarrhea or constipation, intestinal cramps, and bloating can affect the quality of life of patients and current treatments are symptomatic. Non-pharmacological treatments for IBS include diet modification, hyponatremia, and hypotension. In this article, the mechanism of action, side effects, and studies of new approved drugs, including plecantide, dolcantide, and tenapanor, are studied. The mechanism of new targets, including selective glucagon like peptide 1 antagonist) GLP 1(,HT (hydroxytryptamine receptor ) ،Tachykinin receptor antagonist ،Inhibition of miRNA 29a ،Melatonin ،peptide YY (PYY) HMG COA reductase ،Endocannabinioid receptor agonist ،AST-120 Tryptophan metabolites ،Histamine 1 receptor antagonist Bile acids and ileal bile acid transporter (IBAT) antagonists,many of which are in the clinical trial stages and require further study to become a new treatment option for IBS.

## P42

# Effect of Sage on Alzheimer's Disease: A Systematic Review of Clinical Trials

*Mahshid Zarei*[1,2], *Sanam Soltani*[1,2], *Parham Jahani*[2,3], *Kowsar Rastegar*[2,3], *Nilofar Masoumi*[4], *Ehsan Amiri-Ardekani*[5,6]

[1]Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

[2]Student Association of Indigenous Knowledge, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Student Research Committee, Shiraz University of Medical Sciences, Shiraz. Iran

[4]Student Research Committee, Shahid Beheshti University of Medical Sciences, Tehran. Iran

[5]Department of Phytopharmaceuticals (Traditional Pharmacy), Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[6]Research Center for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
Corresponding author: *Ehsan Amiri-Ardekani*
Corresponding author Email : ehsanamiri@sums.ac.ir

Introduction: Alzheimer's disease (AD) is the most common dementia. This illness currently lacks effective treatment .AD etiology is oxidative stress caused by all the incorrectly accumulated proteins involved in neurological disorders. Up to now, we have cholinesterase enzyme inhibitors and N-methyl-d-aspartate to manage signs of Alzheimer's. However, unfortunately, they are not useful for some remediation or prevention of AD. *Salvia officinalis* L. is a plant that is used for various medicinal purposes. Research has shown that sage inhibits acetylcholinesterase activity. Exploring the literature showed no updated systematic review effect of sage on AD. Thus, our study aims to systematically review all papers reporting the effect of sage on AD and memory.Material and methods: We searched Science Direct, Pubmed, Cochrane, Scopus, and Google Scholar databases for all original English randomized clinical trials studying the effect of Salvia officinalis or its molecules on AD published based on PRISMA. Searched keywords were the following: ("salvia" OR "sage" OR "salvia officinalis") AND ("Alzheimer" OR "dementia" OR "memory"). We included original clinical trial articles and analyzed published articles up to March 2021. We reviewed the articles qualitatively and included only those that had JADAD index more than three and only used articles published in English. Reviews, case reports, editorials, observational studies, and studies on other diseases or using different formulations not containing *S.officinalis* were excluded.Results and discussion: We identified six studies with a total subject of 403 participants .All studies were clinical trials. As we know acetylcholinesterase inhibitor disregulation can resulting difficulty in remembering. It appears that sage monoterpenoids (1,8-cineole, α-pinene, borneol, and camphor) can regulate acetylcholinesterase inhibitor and increase remembering ability. Experiments have shown that after consuming sage, its monoterpenoids can reach the brain and activate the cholinergic receptor. Studies have shown that people who received sage had lower symptoms severity

compared to those who received a placebo and prevented the progression of AD. Also, patients' memory increased after using sage; this may result from the sage act on hippocampal. Patients' memory indices improved after using sage in clinical studies; this suggests that treatment may work on hippocampal. Analysis of memory components showed that the increase in the quality of the memory factor is related to long-term or secondary memory, and sage has no effect on working memory performance. There were no important side effect in sage group in compared to control groups of included articles.Conclusions: The results showed that sage has significant effects in improving the symptoms of Alzheimer's disease and reducing it through antioxidant pathways.

P43

## Comparison of the effect of propranolol and prazosin on oocyte maturation three-spotted gourami

*Arash Almasirad*[1] *, Ehsan Moslehipour*[1] *, Marzie Monemi*[2] *, Homayoun Hoseinzadeh*[3] *,Tahereh Naji*[4*] *,*

[1]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.

[2]Department of Basic Science, Faculty of Pharmacy & Pharmaceutical Sciences, Islamic Azad University,Tehran Medical sciences, Tehran, Iran.

[3]Iranian Fisheries Research Institute, Agricultural Research, Education and Extension Organization, Tehran, Iran.

[4]Department of Basic Science, Faculty of Pharmacy & Pharmaceutical Sciences, Islamic Azad University,Theran Medical sciences, Tehran, Iran.

Corresponding author: Dr.Tahereh Naji
Corresponding author Email: tnaji2002@gmail.com

Introduction: One of the vital human problems during his / her life long is sexual dysfunction and reduced fertility, on the other hand, blood pressure is a risk factor of developing chronic cardiovascular and kidney diseases, that you are able to reduce these ricks by timely treatment. As a matter of fact, the consumption of drugs and medicines has been growing daily. Therefore, adverse effects of these drugs on reproductive system have been investigated by examining endocrine evidence and the effect level of propranolol and prazosin drugs on the biological model of *Trichogaster Trichopterus*. (1)(2)Materials and Methods: For this purpose, 120 female *Trichogaster Trichopterus* fishes with the average weight of 2-3 grams are divided into 10 groups, including control intact, dissolvent distilled water And 4 groups treated with prazosin and 4 groups treated with propranolol, each group consisting of 12 pieces of fish . treatment groups took dosage of 1, 2, 4 and 10 mg / kg Propranolol and 1, 2, 4 and 10 mg / kg Prazosin . All doses were administered 10 times in 3 replicates every other day about 20 days in form of intramuscular injections between the lateral lines and the dorsal fin of fish in 0.02 ml. Finally, after anesthetizing the fish, the histological structure of ovary and were investigated in the treatment groups and compared with the control group .(3) (4) Results: The results of high-dose prazosin in this study showed that most of the cells are in the cortical and vitellogenic stages. The number of prenuclear cells is reduced compared to the control group.The results of propranolol treatment in this study showed that in general, the number of cells in the vitellogenic stage increased compared to the control group and fewer prenuclear cells were seen.Discussion: The ovarian sections showed that with increasing dosage of prazosin and propranolol, the number of cells in the cortical stage increased compared to the control group.In treatment with 4 mg / kg Propranolol almost all cells were in the vitologenesis stage, while at 4 mg / kg prazosin, a number of cells were also present in the cortical stage. Conclusion:In this study, due to the increase in the number of cortical cells in prazosin treatment and further increase in cortical cells and vitellogenesis in propranolol treatment, it was determined that the development and stimulation of oocytes were more affected by propranolol.(5)

P44

## The effect of *Althaea officinalis* on maturation of oocyte in three spots gourami fish (*Trichopodus trichopterus*)

*Mobina Hashemi*[1]*, Nastaran Amani Shamsabad*[1,] *Homayoun Hosseinzadeh*[2]*, Haniyeh –Esmaeilkhani*[1]*, Sara Nozad Goli Kand*[1]*, Saeed Sharifi*[1,] *Tahereh Naji*[1]

[1]Department of Basic Sciences, Faculty of Pharmacy& pharmaceutical sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[2]Iranian fisheries research institute, agricultural research, education and extension organization, Tehran, Iran

Corresponding author: Tahereh Naji
Corresponding author Email: tnaji2002@gmail.com

Introduction:Phytoestrogens mimic the effects of androgen sex steroids cause the sexual growth of gonads. One of the compounds containing phytoestrogens is a small amount of sterol that is present in *Althaea officinalis* root; due to the similarity of the endocrine control system in *Trichopodus trichopterus* with mammals and having resistance to laboratory conditions, *Trichopodus trichopterus* as a model was examined.Method :The aquariums have been dewatered and chlorinated, as well as oxygen levels and water temperatures were measured. The fish were then released into the aquariums with an average weight of 1.5 to 2.5 grams. After adaptation of the fish to the environment, The fish were in 10 groups, including 4 treatment groups for *Althaea officinalis* (Doses 10-20-30-40-50 mg per kg of fish weight) and there were two control groups (control 1, received 20 µl of ethanol and control 2, without injection (were divided. Injections for 20 days and every other day in the form of 20 microliters each time were injected into the relevant groups. After three days, the length and weight of the fish were measured. They were anesthetized with $PI_{222}$ for dissection and their ovarian tissue was removed for histological studies.Results:An index that was examined after injection was the mean percentage of the Gonadal index. In this index, a significant difference was observed between the 4 treatments and the control group, so that for the treatment of 10 mg/kg *Althaea officinalis* extract, the average percentage of the gonadal index was 1.85 and for the treatment of 50 mg/kg extract, the mean percentage of the gonadal index was 2.5, which was a significant difference compared to the control group with an average percentage of the gonadal index 1.1. Another factor was determining the average diameter of the eggs. The final factor was to count the number of oocytes in the growth stage. In this factor, it was observed that the growth and maturation of oocytes increased from 10 mg/kg to 50 mg/kg.Discussion:The main discussion in this article was to investigate the effect of *Althaea officinalis* extract on the growth and maturation of oocytes in immature gourami triangular fish due to the similarity of reproduction control by HCG (Human chorionic gonadotropin) axis in fish and mammals and also the relationship between ovulation and egg fertility with gonadotropins secreted from Gonads These tests can be used to achieve hormonal applications and the effect of substances such as phytoestrogens on the sexual growth of gonads. Items such as the use of *Althaea officinalis* in the treatment of infertility, prevention of menopausal symptoms, to induce puberty and prevent some cancers can be explored in future research.Conclusion: *Althaea officinalis* does not stimulate weight and length, as a phytoestrogen, it accelerates the growth and maturation of *Trichopodus trichopterus*, Increases the average egg diameter and the number of sex hormones, thus causes the egg to grow and mature.

P45

## Novel targeted cancer Aptamer Nanotheranostics drug delivery for Cancer Treatment

*Sadi fathi*[*1] *amir amir amini*[2]

[1]Islamic Azad University Pharmaceutical Sciences Branch , Tehran , iran

[2]Islamic Azad University Pharmaceutical Sciences Branch , Tehran , iran

Corresponding author: amir amir amini

Corresponding author Email: sadifathi@ymail.com

Introduction: Cancer defined as abnormal cell growth with the potential to invade or spread to other parts of the body. Nanotechnology is a field of science that incorporates particles having the dimension less than 100 nm. Nanoparticles are developing new approach in health including diagnosing, treatment, imaging, drug delivery, and industry. Carbon quantum dots are nanoparticles with the size less than 10 nm and 33 Nanomaterials are increasingly used as drug carriers for cancer therapy.This review discusses and elaborates on the aptamer nanoparticles leveraging active targeting and its applications in multifarious therapeutic interventions for the eradication of cancer.Material methods:This review article was written in PRISMA statement manner. Three databases including PubMed, Scopus and Google Scholar were searched with MESH terms. The searches were limited to full-text written in English with no limitation in date.Results:Chemotherapy is a class of cancer treatment that uses one or more chemotherapeutic agents via a defined regimen.the majority of anticancer drugs are not molecularly targeted for cancer cells thereby, leading to toxicity on normal cells. It means that developing novel drugs with higher efficacy, but less toxicity and fewer side effects are a major aim for cancer therapy. To date, although only two aptamer-based cancer therapeutics have undergone clinical trials, several more aptamers have shown great potential for cancer imaging, diagnosis, and therapy. Use of covalent or non-covalent conjugation strategies allows different aptamers to serve as easily exchanged building blocks for functionalizing other therapeutic agents. Although bi-specific antibodies, such as BiTE, are currently used for this purpose. A nucleic acid aptamer-based platform is superior to current antibody-based strategies, as aptamers allow:(1)better tissue penetration;(2)lack of immunogenicity;(3)faster target accumulation and shortened body clearance, enabling the use of shorter-lived radioisotopes;(4)simpler, better controlled, and thus less expensive chemical production;(5) amenability to a variety of chemical modifications that are needed for production and storage, such as pH changes or elevated temperature.Discussion:Aptamers are small (5-40 kDa) single-stranded oligonucleotides that through intramolecular interactions fold into unique 3D structures to bind effectively to their targets with high affinity and specificity also Aptamers are synthetic, short single stranded oligonucleotides (DNA or RNA) that with high affinity and specificity bind to their target molecules as a valid alternative to antibodies. This powerful class of ligands has shown many applications in various biomedical fields, especially as targeted drug delivery agents . Nowadays, They are subjected to intensive investigation in vivo as targeted therapeutics or targeted delivery agents for chemotherapeutic, small interfering RNAs, and molecular imaging probes . Such functionalized nanocarriers can act as smart bombs. From the pharmaceutical point of view, aptamers are powerful targeting agents for nanoparticles due to their relatively straightforward immobilization on nanosurfaces without changing the affinity properties. Conjugation of aptamers with nano-vehicles and antineoplastic agents will facilitate inventive applications of aptamer-based anticancer systems.Conclusions:An extensive literature review was performed using internet database, mainly PubMed. The search results revealed that based on their pharmacokinetics properties, aptamers can be modified and conjugated to various molecules making them promising agents for targeted cancer therapy. Aptamers are becoming increasingly common as therapeutics; as of March 2018, there were ten aptamers investigated for clinical applications, and one had received FDA approval.

P46

## The Role of Zinc Supplementation in Acute Gastroenteritis in Pediatrics; A Review of Clinical Trials.

*Fateme Tavakolifar*[1], *Reza Mostafazade*[2]

[1]Islamic Azad University, Ayatollah Amoli Branch, Amol, Iran

[2]Mashhad University of Medical Sciences

Corresponding author: *Fateme Tavakolifar*

Corresponding author Email: fatemetavakolifar@gmail.com

Introduction: Diarrheal diseases stand the third reason for death among children under five years old. Acute gastroenteritis(AGE) is a rapid onset diarrheal disease, with or without other symptoms, such as nausea, vomiting, or fever. Gastroenteritis was considered for over 500,000 deaths of children before five years old in 2013. The backbone of the management of diarrhea is fluid replacement. Oral rehydrated solutions(ORS) do not reduce the duration or severity of diarrhea and its side effects, such as malnutrition, and are not recommended for patients with vomiting. Zinc deficiency, widespread among children in developing countries, is a common cause of decreased cellular immunity, determining the duration of diarrhea. Herein, we aimed to review the role of zinc supplementation in AGE in pediatrics.Material and methods: We searched Scopus, PubMed, and Google Scholar databases in titles, abstracts, and keywords for all articles published until July 2021 in English and Persian. Following keywords were searched: [(Zinc AND Gastroenteritis), (Zinc AND Diarrhea), (Zinc AND Antidiarrheal), (Zn AND Gastroenteritis), (Zn AND Diarrhea), (Zn AND Antidiarrheal). We found 39 clinical trials articles that investigated the effects of zinc supplementation in improving AGE symptoms. Animal, cross-sectional, and reviews were excluded. Finally, six clinical trials were reviewed.Results: All studies were clinical trials. The shortest duration of treatment with zinc was three days, whereas the longest was 14 days. The frequent dose of zinc was 15 mg. Other studies used 5, 12, 20, 30, and 40 mg of zinc as an intervention. Clinical trials were performed on 1014 children with AGE, the youngest of whom was three months old, and the oldest of whom was 12 years. All except one study evaluated the duration of diarrhea.Discussion: Zinc is an essential trace element with far-reaching effects on multiple systems, assists up to 300 biological functions. Zinc is not accumulated in the body, so the balance of dietary intake, absorption, and losses controls its levels. The influence of the diarrhea duration is when its prolongation leads to serious complications, such as the increased risk of malnutrition, impaired cognitive development. Zinc can decrease the diarrhea duration in 10-20mg, which WHO has confirmed, too.Diarrhea is considered 200,000 hospitalizations per year in children, which has a mental and economic burden on patients, families, and the health system. Two of six articles analyzed the duration of hospitalization due to the Zn intake, which 15 mg zinc bisglycinate for seven days significantly reduced hospitalization. Zinc supplementation besides ORS is less costly and more effective than ORS alone.Vomiting is a common clinical manifestation of AGE that causes distress for pediatrics. Severe and intractable vomiting may induce dehydration, requiring emergency hospital admission. Zinc can induce nausea and vomiting because of its metallic taste, which may be the reason for the lack of change in the vomiting duration and not be proper for vomited patients.Conclusions: The positive effect of zinc in AGE is regulating intestinal fluid transport, mucosal integrity, immunity, and oxidative stress. Zinc reduces diarrhea duration and hospitalization, which can be considered as a complementary therapy in AGE.

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## Spike protein and involved proteases in SARS-COV-2 pathogenicity and treatment; a review

*Fateme Tavakoli-Far[1], Ehsan Amiri-Ardekani[2]*

[1]Faculty of Pharmacy, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran.

[2]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran.

Corresponding author: Fateme Tavakoli-Far

Corresponding author Email: Fatemetavakolifar@gmail.com

Introduction: The SARS-CoV-2, a zoonotic virus from the coronavirus family, manifests fever, nonproductive cough, dyspnea, myalgia, fatigue, and pneumonia. Virus pathogenesis starts with the virus attaching to host receptors and entering its genome into the host cell. The virus employs host cell machinery, including proteolytic enzymes, to encode its proteins and infect the host cell. Due to the significant roles of these enzymes in COVID-19 pathogenesis, inhibiting them may be a therapeutic approach. Because of the rapid widespread of this novel virus and the lack of efficient treatments, we reviewed the SARS-CoV-2 host receptor, spike protein, and enzymes involved in pathogenicity processes. Material and methods: We searched title, abstract, and keywords for related English articles in Google Scholar, Scopus, and PubMed databases for all articles from up to April 2020. The following keywords were searched: [(COVID-19 AND ACE2)OR(COVID-19 AND Spike protein)OR(COVID-19 AND Protease)OR(SARS-CoV-2 AND ACE2)OR(SARS-CoV-2 AND Spike protein)OR(SARS-CoV-2 AND Protease)]. We searched keywords to find basic information about the SARS-CoV-2 structure and the protease-associated spike protein cleavage mechanisms that provide the virus entrance to host cells. Results and discussion: The envelope(E), nucleocapsid(N), spike protein, and M protein are functional proteins essential for the virus's replication. The spike is a trimeric protein, which its amino acid residues are essential for the interaction between the spike and receptor; ACE2. Cellular proteases at S1/S2 and S2 cleave spike. S1 acts as a specific Receptor-Binding Domain(RBD) and the fusion between virus membrane and membrane of the host cell. S2 enables the virus to release its single-stranded RNA into the host cell. There is no evidence of ACE2 expression variations relating to age, smoking, and sex. Medications including Angiotensin receptor blockers (ARBs) and ACE-inhibitors increase ACE2 expression, while methyldopa decreases it. No evidence supports changing therapeutic regimens in patients who received ACE-inhibitors and ARB. One serine protease is the transmembrane serine protease type 2(TMPRSS2), essential for spike priming with proteolytic effects on the spike to allow virus and cell membrane fusion. Trypsin as a TMPRSS cleaves the spike. Proprotein convertases, especially furin, play roles in spike processing, cleave the envelope for viral fusion with the host cell membrane. Different furin-like proteases cleave the S2' site. It is supposed that S2' processing is a significant stage in final spike activation. Cysteine proteases, such as cathepsin B and L(cat B/L) are essential for spike priming in SARS-CoV-2. The intracellular acidity is required for viral entry in cat-B is higher than cat-L pH. Low endosomal pH is essential for virus uncoating. Inhibition of both proteases is required to block virus entry.Conclusions: SARS-CoV-2 spike facilitates virus entry to host cells by attaching to the ACE2 receptor. Enzymes involved in spike priming include the TMPRSS2, cat B/L, furin, and trypsin. Structures that can inhibit the mentioned enzymes and processes can be employed as a treatment choice. Protease inhibitors, including camostat mesylate, a TMPRSS2 inhibitor, and E-64d as a cat B/L inhibitor, can be evaluated as SARS-CoV-2 treatments. Further research on mechanisms and blocking the function of E and M proteins may result in SARS-CoV-2 prevention and treatment.

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# Iranian Medicinal Plants Role in COVID-19 prevention

*Dorsa Alizadegan[1], Ehsan Amiri Ardakani[2], Fatemeh Tavakolifar[1]*

[1]Faculty of Pharmacy, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran.

[2]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran.

Corresponding author: Fateme Tavakoli-Far

Corresponding author Email: Fatemetavakolifar@gmail.com

Introduction :The SARS-CoV-2 is the third pandemic of the 21st century. Effective prevention is necessary to curb the spread of COVID-19 and prevent similar pandemics in the future. Vaccines, serums, monoclonal antibodies, immunomodulators, and antiviral drugs on the pharmaceutical market are the most promising options to prevent the disease. Recently, there have been significant advances in antiviral herbal remedies due to growing concerns about drug resistance and limited progress in antiviral drug discovery. In almost every country, different herbal medicines with promising results have been used alone or combined with conventional drugs to treat infected patients. So, this study aims to review and discuss Iranian medicinal plants that are mechanistically useful for COVID-19 prevention.Material and Methods :Scopus, Science Direct, Google Scholar and, PubMed were searched up to March 2021. Searches were made using Herbal Medicine, Phytotherapy, Traditional Medicine, Complementary Medicine, Alternative Medicine, Integrative Medicine, COVID-19 Prevention, Prevention, SARS-CoV-2, and COVID-19 as keywords in combination. After extracting articles related to medicinal plants use in COVID-19 management, articles involving plants available in Iran were included in the study, and Their mechanism for COVID-19 prevention were investigated. Also Editorial Articles, Case Reports and Case Series were excluded in the studyResults :Our proposed mechanisms to prevent COVID-19 infection by medicinal plants are divided into three categories; Immune boosters and modulators, inhibitors of virus attachment to the host cell, and antioxidants. Of course, medicinal plants may work through a variety of mechanisms, knowing that they contain different active ingredients. Hence, it is evident that a plant can fall into all three of these categories. These plants seem to effectively prevent COVID-19 by having anti-inflammatory effects, strengthening the immune system, and inhibiting virus attachment to the host cell: Thyme, Rhubarb, marshmallow, Green tea, Echinacea, Aloe vera, Black seed, Eucalyptus, Chicory, Cloves, Licorice, Garlic, and Saffron.Discussion:SARS-CoV-2 targets cells by binding a viral structural protein (spike protein S) to Angiotensin-converting enzyme 2(ACE2), injecting endosomes into the cell. Transmembrane protease serine 2 (TMPRSS2) is a type 2 host protease enzyme that helps the virus enter the cell through the spike protein. Once the virus penetrates the cell, viral peptides and RNA are synthesized, and new virus particles are assembled and released. Plants categorized as Host cell receptor-attaching Inhibitors, inhibit viral attaching to ACE by 70-100%. Immune system boosters and modifiers are able to strengthen the immune system by increasing the proliferation of lymphocytes and white blood cells, enhancing phagocytosis, modulating the expression of cytokines, enhancing humoral and cellular immunity. Antioxidants are also involved in destroying CD4 T cells by apoptosis. Antioxidants along with factors interfering with the harmful effects of cytokines and lipid mediators, may play a role in treating viral diseases. :Conclusions : As mentioned, many medicinal plants available in the Iranian medicinal plants market have laboratory, animal, and clinical evidence for potential using in COVID-19 prevention. Since these plants are available and well appreciated, additional clinical studies under physicians and Pharmacists' supervision could improve public health.

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## Allium sativum L. (Garlic) role in osteoarthritis: A systematic review of clinical trials

*Fateme Tavakoli-Far[1], Ehsan Amiri-Ardekani[2]*

[1]Faculty of Pharmacy, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran.
[2]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran.
Corresponding author: Fateme Tavakoli-Far
Corresponding author Email: Fatemetavakolifar@gmail.com

Introduction: Osteoarthritis (OA) is a chronic degenerative disease involving the joints and bones, causing their degradation over time. Inflammation, pain, and stiffness in joints are indicators of the disease. Pharmacotherapy cannot always be efficient and may cause side effects. So, adjuncts such as complementary therapies became notable. Garlic is an herb well-known for its various therapeutic effects, such as anti-bacterial, anti-hypertension, antioxidant and anti-inflammatory. Since garlic is one of the most widely used medicinal plants, studying its effects and mechanisms in inflammatory diseases, such as OA, has been noteworthy.Material and methods: We searched Science Direct, PubMed, Cochrane, and Google Scholar databases for all original English randomized clinical trials studying effect of garlic or its constituents on OA published until October 2020, based on PRISMA. Searched keywords were the following: [(Garlic AND Arthritis), (Garlic AND Osteoarthritis), (Garlic AND OA), (Allium Sativum AND Arthritis), (Allium Sativum AND Osteoarthritis), (Allium Sativum AND OA)]. Cited articles and references were checked. Animal studies, cross-sectional, and reviews were excluded. Five articles were reviewed.Results and discussion: The results showed Garlic and its constituents have remarkable effects on improving OA symptoms through antioxidant and anti-inflammatory pathways.Obesity, a risk factor involved in OA, is directly related to increased concentrations of adipocytokines, such as resistin. Garlic may decrease BMI, perhaps dose-dependently. Both innate and adaptive immunity perform OA progression. Pro-inflammatory factors induce OA pathogenesis, causing pain or cartilage destruction. Imbalance in the production of reactive oxygen species leads to the destruction of normal cells, ultimately cell dysfunction, which garlic extracts may alter with antioxidant effects; allicin, thiosulfinates, S-allyl cysteine (SAC), phenolic compounds, ajoenes, S-allyl-mercapto cysteine (SAMC).TNF-α, a critical inflammatory factor, causes pain, stimulating the other pro-inflammatory factors production. SAMC could down-regulate the IL-1β, IL-6, and TNF-α in OA remarkably.Resistin, an adipokine hormone, upregulates IL-6, IL-1β, and TNF-α production in cartilage correlates with local pro-inflammatory factors and cartilage degradation, reduced by garlic component 1,2-vinyldithiin. So, garlic topical formulation may be more efficient in diminishing resistin concentration.IL-6, another pro-inflammatory cytokine that is upregulated commonly in OA, is down-regulated by garlic extracts, especially allicin and SAMC. IL-1β, another pro-inflammatory cytokine, the most critical cytokine in OA progression, expedites cartilage degeneration, decreased by garlic composites.Matrix metalloproteinases (MMPs) as a critical factor in joint destruction is significantly decreased by SAMC, besides other garlic components extract.Pain, the most apparent OA symptom, may originate from inflammatory factors. We suggest reducing pain severity is due to reducing inflammatory factors rather than the efficacy of garlic in mechanical mechanisms. The garlic topical formulation may be more potent in local pain because of the local secretion of pro-inflammatory factors. Also, improvement in physical function follows the progression in pain severity, which promised that TNF-α concentration reduction is the mechanism involved in pain improvement by garlic. Also, stiffness, restricted range of motion significantly got improved after consumption of garlic.Conclusions: Our review shows that groups receiving garlic as a treatment showed a significant reduction in pain and inflammatory factor levels and an improved physical function, as opposed to the control group.

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## Sensitive determination of cysteamine in human plasma based on $MoS_2$/reduced graphene oxide nanocomposite

*Shiva Fallahian[a], Fereshteh Chekin[b,*]*

[a] Department of Pharmacy, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran
b Department of Chemistry, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran
Corresponding author: Fereshteh Chekin
Corresponding author Email: fchekin@yahoo.com

Cysteamine (β-mercaptoethylamine; CA) bitartrate is a drug approved for the treatment of cystinosis, a rare autosomal recessive disease caused by the abnormal intralysosomal accumulation of the amino acid cysteine with in various tissues [1]. The specific and sufficiently sensitive analytical method was required for total cysteamine determination in biological and pharmaceutical samples [2]. The electrochemical methods have the advantages of simplicity, low expense, and high sensitivity. So, electrochemical methods for the determination of CA have received more attention in recent years [3-5].The hybrid nanocomposite composed of $MoS_2$ nanosheets and reduced graphene oxide was fabricated by a facile and effective method. The morphology and structure of the nanocomposite ($MoS_2$-rGO) were characterized by scanning electron microscopy, X-ray photoelectron spectroscopy, Raman spectroscopy, electrochemical impedance spectra and voltammetry. The $MoS_2$ nanosheets were uniformly anchored on the 3D rGO framework with strong adhesion. The deposited $MoS_2$-rGO on GC substrate was used for electro-oxidation of cysteamine (CA). Under optimum conditions, the anodic peak current of CA at the surface of modified electrode is lineared to its concentration ranges at 0.01 to 20 µM with a detection limit of 7 nM by amperometry. The proposed electrochemical sensor was used for determination of CA in human plasma. The accuracy of the method was as excellent comparing with the obtained results using reference method. The proposed method showed a good result, indicating that the present modified electrode can be used for determination of CA in real samples.

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## Evaluation of dynamic changes in antibody titer (IgM and IgG) in recovered patients with Covid-19 at 3 and 6 month intervals

*Hamidreza Ebrahimi Nejad Kohani[1]*

[1] Baqiyatallah University of Medical Sciences
Corresponding author: Hamidreza Ebrahimi Nejad Kohani1
Corresponding author Email: hamidrezaebi@yahoo.com

Introduction: Covid-19 or SARS-CoV-2, is a beta-coronavirus of the coronaviridae family that can cause acute respiratory distress and systemic involvement of other organs. IgM and IgG-specific titers of the virus not only play an important role in diagnosis , clearing the virus and treating patients, but also actively prevent the recurrence of infection. In patients, the IgM titer increases in the first few days and the IgG titer begins to increase with a delay. The titer of antibody starts to peak and

then decreases after a while. This decrease is a sign of a lack of persistence in natural immunogenicity. Thus, monitoring the titer of covid 19 antibodies over time can show how long the immune system can protect the body against re-infection.Material and methods: A total of 60 recovered patients of Covid 19 who were admitted to Baqiyatallah Al-Azam Hospital in Tehran and then discharged were included in this study. In the selection of these 60 patients, 30 patients were hospitalized in different wards of Baqiyatallah Al-Azam Hospital and 30 patients have also been hospitalized in the intensive care unit. Serum IgG and IgM antibodies were measured at the time of admission and at intervals of 3 and 6 months (as second and third monitoring points), patients were called for retesting. Results: The results were completely dependent on the severity of the disease and the quality of hospitalization. Demographic variables, clinical characteristics, duration of hospitalization and even drugs used during hospitalization showed a clear effect on patients' results. IgG levels showed significant decrease , and about 55.6% of patients had below the kit detection limit after 6 months. There was a significant relationship between the initial titer and the degree of stability of natural immunity with demographic factors, disease severity and age of patients, which showed that with increasing disease severity and age, the rate of immune system response also increases.Discussion: Monitoring the titer of covid19 antibodies over time can show how long the immune system can protect the body against re-infection and expand the role of antibodies in addition to the diagnostic dimension to newer dimensions such as treatment, prevention and vaccination. Also, these results can act in determining epidemiological models and health management at the community level, as effective factors in macro decision making.Conclusions: The level of antibodies against covid 19 initially starts to increase rapidly and peaks 2 to 3 weeks after the onset of the disease, but a decrease in the level of serum antibodies appears at 5 to 8 weeks, which is a sign of Immune instability against Covid 19 virus. IgG levels showed significant decrease , and more half of patients had below the kit detection limit after 6 months.

## P52

# Evaluation of pharmacotherapy protocols for COVID 19 patients in Baqiyatallah Hospital and their outcomes

*Hamidreza Ebrahimi Nejad Kohani*[1]

[1] Baqiyatallah University of Medical Sciences

Corresponding author: Hamidreza Ebrahimi Nejad Kohani1

Corresponding author Email: hamidrezaebi@yahoo.com

Introduction: The propagation of new coronavirus, COVID 19, is still a major priority for the many countries around the word. Because of lack of effective certain antiviral therapy for COVID 19. The special medicinal protocols are needed in medical centers to reduce mortality rate.Material and methods: A total of 614 COVID-19 patients , hospitalized from February 19, 2020 to April 15, 2020 in Baqiyatallah hospital were enrolled for this retrospective analytical study. Due to constant change of national pharmacotherapy protocols for COVID-19 patients, this study compares the outcomes of three specific pharmacotherapy regimens (regimen 1 (twice daily for 5 days) : Oseltamivir Cap. 75 mg + Lopinavir/Ritonavir 400/100 mg Cap. + Hydroxychloroquine 200 mg Tab , regimen 2 (for 5 days) : Prednisolone 5 mg Tab. daily + Naproxen 500 mg Tab. every 12 h + Azithromycin 500 mg Tab. 1000 mg 1st day, 500 mg/day for 4 days, regimen 3 (for 5 days): Hydroxychloroquine 200 mg Tab. every 12 h + Azithromycin 500 mg Tab. 1000 mg 1st day, 500 mg/day for 4 days + A nonsteroidal anti-inflammatory drug (NSAID; mainly Naproxen or Diclofenac) or steroidal anti-inflammatory drug (glucocorticoids; mainly Prednisolone)) and the combination of all 3 regimens for management of COVID-19 patients which hospitalized in Baqiyatallah hospital in Tehran, this hospital became a referral centers for receiving COVID 19 patients in Iran.

Results: The more reliable result of treatments belongs to regimen 3 which indicated to 98.26% recovered patients and 1.15% mortality rate and the lowest period of hospitalization with 4.4±0.21 days duration. Discussion: This retrospective analytical study has evaluated several common regimens based on two indexes including the length of hospital stay and mortality rate for COVID19 patients. This study also compared clinical outcomes of drug regimens, focusing on 3 typical regimens that were applied in treating COVID 19 patients.Patients receiving hydroxychloroquine, azithromycin, and an anti-inflammatory drug received better responses both in terms of reduced length of hospital stay and mortality than patients receiving hydroxychloroquine/prednisolone or patients receiving oseltamivir, lopinavir, ritonavir, and hydroxychloroquine.Conclusions: It seems that regimen 3 (with special combination of antiviral and Azithromycin ant anti-inflammatory drugs) had the best result in improving patients with COVID 19 and furthermore this result has not conflict with comorbidity status of patients.

## P53

# The effect of bilateral injection of naloxone in amygdala basolateral on sleep and wakefulness under stress

*Amir Mohammad Dehghan*[1,3], *Mehdi Graily-Afra*[1,2], *Farideh Bahrami*[2] , *Zahra Bahar*[2]

[1]Students' research committee, Baqiyatallah University of Medical Sciences, Tehran, Iran.Applied

[2]Department of Physiology and medical Physics, Faculty of Medical Science, Baqiyatallah University of Medical Sciences, Tehran, Iran

[3]Department of Pharmacy, Faculty of Pharmacy, Baqiyatallah University of Medical Sciences, Tehran, Iran

Corresponding author: Amir Mohammad Dehghan

Corresponding author Email: amdehghanedu@gmail.com

Introduction: Acute and chronic stress can also have important effects on sleep structure and circadian rhythm. Studies have shown that stress reduces SWS sleep and inhibits REM sleep if the animal is exposed to stress. One of the most important nuclei in the amygdala, which plays an essential role in stress condition. In this study the role of Amygdaloid opioid system on the relation between sleep and stress has been investigated through Naloxan injection in to this neucleus.Method: Electrodes placement for EEG and EMG recording was done in Wistar rats and bilateral cannulation was performed in BLA area and recording of REM and NREM sleep. In order to evaluate sleep, first, the EEG and EMG waves obtained are visually examined and the percentage of REM sleep, NREM sleep, and wakefulness were considered as baseline sleep for three consecutive days prior to any protocol or injection. The data were then compared with the mean percentage of REM, NREM, and wakefulness after protocol or drug injection.Naloxone was injected into each BLA at a dose of 0.05 µg or 0.1 µg in a volume of 0.5 µl on 3 consecutive days before the stress protocol. Result: The results obtained from sleep waves related to rats after 3 hours of stress showed a significant decrease in REM sleep when compared to the control group ($P < 0.01$) as well as decreased NREM sleep ($P < 0.05$) in stressed rats, while wakefulness was increased ($P < 0.05$).The results showed that bilateral injection of naloxone 0.05 and 0.1 µg in basolateral amygdala significantly increased REM ($P < 0.001$) and NREM ($P < 0.01$) sleep values despite the presence of stress. It also significantly decreased wakefulness ($P < 0.01$).Conclusion: In general, stress reduces the REM, NREM and Naloxone injection in BLA improves the sleep and reduce

the adverse effect of stress on sleep.

P54

## Economic Effects of Domestic Production of Biosimilar Medicines in Iran

*Seyyed Ali Hashemi*[1], *Behniya Azadmehr*[1], *Farzad Peiravian*[2] and *Nazila Yousefi*[2*]

[1]Student Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2]Department of Pharmacoeconomics and Pharma Management, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran , Iran

Corresponding author: Nazila Yousefi

Corresponding author Email: nazilaa.yousefi@gmail.com

Introduction: The high costs of biological medicines can prevent the access of patients to appropriate treatment and cause poverty and Life expectancy reduction(1). One of the ways to reduce the costs is the production of biosimilars. Material and methods: After designing questionnaires and a semi-structured interview with biologists, the data were qualitatively Analyzed, using MAXQDA software in the way of content analysis and economic indicators affected by domestic production of biosimilars in Iran were determined. In the second step, as an economic indicator, a list of domestic biosimilar prices was prepared by examination. The prices were compared with similar samples in selected reference countries. In addition, prices of domestically produced biosimilars in selected reference countries were compared with equivalent imported biological medicines.Results: The most economic effect of domestic production of biosimilars, is price reduction that leads to enhanced affordability. In this study, enhanced affordability is considered as an access index. Expansion of pharmaceutical markets and the reduction of health system costs were the other results of domestic production of biosimilars. the price of 23 domestically produced biosimilars with similar biological medicines in reference countries were compared. The price of 18 biosimilar medicines were lower than the minimum of the reference countries, and 21 medicines were lower than the average. Among the imported medicines, 28 biological medicines were studied. 23 items were less expensive than the minimum cost of the reference countries, and 26 medicines were less expensive than the average cost of the reference countries. Discussion: As all over the world, Biosimilar medicines have increased patient's access to biological medicines at more reasonable prices. in addition to reducing the costs of the health system, it can lead to an increase in the societal level of health. As seen in the quality section of the study, domestic production of these products can have other effects beyond the health system and increase entrepreneurship, especially among specialized workforces and leading to the increased total welfare of society(2).Conclusions: The domestic production of biosimilars, in addition to enhancing access to biological medicines with reasonable prices, will adjust prices of other imported biological medicine brands as a following result. The growth of ancillary industries and job creation for well-educated and specialized workforces are the other consequences of domestic production. By the comparison of prices, it is also found that domestic production of biosimilars will significantly reduce health costs.

P55

## Influencing Factors in Physician's Loyalty to a Particular Brand

*Behniya Azadmehr*[1], *Milad Mehregan Ara*[1], *and Gholamhossein Mehralian*[2*]

[1]Student Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2]Department of Pharmacoeconomics and Pharma Management, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran , Iran

Corresponding author: Gholamhossein Mehralian

Corresponding author Email: gmehralian@gmail.com

Introduction: Increasing the cost of medicines in developing countries has been prompted researchers to research in the field of factors that influences physician prescription behavior. In the present study, we aimed to assess the attitudes of specialists about the factors that influence physician prescription loyalty behavior in Tehran. Due to the large number and variety of Brands, it is not easy for physicians to identify and compare brands and might not lead to the right decision in writing a prescription, eventually. Brand Loyalty is a key issue for many commercial and marketing managers and it's a strategic fundamental concept. In this research, we will find and classify the reasons for brand loyalty by doctors and also examine dimensions and their implications. Material and methods: By extracting the possible factors associated with physician loyalty to a brand, a standard questionnaire with 37 questions were designed and given to 437 specialists. The collected data from the questionnaire were analyzed by using SPSS software and the results were prepared in the form of relevant diagrams and tables.Results: Doctors will not prescribe a medicine until they make sure about the side effects, quality and efficacy of them. Therefore, further studies should be done in this field. policymakers, government and official health associations play an important role in making the best choice and guarantee or insure patients about what has been prescribed for them. Friedman's test showed advertising and marketing have the last priority on loyalty to a brand's name which choosing by specialists. It means that doctors will not prescribe a medicine until they make sure about its side effects, quality and efficacy.Discussion: If physicians recognize the quality of a medicine, they will be loyal to that particular brand. profile of side effects of a brand medicine and the patient's comfort are important factors of physician's tendency to prescribe a brand. In the present study, it was found that if the effectiveness of the medicine is higher than similar drugs, surely it will be an important factor impacting the selection of the physician. As a result, companies can encourage physicians to become loyal to a brand by holding seminars and specialized training courses for physicians and increasing physician's knowledge of the quality of medicines. According to other prescription behavior examination studies, such as our study, the quality of the drug is an important selection factor considered by the physician(1).Conclusions: As a consequence, according to Friedman's test, affording and Patient access to medicines is the most important factors which chose by doctors. Advertising and marketing are the last priority in physician's loyalty to a particular brand.

P56

## Cost-effectiveness of Calfactant vs Poractant alfa in neonates respiratory distress syndrome: A review

*Hamidreza Rasekh*[1], *Nazila Yousefi*[2], *Zahra Karimi Majd*[3], *Golara Nik Akhtar*[4]

Corresponding author: *Hamidreza Rasekh*
Corresponding author Email: hrasekh@gmail.com

Background: respiratory distress syndrome (RDS) is the second cause of death among infants in the world. Currently, the mainstay of treatment is exogenous surfactant therapy. Objective: To compare the cost-effectiveness of Calfactant and Poractant alfa in neonates with RDS Data source: PubMed and google scholar were searched for relative articles published until May 2021.Study selection: Studies that evaluated the cost-effectiveness of Calfactant vs Poractant alfa in neonates with RDS.Method: study characteristics and outcomes from full-text articles from a systematic search for studies that compared Calfactant with Poractant alfa for RDS in preterm infants were extracted.Conclusions: the efficacy of both surfactants were similar. studies showed pharmacoeconomic advantage for the use of Calfactant compared to Poractant alfa because of similar average dosing and lower per patient drug costs.

P57

## Evaluation of the Prophylactic Effect of Hydroxychloroquine on People in Close-Contact with Patients with Covid-19

*Minoosh Shabani [a,b,§], Mehdi Totonchi[c,d,§], Omidvar Rezaeimirghaed [e], Latif Gachkar [a,b], Mohammadreza Hajiesmaeili [f], Ali Khoshkar [g], Mahdi Amirdosara [f], Ali Saffaei [h], Shervin Shokouhi [a,b], Masoud Mardani [a,b], Ilad Alavi Darazam [a,b], Alireza Karami [i], Milad Sharifi [i], Mana Zaman [j], Elham Abedheydari[k], Zahra Sahraei [l,m*]*

a Department of Infectious Diseases and Tropical Medicine, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

b Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran .

c Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran.

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

e Skull Base Research Center, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

f Anesthesiology Research Center, Loghman Hakim Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

g General Surgery Department, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

h Student Research Committee, Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

i Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

j Student Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

k Department of Embryology, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran.

l Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

m Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

§ Co-first Authors: Minoosh Shabani and Mehdi Totonchi

Corresponding Author: Dr. Zahra Sahraei

Corresponding author Email: zahra.sahraei@yahoo.com

Introduction: The coronavirus disease 2019 (COVID-19) pandemic has caused significant mortality worldwide. The disease attacks the lung tissue and may lead to acute respiratory distress syndrome. An in vitro study showed that hydroxychloroquine (HCQ) has a prophylactic effect against COVID-19 due to its anti-inflammatory effects. The present study aimed to evaluate the prophylactic effect of HCQ on individuals in close contact with patients with COVID-19. Method: In this quasi-trial study, we prescribed HCQ for 7 days to all people who had close contact with a patient with COVID-19. All contacts underwent a nasal swab in two steps, and those positive for COVID-19 were excluded from the study. After 14 days of follow-up, the clinical and laboratory manifestations of COVID-19 were evaluated. Results: A total of 113 participants completed the study. The HCQ group comprised 51 (45.13 %) contacts, and 62 (54.86 %) contacts were allocated to the control group. According to the results of clinical examination and real-time polymerase chain reaction test, 8 (12.90%) contacts in the control group were reported to have contracted COVID-19. In the HCQ group, 7 (13.72%) contacts were confirmed to have contracted COVID-19. There was no relationship between HCQ use and age, sex, underlying disorders, and laboratory data (all $p > 0.05$). In terms of HCQ side effects, five participants experienced gastrointestinal and cutaneous side effects that subsided on discontinuation of HCQ.

Conclusion: The current study showed that HCQ had no prophylactic effect with regard to COVID-19 prevention.

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## Selective toxicity of Cistanche tubulosa root methanolic extract on cancerous skin mitochondria isolated from melanoma induced rat

*Mobina Heidary[1], Jalal Pourahmad [2], Aida Jabbarzadeh [1], Yalda Arast[3], Amir Vazirizadeh[4]*

[1]Student Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran

[2]Department of Toxicology and Pharmacology, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran

[3]Department of Occupational Health, Qom University of Medical Sciences, Qom, Iran

[4]Persian Gulf Research Institute, Marine Biology and Fishery Sciences Department, Persian Gulf University, Iran.

Corresponding author: *Mobina Heidary*

Corresponding author Email: mobina.heidary@yahoo.com

Introduction:Melanoma, a life threatening skin cancer, is among the most common cancers all over the world. It initiates in melanocytes and can metastasize rapidly, so the treatment will be complicated. This made researchers getting attracted in finding novel compounds and investigating them for treatment of this cancer.Antioxidant and antitumoral effects of *Cistanche tubulosa* root methanolic extract, a Persian gulf coastal medicinal plant has been evaluated in this research. Material and methods:We have studied the mitochondrial toxicity parameters specially the upstream apoptosis inducing effects of three concentrations of *C.tubulosa* root extract (1250 µg/ml, 2500 µg/ml, 5000

µg/ml) on cancerous skin mitochondria isolated from melanoma induced rats as main inducers of apoptosis.Upstream apoptosis inducing effects include the decreased succinate dehydrogenase activity determined by (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide assay (MTT), and Mitochondrial Membrane Potential (MMP) collapse, in addition to increased reactive Oxygen Species (ROS) production and mitochondrial swelling.Results:Our results showed that aforementioned extract can significantly and selectively induce toxic alterations only in cancerous but not normal healthy skin mitochondria including increased mitochondrial swelling and ROS formation and declined mitochondrial MMP and SDH activity and release of cytochrome c And finally, all the applied concentrations of the *Cistanche tubulosa* root methanolic extract increased apoptosis phenotype percentage (measured by Flow-cytometry analysis) only in cancerous melanocytes but not healthy control skin cells.Discussion:Our results showed that cytotoxic action of this extract is mediated by mitochondrial upstream apoptosis inducing effects such as MMP collapse and mitochondrial swelling. MMP which can be estimated by mitochondrial uptake of the cationic fluorescent dye rhodamine 123. As we know, mitochondria MMP is one of the gold standards for indicating cell health and any alterations in its content can indicate cellular damages such as cancer, cardiovascular disease, diabetes, neurodegenerative problems and so on. Furthermore, our data revealed that this extract can cause a selective increase in ROS formation only in cancerous skin mitochondria which will selectively initiate ROS mediated apoptosis in melanoma cells. This mechanism is known as one of the most effective treatments for cancer. Conclusions:Our results suggested that bioactive compounds of *Cistanche tubulosa* root could be a hopeful candidate for further studies and clinical trials designed for new treatments for melanoma.

## P59

## Mitochondrial Transplantation: an Innovative Therapeutic Strategy for Mitochondrial Diseases

*Melika Mashhadi*[1], *Jalal Pourahmad*[1*]

[1]Department of Toxicology and Pharmacology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding author: Jalal Pourahmad

Corresponding author Email: pourahmad.j@sbmu.ac.ir

Introduction: Mitochondria are intracellular organelles that assume a pivotal role in regulating cellular activity, including energy production, growth, life, and apoptosis due to their key role in cellular function, Mitochondrial dysfunction is associated with many diseases and clinical disorders. Although advances in cellular and molecular sciences have led to the discovery of many mechanisms associated with mitochondrial disorders, To this date, there is no effective treatment that can target high-grade mitochondrial defects. Mito therapy or Mitochondrial Transplantation is an innovative strategy that has recently been proposed in the treatment of various disorders. In this method, which has been experimented with in a considerable number of animal studies and also patients; viable and intact mitochondria replace the damaged ones. In this review, we attempt to provide an overview of the number of diseases associated with mitochondrial dysfunction and explain the application, therapeutic effectiveness of mitochondrial transplantation, and mechanisms of mitochondria intake.(1, 2)Material and methods: To conduct this research, google scholar, PubMed, and the Scopus databases were searched using keywords such as "mitochondrial transplantation, mitochondrial replacement, and mitotherapy". In the following, we reviewed the found documents.Results: The results of animal and clinical studies have demonstrated that exogenous and endogenous mitochondrial transplantation can promote cell survival. Various parameters associated with mitochondrial dysfunction, including ATP production, ROS generation, oxygen consumption, and enzymatic activity, have been measured and confirmed improvement in cell function.in addition to disease control were reported. Although clinical data are indeed limited, there are numerous reports which claim that autologous or homologous mitochondrial transmission does not elicit significant immune response which is very good news. (3) Discussion: To date, there are many mitochondrial diseases such as neurodegenerative diseases, ischemia-reperfusion injury, fatty liver disease, diabetes, and malignancies for which there is no definitive cure. Mitotherapy is a promising and potentially effective approach that can be used; Nevertheless, interfering factors such as the method of transfer, degree of mitochondrial defects, type of host cell and source of isolated mitochondria will influence the success of the treatment.(4)Conclusions: Based on the current evidence it can be concluded that mitochondrial transplantation is a valued and novel therapeutic strategy which still needs of more investigations.

## P60

## Selective toxicity of methanolic extract of Persian Gulf Snail (*Peronia peronii*) on cancerous skin mitochondria isolated from melanoma induced rat

*Aida Jabbarzadeh*[1], *Jalal Pourahmad*[2] , *Mobina Heidary*[1], *Yalda Arast*[3], *Amir Vazirizadeh*[4]

[1]Student Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran

[2]Department of Toxicology and Pharmacology, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran

[3]Department of Occupational Health, Qom University of Medical Sciences, Qom, Iran

[4]Persian Gulf Research Institute, Marine Biology and Fishery Sciences Department, Persian Gulf University, Iran.

Corresponding author: Aida Jabbarzadeh

Corresponding author Email: Aida_jabbarzadeh@hotmail.com

Introduction: Melanoma is one of the most prevalent and a highly aggressive cancers and one of the major causes of mortality worldwide. Marin animals have attracted much attention as useful substances having application in medicine. One of the important examples of marine animals with medical use is Persian Gulf snail, *Peronia peronii (P. peronii)* which could play an important role in cancer therapy based on traditional and regional medicine. Compounds obtained from *P. peronii* (Peroniatriols I,II )have shown to have anticancer activity through induction of apoptosis signaling .Material and methods: In the present study, selective apoptotic effects of a metanolic extract of P. peronii were assessed on cancerous skin mitochondria isolated from the melanoma induced rats. The mitochondria was isolated from melanoma cells via differential centrifuges and treated with various concentrations (650, 1300, 2600 µg/ml) of methanolic extract of P. peroniiResults: our results showed that all the applied concentrations (650 , 1300 , 2600 µg/ml) of the metanolc extract of *P. peronii* increased the reactive oxygen species (ROS) generation only in the skin mitochondria isolated from melanoma rats in comparison to the normal rat skin mitochondria. *P. peronii* extract also selectively induced collapse of the mitochondrial membrane potential (MMP), swelling within the mitochondria and release of cytochrome c only in the cancerous skin mitochondria isolated from melanoma rats. And finally, all the applied concentrations of the

metanolc extract of *P. peronii* increased apoptosis phenotype percentage (measured by Flow-cytometry analysis) only in cancerous melanocytes but not healthy control skin cells.Discussion: Our results demonstrated that *P. peronii* methanolic extract can selectively induce a notable toxic effect only on cancerous but not normal healthy skin cells and mitochondria such as increasing mitochondrial ROS formation and inducing subsequent ROS mediated apoptosis events such as mitochondrial membrane potential collapse and mitochondrial swelling, cytochrome c release and finally induction of apoptosis phenotype.Conclusions: our results suggest that the bioactive molecules found in *P. Peronii* may be a promising potential candidate for further research designed for discovering new drug treatment for melanoma including precise molecular identification, confirmatory in vivo studies and clinical trials.

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## Design and synthesis of new imidazole derivatives as selective COX-2 inhibitors

*Pardis Kondori[1,2], Mahsa Azami Movahed [1], and Afshin Zarghi [1]*

[1]Department of Medicinal Chemistry and Radiopharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2]Student Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding author: Afshin Zarghi

Corresponding author Email: zarghi@sbmu.ac.ir

Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs) has been developed over a century to reduce inflammation and fever. Unfortunately, they have unpleasant effects on the gastrointestinal system, and it restricts the use of NSAIDs. They show their effects by inhibition of cyclooxygenase enzyme (COX). Hence, inhibition of COX enzymes reduces the production of prostaglandins which cause inflammation, fever and pain. Cyclooxygenase has two isoforms. COX-1 produces prostaglandins involved in a normal cellular activity such as maintaining kidney functions and gastric mucosa protection; COX-2 is responsible for inflammation and is released by the rise of endotoxins, mitogens, and cytokines. Also, COX-2 participates in the pathophysiology of many diseases such as cancer, Alzheimer and Parkinson's disease . Therefore, selective inhibition of COX-2 provides anti-inflammatory effects with lower gastrointestinal adverse effects.Nowadays, we are looking for new compounds with selective inhibition of COX-2 enzyme, higher safety and lower adverse effects; therefore, in this study, we focused on a new series of imidazole derivatives as potential COX-2 inhibitors.Materials and methods: The molecular modeling studies of designed compounds were performed using AutoDock software to search for favorable interactions between the ligands and the enzyme. Different aniline derivatives, bromoacetophenon in the presence of sodium bicarbonate, were reacted in ethanol to produce 1-phenyl-2-(phenyl amino)ethan-1-one, as an intermediate. The final 1,2,4-triphenyl imidazoles were obtained from the reaction of intermediates with para-(methylsulfonyl)benzaldehyde in ethanol.Results: The docking studies demonstrated that para-SO2Me pharmacophore inserted into the secondary pocket present in COX-2 isozyme and formed the proper interactions with Arg513 and His90. The structures of these compounds were characterized by Mass, IR and 1H NMR spectrums. Also, biological evaluation of these compounds is in progress.Discussion: The docking studies indicated the acceptable interaction of designed compounds with crucial amino acids of the active site. The final products were afforded by a two-step reaction. Different types of spectroscopy were used to confirm the structure of these compounds.Conclusions: The new imidazole derivatives were designed according to COX-2 inhibitor SAR. Based on molecular modeling and docking studies, it is expected that these molecules have high potency and fewer adverse effects, which is due to selective inhibition of the COX-2 isoenzyme.

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## Design and synthesis of new pyrrole derivatives as selective COX-2 inhibitors

*Mohammadsaeed Kordi [1,2], Mahsa Azami Movahed [1], and Afshin Zarghi [1]*

[1]Department of Medicinal Chemistry and Radiopharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2]Student Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Corresponding author: Afshin Zarghi

Corresponding author Email: zarghi@sbmu.ac.ir

Introduction: Non-steroidal anti-inflammatory drugs (NSAIDs) have been around for nearly a century. They are highly valued for their widespread use to relieve fever and pain. The therapeutic effects of these drugs are mediated by inhibiting the enzyme "cyclooxygenase" responsible for the conversion of arachidonic acid to PG and thromboxane. Cyclooxygenase (COX) has at least two important isozymes: COX-1 and COX-2. COX-1 is a constitutive form found mostly in gastric mucosa, kidneys and is involved in renal and hemostatic activities. On the other hand, COX-2 is primarily an inducible enzyme and is in charge of inflammatory responses in pathophysiological conditions. The main clinical benefit of selective COX-2 inhibitors is the reduced incidence of gastrointestinal bleeding, with conventional NSAIDs treatments, particularly in the elderly. The widespread and common use of selective COX-2 inhibitors in the treatment of pain and inflammation, as well as the demonstration of the enzyme's pathological role in a variety of diseases such as cancer and neurodegenerative diseases like dementia and Parkinson's, has led to a greater acceptance and discovery of these drugs. Subsequently, in this study, a series of novel pyrrole derivatives with the potential of selective inhibition of COX-2 and a more acceptable safety profile were designed and synthesized using the structure-activity relationship of these inhibitors.Material and methods: A new series of pyrrole derivatives have been designed using molecular modeling and docking software. Different derivatives of aniline and para-(methylsulfonyl)phenacyl bromide react in methanol with sodium carbonate to yield 1-phenyl-2-(phenylamino)-ethanone derivatives. The final derivatives of 1,3,4-triarylpyrrole are formed by reacting these intermediates with phenylacetaldehyde in the presence of iodine and zinc chloride.Results: Docking studies of designed compounds into the COX-2 active site indicated that para-SO2Me substituent inserts into the secondary pocket of COX-2 active site and oxygen atoms formed hydrogen bonding with Arg513 and His90 of secondary pocket. IR, Mass and 1H NMR were used to characterize the structure of the final compounds. The enzyme inhibition assay is under evaluation.Discussion: The molecular modeling and docking studies indicated that 1,3,4-triarylpyrrole derivatives possessing SO2Me at the para position of 3-phenyl occupied the COX-2 active site and SO2Me oxygen atoms form hydrogen bonding with essential amino acids.Conclusions: IR, MS and 1H NMR spectrums were used to validate structures of synthesized compounds. The biological assay will be evaluated. Considering rational design based on structure-activity relationship (SAR) of selective COX-2 inhibitors and molecular modeling studies of designed molecules, high selective inhibition of COX-2 is expected.

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## Design and synthesis of new diaryl-3,4-dihydropyrimidine derivatives as selective COX-2 inhibitors

*Mahshad Mohammadizade[1], Mahsa Azami Movahedi[2], Afshin Zarghi[3]*

[1]Student of Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences
[2]Faculty member of Department of Pharmaceutical Chemistry and Nuclear Pharmacy, Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences
Corresponding author: Afshin Zarghi
Corresponding author Email: zarghi@sbmu.ac.ir

Introduction: Cyclooxygenase- 2 is an isoform of cyclooxygenase (COX) enzyme that is not expressed in most non-pathological tissues and is induced in situations such as inflammation by catalyzing the formation of prostaglandins. COX-2 also has been known to play roles in cancers. It is confirmed that COX-2 is overexpressed in many types of cancers. It has several roles in angiogenesis, apoptosis resistance, metastasis, tumor growth and cancer cell invasion. Therefore, selective inhibition of COX-2 has been considered to be a rational strategy for cancer treatment. In this study, new diaryl-3,4-dihydropyrimidine derivatives were designed and synthesized as selective COX-2 inhibitors, to evaluate their COX-2 inhibitory potency and selectivity as new anticancer agents.Material and methods: To study on possible binding interactions between designed ligands and COX-2 enzyme, docking studies were performed using Autodock software. Diaryl-3,4-dihydropyrimidine derivatives were synthesized via a multiple-component reaction named Biginelli reaction. In the first step, different substituted acetophenones were refluxed with dimethylformamide dimethyl acetal (DMF–DMA) under the solvent-free condition to create the intermediates. Then, obtained intermediates were reacted with para-(methylsulfonyl)benzaldehyde and urea in the presence of glacial acetic acid to produce the final products. All compounds were characterized by Mass spectroscopy, IR and 13C/ 1H-NMR.Results: The docking study results indicated that the para-SO2Me substituent was inserted properly into the secondary pocket present in COX-2. One of the oxygen atoms of SO2Me forms a hydrogen bond with Arginine513 and the other oxygen atom forms a hydrogen bond with Histidine90 of the active site. The synthesis of new diaryl-3,4-dihydropyrimidine derivatives was carried out successfully through two steps. The structures of the synthesized compounds were confirmed by Mass spectroscopy, IR and 13C/ 1H-NMR. The in-vitro enzyme inhibition test is in progress.Discussion: According to the docking results, the designed compounds fit properly into the COX-2 active site and the methylsulfonyl pharmacophore group participates in hydrogen bonding with critical secondary pocket aminoacids. The final products were synthesized successfully via two-step reactions. Based on the docking study and structure-activity relationship (SAR) of COX-2 inhibitors, it is expected that the synthesized compounds could selectively inhibit the COX-2 enzyme.Conclusions: The new diaryl-3,4-dihydropyrimidine compounds were designed according to COX-2 inhibitor SAR. According to the rational design based on the SAR of selective COX-2 inhibitors and molecular modeling studies of designed molecules, high potency values and selectivity indices are expected for the synthesized compounds.

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## Preparation and characterization of diclofenac sodium loaded multivesicular liposomes as a biocompatible sustained release carrier

*Kimia Jandaghi Alaee*[1], *Melody Vatan khah*[2], *Azadeh Haeri*[1], *Mohammad Ali Mahjoub*[1], and *Simin Dadashzadeh*[1,*]

[1]Department of Pharmaceutics and Nanotechnology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[2]Pharmaceutical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Corresponding author: Simin Dadashzadeh
Corresponding author Email: sdadashzadeh@sbmu.ac.ir

Introduction: Adhesion formation is exceedingly common after abdominal and pelvic operations, resulting in chronic abdominal and pelvic pain, infertility, small-bowel obstruction, and difficult reoperative surgery in the majority of patients (1,2). Diclofenac sodium, as a nonsteroidal anti-inflammatory medicine with a fibrinolytic effect can be used in various ways as an adhesion inhibitor (3).Encapsulation of drugs into multivesicular liposomes (MVLs), known also as DepoFoam, offers a novel approach to sustained-release drug delivery. MVL is composed of non-concentric multiple lipid layers and is a biodegradable and biocompatible carrier. Studies have shown that the arrangement of non-concentric lipid layers exhibits desirable properties over the conventional unilamellar and multilamellar liposomes, such as a higher stability, minimum burst release, and extended drugs release from a few days to several weeks (4). The main objective of this study was to formulate a sustained release diclofenac sodium-loaded MVLs (DS-MVLs) as a potential delivery system in prevention of peritoneal adhesion.Material and methods: Various formulations of DS-MVLs were prepared by double emulsion (w/o/w) method as described in previous reports (4,5). Briefly, a water in oil emulsion was prepared by mixing 1 ml aqueous phase containing diclofenac sodium and dextrose 5%, and 1 ml oil phase containing chloroform solution of egg phosphatidylcholine (PC), cholesterol, triolein and dicetyl phosphate (DCP) using 15 min vortex (12,000 rpm). Subsequently, the second aqueous solution containing 40 mmol/L lysine was mixed with the primary emulsion. Then the chloroform was removed by using a rotary evaporation. The resulting MVLs were isolated by centrifugation and washed twice to remove unentrapped drug, then resuspended in a L-lysin solution and stored at 4°C. MVLs were characterized in terms of encapsulation efficiency (EE), particle size, morphology and drug release rate. The effect of some formulation parameters on EE%, and drug release rate were examined.Results: Diclofenac sodium was efficiently encapsulated in DS-MVLs with a proper yield and showed the spherical, smooth, and multivesicular characteristics of particles by a light microscope. The average drug EE was higher than 50% and the mean diameter of the optimum formulation was around 10 µm. The selected formula showed an in vitro sustained drug release characteristic without initial burst release.Discussion: Study of the effect of formulation parameters including total lipid concentration, Chol/PC ratio, and pH of the first aqueous phase on the characteristics of the MVLs showed that lipid concentration and the pH of the first aqueous phase are key parameters and have significant influence on EE and drug release rate.Conclusions: The present study suggests that DS-MVLs might have the potential to be used in the prevention of intraperitoneal adhesion as a biocompatible drug carrier with a controlled drug release.

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## فرمولاسیون و ارزیابی پچ های دهانی بتامتازون با استفاده از روش چاپ سه بعدی

*Pegah Torabi[1], Leila Rezaei Shirfard [2], Shahab Bohlooli[2]*

[1]Shahid Beheshti University of Medical Sciences
[2]Ardabil University of Medical Sciences

Corresponding author: Pegah Torabi
Corresponding author Email: ptorabi99@gmail.com

introduction: There have been significant advances in the additive manufacturing techniques such as 3D printing over the past 30 years; so that they are considered the industrial revolution of the 21th century. these methods can be replaced for most of the traditional and conventional drug manufacturing methods. Attempts are now being made to provide individualized treatment based on individual differences. Individual pharmacotherapy or individual therapy is so effective in meeting the patients' needs for treatment of the special diseases based on the individual anatomical and physiological differences, drug sensitivities, genetic polymorphisms, and the needed dosage. 3D printing has a high accuracy and it will soon be used for large scale production. By using 3D printing, unique products can be produced quickly and at low prices, so that these products cannot be produced by conventional methods.Aphthous ulcers has no specific cause. The patients affected by this condition usually suffer from an unfavorable feeling and pain for a long time. There is no effective drug for treatment of this complication. The products available in the treatment of oral lesions include soluble cocktails, topical pastes, mouthwashes and herbal drops that have a temporary effect and are washed off the site with saliva. . According to the collected data and the inefficiency of the manufactured drugs in improving the oral ulcers, we have used 3D printing to manufacture a drug delivery system proportional to the lesion size and site, the individuals' anatomical and physiological differences, and their medical allergies which is last longer on lesion compared to existing products.Method: Due to the problems in the treatment of oral ulcers and the inefficiency of pharmaceutical products in this field, a suitable drug delivery device was made using the 3D printing method using a warm syringe printing. The warm syringe printer moves in x, y, z coordinate positions with an accuracy of 0.1 mm and prints the desired product with the feedstock inside the machine, depending on which method is used for printing. The feedstock of the warm syringe printer is beeswax and we want this wax to be soft so that it can be printed. The device is a metal syringe that has a piston and a cylinder, the cylinder is heated by a heater that can adjust the temperature, and when the engine is rotating, the piston moves to create enough pressure to extrude the material inside the syringe. Discussion: In this method, low temperature is used to soften the polymers and there is no need to use organic solvent and it will not be toxic to the patient and printing will be done through a syringe with a specific nozzle size. In these patches, we loaded betamethasone. Result: Patches containing betamethasone were printed using beeswax and poly vinyl alcohol polymers. The resulting patches had a smooth surface and was flexible. The patches contained 3.2 mg of betamethasone, which was released slowly over 4 hours. Electron microscopy showed well the order of the patch structure and drug loading. Conclusion: The use of 3D printers in the pharmaceutical industry realizes the possibility of increasing the accuracy and precision of drug dosage by manufacturing layer by layer products. The prepared formulation was well printed by the warm syringe printer and also all the patches had a soft texture and flexibility. Various polymers and excipients can be used in the production of oral patches. Depending on the type of material and their percentage composition, the properties of the final patches will vary in terms of flexibility and drug content and drug release profile.

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## An overview on the new strategies for enhancing anti-wrinkle effect and skin permeation of GHK peptide

*Yasaman Khajeamiri[1], Samira Sharifi[2]*

[1] School of Pharmacy Shahid Beheshti University of Medical Sciences, Tehran, Iran.
[2]School of Medicine Koç University, Istanbul, Turkey.
Corresponding author: Samira Sharifi
Corresponding author Email: ssharifi18@ku.edu.tr

GHK is a tripeptide with the amino acid sequence glycyl-histidyl-lysine which is naturally present in human skin and plasma. This tripeptide has impacts on the health of different tissues such as skin and it declines with age. GHK has antioxidant effects and it has been proposed as a therapeutic agent for improving wound healing, skin and hair follicles regeneration, collagen levels and dermal repair. Moreover, GHK is involved in regulating at least 4,000 human genes and it can improve DNA functions. Previous studies have clearly proven that GHK has a strong affinity for copper 2+ which is similar to the copper transport site on albumin and forms a complex with Cu(2+) and GHK-Cu functions as this complex. Different researches demonstrated that GHK-Cu cosmetic products can upgrade skin quality in humans around the age of 50 and higher and it also have effects such as; improving skin elasticity, density, firmness, clarity, keratinocyte proliferation and reducing fine lines, deep wrinkles, photodamage and hyper-pigmentation. Although this peptide plays very important roles in the skin, due to its hydrophilic nature, there is a great challenge for its transdermal delivery and absorption through the skin. In recent studies, various strategies have been developed and examined to increase and accelerate skin permeation and anti aging effects through using new drug delivery systems and molecular changing. In the light of low transdermal delivery of this GHK-Cu and huge need for investigating appropriate ways to enhance its effects, In the present study we aim to review different new strategies for enhancing skin absorption and anti-wrinkle effects of GHK peptide.

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## Metformin effect on Ki-67 in Non-Diabetic Cancer Patients: A Meta-Analysis Study

*Masoome Qanbari [1]Tahereh Farkhondeh[2], Alireza Amirabadizadeh[3], Hamed Aramjoo[4], Babak Roshanravan[4], Saeed Samarghandian[5]*

[1]Student Research Committee, Faculty of Pharmacy, Birjand University of Medical Sciences, Birjand 9717853577, Iran. Iran.

[2]Faculty of Pharmacy, Birjand University of Medical Sciences, Birjand 9717853577, Iran. Iran. farkhondeh2324@gmail.com, farhadsaeedi1997@bums.ac.ir
[3]Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran. amirabadiza921@mums.ac.ir
[4]Medical Toxicology and Drug Abuse Research Center (MTDRC), Birjand University of Medical Sciences, Birjand 9717853577, Iran; Hamed.Aramjoo@bums.ac.ir, babak.roshanravan@bums.ac.ir
[5]Noncommunicable Diseases Research Center, Neyshabur University of Medical Sciences, Neyshabur 9318614139, Iran. samarghandians1@nums.ac.ir

Corresponding author: Masoome Qanbari
Corresponding author Email: masoomeQanbari1831@gmail.com

Background: Our aim was to investigate and evaluate the influence of metformin on Ki-67 in clinical trials. Methods: This systematic study was conducted according to PRISMA guidelines. Major databases including Scopus, Web of Sciences, PubMed, Ovid-Medline, and Cochrane were systematically reviewed by February 2020. Clinical trials investigating metformin effects on the evaluation of Ki-67 were selected for further analysis. The quality assessment was performed with version 2 of the Cochrane tool for determining the bias risk for randomized trials (RoB 2). Heterogeneity among the included studies was assessed using the Chi-square test. After quality assessment, a random effects model was performed to summarize the data related to Ki-67. Results: The pooled analysis indicated that Metformin could decrease ki-67 in patients with operable endometrial cancer versus healthy subjects (SMD=0.47, 95%CI [-1.82, 2.75], p=30.1). According to Egger's test, no publication bias was observed for Ki-67. Conclusions: It was found that metformin could decrease ki-67 in patients with operable endometrial cancer. In comparison to the results obtained of our meta-analysis, due to the high heterogeneity and bias of the included clinical trials, the present findings could not confirm or reject the efficacy of metformin for patient with breast cancer and endometrial cancer.

## P68

## Evaluation of the antioxidant protective effect of silymarin against gentamicin-induced nephrotoxicity

Motahare Mahi[1], Iman Karimzadeh[2], Masoud Ziaee[3], Shima Jafariy[4], Sajede Karimi[5]

[1]Infectious Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran
[2]Department of Clinical Pharmacy, School of pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.
[3]Infectious Diseases Research Center, Birjand University of Medical Sciences, Birjand,Iran
[4]Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran
[5]Birjand University of Medical Sciences, Birjand, Iran
Corresponding author: Masoud Ziaee
Corresponding author Email: dr.m.ziaee@gmail.com

Background: The aim of this clinical trial was to explore the effect of SM on GEN-induced nephrotoxicity.Materials and Methods: This randomized double-blinded placebo-controlled clinical trial was conducted from April 2017 to October 2019 on patients diagnosed with infectious diseases that were planned to receive GEN for at least 7 days. After approving the study and obtaining informed consents from the patients, 60 patients were included in this study. Patients in the treatment (30) and control (30) groups were given injectable GEN along with 140 mg of SM tablets or placebo orally three times a day. Demographic, laboratory, and therapeutic information of the patients were recorded. Urine and blood samples were collected before and on days 1, 2, 3, 5 and 7 after GEN administration and intervention.Results: There was no significant difference between the two groups in terms of sex, age and weight (p> 0.05) and no significant differences between SM- and placebo-treated groups (p> 0.05) in the mean laboratory findings. No nephrotoxicity episode was observed on the first and second days after GEN administration. But The overall rate of GEN nephrotoxicity in the SM group was significantly lower than that in the placebo group. (16.7% and 53.3% respectively. p value:0.003). serum Cr levels increased (p<0.001) in both SM- and placebo-treated patients, particularly; showing significant increases on days 2, 3, 5, and 7 as compared with the baseline value. Importantly, this increase in serum Cr was significantly higher in the placebo than that in SM group (p <0.05).
Conclusion:SM co-treatment (140 mg orally three times a day) during the course of GEN treatment (1 week) was well-tolerated and significantly attenuated or prevented the nephron- toxicity of GENin patients with different infectious diseases.

## P69

## *Halva*, a Possible New Dosage Form

*Fatemeh Tolouei[1, 2] Fatemeh Hoseinzadeh-chahkandak[3, 4], and Sayyedeh Fatemeh Askari[5, 6]*

[1]Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran
[2]Faculty of Pharmacy, Birjand University of Medical Sciences, Birjand, Iran
[3]Social Determinants of Health Research Center, Birjand University of Medical Sciences, Birjand, Iran
[4]Department of Public Health, Faculty of Health, Birjand University of Medical Sciences, Birjand, Iran
[5]Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran
[6]Department of Phytopharmaceuticals (Traditional Pharmacy), Faculty of Pharmacy, Birjand University of Medical Sciences, Birjand, Iran
Corresponding author: Fatemeh Tolouei
Corresponding author Email: fatmetoloue@gmail.com

Introduction: Traditional medicines (TMs) are increasingly vital for treatment strategies in modern and developing countries. The World Health Organization highlights the role of including traditional medicines for seeking new remedies. Besides illness prevention, health maintenance, and treatment based on natural remedies, traditional medicines provide an excellent opportunity for introducing a new pharmaceutical system such as traditional Persian medicine. For instance, in traditional Persian pharmacy manuscripts, Halva has been considered as a medicinal base. Nowadays, functional food or nutraceuticals are well-known issues in modern medicine, and Halva is one of the highly recommended nutrients consisting of oil, flour, cereals, flavors, and other additives. In this research, we aim at discovering the differences and similarities between modern Halva formulations and traditional ones. Moreover, we try to introduce evidence-based formulations with specific applications.Material and methods: Qarabadin-e Salehi (18thAD) (4), a multi-dimensional encyclopedia, was studied to extract various Halva formulations. In addition, by searching on Scopus and PubMed, recent studies were analyzed, and as keywords, the scientific name of Halva ingredients and mentioned applications were used.Results: Using the procedures mentioned earlier, we found 35 types of Halvah advantageous for various therapeutic and nutritional properties such as a complete meal, brain system booster, sexual enhancers, cough and fever reducer, and weight gainer. Sixty-five components were used in formulations which include 15 animals and 51 herbal. Also, by searching and analyzing the scientific databases, pharmacological functions were confirmed.Discussion: According to the results, various Halva formulations existed from simple to complex, and there is enough evidence to start human studies. Halva has a wide range of nutritional and therapeutic effects. It is also suitable for special groups such as children and slim people who take food instead of medicine. Therefore, Halva can be considered more as medicinal food by researchers and pharmaceutical manufacturers . Conclusions: According to the traditional Halva formulations and achieved evidence, Halva can be considered a new form of drug delivery or new drug forms. Therefore, it can be used for treating different diseases .

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## Evaluation the effect of buprenorphine on oxidative stress indices in the liver of rat pups born to exposed mother during lactation

*Amirali Hosseini,[1] Danial Gharaee Amirabadi,[2] Babak Roshanravan,[3] Hamed Aramjoo,[4] Saeed Samarghandian,[5] Tahereh Farkhondeh[6,7]*

[1]Student Research Committee, Faculty of Pharmacy, Birjand University of Medical Sciences,

Birjand, Iran.

[2]Student Research Committee, Faculty of Pharmacy, Birjand University of Medical Sciences, Birjand, Iran.

[3]Student Research Committee, Birjand University of Medical Sciences, Birjand, Iran.

[4]Student Research Committee, BSc Student in Medical Laboratory Science, Birjand University of Medical Sciences, Birjand, Iran.

[5]Noncommunicable Diseases Research Center, Neyshabur University of Medical Sciences, Neyshabur, Iran.

[6]Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran.

[7]Faculty of Pharmacy, Birjand University of Medical Sciences, Birjand, Iran.

Corresponding author: Prof. Saeed Samarghandian, Dr. Tahereh Farkhondeh.

Corresponding author Email: samarghandians1@nums.ac.ir , farkhondeh2324@gmail.com.

Buprenorphine (BUP) is a semi-synthetic drug usually used for the management of opioid addiction. The effect of BUP on the liver function of neonate rats born to mother exposed to this drug during lactation was not clear.This study was designed to assess the effects of BUP on the oxidative parameters in the liver of pups born to mother exposed to this drug during lactation. BUP at dose of 0.5 or 0.1 mg/kg was subcutaneously administrated to lactating rats for 28 days. At the end of experiment, the pups were anesthetized and the liver of the animals were dissected out to measure oxidative stress parameters [malondialdehyde (MDA), glutathione (GSH), nitric oxide (NO), and the activity of superoxide dismutase (SOD)]. The findings indicated that BUP could not change MDA, NO, GSH levels, nor SOD activity in the liver tissue of animals. We suggest performing additional studies to determine the association between BUP and oxidative modifications in liver tissues of pups born to mothers under BUP therapy during lactation.

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## Pharmacist-Directed Self-Management of Blood Pressure versus Conventional Management in Patients with Hypertension: A Randomized Control Trial

*Sajad Khiali[1], Naser Khezerlo-aghdam[2], Hossein Namdar[2], and Taher Entezari-Maleki[1,2]*

[1]Department of Clinical Pharmacy, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Drug Applied Research Center and Cardiovascular Research Center, Faculty of Pharmacy, Tabriz University of Medical Sciences, Daneshgah St., Tabriz, Iran

Corresponding author: Taher Entezari-Maleki

Corresponding author Email: tentezari@gmail.com

Introduction: A mounting evidence has shown that pharmacist-directed health services play a fundamental role in the management of patients with cardiovascular diseases such as management of warfarin therapy.1 We aimed to carry out the present study to compare the pharmacist-directed home blood pressure monitoring (HBPM) method with the conventional office-based BP control as the standard method.Material and methods: In this randomized control trial, we randomly assigned, in a 1:1 ratio, patients with uncontrolled blood pressure (BP) into pharmacist-directed HBPM and conventional office-based BP control groups. In the intervention group, the patients were trained to measure their BPs and adjust their medications according to the designed protocol under the supervision of a clinical pharmacist. The primary outcome was the comparison of the BPs at baseline and months 1, 3, and 6.Results: A total of 126 patients underwent randomization. One month after the allocation, the baseline systolic BP ($150.5 \pm 13.1$ vs. $149.7 \pm 11.2$ mm Hg; p-value = 0.71) and diastolic BP ($97.2 \pm 9.8$ vs. $93.6 \pm 14.5$; p-value = 0.11) significantly decreased to the control range in 85.2% of the patients in both groups (systolic BP: $128.8 \pm 6.4$ vs. $125.6 \pm 7.1$ mm Hg; p-value = 0.01 and diastolic BP: $89.1 \pm 6.2$ vs. $81.5 \pm 6.0$ mm Hg; p-value= 0.01). This pattern continued during the study period (month 6; systolic BP: $115.6 \pm 10.1$ vs. $116.1 \pm 9.6$ mm Hg; p-value = 0.78; diastolic BP: $79.0 \pm 5.0$ vs. $77.2 \pm 5.8$ mm Hg; p-value = 0.08).Discussion: Many international hypertension guidelines have recommend using of the self-monitoring method. Furthermore, cooperation between patients and pharmacists as well as education of patient could lead to better management of hypertension.2-5 Our study showed that clinical pharmacists and educated pharmacists can play an essential role in hypertension management through medication therapy management.Conclusions: No significant difference was observed between the pharmacist-directed HBPM and usual care methods in the control of BP. Moreover, both methods have significant effects on the control of BP. Multicenter studies with larger sample size and longer study period are required to achieve accurate results.

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## Predictors of acute kidney injury in hematological cancer patients: A prospective cross-sectional study

*Maryam Ghasemi[1], Mohammad Solduzian[2], and kourosh sadeghi [1]*

[1]Clinical pharmacy, faculty of pharmacy, Tehran university of medical sciences , Tehran, iran

[2]Clinical pharmacy, faculty of pharmacy, Tabriz university of medical sciences , Tabriz, iran

Corresponding author: Mohammad Solduzian

Corresponding author Email: dr.mohammadsolduzian@gmail.com

Introduction: Different factors might contribute to the development of (Acute Kidney Injury) AKI in hematological cancer patients including sepsis, hypo perfusion and Chemotherapy. Data about the contribution drugs to development of AKI are scarce. The current study was designed to evaluate the relationship between receipt of different medications and AKI development in hematological cancer patients to identify risk factors in order to minimize their effects.Material and methods: This study was designed as a prospective observational and cross-sectional study. All patients admitted between April 2019 and February 2020 to hematology wards of Shariati Hospital of Tehran University of Medical Sciences, were evaluated for enrollment in the study. Patients younger than 18 years of age, those who were not able to consent to participate and those who presented with AKI were excluded. AKI was diagnosed per KDIGO criteria.Results: Overall, 446 patients were evaluated in this study, 88 (19.7%) cases of AKI were detected. Patients with AKI had longer duration of hospital stay, but mortality rate was not different between two groups (p values of <0.001 and 0.054 respectively). Hypotonic fluids, doxorubicin Idarubicin, vancomycin (Median vancomycin levels of patients evaluated in the current study was 19.24 (IQR, 10.55) and methotrexate (ORs of 3.094, 6.069, 2.337 and 2.685 respectively) increased the odds of AKI while hydrocortisone and statins lowered it (ORs of 0.044 and 0.078 respectively).Discussion: While the results of this study indicated that age, gender and history of type 2 diabetes were not significantly related to AKI development, hypotonic fluids, may be because of impaired tissue perfusion, anthracyclines, and vancomycin with levels higher than 15mg/dl increased the odds of this adverse effect. The observed increased odds of AKI development with vancomycin in this study is in correlation with the findings of the previous studies in patients with hematological malignancies. Of interesting findings of this study which should be noted, are the protective effects of statins and hydrocortisone against AKI development, which might be because of their anti-inflammatory effects. Treatment with methotrexate could have nephrotoxic effects and this adverse effect occurs in a dose related manner and the results of our investigation endorsed the previously reported nephrotoxic effects of MTX as multivariate analysis showed significantly increased odds of AKI development with this medication. Because of specific ward protocol, which mainly utilizes doses or medications with less nephrotoxicity, multivariate analysis did not show causality effects for medications such as Amphotericin-B in AKI development.Conclusions: This study showed that treatment with vancomycin, anthracyclines, hypotonic fluids and methotrexate could increase the odds of AKI development and optimal management of drug and fluid therapy in combination with close monitoring could help lower the rates AKI and its following complications.

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# Pharmacist-Directed Self-Management of Blood Pressure versus Conventional Management in Patients with Hypertension: A Randomized Control Trial

*Sajad Khiali[1], Naser Khezerlo-aghdam[2], Hossein Namdar[2], and Taher Entezari-Maleki[1,2]*

[1]Department of Clinical Pharmacy, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Drug Applied Research Center and Cardiovascular Research Center, Faculty of Pharmacy, Tabriz University of Medical Sciences, Daneshgah St., Tabriz, Iran

Corresponding author: Taher Entezari-Maleki

Corresponding author Email: tentezari@gmail.com

Introduction: A mounting evidence has shown that pharmacist-directed health services play a fundamental role in the management of patients with cardiovascular diseases such as management of warfarin therapy.[1] We aimed to carry out the present study to compare the pharmacist-directed home blood pressure monitoring (HBPM) method with the conventional office-based BP control as the standard method.Material and methods: In this randomized control trial, we randomly assigned, in a 1:1 ratio, patients with uncontrolled blood pressure (BP) into pharmacist-directed HBPM and conventional office-based BP control groups. In the intervention group, the patients were trained to measure their BPs and adjust their medications according to the designed protocol under the supervision of a clinical pharmacist. The primary outcome was the comparison of the BPs at baseline and months 1, 3, and 6.Results: A total of 126 patients underwent randomization. One month after the allocation, the baseline systolic BP ($150.5 \pm 13.1$ vs. $149.7 \pm 11.2$ mm Hg; p-value = 0.71) and diastolic BP ($97.2 \pm 9.8$ vs. $93.6 \pm 14.5$; p-value = 0.11) significantly decreased to the control range in 85.2% of the patients in both groups (systolic BP: $128.8 \pm 6.4$ vs. $125.6 \pm 7.1$ mm Hg; p-value = 0.01 and diastolic BP: $89.1 \pm 6.2$ vs. $81.5 \pm 6.0$ mm Hg; p-value= 0.01). This pattern continued during the study period (month 6; systolic BP: $115.6 \pm 10.1$ vs. $116.1 \pm 9.6$ mm Hg; p-value = 0.78; diastolic BP: $79.0 \pm 5.0$ vs. $77.2 \pm 5.8$ mm Hg; p-value = 0.08).Discussion: Many international hypertension guidelines have recommend using of the self-monitoring method. Furthermore, cooperation between patients and pharmacists as well as education of patient could lead to better management of hypertension.[2-5] Our study showed that clinical pharmacists and educated pharmacists can play an essential role in hypertension management through medication therapy management. .Conclusions: No significant difference was observed between the pharmacist-directed HBPM and usual care methods in the control of BP. Moreover, both methods have significant effects on the control of BP. Multicenter studies with larger sample size and longer study period are required to achieve accurate results.

## P74

# Evidence-Based Review of Potential COVID-19 Therapeutic Agents

*Elnaz Khani[1], Taher Entezari-Maleki[2]*

[1]Student Research Committee, Tabriz University of Medical Sciences, Tabriz , Iran

[2]Department of Clinical Pharmacy, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz , Iran

Corresponding author: Taher Entezari-Maleki

Corresponding author Email: tentezari@gmail.com

Introduction: Since the early days of 2020, coronavirus disease 2019 (COVID-19) has become a global health issue. Currently, some medications have gotten the FDA approval or emergency use authorization (EUA) for disease management.Material and methods: We searched the available literature in PubMed, Google Scholar databases and categorized the potential medications based on the American College of Cardiology/American Heart Association Clinical Practice Guidelines Recommendation Classification System.Results: Reviewing the available data showed that remdesivir has a high class of recommendation and level of evidence against severe COVID-19. Among patients receiving either invasive mechanical ventilation or oxygen alone, dexamethasone can be beneficial, particularly with tocilizumab. Based on the available studies, hydroxychloroquine and lopinavir-ritonavir have no benefit and are even harmful that their use is not recommended. In patients on high-flow oxygen or noninvasive ventilation baricitinib can be favorable in combination with remdesivir. Also, outpatients with mild to moderate COVID-19 can take advantage

of casirivimab/imdevimab in settings that patients' condition progresses to severe. The efficacy of IFN-β-1a, colchicine, ruxolitinib, convalescent plasma, ivermectin, and anti-HCV medications is unclear according to the clinical trials and needs more studies. Since the limited clinical trials regarding the use of anakinra, favipiravir, IFN-α-2b, and methylprednisolone, their effectiveness on COVID-19 should be evaluated by further studies.Discussion: According to the promising effects of remdesivir in clinical trials, the FDA approved the first agent in hospitalized patients aged ≥ 12 and weighing ≥ 40. However, the WHO SOLIDARITY trial recommended against the use of remdesivir with the same doses and duration. It should be noted that patients in this trial were not categorized based on the disease severity. Second, this trial was conducted in over 30 countries with variable health care quality and treatment guidelines, affecting the results. Third, the lack of a placebo increased the risk of bias. Similarly, the National Institutes of Health (NIH) recommended remdesivir in patients on supplemental oxygen. In parallel with NIH and WHO guidelines, we strongly recommended against the use of lopinavir plus ritonavir and chloroquine or hydroxychloroquine in patients with COVID-19. This can be rationale due to the results of randomized clinical trials, especially the RECOVERY collaborative group's trial. Moreover, the evaluation of pharmacokinetics of lopinavir/ritonavir in patients with COVID-19 showed that the usual doses of lopinavir plus ritonavir could not affect the virus replication due to low concentrations. Also, the adverse effects and drug interactions of chloroquine and hydroxychloroquine raise concerns about safety issues. As immunomodulatory agents, dexamethasone and tocilizumab were medications with the highest class of recommendation and level of evidence. According to the NIH recommendation, dexamethasone combined with tocilizumab could improve survival in hospitalized patients with COVID-19 who need mechanical ventilation. According to the NIH recommendations, the combination of baricitinib plus remdesivir is a rational treatment option in conditions in which corticosteroids cannot be administered and non-intubated patients with oxygen supplementation.Conclusions: Remdesivir and dexamethasone are the most beneficial medications in the viral and inflammatory phases, respectively. Other medicines need more studies to confirm their efficacy and safety.

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# Time-dependent influence of infliximab oh hemodynamic responses and cardiac injuries of isoproterenol-induced myocardial infraction in rats

*Seyyed Amin Shafaei Bagheri, Nasrin Maleki Dizaji, Alireza Garjani, Samin Mousavi, Mahdieh Mohammadi and Haleh Vaez*

[1]Pharmacology and Toxicology Department, Faculty of Pharmacy, Tabriz University of Medical sciences, Tabriz , Iran

[2]Student Research Committee, Faculty of Pharmacy, Tabriz University of Medical sciences, Tabriz , Iran

Corresponding author: Haleh Vaez

Corresponding author Email: Haleh.vaez@gmail.com

Introduction: Cardiovascular diseases are the leading cause of morbidity and mortality worldwide. Myocardial infarction (MI) is the most frequent cause of heart failure with high prevalence. Immune-induced inflammation plays an important role both in aggravating and healing post-myocardial infarction (MI) injuries. It has shown that the serum and heart tissue levels of pro-inflammatory cytokines elevated in isoproterenol-induced myocardial infarction, amongst which, TNF-alpha produced by cardiomyocytes, mediated a predominant inflammation, suggesting its essential role in initiating pathophysiological responses following MI. Infliximab, a potent chimeric monoclonal IgG1 anti-TNFα antibody, binds to both the soluble subunit and the membrane-bound precursor of TNF-α interfering with endogenous TNFα activity. Potent anti-inflammatory and local immunomodulatory activity of infliximab have been suggested to have modulating effects on immune responses after MI. Due to the insufficient outcomes of clinical investigations of efficacy and safety of infliximab in patients with moderate-to-severe heart failure, more fundamental non-clinical studies are required to make a proper judgment in this regard. The aim of the present study was to evaluate the efficacy of infliximab on hemodynamic responses and myocardial injuries following isoproterenol-induced myocardial infarction.Material and methods: Male Wistar rats, weighting 260 ± 20 g were assigned into ten groups (n = 6) of saline (normal saline), infliximab (7 mg/kg), isoproterenol (100 mg/kg for two consecutive days), and isoproterenol plus infliximab (30 min after the second injection of isoproterenol). The heart tissues and serums were analyzed 24, 48, 72, and 96 h post-MI ,and hemodynamic parameters, histopathological changes, malondialdehyde (MDA), Total antioxidant capacity, lactate dehydrogenase, and lactate levels were assessed in the respective groups.Results:Infliximab partially improved hemodynamic depression in the first days after MI, but the heart became more suppressed later. A similar result also obtained at the MDA tissue levels but not serum levels. Anti-inflammatory effects of Infliximab may improve cardiac function and prevent heart tissue injury early after MI; however, it can worsen the condition later by inhibiting compensatory reactions such as cardiac remodeling and tissue repair.Discussion: In a rat model of isoproterenol-induced myocardial infarction, we demonstrated that a single dose of infliximab had a slight protective effect in the early hours after MI but in the following days it deteriorated the cardiac dysfunction due to suppressing heart tissue remodeling and restoration. Despite a significant increase in the heart weight on the fourth day, no considerable effect on the heart-to-body weight ratio in the first days has been reported. The MI-induced heart tissue weight gain gradually decreases over time.Conclusions:Obviously, inflammation and the recruitment of neutrophils to the area of infarction are the main participants in the development of both post-MI injury and healing. Due to the insufficient therapeutic approaches targeting the immune system's reaction to MI injury, understanding the time course of the cellular responses in inflammatory cascade and precise characterization of the systemic and cardiac immunity are critical for the ideal design of therapeutic strategies which result in reducing the high morbidity and mortality rate by lowering excessive inflammatory injury and opening a new window of opportunity for safe and effective treatment.

## P76

# Investigation of the production and purification of teduglutide effective in short bowel syndrome

*Saba Rasouli*[a,b]

*Supervisors : Siavoush Dastmalchi*[a, b] *, Ali Akbar Alizadeh*[a]

[a]Biotechnology Research Center, Tabriz University of Medical Sciences [b]School of Pharmacy, Tabriz University of Medical Sciences

Corresponding author: Saba Rasouli

Corresponding author Email: sabarasouli93@gmail.com

Short bowel syndrome (SBS) is a disabling condition characterized by diarrhoea, steatorrhoea, abdominal pain, electrolyte disturbances, dehydration and malnutrition, resulted from the loss of substantial portions of intestine . In a few years following removal, the remnant intestine is able to compensate for the reduction of absorptive surface area as a result of the endogenous trophic hormones and peptides such as glucagon-like peptide-2 (GLP-2), which regulate the growth, proliferation and maintenance of cells lining the gastrointestinal tract .Growth factors and seven other trophic

hormones have been used to enhance the quality of lives and among them; human growth hormone, somatropin and L-glutamine have been approved to be used in SBS for short-term usage with limited efficacy .Teduglutide (Gattex, Revestive) is an analogue of GLP-2, which has longer half life compared to GLP-2 due to a single residue substitution. It is the first drug which has been introduced for long-term treatment of SBS with beneficial effects in different clinical trials. Teduglutide increases intestinal and portal blood flow, inhibits gastric acid secretion and decreases intestinal motility via binding to the GLP-2 receptors located in intestinal tissue .The glucagon-like peptide-2 receptor (GLP2R) belongs to glucagon/secretin receptor superfamily of GPCRs whose activation leads to increased intracellular level of cAMP.Clinically used teduglutide is the product of both chemical synthesis (patent number: CN104418949A) and application of recombinant DNA technology (US Patent Number:9987334*PED), and the current study aimed to produce recombinant teduglutide in bacterial expression system. For this, teduglutide was expressed attached to glutathione S- transferase (GST) tag and purified using affinity and size exclusion chromatographies. The secondary structure content and biological activity of teduglutide were determined by circular dichroism spectropolarimetry and cell proliferation assay. We believe, this method of production can provide advantages over the industrial-scale peptide synthesis which is a costly, time-consuming, and highly polluting process, especially for long peptides such as teduglutide.

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## Prediction of solubility class in biopharmaceutics classification system

*Farnaz Aghazadeh Shabestari[1], Ali Shayanfar[2,3]*

[1]Student Research Committee, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Pharmaceutical Analysis Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

[3]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

Corresponding author: Ali Shayanfar

Corresponding author Email: shayanfara@tbzmed.ac.ir

Introduction: The Biopharmaceutics Classification System (BCS) has turned out to be commonly accepted in academia, industry, and regulatory world. Biopharmaceutics Drug Disposition Classification System (BDDCS) is a modification of BCS which is a four-class system based on solubility and metabolism. This system assigns the role of carriers in pharmacokinetics and their interaction with metabolizing enzymes (1, 2). Drugs are classified into four groups in terms of the extent of permeability (BCS) or metabolism (BDDCS) and solubility, high and low, based on BDDCS (3). In order to predict classes, structural enzymes (1, 2). Drugs are classified into four groups in terms of the extent of permeability (BCS) or metabolism (BDDCS) and solubility, high and low, based on BDDCS (3). In order to predict classes, structural parameters of drugs were used to create classification-based models. Against metabolism and permeability, the previous models cannot predict solubility class with good accuracy (4). Therefore, the aim of this study is to improve the capability of the models for estimating solubility class.Material and methods: Firstly, drugs' BDDCS data were collected through the literature, then, the structural descriptors including Abraham solvation parameters, distribution coefficient (log D) and octanol–water partition coefficient (log P)) were computed by ACD/Labs software. Later, data were divided into two portions including training and test. The training set was applied to develop the models based on structural parameters by logistic regression. Results: The developed models based on Abraham solvation parameters and log P and log D could predict the class of solubility with good accuracy. Discussion: The outcomes of this research revealed that the accuracy for the prediction of the class of solubility was improved after the inclusion of drugs ionization in biological pHs, in addition to Abraham solvation parameters and log P. Hence, the developed classification models can estimate solubility class with satisfactory accuracy.Conclusions: The class of solubility can be estimated with high accuracy with the aid of the applied structural descriptors of drugs.

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## Changing the daily injection of Glatiramer acetate to a monthly long acting product through designing polyester based polymeric microspheres

*Fatima Molavi[1] , Mohammad Barzegar-Jalali[1] , Hamed Hamishehkar[2]*

[1]Biotechnology Research Center, Student Research Committee, Department of pharmaceutics, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

[2]Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Corresponding author: Hamed Hamishehkar

Corresponding author Email: Hamishehkar.hamed@gmail.com

Introduction: Glatiramer acetate (GA) is a newly emerged therapeutic peptide to reduce the frequency of relapses in multiple sclerosis (MS). Despite its good performance in control of MS, it is not widely applied because of its daily or biweekly SC injections due to the fast degradation and body clearance. Therefore, designing sustained release implant results in long biological effect by gradually increasing drug exposure through convection system and by protecting GA from local rapid degradation. *Methods:* Different emulsion methods, PLGA type, surfactant concentration, drug/polymer ratio, drying processes, stirring method and other variables in preliminary studies modified the final formulation. The release kinetics was studied through mechanistic kinetic models such as zero-order, Weibull, Higuchi, etc. In this study, all challenges for easy scale up, methodological detail and a simple feasible setup in the mass production were discussed. *Results:* The optimized formulation was obtained by 1:6 drug/PLGA, 0.5% w/w polyvinyl alcohol (PVA) and 0.75% w/w NaCl in external aqueous phase, 1:10 continuous phase to dispersed phase (CP/DP) ratio and without any surfactant in primary emulsion. The final freeze-dried particles presented a narrow distributed size of 1-10 µm with 7.29% ± 0.51 drug loading (DL) and zero-order release behavior with appropriate regression correlation ($R^2$ 98.7, k= 0.001), complete release and only 7.1% initial burst release. *Conclusion:* Therefore, to achieve improvement in patient compliance through better and long efficacy, designing the parenteral sustained released microspheres of this immune modulator is a promising approach to be considered.

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## Budget Impact Analysis of Inactivated Polio Vaccine (IPV) introduction into the Iranian national immunization program

*Rozhin Khalili[1], Toktam Faghihi[2], Naeim Karimpour-fard[3], Akbar Abdollahi-asl[3], Seyed Mohsen Zahraei[4] and Shekoofeh Nikfar[3]*

[1]International Campus, School Of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[2]Department of Pharmacotherapy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[3]Department of Pharmacoeconomics and Pharmaceutical administration, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[4]Center for Communicable Diseases Control, Ministry of Health and Medical Education, Tehran, Islamic Republic of Iran

Corresponding author: Shekoofeh Nikfar

Corresponding author Email: Nikfar_sh@tums.ac.ir

Introduction: Due to the increasing costs of the health sector in all countries of the world and on the other hand the existence of limited budgets in this area, so the efficient and effective use of resources is essential. Due to the unequal health conditions and financial resources in different countries, decision makers have to make decisions based on the existing conditions and needs of their country and the use of evidence. One of these evidences is economic evaluations. Economic evaluation studies seek to show ways to use limited resources efficiently (1).There are currently 154 countries using the oral vaccine in the immunization program against the wild polio virus. Three polio serotypes should be collected from the cold chain in all vaccination service centers and vaccine storage centers, whether public or private, and replaced with the two oral serotypes 1 and 3. Also, a dose of three-serotype injection vaccine should be added to the Iranian national immunization program the age of 4 months (2).Introducing a new vaccine as a new technology need economic evaluation studies such as Budget impact analysis (BIA) for entering to the national vaccine program. A budget impact model can help decision makers predict the expected changes in health care spending after adopting any new interventions and/or medications (3,4). Therefore, the aim of the present study is to analyze the budget impact of the introduction of the injectable polio vaccine into the Iranian national immunization program.Material and methods: In this study, the pre- and post-vaccine introduction costs of the IPV into the national immunization program were compared. Pre-vaccination costs include the direct cost of treating polio patients for inpatient and outpatient services. post-vaccine introduction costs include the total cost of vaccination and the direct cost of treating patients with polio who have been infected, despite receiving the vaccine; However, due to the effectiveness of the vaccine, the number of vaccinated patients is expected to be significantly lower than the number of patients before receiving the vaccine, and consequently treatment costs will be reduced. In this study, costs for a period of 5 years, from 2021 to 2025, are considered separately (3).Results: The total cost of vaccination for five years in Iran before IPV vaccination would be more than 3.29 million USD and after IPV vaccination would be more than 3.57 million USD. The introduction of the IPV resulted in a net increase about 290,000 USD in the healthcare budget.Discussion: Other studies have shown that applying at least one dose of IPV alongside OPV in the national immunization program will increase cost of vaccination, but the increase in the overall cost of the health budget is not significant (4,5).Conclusions: The results of this study showed that inclusion of the IPV into the national immunization program will have an increase effect on the health budget and will increase government spending.

## P80

# Study of decision-making manner in managers of Iranian pharmaceutical system

*Abas Kebriaeezadeh[1], Amirhossein Abdi Karimipour[2], Masoumeh Nematbakhsh[3], Meysam Seyedifar[4]*

[1]Department of Economics and Drug Management,Tehran University of Medical Sciences, Tehran, Iran

[2]Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Abbas Kebriaeezadeh

Corresponding author Email: kebriaee@tums.ac.ir

Introduction: Iranian pharmaceutical industry is one of the most important strategic industries. The changing policies and changes of the managers of the regulatory bodies on the pharmaceutical industry, and also the fluctuations, financial and commercial challenges of the country have created turbulent conditions for all pharmaceutical industries and other industries. Studying the pattern and decision-making manner of managers is one of the most important methods used in the in-depth evaluation of organizations. To evaluate development models with a forward-looking approach, managers' decision patterns are usually turned into models.Method: We selected 23 managers from the policy sector and important economic firms of the Iranian pharmaceutical industry (include: manufacturing, importation, and distribution) and conducted in-depth interviews with them. In order to do this, we have already stated the objectives of the study to the Interviewees, and this analysis started by interviewing them in random order. We analyzed their management style, model of decision making, and strategies by mentioned tools. Mintzberg's artistic view of management styles, decision-making manners, and types of strategies was considered as a theoretical framework of the research and the collected data were analyzed by thematic analysis method based on Mintzberg's view.In the interview, their biographies, activities and achievements, and their life and work history were questioned. In this report, each chapter is dedicated to a manager and includes all four mentioned sections.Result: The results of the interview analysis, show the management style of managers can be divided into three general groups. (These three styles are the result of 3 different criteria of management based on Mintzberg's view, includes: management based on art, craft, and science). Then it was determined how many of these managers are in each category and the successes and achievements of each manager are related to which period of their work experience. (Political, economic, social conditions, etc. are very variable in different Government courses of Iran and this has affected the performance of managers. So what performance each manager has in what time trend is another result of this analysis). Also, 3 different decision-making manners were extracted from interviews which are “Thinking first”, “Seeing first” and “Doing first”. In addition, 4 different ways of forming a strategy in the managers’ mind (“Planning”, “Visioning”, Venturing, and Learning) were determined in this research.Discussion: This research is descriptive and does not make judgments about a manager's success or failure, but analyzing and identifying people's management styles can help readers achieve a clearer analysis of the issue. For example, the analysis shows that most of the managers who have had significant success in small and innovative private companies have the “Craft” management style and their type of strategy is “venturing”, this analysis helps to strengthen this hypothesis. The same styles will be more effective for some pharmaceutical companies with a similar theme and environment.Conclusion: We conclude that management style, decision-making manners, and way of forming the strategy of the effective managers in Iranian pharmaceutical history were various according to different time trends with different political, economic, and social situations.

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## Design, Synthesis and Molecular Docking of *p*-Aminobenzamide Derivatives as Potent Urease Inhibitor

*Movahed Abdi[1], Fatemeh Niasari-Naslaji[1], Mansour Nasirian Koupani[1] and Meysam Talebi[1]*

Department of Medicinal Chemistry, Faculty of Pharmacy, Drug Design and Development Center, Tehran University of Medical Sciences,16Azar Ave. Tehran, Iran.

Corresponding author: Massoud Amanlou

Corresponding author Email: amanlou@tums.ac.ir

Introduction: Until 1982, it was believed that peptic ulcer disease (PUD) is caused by hyper acidity. Then, *H. Pylori* discovery has changed the concept of PUD pathogenesis to a bacterial infection[1]. *H. Pylori* is a Gram-negative bacterium that triggers the inflammation of the gastrointestinal epithelium lining by its means of multifaceted surviving system[2]. One of its crucial strategies to obtain epithelial colonization is an enzyme known as urease, that initiates the conversion of urea to ammonia and carbon dioxide[3]. The ammonia produced in this pathway, neutralizes gastric hydrochloric acid, and therefore, enables the microorganism to thrive[4]. By diminishing this deactivating tactic, we can reach the goal of treatment. The intention of this study was to design and synthesize new potent urease inhibitors, to boost *H. pylori* eradication.Methods: Synthesis of p-Aminobenzamide derivatives was obtained in a three-step reaction procedure. First of all, Ethyl-4-aminobenzoate was prepared in ethanol from 4-aminobenzoic acid. Then, excess addition of hydrazine hydrate in ethanol, gave 4-aminobenzohydrazide. Finally, the p-Aminobenzamide derivatives were synthesized through a condensation reaction of 4-aminobenzohydrazide with different aromatic aldehydes in 1:1 molar ratio, in ethanol medium. Inhibitory activity against jack bean urease enzyme was determined by Berthelot reaction.Results: Twelve novel derivatives were synthesized and their structure was confirmed by C-NMR, H-NMR and MS analysis. Subsequently, the potency of the derivatives was verified by urease test. Besides, the interaction of our inhibitors with the active site of the enzyme was studied by docking. Discussion: The attained results, demonstrated that all of the synthesized compounds have more potent activity than Thiourea, as a standard urease inhibitor, in hindering *H. Pylori*’s urease enzyme. Docking studies showed that all of the compounds successfully occupy and interact with the active site of the urease enzyme. Eventually, among all compounds, compound d indicates the lowest $IC_{50}$ value of urease inhibitory activity and the lowest docking binding energy, therefore it is considered as the most potent compound of this series.Conclusion: According to the urease inhibitory activity of our final compounds, it seems beneficial to consider p-Aminobenzamide as an important moiety for design and synthesize of potent urease inhibitors.

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## Discovery of some novel racetams as potential anti-seizure and nootropic agents: Pharmacophore study and molecular docking

*Mohammad Amin Manavi [*1]*

[1]Department of Medicinal chemistry, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Mohammad Amin Manavi

Corresponding author Email: ma-manavi@student.tums.ac.ir

Introduction: Synaptic vesicle protein 2A (SV2A) is an integral membrane protein necessary for the proper function of the central nervous system and is associated to the physiopathology of epilepsy. SV2A is the molecular target of the anti-epileptic drug levetiracetam and its racetam analogs. Levetiracetam is a multiple action drug that primarily acts through an interaction with the synaptic vesicle protein 2A. Levetiracetam is the first drug of its kind to be approved for the treatment of epilepsy and is now the most prescribed among the newer antiepileptic drugs. The racetam binding site in SV2A and the non-covalent interactions between racetams and SV2A are currently unknown; therefore, an in-silico study was performed to explore these issues. This study aims to recognize a possible small molecule as a racetam analogue by the computational program. Material and methods: Files were download in SDF format; 3D structures of about 2500 racetam and racetam like ligands, were downloaded from the ZINC database in structure-data file (SDF) format. PyMol version 1 and then Open Babel (version 2.3.1) were used to convert SDF format to PDB. The crystal structure of the Synaptic vesicle protein 2A (SV2A) was downloaded as a PDB file from a website related to protein data bank (http://www.rcsb.org) with PDB ID: 4v11. Water molecules in the crystal structure were removed. RMSD cut off 0.30 ˚A was applied during minimization. There are many methods for molecular docking that Each has its own mechanism with Different methods, equations and results. Molegro Virtual Docker (MVD) 2013.6.0.1 was used for docking study. The procedure of docking was done automatically by codes and scripts written in-house. The ADME (i.e., absorption, distribution, metabolism and excretion) and toxicity prediction of selected racetam derivatives were performed by Swiss database and OSIRIS Property Explorer Osiris property explorer software that available at http://www.organic-chemistry.org/prog/peo/. Results: 22 known racetams were selected and with the help of a zinc database, compounds with have at least 40% Similarity were download in SDF format. After selecting and downloading all Desired ligands, 2464 ligands saved. 28 Compounds was identified based on their affinity to receptor: 16 compounds were found by AutoDock Vina and 12 molecules were identified by Molegro Virtual Docker. Top 10 of them was selected and their pharmacokinetic (such as: absorption, distribution, metabolism and elimination) and also their toxicity were evaluated. best compound was chosen. Discussion: ZINC000408972527, a Phenyl piracetam derivative, has high affinity to SV2A with BBB permeability and without mutagenicity, tumorigenicity and irritancy effect and finally without has been P-gp substrate with good score of Lipinski and synthetic accessibility. Conclusions: In this study About 2500 compounds were used with help of ZINC database and we identified 26 novel compounds with the highest score from molegro virtual docker and AutoDock vina software. after selecting these Chemical structures, ADME and toxicity and other parameters related to medicines chemical structures was evaluated and 1 compound was identified as best compound for in vitro and in vivo studies.

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## Synthesis of phloroglucinol chalcone derivatives as potential anti-bacterial agents

*Fatemeh Najafi [1], Shaya Mokhtari[2,3], Farzad Kobarfard[*3,4]*

[1]Department of Medicinal Chemistry, School of Pharmacy, Islamic Azad University of Medical sciences, Islamic Azad University, Tehran, Iran.

[2] Central Research Laboratories, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[3]Phytochemistry Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[4]Department of Medicinal Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Corresponding author: Fatemeh Najafi

Corresponding author Email: miss.fatemeh73@gmail.com

Methicillin-resistant Staphylococcus aureus (MRSA) is a potentially life-threatening pathogen that has increased the need for new antibiotics for both hospital-acquired and community-acquired bacterial infections.Chalcones are products of the reaction between aromatic ketone and enones and they are the central core for a variety of important biologically active compounds. The bacteriocidal effects of chalcones are related to the ability of the unsaturated alpha and beta ketone susceptible to be attacked by a nucleophile.Phloroglucinol was converted to acetylphloroglucinol using a friedel crafts reaction with acetyl chloride. The methylketone thus obtained was reacted with aromatic aldehydes to obtain the desired chalcones of phloroglucinol.In this study a group of new chalcone derivatives of phloroglucinol was synthesized and purified. The compounds structures were confirmed using IR, MASS and NMR spectra. Anti bacterial activity of the synthesized compounds was evaluated against a group of gram negative and gram positive bacteria as well as meticillin resistant staphylococcus aureus (MRSA). Some of the compounds showed promissing activities against MRSA as one of the challenging pathogen in today`s medicine.

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## Design, Synthesis and In Vitro Evaluation of Acetamide Derivatives Incorporating Oxoindolin Hydrazine Carbothioamide Moiety as Potential Tyrosinase Inhibitors

*Reyhaneh Saburian[1], Manan Hajimahmoudi[2], Mohammad Mahdavi[3]*

[1]Department of Drug and Food Control, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

[2]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Mohammad Mahdavi

Corresponding author Email: momahdavi@tums.ac.ir

Introduction: Tyrosinase (EC1.14.18.1) (also known as TYR, monophenol and polyphenol oxidase) is a type-III coppercontaining metalloenzyme that have a key role in melanin synthesis in wide range of organisms and microorganisms, from bacteria to mammals. TYR enzyme take part in the melanin biosynthesis pathway, Initially, the hydroxylation of L-tyrosine to 3,4-dihydroxy-L-phenylalanine (L- DOPA) and in the second step, the oxidization of L-DOPA to dopaquinone catalyze by tyrosinase1. Hyperpigmentation including senile lentigines, melasma, and freckles in human skin

are disorder that may occur by an excess production of melanin and increase of tyrosinase activity. In addition, tyrosinase has a crucial role in enzymatic browning of fruits and vegetables via oxidation of phenolic compounds that leads deteriorating food during the postharvest and handling processes2. Therefore, the discovery and development of novel tyrosinase inhibitors in various applications of medicine, cosmetics and food industries have great values.Material and methods: A series of oxoindolin hydrazine carbothioamide bearing acetamide derivatives were synthesized and evaluated for their tyrosinase inhibitory. The inhibitory activities of the Carbamothioyl hydrazono-2-oxoindoline acetamide compounds were measured on mushroom tyrosinase enzyme according to the literature protocol3. The most potent compound 7m was selected to investigate the mechanism of inhibition type on mushroom tyrosinase.Results: According to tyrosinase inhibition results, all synthesized compounds exhibited moderate to potent tyrosinase inhibitory activity with IC50 values ranging between 0.08 and 3.88 µM. Among tested compounds, analog 7m, containing the 2-methyl-4-nitrophenyl on acetamide moiety displayed superior tyrosinase inhibition at IC50 value=0.80 µM. Discussion: Structure activity relationship studies indicated that substations at 2- position of acetamide moiety maybe a key factor in improving the tyrosinase inhibitory activity. The kinetic analysis of 7m was also presented a mixed-type inhibition for tyrosinase. Furthermore, molecular modeling study showed the ability of 7m for favorable interaction with critical Histidine residue within TYR enzyme active site. Overall, the results suggest that compound 7m could be considered for the development of potent inhibitor of tyrosinase.Conclusion: In conclusion, molecular hybrid design and fragment based strategies were used to design a novel series of TYR inhibitors. In this study, oxoindolin hydrazine carbothioamide scaffold bearing different acetamide moiety were designed according to the isatin backbone, thiosemicarbazid and acetamide derivatives that reported in the previous studies as potent tyrosinase inhibitors. The results showed that all of the synthesized compounds possess high tyrosinase inhibitory activities with IC50 values less than kojic acid as positive control (IC50 = 36 µM). 7m derivative containing a methyl as a small electron-donating group on the 2rd position and nitro on the 4th position of the acetamide moeity showed a promising antityrosinase activity with IC50 = 0.80 µM and the kinetic analysis revealed its competitive inhibition mode of action. Consequently, compound 7a-m could be a promising lead introduce in the field of effective tyrosinase inhibitors discovery, and further development towards the cosmetics, medicine, or food industries.

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## Efficacy Comparison of TAT Peptide-Functionalized PEGylated Liposomal Doxorubicin in C26 and B16F0 Tumor Mice Models.

*Farjad Zarazvand[1], Mohammad Mashreghi[2], and Niloofar Zonoubi[3]*

[1]Department of Pharmaceutical Nanotechnology, Faculty of pharmacy, Tehran university of medical sciences, Tehran, Iran

[2]Department of Pharmaceutical Nanotechnology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[3]Department of pharmacognosy, Faculty of pharmacy, Tehran university of medical sciences, Tehran, Iran

Corresponding author: Mahmoud Reza Jafari

Corresponding author Email: jafarimr@mums.ac.ir

This study aimed to evaluate the antitumor activity of PEGylated liposomal doxorubicin (Dox) functionalized with TAT peptide through PEG1000 while the surface of the liposome is covered by PEG2000 molecule. The size (nm) of liposomal formulations ranged from 90 to 140 nm, and all formulations had a negative zeta potential. The in vitro cellular uptake and cytotoxicity effects of formulations were investigated on C26 and B16F0 cell lines. Biodistribution and antitumor activity of formulations were investigated on BALB/c and C57BL/6 mice bearing C26 and B16F0 tumor models, respectively. In vitro and results on the C26 cell line indicated the higher efficacy of 100-ligand formulation, while in the case of B16F0 cell line 400-ligand formulation was the most efficient formulation. Since the TAT-peptide enters the cell through heparan sulfate proteoglycans, the difference in results may be due to the differences in expression levels and the intraspecies distribution between proteoglycans. Altogether our data indicate that surface-functionalization of liposome with TAT peptide via PEG1000 improves its antitumor efficacy and merit future considerations.

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## The place of transparency against corruption in the health system

*[1]Armin Rezaee shahrabi*

[1]Faculty of Pharmacy, Damghan Azad University of Medical Sciences , Damghan , Iran

Corresponding author: Armin Rezaee shahrabi

Corresponding author Email: arminre824@gmail.com

Introduction: Corruption has a long history in the life of mankind. Specifically, corruption in the health system has been important due to its tension with the health of the people. Eliminating corruption from societies facilitates overcoming the requirements of each society via the lowest costs and least supplements. Therefore, it seems necessary to study corruption and ways to fight it. Examining the roots of corruption in the health system and therefore possible and practical ways to combat it was this literature's ideal. Material and methods: This research is a descriptive-analytical one that has been done in two stages. In the first stage, a comprehensive definition of corruption in the health system and the reasons for its occurrence has been provided, then in the second stage, transparency and its effects on corruption have been discussed. For the first stage, articles related to corruption and its types with "corruption, corruption in the health sector, corruption and corruption in the health system" keywords, were collected and entered into the research based on their abstracts. Then in the second stage, keywords like "transparency, democracy, accountability, comparative politics and good governance were discussed" have been studied to examine the transparency in the health system, its possible effects, and factors improving the effect of transparency to analyze the impact of transparency in the fight against corruption. Results: This study indicates that the most important factors underlying corruption are divided as follows: monopoly, authority, lack of accountability, lack of voice of citizens, lack of transparency and defects in the rule of law. On the other hand, studies show that in order to fight corruption, tools such as good governance can be used in the fight against corruption with a focus on the rule of law, transparency and accountability.Conclusion: Corruption is one of the most important challenges of human societies. One of the most derivative types of corruption is administrative corruption, which is doubly vital in the health care system due to its involvement with public health. The results of this study show that corruption in the health system can be affected by the performance of regulatory, paying, providing, consumer and supplier organizations or even their relationships with each other.Transparency is found as a very practical way to fight corruption. Transparency can be classified into two types: agent-controlled and non-agent-controlled. Discussion: Transparency is not enough to fight corruption and must be accompanied by public awareness. Education, media literacy, and democracy are some of the most important factors that affect the impact of transparency on corruption. Moreover, the effect of education and level of education and newspaper circulation on

transparency and its effect on corruption indicates that if the public awareness perspective is short, the effect of transparency on corruption will be insufficient.

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## Investigating The Effect of Some Minerals and Vitamin Supplementation on Improvement of The Situation of Hospitalized Patient with COVID-19

*Zeinab khoramshahi[1], Farzan lotfi[1] , Habib Ghaznavi[2], Omolbanin Shahraki[2,3], Jafar Shahraki[4]**

[1]Student Research Committee, Zabol University of Medical Sciences, Zabol. Iran

[2]Pharmacology Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.

[3]Cellular and Molecular Research Center, Resistant Tuberculosis Institute, Zahedan University of Medical Sciences, Zahedan, Iran

[4]*Department of Pharmacology and Toxicology, Faculty of Pharmacy, Zabol University of Medical Sciences , Zabol , Iran

Corresponding author: Jafar Shahraki

Corresponding author Email: jafar.shahraki@gmail.com

Introduction: Taking into the account that during a pandemic like the current SARS-CoV-2 outbreak (started from March 2019), a worldwide vaccination is a really time demanding process; supplementation could be considered as a potential cheap and available preventive or even a cure agent for recovery of COVID-19 patients. Related studies indicated that vitamin C plays a significant role in promoting immune function due to its effects on various immune. vitamin D is assumed to be important in the regulation of the inflammatory cytokine response. vitamin B, by reducing the pro-inflammatory cytokine levels, could improve respiratory function and thus reduce hypercoagulability, also it could promote endothelial structural integrity. zinc is a trace mineral that has been reported to inhibit viral replication and attachment to the nasopharyngeal mucous. Administration of omega-3 can decrease inflammatory mediators and also prevent cytokine storms. This study aimed on investigating the relationship between taking the supplements such as vitamin D, vitamin C, calcium citrate, omega 3, thiamine, B complex and zinc, and the rate of mortality in COVID-19 patients who referred to Zabol Respiratory Hospital.Material and methods: Our population study was among coronavirus patients, hospitalized in Zabol Respiratory Hospital, from the time of the epidemic to the end of February 2021. All information received from the HIS (Hospital Information System) of Zabol Respiratory Hospital including age, gender, underlying disease, underlying factors, duration of hospitalization, clinical symptoms on arrival, radiological information, supportive measures and medication during the length of hospital stay. Which has been studied between the improved and dead groups by analytical and descriptive methods. Utilized instruments for both groups were demographic information questionnaire.Results: From whole 848 evaluated patients, there were 371(43.75%) female and 477(56.25%) male. According to the results of data analysis, taking the studied supplements, was associated with a reduced risk of mortality.

Vitamin C: OR=0.13, 95%CI (0.09 , 0.21). P value= <0.001

Vitamin D: OR=0.11, 95%CI (0.08 , 0.17) . P value=<0.001

Thiamine: OR=0.07 , 95%CI (0.01 , 0.58) . P value=0.013

Omega 3: OR=0.25, 95%CI (0.13 , 0.49). P value=<0.001

Calcium citrate: OR= 0.28, 95%CI (0.15 , 0.53) . P value= <0.001

B complex: OR=0.50, 95%CI (0.34 , 0.73) . P value=<0.001

Zinc: OR=0.19 , 95%CI (0.11 , 0.32) . P value=<0.001

Discussion: We could assert that consuming the studied supplementations including vitamin C, vitamin D, thiamine, omega 3, calcium citrate, B complex, zinc respectively 0/13 , 0/11, 0/07, 0/25, 0/28, 0/ 50, 0/19 could increase the chance survival of patients during COVID-19 pandemic.Conclusions: Thanks to strengthening the immune system, taking mineral supplements and vitamins could be suggested to have a great positive effect not only on decreasing the chance of succumbing by COVID-19 within the pandemic.

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## Evaluation of neuroprotective effects of hesperidin on brain necrosis and spatial memory deficit in acute CO poisoning in male rats

*Zahra Dadrezaei[1], Mahmood Hashemzaei[2], Kaveh Tabrizian[3], Gholamreza Bagheri[4]*

[1]Department of Toxicology and Pharmacology, School of Pharmacy, Zabol University of Medical sciences, Zabol, Iran

Corresponding author: Zahra Dadrezaei

Corresponding author Email: zahradrezaei@gmail.com

Background: Carbon monoxide poisoning is the third leading cause of death from poisoning in the world. Carbon monoxide disrupts the delivery of oxygen to tissues and quickly disrupts the brain. Hesperidin has neuroprotective effects and reduces oxidative stress and apoptosis in nerve cells. this study aimed to evaluate the neuroprotection of Hesperidin in acute carbon monoxide poisoning and its influence on spatial memory and cerebral necrosis in rats.Methods: Thirty adult male rats were divided into five groups: control group, CO + DMSO receptor group, and CO + Hesperidin receptor groups (in three doses of 25 mg / kg, 50 mg / kg and 100 mg / kg). Mice in all groups except the control group were exposed to 1000 ppm CO for 40 minutes and then exposed to 3000 ppm CO for 20 minutes. After receiving CO, Hesperidin was injected intraperitoneally to mice in the CO + Hesperidin receptor groups for five consecutive days. The CO + DMSO receptor group also received DMSO and normal saline. One day after the poisoning, the Morris water maze test began. In this test, each group was given 60 seconds to find the platform. The escape latency and traveled distance parameters were checked. Time spent in the target quadrant parameter was also examined in the probe test. Hematoxylin and Eosin staining was performed to examine structural changes in the brain after poisoning.Results: Hesperidin leads to a significant decrease in escape latency ($P<0.01$) and traveled distance ($P<0.01$) and increase in time spent in the target quadrant. HE staining showed that Hesperidin promotes necrosis recovery.Conclusion: Hesperidin improves impaired spatial memory and improves cerebral necrosis in rats by carbon monoxide.

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## Preparation and characterization of nanostructured lipid carriers containing Hesperidin and evaluation of the release via cell diffusion method

*Mahdiye Dehghan tanha[1], Shima Jafarinasab [1],Farzan Lotfi[1], Sara Daneshmand [*]*

[1]Faculty of Pharmacy, Zabol University of Medical Sciences, Zabol, Iran

Corresponding author: Sara Daneshmand

Corresponding author Email: sdmehrpooya@gmail.com

Introduction: Hesperidin is a natural flavonoid found mainly in citrus with valuable pharmacological properties. Hesperidin is insoluble in water and has low solubility in bio-solvent. Low solubility is the main reason for the low bioavailability of this flavonoid (1). The main purpose of this study was to investigate the potential of lipid nanoparticles for topical drug delivery of hesperidin. Nanostructured lipid carriers (NLCs) provide a controlled drug release and an increase in chemical stability of the incorporated drugs. Moreover, they are safe carriers which can be produced easily in a large scale.Material and methods: NLCs were prepared by hot homogenizer and Ultra sound method. 26 formulations were designed using Design Expert software. differential scanning calorimetry (DSC) and IR spectroscopy tests were performed and also encapsulation percentage was determined and drug release was performed by Franz Diffusion Cell method in mouse skin (2).Results: Based on DLS data, and via Design Expert software the optimum formulation was selected. Morphological tests on the selected formulation showed that it was spherical. Encapsulation percentage was 95.47%.The formulation with size of 165.7 nm, PDI of 0.223 and zeta potential of -22.3 mV was selected as the final formulation. The in vitro permeation studies exhibited that HESP-NLC could significantly enhance cutaneous uptake of HESP and skin targeting.Discussion: These data revealed that the prepared nano formulations exhibited sustained release compared with the HESP-cream. There was a significant drug diffusion difference between the HESP-cream and the HESP-NLC over the 24 h period. Results showed that there is an initial burst release in the first 30 minutes and a sustained release over 24 hours. The reason for the burst release is the presence of free drug molecules on the surface of nanoparticles. Considering the hydrophobic and solid nature of the nanocarriers, resulted sustain release of HESP. Therefore, Two-stage release for topical administration is a desirable phenomenon. The HESP-loaded NLCs achieved higher localization of HESP in the skin than the HESP-cream. Therefore, the lipoidal nature of NLCs, has a beneficial drug-localizing effect that increases drug penetration and localization to the skin.The main factors that increase skin delivery by NLCs are the large surface area and the occlusive effect of nanoparticles. Therefore, cutaneous diseases could be successfully treated by localized release of HESP and more accumulation may enhance the controlled release of the HESP.Conclusions: It is found that the NLCs system indicates the possibility of increasing drug loading and higher improvement in topical delivery of Hesperidin. Overall, the results confirm that NLCs can be suitable carriers for hesperidin as a natural product.

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## Targeting evaluation of nanostructured lipid carriers containing caffeine and argan oil to the hair follicles of mice

*Asra dadkani [1], Elahe Mir[1], Sara Daneshmand [1*]*

[1]Faculty of Pharmacy, Zabol University of Medical Sciences, Zabol, Iran

Corresponding author: Sara Daneshmand,

Corresponding author Email: sdmehrpooya@gmail.com

Introduction: Hair loss is one of the problems that many people in the world face at some point in their lives; in addition, it can cause many other diseases. The role of androgens in causing androgenetic hair loss has been known for more than 50 years. The aim of this study was to evaluate the efficacy of nanostructured lipid carriers (NLCs) containing caffeine and argan oil in drug delivery to hair follicles in mice.Material and methods: In this study, lipid nanoparticles containing caffeine and argan oil were used. The formulation was prepared previously via hot homogenization and ultra sound method with size of 256.2 nm, PDI of 0.225 and zeta potential of -25.4 mV and encapsulation percentage was 96%. the experiment was performed on mice using stripping and slide test. The penetration rate of the formulation was determined using a spectrophotometric device.Results: According to the results of the differential striping method, the amount of caffeine-containing NLCs in the hair follicle is still found to be significant after six days ($p<0.001$), while the amount of caffeine solution in the hair follicle drops sharply on the third and sixth day.Discussion: Nanoparticles penetrate well into hair follicles and reach deeper structures where they can re stored for several days.Lipid nanoparticles can deliver the encapsulated drug to the desired location and are in fact a targeted drug carrier and are found in hair follicles even after 24 hours of use.Hair follicles are a good reservoir for medicines , allowing the drug to be delivered slowly and reducing the frequency of use. Caffeine penetrates through the follicular pathway more effectively than the skin pathway.Caffeine solution is limited to the stratum corneum and does not have significant durability over time and also does not have high penetration into the hair follicle, but NLCs containing caffeine due to the particle size in the form of nanoparticles and pumping phenomenon gradually penetrates into the hair follicle. It has a long shelf life in hair follicles and is present in significant amounts on the third and sixth days.In this study, the time of application of each substance on the back of the mouse was 2 minutes with the application of massage. The massages were performed with the fingertip with almost the same pressure on the back of the mouse.Conclusions: Nanostructured lipid carriers specifically increase the penetration of caffeine in to the hair follicle and remains in the hair follicle for a long time and serve as a reservoir for slow drug release.

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## In silico studies for Identification of Potent Angiotensin Converting Enzyme 2 (ACE2) Inhibitors to Counteracts COVID-19

*Arash Iliamehr*[1], *Hamed Bahrami*[2], and *Hafezeh Salehabadi**[1]

[1]Department of Medicinal Chemistry, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

[2]Chemistry Department, University of Zanjan, Zanjan 45371-38791, Iran

Corresponding author: Hafezeh Salehabadi

Corresponding author Email: hsalehabadi@zums.ac.ir

Introduction: Coronavirus disease 2019 (COVID-19) was first appeared in Wuhan, China. Then was spread all over the world and led to more than 2 million of deaths globally since December 2019 (1). COVID-19 leads to different symptoms including fever, dry couch, dyspnea, and respiratory syndrome. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the virus causing the COVID-19 disease, is a beta coronavirus. Beta coronaviruses contain a large family of single-stranded RNA viruses that infect a wide variety of avian and mammalian hosts (2). Recent studies showed that SARS-CoV-2 begins its life cycle by binds to the angiotensin-converting enzyme 2 (ACE2) receptor to entry the host cells (3). To date there are no FDA approved drugs targeting SARS-CoV-2. Therefore, researches targeting ACE2 is vital to improve

life quality of human and combat to COVID-19. Computer-aided drug design (CADD) have developed during the last decade as a substantial tool to help and supplement experimental information (4). Application of bioinformatics could help to rational drug design and identification of new potent lead compounds. Here, a hybrid strategy including docking and pharmacophore based virtual screening was used to identify new ACE2 inhibitors, as potential compound to counteract COVID-19.Material and methods: The Crystal structure of Angiotensin Converting Enzyme-2 (ACE2), with the PDB ID of 1R4L and resolution of 3.00Å was achieved from Protein Data Bank (www.rcsb.org). An appropriate pharmacophore model was generated via Ligand Scout 3.12 based on most critical area on the ACE2 active pocket. The pharmacophore model as a filter was applied for virtual screening of ZINC database (over 35 million purchasable compounds). Molecular docking studies have been used to follow the collected compounds from ZINC database.Results and discussion: The crucial interactions between the selected compounds from ZINC database and ACE2 active site were precisely investigated in detail by molecular docking studies. Finally, 6 ligands were selected by limiting on the binding free energies less than -10 kcal.mol$^{-1}$ and having an appropriate orientation in active pocket.Conclusions: Herein computational approaches were used to identify new compounds with inhibitory effects on ACE2. Structure - based virtual screening an integrated database followed by docking studies was employed in order to find novel ACE2 inhibitors to counteract COVID-19. Most active compound with appropriate position in active pocket were identified. These compounds can be used and optimized for future drug development.

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# Injectable Photothermal Hydrogel with Antibacterial Activity for Wound Healing Acceleration

*Vahideh Nosrati Siahmazgi[1], Samin Abbaszadeh[2], Kian musaei[1], Mohammad-Reza Eskandari[3] and Mohammad-Ali Shahbazi[1,4]*

Department of Pharmaceutical Biomaterials, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

Department of Pharmacology, School of medicine, Zanjan University of Medical Sciences, Zanjan, Iran

Department of Pharmacology and Toxicology, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

Department of Biomedical Engineering, University Medical Center Groningen, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, Netherlands

Corresponding author: Mohammad-Ali Shahbazi

Corresponding author Email: m.a.shahbazi@umcg.nl

Introduction: Although the wound healing process occurs naturally in the body, full-thickness wounds are usually hard to heal. Moreover, bacterial infection delays this process. Therefore, efficient strategies to simultaneously improve the wound healing and prevent bacterial infection are needed. Among different biomaterials, injectable hydrogels have attracted attention of researchers due to similarity to extracellular matrix, maintaining a moist environment, and ability to fill the irregular shape of the wounds to act as a barrier to hinder bacterial infection. In this study, a multifunctional hydrogel composed of poly methyl vinyl ether-alt-maleic acid (PMVE-MA), allantoin, and copper oxide (CuO) nanosheets was synthesized. The CuO nanosheets possess controllable photothermal property under near-infrared (NIR) light irradiation at 808 nm. Allantoin as a metabolite isolated of the comfrey plant improves skin regeneration through reducing inflammation, triggering cell migration and enhancing the activity of keratinocytes. Material and methods: The hydrogel was successfully prepared through the chemical crosslinking between PMVE-MA and gelatin incorporated with CuO and allantoin (PGCA hydrogel). Characterization tests were performed to confirm the structure of the hydrogel. The injectability and the antibacterial activity of the hydrogel were investigated. Moreover, to determine the photothermal effects of the hydrogels, different concentrations of CuO were irradiated by NIR light with a power density of 1W/cm2 over a period of 10 min.Results: The Fourier transform infrared spectroscopy and X-ray Diffraction analysis results confirmed the successful preparation of the hydrogel. Swelling results showed a maximum of water absorption ≈400% of the initial weight after 24 h, which is beneficial to absorb the wound drainage. As showed in the rheological analysis, the viscosity of PGCA hydrogel decreased from 12.4 to ~2 Pa·s with the shear rate changing from 10 to 100 1/s, showing the shear-thinning behavior of the hydrogel and confirming the suitable injectability. The in vitro photothermal performance exhibited that increase in temperature of the hydrogel depends on the concentration of the nanomaterials incorporated in the hydrogel. The surface temperature increased to 44 °C (200 µg/mL of CuO nanosheets) under NIR irradiation (1W/cm2, 10 min) which is the required temperature to promote wound healing and also eliminate bacteria, displaying the excellent photothermal performance of PGCA hydrogel. Moreover, the hydrogel exhibited excellent in vitro antibacterial efficacy of 99.9% against both staphylococcus aureous and Escherichia coli.Discussion: The aim of this study was to employ photothermal therapy for skin regeneration. To this end, an injectable hydrogel integrating CuO and allantoin was developed. The results showed an excellent and controllable photothermal effect of the hydrogel. The bacteria could be effectively killed through NIR-irradiation as well as the inherent antibacterial activity of CuO. Moreover, CuO, in contribution with allantoin, could support proliferation, migration and angiogenesis of cells that makes this biomaterial an attractive candidate for bacterial infection-induced chronic skin wounds.Conclusions: A multifunctional hydrogel with CuO nanosheets and allantoin was prepared. The hydrogel indicated high swelling ratio, suitable injectability, excellent photothermal therapy, and antibacterial activity. All these results meet the requirement of a proper hydrogel for skin regeneration.

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# Multifunctional hydrogel for acceleration of wound healing based on controlled- temperature photothermal therapy

*Kiyan Musaei[1], Samin Abbaszadeh[2], Vahideh Nosrati Siahmazgi[1], Mohammad-Reza Eskandari[3], Aziz Maleki[1] and Mohammad-Ali Shahbazi[1,4]*

[1]Department of Pharmaceutical Biomaterials, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

[2]Department of Pharmacology, School of medicine, Zanjan University of Medical Sciences, Zanjan, Iran

[3]Department of Pharmacology and Toxicology, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

[4]Department of Biomedical Engineering, University Medical Center Groningen, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, Netherlands

Corresponding author: Mohammad-Ali Shahbazi

Corresponding author Email: m.a.shahbazi@umcg.nl

Introduction: Treatment of full-thickness wounds, as a major clinical challenge has caused a tremendous economic burden worldwide. Therefore, an efficient new strategy is a high demand that could promote

wound healing. Herein, we report a photothermal therapy (PTT) assisted antibacterial system utilizing hyaluronic acid-coated Bismuth nanoparticles (BiH). Moreover, allantoin (Alla) as a hydrophilic drug derived from plants could stimulate proliferation and cell migration leads to acceleration of wound closure.Material and methods: Gel-BiH-Alla hydrogel was prepared through abundant metal coordination among the functional groups of Farsi gum and ferric ions containing allantoin and BiH. Characterization tests were performed to confirm the structure of the hydrogel. The photothermal effect of the hydrogel was assessed under near-infrared (NIR) light irradiation at 808 nm with a power density of 1 W/cm2 for 10 min. Moreover, antibacterial activity, blood clotting test, and *in vivo* toxicity of the hydrogel were evaluated. Results: Scanning electron microscopy and Fourier transform infrared spectroscopy results confirmed successful synthesize of BiH and preparation of the hydrogel. The photothermal evaluation of the Gel-BiH-Alla showed an increment of temperature up to 43 ˚C under NIR irradiation that could promote wound healing. In addition, the hydrogel showed a desirable antibacterial activity due to the bacterial killing effect of BiH and allantoin. The hematoxylin and eosin staining of the main organs of rats showed no organ damage, like necrosis and inflammation. Moreover, the blood clotting test showed a significant decrease in hemostatic time and blood loss in comparison to the control group.Discussion: In this study, a hydrogel containing allantoin and BiH was used to accelerate the wound healing process. This hydrogel provides antibacterial activity as well as activating hemostasis cascade. In addition, the prepared hydrogel under NIR laser irradiation can significantly accelerate skin tissue regeneration. Conclusions: This novel multifunctional hydrogel demonstrates excellent hemostatic performance, antimicrobial activity, and photothermal-induced skin regeneration, which has great application potential as a promising wound healing material in clinical use.

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## کلونینگ و بیان سازه ژنی حاوی PTPRZ1و TNC در وکتور بیانی pET-28a و میزبان بیانی BL21 E. coli

*Maedeh Parchianloo[1], Mohammadjavad Motamedi[2],Mahmood Gharbavi[3], Ali Sharafi[4]*

[1]School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

[2]departement of molecular biology and genetic engineering,stem cell research center,tehran,iran

Corresponding author: Maedeh Parchianloo

Corresponding author Email: mparchianloo@gmail.com

گلیوبلاستوما از جمله تومورهای مغزی می باشد که بطور عمده در سلول های گلیال ایجاد می شوند. سلول ها این تومور به دلیل ماهیت تهاجمی و منتشر شونده در فضای جمجمه، از جمله تومورهای بدخیم مغزی می باشند. که درمان این سرطان تقریبا غیر ممکن می باشد.در این بین استفاده از پروتئین های سطحی به عنوان عوامل آنتی ژنیک، جهت تولید یک کاندید واکسن نوترکیب بر علیه سرطان گلیوبلاستوما افق جدیدی جهت درمان این سرطان را باز می کند که می توانند به عنوان عوامل آنتی ژنیک جهت درمان و حتی پیش گیری از این سرطان استفاده شوند.انتظار می رود که سیستم ایمنی بدن به واکسن حاوی آنتی ژن یا آنتی ژن هائی که در سلول های توموری هدف ترشح می شوند، پاسخ داده و بر علیه این تومور واکنش نشان دهد .در این مطالعه از واکسن کایمریک که حاوی دو آنتی ژن موثر بر سرطان گلیوبلاستوما استفاده می شود. این پروتئین آنتی ژنیک می تواند جهت تقویت و تحریک سیستم ایمنی بدن بر علیه سلول های تومور گلیوبلاستوما و در نهایت درمان این تومور استفاده شود.با توجه به اینکه که بیان ژنهایPTPRZ1 و TNC در سلول های سرطانی مغز یا گلیوما افزایش می یابد، بنابراین این ژنها در مطالعه حاضر مورد بررسی بیوانفورماتیکی، طراحی سازه ژنی و بیان در میزبان پروکاریوتی قرار گرفتند تا محصول حاصل به عنوان یک کاندید ساخت واکسن علیه گلیوما مورد ارزیابی های بعدی در مدل حیوانی قرار گیرد.ابتدا توالی های اسید آمینه هر یک از پروتئین های-TNC,PTPRZ1را با استفاده از بانک ژنی NCBI به دست آورده و آن را به فرمت FASTA ذخیره می کنیم. سپس جهت بررسی ساختار پروتئین ، به کمک سایت UniProt به بررسی توالی های اسید آمینه پرداخته و آن قسمت از توالی ها که سایت های قابل تغییر نداشته باشند می توان جهت پیش بینی میزان آنتی ژنیسیته آنها انتخاب نمود. بیان کاندید واکسن نوترکیب گلیوبلاستوما حاوی بخشهایی از پروتئینهای سطح سلولیPTPRZ1 و TNC در این تحقیق سازه ژنی دوگانه با لینکر A (EAAAK) 3A طراحی و جهت سنتز فرستاده شد.این سازه ژنی نوترکیب در پلازمید بیانی pET28a و داخل سویه بیانیBL21 و نیز سویه کلونینگ TOP10 کلون گردید. سپس به کمک پرایمر های اختصاصی کلونی PCR انجام شد .همچنین تائید مولکولی با هضم آنزیمی پلازمید صورت گرفت.به منظور القأ بیان پس از انتقال وکتورهای نوترکیب به باکتری E.coli (DE3)، از غلظتهای مختلفی از IPTG استفاده شد. به منظور بررسی بیان پروتئین، استخراج پروتئین صورت گرفت و ژل SDS-PAGE استفاده شد.پروتئین نوترکیب در حدود ... KDa را نشان داد .تخلیص پروتئین نوترکیب بوسیله¬ ستون کروماتوگرافی میل ترکیبیNi-NTA انجام شد.جهت اندازه گیری مقدار پروتئین ها روش برادفورد انجام شد .تأیید پروتئین نوترکیب بیان شده نیز با کمک روش وسترن بلاتینگ با آنتی هیستیدین با موفقیت صورت گرفت.(بیان موفق کاندید واکسن نوترکیب آنتی ژنیک دو گانه گلیوبلاستوما با وکتور بیانی pET28a تحت پروموتر فاژT7 در میزبان باکتریاییBL21 E. coli)

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## Expression of recombinant vaccine candidate for Glioblastoma contains parts of cell surface proteins of IL13R2a and TNC

*Erfan Behseresht[1], Mohammadjavad Motamedi[2], Mahmoud Gharbavi[3], Ali Sharafi[4]*

Department of Pharmaceutical Biotechnology, School of pharmacy, Zanjan university of medical sciences, Zanjan, Iran

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

Corresponding author: Erfan Behseresht

Corresponding email address: erfanbehseresht@gmail.com

Given that gene expression of IL13R2a and TNC in cells of Glioma increase, therefore these genes were subjected to bioinformatics analysis, gene construct design and expression in *E. coli* BL21 host as acandidate for introducing a recombinant vaccine against glioma to be evaluated in animal model. In this study dual gene structures with the linker of A(EAAK)3A designed and synthesized. This recombinant gene construct in expressive plasmid of pET28a and inside the expressive strain BL21 and also inside the cloning strain of *E. coli* TOP10 was cloned.Then,colony PCR and plasmid extraction and digestion was performed.In order to expression, after transformation of recombinant vectors to bacteria of *E.coli*BL21 (DE3) induction was used from different concentration of IPTG. In order to checking of protein expression, protein extraction was done and the gel of SDS-PAGE was used .The recombinant protein was showed about 42 KD. Purification of recombinant protein was performed by chromatographic column with Ni-NTA. For measurement of amount of protein, Bradford method was used . Finally, for confirmation of expressed recombinant protein, Western blotting method with anti histidine successfully performed.

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## Comparing the cost-effectiveness of Iranian Sevelamer carbonate (Sevelagen®) with liecensed brand of Sevelamer carbonate (Genthon®) in patients with chronic kidney disease

*Seyed Shahab Shokri [1] Iman Karim Zadeh [2]*

[1]School of Pharmacy, Student research committee, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Department of Clinical Pharmacy, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Seyed Shahab Shokri

Corresponding email address: shahabbshk@gmail.com

Introduction: Men with CKD stages 3–5 and on dialysis (5D) have shown great increase in mortality and morbidity, which has been associated with hyperphosphatemia in many studies. Oral phosphate binders are commonly prescribed in order to achieve a lower serum phosphate level. A frequently used phosphate binder is called sevelamer which is generally in the form of either carbonate or hydrochloride. Sevelamer carbonate is found with different brands in Iranian pharmaceutical markets. In this study we determine the cost-effectiveness of Iranian sevelamer brand (Sevelagen®) and the licensed brand (Genthon®).Material and methods: This observational, cross-sectional study was performed during 4 months period from Mehr 1399 to Day 1399. A questionnaire was designed and it was composed of 4 parts including demographic characteristics of patients, plasma Level of Phosphate, Calcium, PTH in dialysis patients, The brand of sevelamer each patient is using and Cost-effectiveness of different sevelamer brands. Questionnaires were filled by a pharmacy student through face-to-face interviewing with patients in Namazi and Ibn Sina dialysis center, Shiraz. Data were analyzed by IBM Statistics SPSS® 20.Results: Data of 70 dialysis patients were collected during this period. 76.6% of patients whom used Genthon® achieved controlled range of Phosphate plasma level; (23.4% uncontrolled) while Those using Sevelagen® achieved 66.6% in controlled and 33.4% in uncontrolled range. 60% of patients on Genthon®, achieved the controlled range of Ca plasma level and 40% could not achieve the target level, while these statics were 63.8% and 36.2% for Sevelagen® respectively. 24.1% of Patients on Genthon® for at least one month, developed a desirable PTH plasma level but PTH plasma level was considered as uncontrolled in 75.9% of patients. While 22.2% of patients on Sevelagen® had a desirable PTH plasma level, and 77.8% of them were not under controlled.Discussion: As it can be seen, there is not any significant difference between using Genthon® and Sevelagen® in controlling Phosphate, Calcium and PTH plasma level. According to the prices, Genthon® is much more expensive than Sevelagen®. (each cap of Genthon® costs 27300 R, each cap of Sevelagen® costs 23400R). Conclusions: Due to heavy annual dialysis patients expenditures, it is necessary for health care politicians to revise or arrange the policies related to importing the medicine, physician prescribing and also therapeutic guidlines . It was resulted from the study that administrating Sevelagen® appears to have a better cost-effectiveness ratio than administrating Genthon®.

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## COVID-19 Vaccination in Immunocompromised Patients

*Shiva Rasekh [1, 2], Seyed Mohammad Iman Moezzi [1, 2], Sogand Amiri [1, 2], Ashkan Bagheri [2], Mojtaba Shafiekhani[3], Afsaneh Vazin [4], Manica Negahdaripour [2, 5*], Pouria Mosaddeghi [1,2]*

[1]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Shiraz Transplant Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[4]Clinical Pharmacy Department, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[5]Department of Pharmaceutical Biotechnology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
Corresponding author: Manica Negahdaripour
Corresponding author Email: negahdaripour@sums.ac.ir

Introduction: After outbreak of the COVID-19 pandemic, vaccinating the healthy population to prevent disease prevalence was mentioned as one of the main solutions. Thus, many pharmaceutical companies started developing vaccines with different structures, which could be categorized in four main groups: inactivated, protein subunit, RNA, and viral-vector vaccines. People with immunocompromising diseases could encounter difficulties in their immunization process by vaccines due to the malfunction of their immune system and using immunosuppressive drugs. Here, information regarding vaccination in immunocompromised patients would be discussed.Methods: Keywords "cancer", "hematopoietic stem cell transplantation", "solid organ transplant", "multiple sclerosis", "inflammatory bowel disease", and "rheumatologic disorders" combined with "vaccination", and "COVID-19 vaccine", were searched thoroughly based on the trials conducted so far and previous information about vaccinating these patients.Discussion: Studies suggest that patients with cancer and hematopoietic stem cell transplantation are at a higher risk of acquiring COVID-19 infection, thus vaccination is recommended. Vaccination is usually effective in creating adequate immune response; unless, the patient is under intensive chemotherapy. A six-month interval between plasma cell or lymphocyte−depleting therapies and vaccination is recommended to ensure maximum immunization. Trials indicate that the Pfizer-BioNTech vaccine showed proper immune response in these patients. Moreover, in patients with solid organ transplant due to the administration of immunosuppressive medication and underlying chronic diseases, weak immune response is anticipated. Thus, timing is extremely important to ensure maximum efficacy. The best time for vaccination is before transplantation or at least three months after transplantation. In patients with "multiple sclerosis", there is a risk of relapse and progression in case of COVID-19 infection; hence, vaccination is recommended, and fortunately there is no evidence of post vaccination relapse or progression in these patients. Discontinuing the disease-modifying therapies is not advised, but monitoring after vaccination is recommended to ensure satisfying immune responses. The effect of inflammatory bowel disease (IBD) on COVID-19 infection is controversial. However, vaccination is still recommended unless the patient is in a severe IBD flare period or in the need of hospitalization in which postponing the schedule is preferred. Vaccination is recommended when the intake of corticosteroids is at the lowest. In general, all types of vaccines are safe in IBD patients except for live-attenuated vaccines. Lastly, in patients with "rheumatologic diseases" due to the existence of underlying inflammation and the administration of immunomodulatory drugs, the risk of acquiring COVID-19 infection is increased. Moreover, there is a possibility of increased morbidity and mortality post infection. Thus, vaccination is recommend specifically using vaccines such as Pfizer-BioNTech and Oxford-AstraZeneca, which are considered safe in these patients. The best time for vaccination is during the quiescent state of the disease.Conclusions: In general, vaccination is recommended in all groups, but considering timing and the right interval between disease-modifying therapies and vaccination can ensure maximum efficacy and minimize the possibility of inadequate immune response. Although evidence is lacking due to omitting these groups from clinical trials, with the progress of vaccination, the pros and cons will be revealed in heterogeneous populations.

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## Design, synthesis and biological evaluation of tyrosinase inhibitors: *symmetrical azine* derivatives

*Somaye Karimian [1], Fatemeh Kazemi[1], Mehdi Khoshneviszadeh [1,2]*

[1]Department of Medicinal Chemistry, School of pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.
[2]Medicinal and Natural Products Chemistry Research Center, Shiraz University of Medical sciences, Shiraz, Iran.
Corresponding author: *Somaye Karimian*
Corresponding author Email: s_karimian@sums.ac.ir

A series of symmetrical azine derivatives containing substituted benzyl moieties were designed, synthesized and evaluated for their inhibitory activity against mushroom tyrosinase. The results showed that six compounds exhibited effective inhibitory activity with IC50 ranging from 7.3 µM to 62.6 µM and compounds 2,4-dihydroxy substitutions(3f) and 4-hydroxy-3-methoxy substitutions(3k) were the most potent tyrosinase inhibitor (IC50=7.3±1.15 and 12.9±.18 µM, respectively) and their inhibitory effects were comparable to kojic acid (IC50=20.24±2.28 µM). Kinetic study of compound 2,4-dihydroxy substitutions(3f) confirmed uncompetitive inhibitory activity towards tyrosinase indicating that it can bind to enzyme-substrate complex. Also, molecular docking analysis was performed to study the interactions and binding mode of the most potent compound 3f in the active site of tyrosinase. Consequently, compounds 2,4-dihydroxy substitutions(3f) and 4-hydroxy-3-methoxy substitutions(3k) could be introduced as a potent tyrosinase inhibitor that might be a promising candidate in the cosmetics, medicine and the food industry, and the development of such compounds may be of interest.

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## بررسی شیوع افسردگی و تداخلات دارویی در سالمندان دارای آرتروز مراجعه کننده به کلینیک طب فیزیکی و توانبخشی دانشگاه علوم پزشکی شیراز

*Seyed Mahdi Sadati[1],Laleh Mahmoudi[2], Hamidreza Farpor[3], Soha Azadi[4], Negar Mortazavi[5]*

[1]Clinical Pharmacy Department, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Physiology and medical Physics, Faculty of Medical Science, Shiraz University of Medical Sciences, Shiraz , Iran
Corresponding author: Laleh Mahmoudi
Corresponding author Email: mahmoudi_l@sums.ac.ir

افسردگی یکی از بیماری های شایع در سراسر جهان می باشد که منجر به ناتوانی فرد در زمینه های شخصی، اجتماعی و اقتصادی می شود و کیفیت زندگی فرد را به شدت تحت تاثیر قرار می دهد در افسردگی، انگیزه، حافظه و عادات حسی، دچار ناکارآمدی می شود و حتی در بعضی از افراد انگیزه های خودکشی نیز ایجاد می شود.استئوآرتریت، شایع ترین بیماری مفصلی است. این بیماری مفاصل سینویال را درگیر می کند که از لحاظ

بالینی با درد و محدودیت عملکرد شناخته می شود.شیوع استئوآرتریت به شدت با سن ارتباط دارد به گونه ای که در سنین قبل از چهل سال شایع نمی باشد و با افزایش سن، شیوع آن افزایش می یابد. اکثر افراد بالای 70 سال تغییرات پاتولوژیک استئوآرتریت در بعضی مفاصل دارند.(اگرچه بدون علامت باشند.) مسئله ی مهم دیگر شیوع بیماری افسردگی در جمعیت سالمند می باشد. این مطالعه بر روی 88 بیمار مبتلا به استئوآرتریت انجام گرفت و شیوع و شدت افسردگی آنها طبق پرسشنامه Hamilton سنجیده شد.جهت بررسی تداخلات دارویی از برنامه ی lexi interact استفاده شد.میزان شیوع افسردگی در سالمندان مبتلا به استئوآرتریت 85.22 درصد گزارش شد . یعنی از 88 نفر، 75 نفر مبتلا به افسردگی بودند.همچنین در بیماران سالمند مبتلا به استئوآرتریت زانو و ستون فقرات، شدت افسردگی نسبت به هر کدام به تنهایی به طور معناداری بالاتر بود. (میانگین نمره افسردگی در هر دو با هم 23.91±6.762 برای هردو با هم ، زانو به تنهایی 6.573±20.16 و ستون فقرات به تنهایی 20.07± 6.367) .نمره افسردگی پس از شروع درمان استئوآرتریت به طور معناداری بهبود یافته بود. (از 18.94±9.737 به 17.12±10.346 ) .همچنین در خانم های خانه دار، شیوع و شدت افسردگی به طور معناداری بالاتر بود شدت افسردگی و grade استوآرتریت زانو رابطه ای معکوس داشت. کسانی که داروهای NSAID مصرف می کردند، شدت و نمره افسردگی بالاتری داشتند. در 88 بیمار بررسی شده، 42 درصد در میان داروهاشان، تداخل C و D یافت شد که بیشترین نوع تداخل ، مربوط به آهن و داروهای قلبی بود.با توجه به شیوع بالای افسردگی در سالمندان مبتلا به استئوآرتریت که تشخیص هم داده نشده است، مداخلات بالینی بین متخصصان در حیطه مختلف را می طلبد و همچنین با توجه به میزان بالای تداخلات دارویی در آنها، لزوم وجود داروساز بالینی یا داروسازی که با بررسی ساده، بتواند از این تداخلات جلوگیری کند.

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## Evaluation of Antioxidant, Acetyl and Butyryl Cholinesterase Inhibitory Activity of Safoof-e-Nesian Polyherbal Formulation from Persian Medicine

*Sara Sanei[1], Ehsan Amir-Ardekani[2], Moein Mahmoudreza[3], Amirhossein Sakhteman[4], Hamidreza Adhami[5], Mohammad-Mehdi Zarshenas[6]*

[1]School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Mohammad-mehdi Zarshenas

Corresponding author Email: zarm@sums.ac.ir

Introduction: Alzheimer's is the most common type of dementia in humans. So far, the mechanism and pathophysiology of this disease have not been adequately elucidated. In this regard, one of the most important hypotheses is the cholinergic hypothesis. It claims excessive acetylcholinesterase enzyme activity reduces the amount of acetylcholine in the brain and causes dementia. Alzheimer's (Nesian in Ancient Persian) has been deeply investigated in Persian medicine. Various remedies have been recommended for prevention, treatment, and symptom management. One of the main prescribed polyherbal formulations is Safoof-e-Nesian. In this study, this formulation effect on acetylcholinesterase and butyrylcholinesterase and also its antioxidant effects are investigated.Material and methods: In this study, Safoof-e-Nesian (extracted from the Qarabadin-e-Azam) was used. Safoof-e-Nesian includes seven plants including cinnamon, ginger, frankincense, cloves, sage, sweet flag, and galingale. Methanolic and dichloromethane extracts of each ingredient and formulation were prepared. The prepared extracts were concentrated using a rotary apparatus. DPPH test was used to evaluate the antioxidant effect in four different concentrations from 6.25 mg/L to 3200 mg/L. Finally, after Standard enzymatic testing using tacrine, Safoof-e-Nesian formulation and ingredients extracts with different concentrations (1.5 mg/ml, 2.5 mg/ml, 5 mg/ml, and 10 mg/ml) were used to evaluate acetyl and butyrylcholinesterase inhibitory effects.Results and Discussion: IC50 of dichloromethane extract of formulation wast 669.0±3.38 µg/ml and 151.0±5.11 µg/ml for methanolic extract. The least IC50 of herbs dichloromethane extract was 51.4±1.4 µg/ml for cinnamon and in the methanolic extract was 13.0±1.03 µg/ml for the sweet flag. The highest Percentage of Inhibition of dichloromethane extracts on acetylcholinesterase enzyme is related to the 5mg/ml concentration of cinnamon with 63% inhibition. Also, its methanolic extract can inhibit acetylcholinesterase enzyme 93% at 2.5 mg/ml concentration. In case of butyrylcholinesterase enzyme inhibition sweet flag dichloromethane extract with 68% inhibition in 10mg/ml concentration and galingale methanolic extract with 82% enzyme inhibition in 10mg/ml concentration were know as most potent ingredients in each extract for acetylcholinesterase and butyrylcholinesterase. Safoof-e-Nesian formulation acetylcholinesterase inhibition was 42% and 65% for dichloromethane and methanolic extracts in 10mg/ml concentration, respectively. Also, formulation butyrylcholinesterase inhibition was 63% and 80% for dichloromethane and methanolic extracts in 10mg/ml concentration, respectively.Interestingly, most plants at 5 mg/ml have more Inhibition than other concentrations. In many studies, this issue has been considered. It has been shown that the relationship between the concentration of the extract and the Percentage of enzyme inhibition is not dose-dependent and can not be predicted. One of the reasons for this can be the presence of polyphenols in the plant as a chelating agent and enzyme inactivator.Conclusions: The results of the enzyme inhibitory effect showed that Safoof-e-Nesian could be considered as an enzyme inhibitor. Also, methanolic extracts showed a more substantial effect than dichloromethane extracts. It appears that the best anti-enzymatic effect of acetylcholinesterase was related to cinnamon and sage, and the best anti-enzymatic effect of butyrylcholinesterase was related to galingale, sweet flag, and clove that are responsible for this formulation anti-Alzheimer activity.

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## "Turmerones" Being Introduced as a New Marker for Turmeric Standardization

*Ala Mohagheghzadeh[1], Shohreh Alipour[2], Abdolali Mohagheghzadeh[3]*

[1]School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Department of Pharmaceuticals Quality Control, School of pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Department of Pharmacognosy and Traditional Pharmacy, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
Corresponding author: Abdolali Mohagheghzadeh
Corresponding author Email: Mohaghegh@sums.ac.ir

Introduction: Dried rhizomes of *Curcuma longa* L. are known as turmeric. Two major bioactive components of turmeric rhizomes are determined as Curcuminoids and Turmerones. Curcumin was the first molecule to be isolated from turmeric, thus researchers paid so much attention to it, as an active component. Turmerones, as neglected compounds, are responsible for the special taste and smell of turmeric. Both Curcuminoids and Turmerones have beneficial effects on men's health. Considering the fact that Curcuminoids and Turmerones are unstable to certain conditions and that turmeric is cultivated only in tropical regions, the shipping process can be taken as an important factor of a great decrease in active components of Turmeric (1, 2). Accordingly, using Curcuminoids and Turmerones as markers for turmeric standardization will help us find out about the imported article's quality. To the best of our knowledge, Turmerones aren't considered as a marker for standardization of Turmeric in Pharmacopoeias yet (3). Considering that Traditional Iranian Medicine suggests using all parts of the plant, so the aim of this research is to establish an appropriate method of standardization for Turmeric, using Turmerones as a new standardization marker. Material and methods: Freshly powdered turmeric was subjected to hydro-distillation. Identification and quantification of essential oil was carried out via GC-MS (Agilent, USA) using kovats indices and literature. Curcuminoids were identified and quantified using Cecil HPLC system. The mobile phase composition was Acetonitrile/water (70/30 v/v), The PH was adjusted to 3 using acetic acid. The analysis was carried out by an isocratic solvent system at a flow rate of 1 $ml/_{min}$. Validation of HPLC system was also done. Results: oil extraction yield was 1.9% (v/w). Two monoterpene hydrocarbons (4.56%), one oxygenated monoterpene (1.43%), five sesquiterpenes hydrocarbons (8.14%) and five oxygenated sesquiterpenes (85.5%) were detected in the oil. The main components were turmerones which leads to a rank order of ar-turmerone (30.75%) > α-turmerone (26.82%) > β-turmerone (23.37%). Using HPLC calibration curve, Curcumin percentage was obtained nearly 0.6%. Discussion: By comparing the results to those mentioned in literature (4), it can be suggested that imported turmeric found in local herbal market, Iran, has a nearly high level of Turmerones, and an acceptable level of Curcumin. Curcumin is very sensitive to heat and light, and the reduction of the molecule during shipping is expected. High level of Turmerones will bring the aroma and good taste. The suggested method of turmeric standardization using HPLC and GC-MS was facile, and it can be used in worldwide herbal Pharmacopoeia.Conclusions: Although turmeric has many uses, it is not cultivated all over the world and only a few countries are responsible of exporting it to all around the world. Since shipping is a very time-consuming step, it is necessary to ensure that the quality of turmeric is not reduced during the process. This is especially more considerable because Curcuminoids and Turmerones are sensitive to improper packaging. Studying various methods of standardization of turmeric mentioned in different Pharmacopoeias, we suggest standardization of turmeric based on turmerones.

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## In silico study of receptor-ligand binding affinity for traditional antitussive formulations

*Reyhaneh Chini[1], Fatemeh Etematpour[1], Nikoo Khalili Moghadam[1], Amirhossein Sakhteman[2], Negar Firuzabadi[3], Parmis Badr[4]*

[1]Pharmacy student, Student Research Committee, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

[2]Department of medicinal chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

[3]Department of Pharmacology and Toxicology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

[4]Pharmaceutical sciences research center, Shiraz University of Medical Sciences, Shiraz, Iran.

Corresponding author: *Reyhaneh Chini*

Corresponding author Email: chinireyhaneh@gmail.com

Introduction: Cough is one of the most common clinical symptoms[1]. more effective treatments are needed along with prevalent products[3]. some herbal compounds such as pseudoephedrine from ephedra and codeine from opium poppy have been developed into drugs[2]. A review reported that from 122 drugs derived from natural sources, 80% were developed for the same indication as to their traditional use. Researchers have proposed that screening the historical literature can be an approach in identifying plants for further investigation of novel pharmacological agents[3]. Searching Traditional Persian Medicine or Pharmaceutical Manuscripts is the key to discover more about antitussive agents and formulations.Material and methods: "Soal" and "Sorfe" were Persian terms for cough that we used to search the 7 selected Traditional Persian Pharmaceutical Manuscripts such as Qanoon, Zakhire Kharazmshahi, Tibb Akbari, Moalejat Aghili, Qarabadin Ghaderi, and Qarabadin Salehi, and Exir Aazam. Different causes of cough and their relative compounding remedies along with their components were extracted. Then equivalent Latin name for each component was highlighted and double-checked on Theplantlist website. Through searching scientific names in databases like Dr. Duke, and other references like PDR, Iranian Herbal Pharmacopoeia, and Dr zargari's book, active ingredients were found. With help of Pycomp (an in-house application), the 1D structure of each bioactive compound was searched through PubChem. Dockface software was used to convert the 1D format to mol2 and the 3D format. Meanwhile, the 3D structure of cough-mediated receptors was extracted from the UNIPROT website and saved as PBD files. A self-docking procedure was conducted to verify the validity of the docking protocols and in the next step, the prepared structures were docked on the target receptors to afford a matrix of binding energies for further analysis. Consequently, the resulting heatmap was used to predict the possible mechanism of action for the compounds.Results: Different indications of cough and their treatment protocol merged into 4 main categories: cold, hot, wet, and dry temperament. Suggested traditional formulations for each type and their RMSD for cough receptors have been listed. RMSD less than 2 indicated an acceptable efficacy. beta-2 adrenergic receptor, histamine H1 receptor, gamma-aminobutyric acid receptor subunit beta-3, delta-type opioid receptor, and sigma-1 non-opioid receptor were more interfered in the antitussive effect of traditional formulations.Discussion: Traditional compound products can be effective in cough and their components follow a logical pattern. There are differences between the receptors involved in the types of coughs introduced in traditional medicine, and different mechanisms for treatment are involved. By gathering information on cough medicines from seven sources of traditional medicine, investigating the receptors they are interfering with, and sorting the medications according to their affinity to each receptor, the validity of traditional recipes and their pattern for different types of cough has been discussed.Conclusions: By confirming the mechanism of action and efficiency of the components of the traditional compound formulations, they can be used in the form of new optimal antitussive herbal formulations along with modern therapies.

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## Preparation of Pellet Dosage Form from Pahkame: a Traditional Pharmacy Formulation

*Leila Khajehesami[a], Hajar Ashrafi[b], Zohre Abolhasanzadeh[c], Abdolali Mohagheghzadeh[d]*

[a] Student of Pharmacy, Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Science
[b] Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences.
[c] Department of Phytopharmaceuticals (Traditional Pharmacy), Shiraz University of Medical Science.
[d] Department of Phytopharmaceuticals (Traditional Pharmacy), Shiraz University of Medical Science.

Corresponding author: *Leila Khajehesami*
Corresponding author Email: leilakhajehhesami@gmail.com

Pahkameh as a traditional formulation is used among the people of Kazerun for gastrointestinal complications such as gastroesophageal reflux disease, flatulence, etc. It is a combination of several natural products including: *Carum copticum* L., *Bonium persicum* Boiss., *Foeniculum vulgare* Mill., *Glycyrrhiza glabra* L. and *Boswellia carteri* Birdw. To improve traditional formulation of Pahkameh, pellets that are small spherical particles with good flowability were prepared, optimized and standardized.Introduction Pahkameh as a traditional formulation is used among the people of Kazerun for gastrointestinal complications such as gastroesophageal reflux disease, flatulence, etc. It is a combination of several natural products including: *Carum copticum* L., *Bonium persicum* Boiss., *Foeniculum vulgare* Mill., *Glycyrrhiza glabra* L. and *Boswellia carteri* Birdw. To improve traditional formulation of Pahkameh, pellets that are small spherical particles with good flowability were prepared, optimized and standardized.Material and methods: Pellets of Pahkameh were prepared using powder of *Carum copticum* L., *Bunium persicum* Boiss., *Foeniculum vulgare* Mill., *Glycyrrhiza glabra* L. and *Boswellia- carteri* Birdw.. Quality control analyses including ash content and water content were performed for main raw material. Based on the result from Design-Expert® software, the optimization was carried out. Pharmaceutical characteristics including particle size distribution, flowability and tap density were evaluated for both powder and finished product. Physicochemical stability and microbial tests were carried out for Pahkameh pellets. The constituents of essential oils obtained from pahkameh were identified by GC-MS. A validated HPLC was used to quantify glycyrrhizic and GC-FID to quantify thymol in optimized formulation of pellet.Results: Optimized formulation of pellet was prepared using 0.51 alcohol:water, with 32 rpm extruder speed and 2022 rpm spheronizer speed. Sixteen compounds of pahkameh essential oil were identified by GC-MS. the results of this study showed that thymol , γ-terpinene, anethol and ρ- cymene were found to be the major constituents of the oil. glycyrrhizic acid were identified with 1.25% by HPLC. GC-FID shows thymol as the major component of pellet essential oil was 31%. Discussion: Regarding acceptable flowability, particle size distribution and physicochemical stability, pellet of pahkameh can be a desired alternative for current formulation of pahkameh powder. Conclusions: Based on traditional notions and preparing a pellet formulation here, designing clinical trials for modernized formulation is suggested.

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## Prevention and management of heart failure-induced remodeling: bioactive constituents with antioxidant and anti-apoptotic activities

*Atefeh Jalali[1, 2], Alireza Abdi Ardekani[3, 4], Mohammad M. Zarshenas[1, 2, 5]*

[1]Medicinal Plants Processing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Phytopharmaceuticals (Traditional Pharmacy), School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Department of Cardiology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
[4]Anesthesiology and Critical Care Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[5]Epilepsy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Mohammad M. Zarshenas
Corresponding author Email: zarm@sums.ac.ir

Introduction: Heart failure (HF) is described as a complicated clinical syndrome affecting about 64.34 million peoples worldwide (1). The most significant burden of HF are individuals aged ≥65 years, as more than 80% of associated deaths to HF occur in this population. The most crucial characteristic of HF is reducing the heart's ability to pump or fill with blood that leads to fatigue and dyspnea with congestion signs and cardiac remodeling (2-5). Abnormal cardiac cells apoptosis is one of the more important heart disease risk factors (6). Based on various studies, the decreased in the levels of antioxidant defenses such as catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), and the increased in the levels of reactive oxygen species (ROS) and lipid peroxidation markers are attributed to HF development (7, 8). Oxidative stress induces cardiac remodeling through several pathophysiological mechanisms and leads to HF development and progression (9). Medicinal plants possess a notable place worldwide and were prescribed over centuries. Although the effectiveness of conventional drugs is proved in the management of cardiovascular disorders, they lead to undesirable effects, especially in HF management (10, 11). Altogether, apoptosis and oxidative stress possess a significant role in HF progression and herbal medicine can balance these processes. Therefore, the prevention of cardiac apoptosis and oxidative stress via medicinal plant or bioactive components can be introducing as an alternative therapy in the prevention and management of HF.Till now, various papers have been conducted on the cardio-protective effect of the plants in HF. Attending to the importance of antioxidant and anti-apoptosis activities in HF progression and the positive result of natural products in HF management, this research is designed to review effective herbal medicines in one of the involvement critical processes in HF for developing novel cardioprotective drugs.Material and methods: In this review, papers related to pharmacology, toxicology, and pharmaceutics were gathered via searching the following keywords trough "Scopus", “Google scholar”, and “PubMed” databases from 1st January 1990 until 1st January 2021:

A. Heart failure and Oxidative stress

Keywords "heart failure" and "plant" or "herbal" and "antioxidant" or "radical scavenging" were synchronously searched.

B. Heart failure and Apoptosis

Keywords "heart failure" and "plant" or "herbal" and "apoptosis" were synchronously searched.

All extracted data summarized in two sections: (A) Heart failure and Oxidative stress, (B) Heart failure and Apoptosis Results: Many medicinal plants and bioactive components have been evaluated for their possible cardio-protective effects via antioxidant and anti-apoptotic activities in HF prevention and management. Among them, 31 papers were linked to antioxidants and 34 papers were related to anti-apoptosis. Also, 10 bioactive constitutes/plants and 1 formulation showed both of antioxidant and anti-apoptotic effects, including the polysaccharide of *Astragalus*, anthocyanins-enriched extract of *Vaccinium corymbosum*, methanol extract of *Brassica oleracea*, *Salvia miltiorrhiza*, *Zanthoxylum bungeanum*, cardamonin, carnosic acid, rhein lysinate, leonurine, and wogonin, as well as Cortex Dictamni formulation. Discussion: Oxidative stress and apoptosis play a major function in HF development by targeting several important signaling pathways in cardiac cells. As the conventional HF treatments lead to several side effects, and the growing tendency to use herbal medicine is highlighted last year, we gathered about 50 medicinal plants or bioactive components with positive effects on HF management. Conclusions: Prevention of cardiac apoptosis and oxidative stress can be introducing as an alternative therapy in HF management via inhibition of cardiac remodeling. Medicinal plants are the major source of antioxidants and can inhibit apoptosis via targeting related signaling pathways. Natural products can use as supplements or prescribe as an alternative approach to HF management.

## P105

# Etiology and treatment of Heartburn in Traditional Iranian Medicine

*Reyhaneh Majidipur*[1], *Zahra Zare*[1], and *Parmis Badr* [2]

[1]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Reyhaneh Majidipur

Corresponding author Email: rhnh.mp.99@gmail.com

Introduction: Every year, millions of people worldwide get sick of gastrointestinal diseases such as heartburn. Heartburn is defined as a burning sensation behind the breast bone. The etiology can be different such as gastroesophageal reflux disease, non-erosive reflux disease, hypersensitive esophagus, functional heartburn, *Helicobacter pylori* infection, stomach ulcer and psychological disturbance. One of the most common treatments for heartburn is application of proton pump inhibitors, but in some cases such as gastroesophageal reflux disease they are not effective, also long-term use of PPIs can lead to a range of adverse effects, including withdrawal symptoms, nutritional deficiencies (specifically, vitamin B12 and magnesium), rebound acid hypersecretion, acute interstitial nephritis, gastric cancer, adverse effects with concomitant medication, bone fractures, enteric infections, and pneumonia. The aim of this study was to investigate the treatment of heartburn, mechanism of the formulations suggested in traditional medicine manuscripts and recent knowledge about heartburn.Material and methods: The keywords of heartburn, in selected Traditional Iranian manuscripts including (horghat mede and soozesh mede), were searched in traditional medicine books including Exir Azam, Moalejat Aghili, Qarabadin salehi, Qarabadin Ghadreri and Zakhire khawrazm Shahi. The treatment protocol was also extracted from Exir Azam, Moalejat aghili and Sharh al-Asbab va al-Alamat. Scientific names were authenticated based on the plant list website. we carried out a literature search through PubMed and Google scholar with the purpose of finding relevant studies about therapeutic effect of each ingredients.Results: After reviewing six selected traditional medicine books, thirty-two formulations were found in dosage form of tablet, syrup, javaresh, safoof, maajun, oxymel and oil. According to the mentioned books, heartburn has three causes: eating foods that are hard to digest, excessive phlegm or black bile in stomach. How to diagnose heartburn is also based on when a patient feels burning sensation (onset of digestion or when the stomach is empty).Discussion: The number of medicinal plants in Lamiaceae and Apiaceae family was in the highest rank. According to findings from recent studies the main mechanisms of action of plants were: antioxidant, anti-inflammatory and antiulcer. In addition, some plants had analgesic and antimicrobial effects. Some had a direct effect on the gastrointestinal tract, such as the gastroprotective activity of *Terminalia chebula* Retz. and the effect of *Phyllanthus emblica* L. on non-erosive reflux disease. Conclusions: Based on the identified treatment mechanisms, it is now possible to suggest multi-component formulations that treat a specific cause and the treatment is done in a personalized way and patient may cooperate more.

## P106

# Assessment of the Cytotoxic Activity of Triphala: A Semisolid Traditional Formulation on HepG2 Cancer Cell Line

*Ali Sahragard*[1], *Mohammad-Mahdi Zarshenas*[2]

Department of Phytopharmaceuticals (Traditional Pharmacy), Shiraz University of Medical Science.

Corresponding author: Ali Sahragard

Corresponding author Email: a.sahragard646@gmail.com

Introduction: Cancer chemotherapies may result in resistance, and therefore, contemporary treatments including natural products may find an increasing consideration. As per Persian medicine (PM), many natural products have been used for malignant and chronic diseases. Triphala, with a combination of Terminalia chebula Retz., Terminalia bellirica Retz., Phyllanthus emblica L., and honey, is a multi-ingredient traditional formulation attributed to anticancer activities in PM. This study is aimed at evaluating the cytotoxic activity of this preparation on HepG2, the human liver cancer cell line.Material and methods: Hydroalcoholic extracts were prepared from the formulation and its components. Compared with the control and Cisplatin, the extracts were tested using MTT assay at different concentrations.Results: All concentrations of the preparation, as well as Cisplatin, were effective significantly against HepG2 cells. All extract preparations at multiple concentrations were significantly effective as evidenced by MTT assay when compared to the control group. The IC50 level for Triphala extract was 77.63±4.3 µg/ml.Discussion: The extract of this formulation can be introduced as a natural cytotoxic agent and an adjuvant to other related drugs to reduce their concentration and help to boost the immune system due to its nutritional effects.Conclusions: Based on the results, Triphala and its components have cytotoxic activity on the HepG2 cancer cell line and they can reduce the survival rate significantly.

## P107

# Volatile composition analysis and quantitative determination of specific markers in a traditional preparation, Jawārish-e-Komooni

*Sanaz Jafari*[1] *, Saeedeh Aghajani* [2] *, Mohammad M. Zarshenas* [3]*,* Zohreh Abolhassanzadeh*[4]

Shiraz University of Medical Sciences, Shiraz, Iran
Corresponding author: Sanaz Jafari
Corresponding author Email: sanazjafaripharma@gmail.com

The control and standardization process of herbal products is a critical point in traditional medicine. Many drugs that are being used today are not standardized and also there is no noticeable control over them. Out of all the different pharmaceutical dosage forms mentioned in Traditional Persian Medicine literature, Jawārish-e-Komooni is an effective formulation due to its positive effect on Gastrointestinal disorders. This formulation includes Zingiber officinale, Bunium persicum, Piper nigrum, and also honey. At this time there have been no noticeable and proven control and standardization or any pharmacognosy studies on this formulation.In this study, Jawārish-e-Komooni was prepared from Qarābadin-e-Salehi, one of the Traditional Persian Medicine literature. Then, by using gas chromatography/mass spectroscopy (GC/MS) and HPTLC, the containing of the formulation were assessed. Also for content determination, using Gas Chromatography/ Flame Ionization Detector (GC/FID), two of the main ingredients were determined. The HPTLC results showed piperine and γ-terpinene as the main components of the formulation. In the standardizing process, piperine and γ-terpinene were respectively proved to be 0.22% and 0.97% of the whole preparation. Also by calculating the standard deviation of the content determination process, we could reach the point where RSD was less than 10%, which is proof of the validity of our method. As mentioned before, standardization is a critical process for all the traditional preparations and it could help us gain repetitive drug responses elsewhere.

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## Ethnopharmacology survey of Bavi tribe (Kohgiluyeh va Boyer-Ahmad province, Iran)

*Ehsan Amiri-Ardekani[1,2,3], Hossein Askari[1], Sedigheh Khademian[1], Shiva Hemmati[4], and Abdolali Mohagheghzadeh[1,5]*

[1]Department of Phytopharmaceuticals (Traditional Pharmacy), Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Iranian Student Association of Indigenous Knowledge, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Student Research Committee, Shiraz University of Medical Sciences, Shiraz. Iran

[4]Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[5]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran.
Corresponding author: Abdolali Mohagheghzadeh
Corresponding author Email: mohaghegh@sums.ac.ir

Introduction: Ethnopharmacology has been one of the important sources of drug discovery from ancient times. The principles of Ethnopharmacology research include compiling a list of plants of an ethnic group and explaining how these plants are used by individuals. Basht and Gachsaran regions in Kohgiluyeh va Boyer-Ahmad province, which Bavi tribe residence place, is the habitat of different plant species that people use for therapeutic purposes.Material and methods: Ethnopharmacology has been one of the important sources of drug discovery from ancient times. The principles of Ethnopharmacology research include compiling a list of plants of an ethnic group and explaining how these plants are used by individuals. Basht and Gachsaran regions in Kohgiluyeh va Boyer-Ahmad province, which Bavi tribe residence place, is the habitat of different plant species that people use for therapeutic purposes.Results: 56 herbal therapeutic agents are used in Bavi tribe. Most of the recommendations were for gastrointestinal diseases with a frequency of 50 therapeutical recommendations. Lamiaceae was recognized as the most used family with 7 plants. The main organs used in this tribe were aerial organs. The most used dosage form in this tribe was decoction with a frequency of 72 uses. The highest informant consensus factor in plant species was related to skin diseases with a value of 0.35 and the highest informant consensus factor in plant families was in the category of pregnancy, childbirth, or the puerperium with a value of 0.75.Discussion and Conclusions: Given the wide range of indigenous knowledge in this tribe, the urgent need to protect the indigenous knowledge of this tribe, using this knowledge for the benefit of ethnic group, and protecting intellectual property rights of this knowledge for this ethnic group is essential. In this regard, it is recommended that appropriate cultural, legal, and regulatory actions be taken to preserve and expand ethnopharmacology of ethnic tribes.

P109

## Assessment of the Cytotoxic Activity of Triphala: A Semisolid Traditional Formulation on HepG2 Cancer Cell Line

*Ali Sahragard[1], Mohammad-mahdi Zarshenas[2]*

[1]Department of Phytopharmaceuticals (Traditional Pharmacy), Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
Corresponding author: Ali Sahragard
Corresponding author Email: a.sahragard646@gmail.com

Introduction: Cancer chemotherapies may result in resistance, and therefore, contemporary treatments including natural products may find an increasing consideration. As per Persian medicine (PM), many natural products have been used for malignant and chronic diseases. Triphala, with a combination of Terminalia chebula Retz., Terminalia bellirica Retz., Phyllanthus emblica L., and honey, is a multi-ingredient traditional formulation attributed to anticancer activities in PM. This study is aimed at evaluating the cytotoxic activity of this preparation on HepG2, the human liver cancer cell line.Material and methods: Hydroalcoholic extracts were prepared from the formulation and its components. Compared with the control and Cisplatin, the extracts were tested using MTT assay at different concentrations.Results: All concentrations of the preparation, as well as Cisplatin, were effective significantly against HepG2 cells. All extract preparations at multiple concentrations were significantly effective as evidenced by MTT assay when compared to the control group. The IC50 level for Triphala extract was 77.63±4.3 µg/ml.Discussion: The extract of this formulation can be introduced as a natural cytotoxic agent and an adjuvant to other related drugs to reduce their concentration and help to boost the immune system due to its nutritional effects.Conclusions: Based on the results, Triphala and its components have cytotoxic activity on the HepG2 cancer cell line and they can reduce the survival rate significantly.

P110

## Conceptual framework of Traditional Persian Medicine based on systems theory and holism

*Motahare Nayebzade[1], Parmis Badr[2]*

[1]Department of Traditional Pharmacy, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
Corresponding author: Motahare Nayebzade
Corresponding author Email: motahare.nayebzadeh96@gmail.com

Introduction: In the last two centuries, reductionism approach has prevailed in various sciences, including several fields of medicine such as prevention, diagnosis and treatment. Additionally, due to the inadequacy of this approach in the treatment of chronic diseases and the development of system biology, anti-reductionism was introduced. Systems medicine has discovered a new concept of the widespread complexity between health and disease which introducing of network medicine and hierarchy theory (1). In the late 1970s, the hierarchy theory was introduced which consider human as a base system, inner world of him is considered as a subsystem and outer world of him called suprasystem (2). In the past centuries, traditional Persian medicine (TPM) had holistic approach to prevention, diagnosis and treatment of disease (3). The aim of this study is a review about examples of holistic, system, network and hierarchy approaches in TPM. Material and methods: In this review, the terms of novel theories such as holism, system medicine, network medicine and hierarchy theory were searched in google scholars, PubMed and ScienceDirect. On the other hand, in order to finding examples of these theories in TPM, terms like six principles of maintenance of health, participatory disease, classification of organs and spiritual function was searched in TPM sources including; Al-Qanun-fi-Tibb, Kholase-al-hekma, spiritual medicine and Tibb-E-Akbari.Results: Jan Christian Smuts (1926), introduced the term "holism" and Bertalanffy developed system theory (of life). Network-based approaches to human disease lead to a more accurate understanding of the interaction between cells and disease progression (4). Scholars of TPM, such as Avicenna, considered the human body that is composed of spirit and body therefore in order to treatment of disease these parameters were considered. For example, along with other medical and food treatments, other important tools were chosen like the right weather and appropriate movement and stillness which can point to the importance of the impact of society and living environmental on person's health which this approach can be the traditional example of novel holism theory. Additionally, in TPM, there are several examples of system and network thinking to the human body, health and disease. Avicenna considered framework of the human body in seven innate principles which can introduced as subsystem of human system, additionally in order to maintenance of health introduced environmental parameters that can be considered as suprasystem. For instance, Avicenna hierarchically classified human organs to the boss, employee, subordinate and other, which these organs had interaction with each other. A trace of novel network medicine in TPM is participatory disease which occurs pursuant of other organ's dysfunction such as heart disease which can occur due to the uterine, liver, brain or stomach disease (3, 5). Discussion: Although the anti-reductionism approach was introduced after the first world war, in the past centuries in TPM, scientists had the holistic approach to the human body and considered him as a network of the seven fundamental parameters which have the hierarchical classification. Conclusions: However, the history of traditional Persian medicine back to many years ago, we can find examples of current theories in holistic approach of TPM.

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## Arginine Deiminase: Applications and optimization

*Niloofar Rezaeifar[a], Mohammad Bagher Ghoshoon[ab], Mohammad Hossein Morowvat[ab], Mahboubeh Zarei[ab], Younes Ghasemi[ab]*

[a] Pharmaceutical sciences researcher center, Shiraz University of Medical Sciences, Shiraz, Iran
[b] Department of pharmaceutical biotechnology, School of pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Background:Arginine deiminase (ADI) is an enzyme that catalyzes arginine to citrulline and ammonium . This enzyme is considered as an anti-tumor agent for the treatment of arginine auxotrophic cancers. Now, *Mycoplasma* arginine deiminase has completed its clinical trial for the treatment of hepatocellular carcinoma (phase Ⅲ) and melanoma (phase Ⅱ). However, some obstacles limit its clinical applications. Despite its concentration on the antitumor activity of arginine deiminase, few studies have been performed to increase the production of this enzyme. To date, no study has been reported on the purification of recombinant *Mycoplasma hominis* arginine deiminase. Objective:This review will summarize the brief history of ADI, its clinical applications, and its limitations . Also to optimize the culture medium of the recombinant enzyme arginine deiminase in *E. Coli* has been paid to increase its production.Method:Cloning, expression, applications of arginine deiminase enzyme and optimization of culture medium have been explained in this review.Conclusion:All the results lead to the use of ADI with optimal characteristics from different sources and

improving suitable host culture conditions and environmental conditions has led to the achievement of efficient and low-cost methods for higher production scales of recombinant arginine deiminase enzyme as well as promising strategies to improve clinical application ADI.

P112

## Staphylokinase Thrombolytic Effects, Advantages, and Drawbacks

*Amin Maleki*[1,2], and *Manica Negahdaripour*[1,2*]

[1]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Department of Pharmaceutical Biotechnology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Manica Negahdaripour

Corresponding author Email: Negahdaripour@sums.ac.ir

Introduction: Cardiovascular diseases (CVDs) are amongst the most important reasons of mortality globally. Clot establishment, as a main cause of CVD, is the major target in therapeutic strategies. Almost always, clots are made upon a damage to vessels or a wound in body. Normally, clots are lysed by thrombolytic factors after a while. If these factors act incorrectly, problems including blocking of the blood flow, strokes, and many other diseases could appear (1).Many approaches have been developed for CVD treatment. Enzymatic thrombolysis has shown high capability in this regard. There are three generations of thrombolytic drugs. The first, such as streptokinase, the second, namely alteplase, and the third generation, i.e. monteplase. A third-generation thrombolytic enzyme is a product of *Staphylococcus aureus* and non-aureus lysogenic strains called staphylokinase (SAK). It is secreted to help bacteria to spread in host's body tissues. SAK is an indirect plasminogen activator, which destroys clots in complex with plasmin(ogen) (1).In this review, SAK effects, advantages, and drawbacks as well as studies that tried to improve this enzyme for therapeutic approaches are briefed.Methods: PubMed and Scopus were searched using following keywords or their combinations: staphylokinase, thrombolytic, cardiovascular diseases, *Staphylococcus aureus*, and fibrinolytic.Results and discussion: Several benefits of SAK compared to other thrombolytic enzymes makes SAK an appropriate option, including its lower production costs, less side effects, as well as production by various strains of *Staphylococcus aureus*. Moreover, many studies and researches have been conducted to improve its activity, safety, and stability. SAK immunogenicity can cause undesirable situations such as thrombocytopenia and aplastic anaphylactic responses. Short half-life of SAK is another disadvantage, which should be improved before its usage in clinics (2).Decreasing its immunogenicity and increasing its stability is studied through different approaches, such as protein engineering or pegylation. For example, using polyethylene glycol carrier to develop a PEGylated recombinant SAK led to 75% less immunogenicity than the natural enzyme. In another research, a lipid-modified SAK (LMSAK) was compared with SAK in a mouse model and showed higher stability and activity than SAK (2).A recombinant SAK, SAK6, was compared with SAK in rhesus monkey, which showed higher secretion level (45%), lower antibody activity, and the same thrombolytic activity (3).A gene-modified staphylokinase, named Fortelyzin®, was developed by a Russian company several years ago and was studied versus Actilyse® (alteplase) in patients with acute myocardial infarction. It showed the same safety but inferior outcome in regards to reduction of fibrinogen level. In another study, in ST-elevated myocardial infarction comparing a single bolus administration of Fortelyzin® versus Metalyse® (tenecteplase), comparable one-year result was reported including low CVD mortality and high survival (4).Additionally, the safety and advantages of a recombinant non-immunogenetic staphylokinase and alteplase are being compared in an ongoing phase 3 clinical study in patients with massive pulmonary embolism (5).Conclusions: Despite several clinical trials with various settings, SAK is not approved yet. However, studies to evaluate its efficacy as well as attempts for developing improved forms of this enzyme are being continued (5).

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## Preparation and evaluation of polyethylenimine-L-DOPA conjugate as a potential targeted gene carrier

*Zahra Taheri*[1, 2], *Ali Dehshahri*[1], *Fatemeh Ahmadi*[2] *and Maryam Kazemi*[1, 2]

[1]Department of Pharmaceutical Biotechnology, School of pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Department of Pharmaceutics, School of pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Ali Dehshahri

Corresponding author Email: dehshahria@sums.ac.ir

Introduction: Neurodegenerative diseases are not effectively treated by conventional therapies. This highlights the need for alternative therapeutic approaches such as gene-based therapies (1). L-Type Amino Acid Transporter 1 (LAT1) is responsible for carrying large, neutral L-amino acids across the blood-brain barrier (2). In this study, we aimed to develop a targeted carrier with the potential of transferring genetic materials through LAT1 transporter.Materials and methods: L-DOPA (3,4-Dihydroxy-L-phenylalanine) was conjugated on 25 kDa polyethylenimine (PEI) at various conjugation degrees. Then, plasmid/polymer DNA complex was prepared and particle size, zeta potential, DNA condensation and gel retardation assay were evaluated. Cytotoxicity and transfection study were performed on 4T1 and Hep-G2 cell lines (3).Results: Three conjugates with different conjugation degrees (1%, 2%, and 4%) were synthesized. $^{1}$H-NMR, FT-IR and buffering capacity tests showed that the conjugates have been prepared properly. DNA condensation assay and gel retardation assay indicated that conjugates could protect the plasmid effectively. Results of zeta potential and particle size measurement demonstrated that the polyplexes were in the optimal size and zeta range. Buffering capacity reduced with increasing the substitution degree. In order to assess the ability of PEI and its derivative to protect plasmid DNA against enzymatic degradation, DNase I was used as the model enzyme and the protection effect of the polymers on plasmid DNA was demonstrated by agarose gel electrophoresis. The results showed that the increasing of conjugation degree enhances the protection against enzymatic degradation.Discussion: The results of this study showed that the conjugation of various degrees of the ligand on PEI structure alters its biophysical properties. These new characteristics may also have impact on its behavior on invitro model to transfer plasmid DNA into the targeted cells.Conclusions:Totally, we expect that our designed conjugate can carry plasmid DNA to the cells through LAT1 transporter.

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## Protein Engineering Approach to Introduce an Improved Calcitonin Mutant

*Benjamin Abedini [1, 2], Mahboubeh Zarei [1, 2], Mohammad Reza Rahbar [1,2], Manica Negahdaripour [1, 2]*

[1]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Pharmaceutical Biotechnology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
Corresponding author: Manica Negahdaripour
Corresponding author Email: negahdaripour@sums.ac.ir

Introduction: Calcitonin, a 32 amino acid peptide from calcitonin family, has a fundamental role in the homeostasis of calcium in kidneys, bones, and intestine. Calcium is involved in key functions such as cell proliferation and junction (1). Calcitonin is used to treat diseases such as osteoporosis, Paget's disease, and other bone diseases (2). Salmon calcitonin (sCT) has a higher potency in humans than human calcitonin, leading to its more clinical usage (3). However, its allergenicity and antigenicity could reduce its pharmacological efficiency (4).The aim of this study was to improve some properties of sCT especially antigenicity through *in silico* peptide engineering.Methods: The available reviewed calcitonin sequences of different organisms were extracted from SwissProt. Several *in silico* tools (ProtParam, Vaxigen, PREDICTED ANTIGENIC) were applied to characterize the sequences. The best structures in regards to immunogenicity were identified.At the second phase, linear B cell epitopes were searched on the sCT using BepiPred 2.0. Its conserved regions, found by ProtSkin server, were exempted from further analysis. Several criteria including B-cell epitope score, surface accessibility, convexity index, hydrophilicity, and flexibility were identified for different residues through several servers to identify hot spot residues. Then, the selected hot spot residues were changed based on the least immunogenic calcitonin peptides identified at the first step of study. The physicochemical properties, antigenicity, and allergenicity of the mutants were studied, and the best mutant was selected. Its modelled 3D structure was superimposed on natural sCT. Results: Among 13 derived calcitonin sequences, four appropriate candidates (P01258, P01257, P41547, P01262) were introduced as the best structures. The residues 14-29 of sCT were predicted as the immune-reactive region with amino acids 27 and 29 as the non-conserved most epitopic hot spot residues. Following mutation on these two residues, six mutants were built. Comparison of antigenicity, allergenicity, stability, solubility, and half-life helped to identify the S29V/T27F mutant as the best peptide. It showed less antigenicity and higher stability and solubility than sCT, while its allergenicity and half-life was equal. Super-imposition of this final selected mutant on natural salmon calcitonin showed low RMSD.Discussion: Structural analysis showed the protrusion of antigenic regions enriched with charged and polar residues on the protein surface, as crucial characteristics of epitopes. Besides, high surface accessibility, flexibility, hydrophilicity, and convexity index indicated other criteria for selecting hot spot epitopic residues [5]. Accordingly, T27 and S29 with high B-cell epitope score were considered as the hot spot residues candidate for mutation.Overall, mutant, S29V/T27F, showed the best features and could potentially be employed as an advantageous pharmaceutical candidate. Its comparable conformation in respect to sCT indicated its comparable functionalityConclusions: An improved peptide was introduced, which could be potentially employed in medical application based on its physicochemical and immunological advantages. Future experimental studies are needed to confirm its clinical efficiency.

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## In silico studying of lipase from different bacterial species

*Aboozar Kazemi [1, 2], Younes Ghasemi [1,2*]*

[1]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, P.O. Box 71365_158, Shiraz, Iran.
[2]Department of Pharmaceutical Biotechnology, School of Pharmacy Shiraz University of Medical Sciences, P.O. Box 71345_1583, Shiraz, Iran.
Corresponding author; Younes Ghasemi
Corresponding author E-mail: ghasemiy@sums.ac.ir

Introduction: In recent years, lipases have played an important role in industrial applications including food technology, biomedical sciences and chemical industry. Lipases exist frequently in nature which are produced by different plants, animals and microorganisms. Microbial lipases, chiefly bacterial and fungal, form the most broadly used class of enzymes in organic chemistry and biotechnological applications. To gain the more information about lipases, the investigation of enzyme structure is important and can be useful for industrial purposes. The aim of this study was the comparison and similarity investigation of lipase enzyme between different bacterial species.Methods: In this study, we selected 15 different bacterial species as source of lipase enzyme. The amino acid sequence of the enzyme was searched through Uniprot server (http://www.uniprot.org/), and motifs was searched by Motif finder (http://www.genome.jp/tools/motif/). Phylogeny analysis was performed by Mega 4.Results: Lipase comprised of an average of 416 amino acids in selected species. According to the phylogenetic tree, species located in two clads which in each clad species contain a close phylogeny relationship. The motifs were searched by motif finder. A total of 36 different motifs found in all species including Abhydrolase_1 , Hydrolase_4, DUF, Esterase, Lipase_GDSL, LCAT. Various species contain a different composition of motifs in their amino acid sequences.Conclusion: Different bacterial species are phylogenetically related as a source of lipase which contain conserved residues. The bacterial lipases can be a suitable candidate for using in industrial purposes.

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## In silico investigating of Theta-Defensin as a furin inhibitor to confront COVID-19

*Manica Negahdaripour [†, [a], [b]] Mohammad Reza Rahbar [†, [a]] Zahra Mosalanejad [†, [b]] Ahmad Gholami [[c]*]*

[a]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz,Iran
[b]Department of Pharmaceutical Biotechnology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[c]Biotechnology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[†]These authors contributed equally to this work.

Corresponding author: Ahmad Gholami
Corresponding Author: Gholami@sums.ac.ir,

The new 2019 coronavirus was characterized as a pandemic by the World Health Organization. SARS-CoV-2 has a spike protein on its surface, which binds to the cell membrane and infects the cell. Furin, which is a host-cell enzyme, possesses a binding site for the spike protein. Thus, molecules that block furin could potentially be a therapeutic solution. Defensins are arginine-rich antimicrobial peptides that can hypothetically inhibit furin since poly-arginine-derived molecules are furin inhibitors. Theta- defensins, a defending family, have attracted attention as drug candidates due to their small size, unique structure, and involvement in several defense mechanisms. Theta defensins could be a potential treatment for COVID-19 by inhibiting furin and their anti-inflammatory mechanisms. Here, the potential of theta defensins against SARS-CoV-2 is investigated through in silico approaches. Based on docking analysis results, theta defensins can function as furin inhibitors. Additionally, a candidate novel peptide against COVID-19 with optimal properties regarding antigenicity, stability, electrostatic potential, and binding strength is proposed.

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## Mechanism of Tramadol-induced Renal Injury

*Sara Bagheri[1], Reza Heidari[2], Khadijah Mousavi[3], Asma Najibi[4], Ram Kumar Manthari[5], Zhipeng Jia[6], Mohammad-mehdi Ommati[7]*

[1]Student Research Committee, Shiraz University of Medical Sciences, School of Pharmacy, Shiraz, Iran
[2]Department of Pharmacology and Toxicology, Shiraz University of Medical Sciences, School of Pharmacy, Shiraz, Iran
[3]Department of Biotechnology, GITAM Institute of Science, Gandhi Institute of Technology and Management, Visakhapatnam-530045, Andhra Pradesh, India
[4]College of Animal Sciences, Shanxi Agricultural University, Shanxi, Taigu, China
[5]College of Life Sciences, Shanxi Agricultural University, Shanxi, Taigu, China

Introduction: Tramadol (TMDL) is an opioid analgesic widely administered for the management of moderate to severe pain. On the other hand, TMDL is widely abused in many countries because of its availability and cheap cost. Renal injury is related to high dose or chronic administration of TMDL. No precise mechanism for TMDL-induced renal injury has been identified so far. The current study aimed to evaluate the potential role of oxidative stress and mitochondrial impairment in the pathogenesis of TMDL-induced renal injury.Material and methods: For this purpose, rats were treated with TMDL (40 and 80 mg/kg, i.p, 28 consecutive days).Results: A significant increase in serum Cr and BUN was detected in TMDL groups. On the other hand, TMDL (80 mg/kg) caused a significant increase in urine glucose, ALP, protein, and γ-GT levels. Moreover, urine Cr was significantly decreased in TMDL-treated rats (40 and 80 mg/kg). Renal histopathological alterations included inflammation, necrosis, and tubular degeneration in the kidney of TMDL-treated animals. Reactive oxygen species formation, lipid peroxidation, increased oxidized glutathione, and protein carbonylation was increased, whereas total antioxidant capacity and reduced glutathione levels were considerably decreased in TMDL groups. Significant mitochondrial impairment was also detected in the form of mitochondrial depolarization, ATP depletion, mitochondrial permeabilization, lipid peroxidation, and decreased mitochondrial dehydrogenase activity in the kidney of TMDL (80 mg/kg)-treated animals.Discussion: To date, there have not been studies dedicated to the precise mechanism for TMDL-induced renal injury. In this study, the significant increase in oxidative stress markers and mitochondrial dysfunction were evident in the kidney of TMDL-treated animals.Oxidative stress and mitochondrial impairment are two tightly related phenomena. Mitochondria are the primary sources of intracellular ROS formation. On the other hand, significant ROS formation and oxidative stress could impair mitochondrial function. Therefore, mitochondria could act as an essential source of ROS formation in the kidney of TMDL-treated animals.Kidneys are high-energy consuming organs and contain a considerable number of mitochondria. Enough energy (ATP) production in the kidney guarantees vital processes such as chemicals reabsorption in renal tubules. The reabsorption of many compounds such as glucose, amino acids, several ions, and phosphate is dependent on ATP availability. As observed in the current study, serum levels of ions such as K+ as well as phosphate levels were significantly decreased in TMDL-treated animals. On the other hand, significant proteinuria in addition to increased urine levels of γ-GT and ALP were detected in TMDL-treated rats. These data could indicate significant tubular injury induced by TMDL. Interestingly, it has been reported that TMDL caused significant hyponatremia. This complication could be associated with impaired reabsorption of ions and chemicals due to mitochondrial impairment and energy crisis in the kidney during TMDL exposure. Therefore, monitoring serum electrolytes and applying appropriate clinical intervention is essential in human cases of TMDL-induced renal injury. Moreover, the administration of mitochondria protecting agents could serve as a viable therapeutic intervention in this complication.Conclusions: These data suggest mitochondrial impairment and oxidative stress as mechanisms involved in the pathogenesis of TMDL-induced renal injury.

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## A repurposing pipeline to candidate suitable inhibitors of tyrosinase

*Mina Zarei, Maryam Kabiri, Ali Khodabandelou, Mehdi Khoshneviszadeh, Amirhossein Sakhteman*

Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Mina Zarei

Corresponding author Email: mina.zarei.7795@gmail.com

Introduction : Tyrosinase as a metalloprotein enzyme plays role in the synthesis of melanin by hydroxylation of L-tyrosine to L-dopa. Inhibition of this enzyme can be considered as a therapeutic target in hyperpigmentation and other skin disorders. In this study we attempted to investigate the interaction of all FDA approved compounds on this target during a repurposing strategy. Methods:All FDA approved compounds were retrieved from https://tripod.nih.gov/npc as SMILES and their structures were converted to pdbqt via OpenBabel (1). The structure of the enzyme was downloaded from RCSB as the PDB code 2y9x, water molecules were removed, Cu atoms were retained and the structure was saved as PDBQT format.Self-docking using Vina and RMSD evaluations of the cognate ligand (tropolone) in the protein crystal structure was used as a measure of validation for the docking protocol (2). Finally, the binding energy of all structures were retrieved and the SMILES with the lowest binding energies were subjected to SWISSAMDE. Visualization of the interactions was done by pose view.(3)The IC50 values of the compounds were assessed by measuring the dopaoxidase activity of the tyrosinase enzyme at 475 nm in the presence and absence of the candidate inhibitors at different concentrations using a UV photo spectrophotometer. Adapalene was used as the positive control during the bioassay study. Results :Based on the binding energies of the docked structures, 36 compounds with the lowest binding energies were submitted to predict skin permeation properties among which montelucast, ergotamine and dihydroergotamine were selected as the most suitable candidates for the

final bioassay. The binding energies of the selected compounds montelucast, ergotamine and dihydroergotamine were -9.1, -9.2 and -10.1 kcal.mol$^{-1}$, respectively. The binding energy for the cognate ligand was obtained as -6 kca.mol$^{-1}$. The result of bioassay confirmed that all three selected structures were showing reasonable IC50 values with respect to the positive control against tyrosinase. Discussion:Based on the results of docking simulations and bioassay IC50 values, it was revealed that all three structures can be considered as suitable candidates against tyrosinase in topical preparations. The most advantage of this study is that all results were obtained in a repurposing pipeline. Therefore, it can be concluded that the cytotoxic and other side effects of the compounds are in a reasonable therapeutic index range. Conclusion:Due to importance of tyrosinase inhibitors in the treatment of different skin disorders, in this study a pipeline was designed in order to present some suitable candidates against tyrosinase. The activity and skin permeation properties of the selected candidates revealed that they can be used in different topical formulations as tyrosianse inhibitors.

P119

## N-benzyl and N-allyl isatin-oximes as potent antitumor agents; Synthesis, Cytotoxicity, Molecular docking and in silico studies

*Ahmad Moeni-Roudbali[1], Zeinab Faghih[2], Soghra Khabnadideh[3], Leila Emami[4], Zahra Faghih[5], Amirhossein Abbasi[6]*

[1]Student Research Committee, Shiraz University of Medical Sciences, School of Pharmacy, Shiraz, Iran
[2]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz,Iran
[3]Research Center of Oncology Studies, Shiraz University of Medical Sciences, School of Medicine, Shiraz, Iran
Corresponding author: Zeinab Faghih
Corresponding author Email: faghihz@sums.ac.ir

Introduction: Cancer is one of the leading causes of death globally. Despite the significant progress in the treatment of cancer, there continues to be a rise in cancer incidence and mortality. Many clinically available anticancer drugs have low tumor selectivity and therapeutic efficacy, giving rise to undesirable side effects. Therefore, the discovery of novel chemotherapeutic agents with increased tumor cytotoxicity and specificity remains an essential domain of cancer therapy research. The isatin nucleus is an important scaffold for the development of novel antitumor agents that are well-tolerated in humans. In recent years, researchers have established isatin-Schiff bases as promising anticancer agents; among them, oxime derivatives have demonstrated significant cytotoxicity against cancer cell lines.Material and Methods: In an effort to generate more cytotoxic agents, we synthesized novel N-benzyl and allyl isatin-oxime derivatives (4a-h and 5a-b) in two steps, screened their cytotoxicity (1-500 μM for 72 hours) against human breast cancer (MCF-7), human lung adenocarcinoma (A-549) and colon cancer (SW1116) cell lines via MTT assay. Then, we selected 4h, as potent compound, to investigate the ability of inducing apoptosis in SW116 cells using an Annexin V/7AAD kit. Molecular docking studies were performed on cancer-related enzymes to investigate the inhibitory potential of the isatin-oximes on c-Jun N-terminal kinase 3 (JNK3), cyclin-dependent kinase 2 (CDK2), and interleukin-2-inducible T-cell kinase (ITK) using AutoDock 4.2. Finally, the pharmacokinetic properties of the isatin-oxime derivatives were examined in silico using SwissADME software to identify their potential as potent anti-cancer drugs.Results: Substitution of Cl to position 5 of the isatin ring yielded more cytotoxic derivatives than 5-F substitution. Additionally, N-benzyation produced more active derivatives compared to N-allylation. Compound 4h was determined to be the most active compound against all studied cell lines. Apoptosis assay of 4h showed that the isatin-oxime derivatives induce early-phase apoptosis in cancerous cells. In silico docking studies explored potential interactions of isatin-oximes with the target site of various cancer-associated proteins; JNK3, CDK2 and ITK. Pharmacokinetics analyses indicated that all of the compounds were in agreement with Lipinski's rules.Discussion: The structure-activity relationship analyses of the various substitutions on the isatin ring (N1 and C5) revealed that 5-chloro-substituted derivatives with bromine in the para and meta positions of the N-substituted benzyl ring (4g-h) showed increased cytotoxicity against all studied tumor cell lines. The molecular docking studies confirmed the results from the cytotoxicity assay as N-benzyl substituted derivatives had stronger binding to the active sites of all enzymes studied compared to the allyl and unsubstituted isatin-oximes, matching the findings from the MTT assays. ADME modeling suggested that these derivatives were predicted to display increased absorption across the intestine and skin as well as enhanced efficiency in transportation across cell membranes.Conclusion: In summary, Compound 4h was determined to be the most active against all cell lines and induced early-phase apoptosis in SW1116 cells. Docking studies demonstrated good correlation with anti-tumor activity. The insilico ADME analysis indicated that all compounds followed Lipinski's rule of five and have good absorption to show proper oral bioavailability

P120

## Anticonvulsant Activity of Some Benzoxazole Derivatives

*Ahmad Moeeni Roodbaly[1], Zeinab Faghih [2], Leila Emami[2], Leila Moezi[3], Soghra Khabnadideh[2]*

[1]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Department of Pharmacology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Soghra Khabnadideh

Corresponding author Email: khabns@sums.ac.ir

Introduction: Epilepsy is not a disease, but a syndrome of diverse cerebral disorders of central nervous system distinguished by the periodic sudden loss or loss of consciousness, frequently followed by convulsions. About 50 million people worldwide have epilepsy, making this condition the second leading neurological disorder with almost 90% of these people being in developing countries. Long-acting antiepileptic drugs with high efficacy and low adverse effects were a major research topic in pharmacology. The substituted benzoxazoles have attracted much attention due to their prominent utilization as anti-inflammatory, antiviral, antifungal, antibacterial, anticancer, anti-tubercular and anticonvulsant activity. In the present study, we have investigated the antiepileptic effects of some newly benzoxazole derivatives which were synthesized in our previous study. Material and Methods: The new benzoxazole derivatives previously synthesized in our group were screened for the anticonvulsant property in PTZ induced seizure model in rats. The benzoxazole derivatives have been evaluated through Maximal Electroshock (MES) and intravenous infusion of Pentylenetetrazole (PTZ) induced epilepsy mice models. Time of onset

of convulsions and time of onset of tonic clonic were recorded in rat for all the target compounds. Results: Our results showed that some of the tested compounds exhibited good anti convulsant potency. In MES model, some of the compounds were effective at 20 mg/kg, 50 mg/kg and 75 mg/kg dose. Meanwhile, some other compounds were significantly better than the vehicle solution in increasing the clonic seizure threshold of PTZ model at 50 mg/kg. Discussion: In conclusion, we can conclude that benzoxazole derivatives which were studied here have anticonvulsant effects and are recommended for being more investigated in further studies. Some of the designed compounds were effective at 20 mg/kg, 50 mg/kg and 75 mg/kg dose. Also, some other compounds were significantly better than the vehicle solution in increasing the clonic seizure threshold of PTZ model at 50 mg/kg.

## P121

## Synthesis, Antimicrobial and Cytotoxic Evaluation of Some new Pyrazole and Benzimidazole Derivatives

*Roya Rahimi Panah[1], Leila Emami[2], Zeinab Faghih[2], Kamiar Zomorodian[4], Ahmad Rostami[3], Asghar Jalilian[3], Leila Zamani[2], Soghra Khabnadideh[2].*

[1]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[4]Center of Basic Researches in Infectious Diseases and Department of Medical Mycology and Parasitology School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran.

Corresponding author: Soghra Khabnadideh

Corresponding author Email: khabns@sums.ac.ir

Introduction: Azole and heterocyclic fused azole derivatives represent an important class of heterocyclic compounds which show various biological activities. Clotrimazole is an azole derivative possessing effective antifungal properties. It has a broad-spectrum activity against different strains of fungi. Here, in this study we aimed to design and synthesis some azole (pyrazole and benzimidazole) based on clotrimazole core structure. We are also going to evaluate biological activities of the new compounds. Material and methods: Some analogues of novel pyrazole and benzimidazole derivatives were synthesized in one step. Different pyrazole or benzimidazole rings reacted with trityl moieties in the presence of tetraethylammonium iodide (TEAI) and NaOH in toluene. Purification of crude compounds were done by plate chromatography. Chemical structures of the compounds were confirmed by different spectroscopic methods. The antimicrobial activities of all designed compounds against different species of microorganisms including fungi, gram positive and gram negative bacteria were evaluated by Broth micro-dilution method. Also, the cytotoxic activity of all compounds were further evaluated on two different human cancerous cell lines including lung cancer (A549) and breast cancer (MCF-7) using MTT method. Results: The target clotrimazole like compounds were conveniently obtained in 57-88% yields. Antimicrobial activity showed that some designed compounds exhibited good antimicrobial potency. Some of the tested compounds represented desire *in vitro* antifungal properties at concentrations ranging from 0.5 to ≤1 µg/mL. The cytotoxic activities were assessed against MCF-7 and A549 cell lines using MTT method. The results indicated that most compounds had fairly good cytotoxic activity. Discussion: We have developed a highly efficient method for the synthesis of clotrimazole derivatives by treatment of pyrazole or benzimidazole derivatives with trityl moiety. Some compounds exhibited great activity against tested fungi. Considering chemical structure of the most active compound, it seems the presence of the triangular structure (cyclopropyl group) with bend bonds and its unique chemical properties along with hydrogen donor and acceptor and electron-rich amino group, is the cause of having such a broad spectrum antifungal activity even against azole resistant strains.

## P122

## Design, synthesis and biological evaluation of tyrosinase inhibitors: *symmetrical azine* derivatives

*Somaye Karimian [1], Fatemeh Kazemi[1], Mehdi Khoshneviszadeh [1,2]*

[1]Department of Medicinal Chemistry, School of pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

[2]Medicinal and Natural Products Chemistry Research Center, Shiraz University of Medical sciences, Shiraz, Iran.

Corresponding author: *Somaye Karimian*

Corresponding author Email: s_karimian@sums.ac.ir

A series of symmetrical azine derivatives containing substituted benzyl moieties were designed, synthesized and evaluated for their inhibitory activity against mushroom tyrosinase. The results showed that six compounds exhibited effective inhibitory activity with IC50 ranging from 7.3 µM to 62.6 µM and compounds 2,4-dihydroxy substitutions(3f) and 4-hydroxy-3-methoxy substitutions(3k) were the most potent tyrosinase inhibitor (IC50=7.3±1.15 and 12.9±.18 µM, respectively) and their inhibitory effects were comparable to kojic acid (IC50=20.24±2.28 µM). Kinetic study of compound 2,4-dihydroxy substitutions(3f) confirmed uncompetitive inhibitory activity towards tyrosinase indicating that it can bind to enzyme-substrate complex. Also, molecular docking analysis was performed to study the interactions and binding mode of the most potent compound 3f in the active site of tyrosinase. Consequently, compounds 2,4-dihydroxy substitutions(3f) and 4-hydroxy-3-methoxy substitutions(3k) could be introduced as a potent tyrosinase inhibitor that might be a promising candidate in the cosmetics, medicine and the food industry, and the development of such compounds may be of interest.

## P123

## Pharmacokinetics and bioavailability of midazolam in rats following single dose administration of intravenous solution, intranasal dispersion and in situ nasal gel

*Zahra Adell[1], Elahehnaz Parhizkar[2], Saba Movaffagh[3], and Shohreh Alipour[3]*

[1]Student Research Committee, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Department of Quality Control, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Dr. Shohreh Alipour

Corresponding author Email: alipour_sh@sums.ac.ir

Introduction: Midazolam (MDZ) is used as a sedative and anxiolytic agent in pediatric operations or dentistry procedures. Considering low solubility in physiologic pH, commercial intravenous MDZ formulation is formulated as an acidic solution, which is unofficially used orally,

rectally, buccally and intranasally in spite of low patient compliance due to irritation, inflammation and caustic effect at administration sites.Material and methods: Due to the pathological safety of our previously designed MDZ poloxamer nasal gel (MDZ-PLX-GEL), its pharmacokinetics parameters were determined and compared to MDZ aqueous dispersion (MDZ-DIS) after intranasal administration in rats. For better comparison, i.v commercial solution was evaluated either. MDZ was analyzed using a validated High performance liquid chromatography (HPLC) method. Male Sprague-Dawley rats (200±20 g weight and 6–8 weeks) used for in vivo experiments.Results: The most important feature of MDZ-PLX-GEL was a rapid onset (20 minutes) with a Mean residence time (MRT) of 170 minutes, which means MDZ effective blood concentration (100-200ng/ml) lasts 3 hours, respectively, which could increase MDZ-PLX-GEL absolute bioavailability up to 66.5%± 4.6%.Discussion: It was confirmed that thermosensitive poloxamer gel was a suitable nasal carrier for MDZ that could increase its residence time. Conclusions: MDZ-PLX-GEL may be a proper alternative for currently unofficial MDZ routes of administration.

## P124

## Targeted polyethyleneimine nanoparticles for Co-delivery of Paclitaxel and anti-p-glycoproteins shRNA

*Maryam Kazemi[1], Fatemeh Ahmadi[2], Ali Dehshahri[3], Elahenaz Parhizgar[4], Soleiman Mohammadi-Samani[5]*

[1]Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
Corresponding author: Maryam Kazemi
Corresponding author Email: makazemi@sums.ac.ir

Introduction: Cancer is the second leading reason for death in the world (1). In order to the treatment of cancer, one of the broad-spectrum anticancer drugs is paclitaxel (PTX)but Cancerous cells get multiple drug resistance(MDR) after prolonged exposure to paclitaxel (2), To overcome MDR to enhanced chemotherapy efficacy can be suggested co-delivery of anticancer drug with an RNA interference(RNAi) knockdown the expression of the target gene to prevent the activity of efflux transporters the same as shRNA(3). This study emphasizes the targeted PEI with 3,4 Dihydroxy phenylalanine (L-DOPA )for delivery of paclitaxel and shRNA anti-P-glycoproteins in order to overwhelm paclitaxel resistance that is complicated the treatments of patients with solid tumors. Material and method:This synthesis was performed in three steps:1)preparation of succinate paclitaxel, The second step was the conjugation of LMW bPEI by succinate paclitaxel, the third step was the attachment of L-dopa with amide linkage to the primary amines of bPEI, the formation of every step was proved by 1H-NMR. Then, The solubility, content, and in-vitro release of paclitaxel were determined by HPLC method.in order to gene delivery, Plasmid transformation and isolation and Preparation of polyplexes with different C/P ratios were done, then below biophysical characterizations were performed: 1)Gel retardation assay:The ability of the conjugated polymer to condense the plasmid by electrostatic interaction, polyplexes with different C/P ratios, then the plasmid bands showed under the UV illuminator.2)Buffering capacity:The buffering capacity of conjugated PEI was evaluated by acid-base titration.3)Protection against enzymatic degradation:In order to demonstrate the protection of plasmid against DNase I by conjugated PEI, 2 series of various C/P ratios of polyplexes were prepared, the influences of polymer for protection against enzymatic degradation were evaluated by agarose gel electrophoresis.4)The size of particles and zeta potential were measured at the C/P ratio of 8.Results: This study demonstrates that condensation of plasmid by PEI causes the formation of nanoparticulate with the size of 270nm with acceptable buffering capacity and protected the shRNA from nuclease in the C/P ratios ≥4.Discussions: this nanoconjugate can deliver chemotherapeutic drug and shRNA anti-p-glycoprotein to the cancer cells and the resulting nanoparticles achieved drug conjugation of 13.8% (W), this nanoconjugate can be used for the sustained and pH-responsive release of the PTX, and this conjugation enhanced the solubility of paclitaxel. formation of polyplexes at C/P ratios ≥4 can condense and protect the plasmid with high buffering capacity for bypassing the lysosomal degradation.Conclusions: These results demonstrated that nanoconjugate could be a good delivery system for chemo/gene co-delivery systems.

## P125

## A Systematic Review of Glycyrrhiza glabra Use Clinical Trials in Recurrent Aphthous Stomatitis

*Gita Vahid-Dastjerdi[1,2,3], Fereshteh Dorsareh[1,2,3]* and *Ehsan Amiri-Ardekani[1]*

[1]Department of Phytopharmaceutical (Traditional Pharmacy), Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Student Association of Indigenous Knowledge, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Ehsan Amiri-Ardekani

Corresponding author Email: ehsanamiri@sums.ac.ir

Introduction: Recurrent aphthous stomatitis(RAS) is the most common ulcerative disease that affects oral mucosa. For patients who experience severe form, painful ulcers, or recurrent form, treatment should be considered. The first line treatment is topical therapy including topical anesthetics, mouthwashes, coating or occlusive agents, topical corticosteroids and intralesional corticosteroids, that result in rapid healing. Tha last choice of treatment is systemic therapy such as systemic corticosteroids for patients who experience the recurrent and severe form of RAS. Since common treatment such as anti-inflammatory steroids have side effect I.e., developing secondary oral candidiasis, and due to many studies that indicate optimal effects of *Glycyrrhiza glabra* on reducing pain, number, and size of oral ulcers with less side effects, we decided to perform a systematic review on effect of licorice consumption on RAS treatment that is a well-known medicinal plant with anti-inflammatory effects.Material and Methods: We searched all original English randomized clinical trials studying the effect of *G.glabra* or its compositions on RAS published based on PRISMA in Science Direct, PubMed, Cochrane, Scopus, and Google Scholar databases up to June 2021. Searched keywords were ("Glycyrrhiza glabra" OR "Licorice"OR"Liquorice") AND ("Recurrent aphthous stomatitis" OR "aphthous"). We just included clinical trial articles and analyzed published articles. We reviewed the articles qualitatively and included only those that had JADAD score ≥3. Non English articles, Reviews, case reports, observational studies, and studies on other diseases or using different formulations not containing *G.glabra* were excluded.Result and discussion: The result showed licorice extract has significant effects on RAS pain reduction and ulcer size. It has been suggested that its effectiveness is related to its anti-inflammatory and antioxidant effects dose-dependently. Licorice can be useful in RAS treatment through several mechanisms; The anti-inflammatory effects cause through blocking COX-2/TxA2 pathway corticosteroid-like effects by inhibiting 11β-hydroxysteroid dehydrogenase that result in blocking conversion of active cortisol to inactive cortisone, inhibiting production of proinflammatory cytokines and CD14, as well as reduction in tumor

necrosis factor plasma level and interleukin-6, and increase IL10 production. Also, licorice has antibacterial effects against *Streptococci mutans* and *Porphyromonas gingivalis* as another mechanism of actions in RAS treatment. As well as, licorice can elevate the EGF level compared to control group that has an essential role in oral mucosal tissue integrity. Licorice extract has been used in dosage forms including paste, patch and mouthwash. Different study used concentration of 1% or 5%. Although all dosage forms show positive effectiveness, licorice patch seems to be more effective due to its mechanical mucosal protection. The healing time after licorice therapy is expected to be within 4-5 days. However small and singular ulcer may be treated after a day while multiple ulcers take more time to complete healing occur. Licorice has shown no adverse effect in intervention group that indicates in its effectiveness and safety for RAS treatment.Conclusion:Our study shows that licorice has a significant effect on promoting healing, reducing pain, healing time, and size of inflammation zone without side effects that makes it a safe complementary therapy for RAS.

P126

## Powder microscopy and Evaluation of Antioxidant, Antifungal Activity and Analysis and Identification of Volatile Compounds in Mentha mozaffarianii In Comparison with a Standard and Market Mint Sample

*Mahmoodreza Moein[1,2], Niloufar sarabi[1], Kamiar Zomorodian[3], Sedigheh khademian[4], Ehsan Amiri-Ardekani[4,5,6], Roxana khalife[5,6]* , and *Mohammad Mehdi zarshenas[1,4]*

[1]Medicinal Plants Processing Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Department of Pharmacognosy, Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Department of Medical Mycology and Parasitology, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

[4]Department of phytopharmaceutical (Traditional Pharmacy), Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[5]Student research committee, shiraz university of Medical Sciences, Shiraz, Iran

[6]Student Association of Indigenous Knowledge, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Mohammad Mehdi Zarshenas

Corresponding author Email: Zarm@sums.ac.ir

Introduction: Mentha is one of the most famous medicinal genera of the Lamiaceae family, including 25 species. The importance of this plant is due to monoterpenes such as menthone, menthol, carvone, and pulegone. They are originating from the southern parts of Iran. Although *Mentha mozaffarianii* (oregano) is an endemic plant in Iran, only three reports of its essential composition and content have, and only one report of antimicrobial effects of this plant has been published. Considering the widespread use of this medicinal herb by people in southern Iran, the present study aims to identify and analyze the chemical constituents of three mint samples essential oils, comparing antifungal effects of these spicies and evaluate free radicals scavenging and antioxidant potential of mint samples essential oils and extracts. Material and methods: This study focuses on powder microscopy, analyzing and distinguishing the chemical constituents of essential oil of *M.mozaffarianii* was collected from Bandar Abbas and two other mint samples (farmland and market). The essential oils were extracted by column chromatography using silica gel, and a solvent system contains petroleum ether and diethyl ether. Chemical constituents of samples essential oil and other sample were analyzed by gas chromatography-mass spectrometry. Besides, antifungal (Microdilution method) and radical savaging (DPPH method) effects of three species were studied. Finally, The antimicrobial effects of essential oils against fungal and bacterial agents were determined by the broth microdilution method based on CLSI protocol.Results and Discussion: Powder microscopy also showed slight differences between oregano and other mint specimens. These differences were differentiable. Essential oil analysis of *M.mozaffarianii* showed that Piperitenone (30.12%), Piperitone (25.81%), and Piperitone-oxide (10.29%) and linalool (6%), and cineol (5.34%) were the main constituents of essential oils. Also, the major constituents in the market mint sample include carvone (9.44%) and limonene (22.27%). Sample collected from farmland constituents include Carvone (31.41%) and limonene (13.38%). Carvone and limonene were detected in similar amounts for market and farmland samples. The results also indicated antifungal activity for all essential oil samples. This effect decreased with increasing polarity of the solvents so that the highest inhibitory and lethal effect was for petroleum ether extract and the least for diethyl ether fraction. Besides, the inhibitory and lethal effects of M.mozaffarianii essential oil had lowest MIC and MLC lower than farmland and marke samples. Antimicrobial effect may be Due to the presence of phenolic rings in the structure of these compounds. Also, no antioxidant activity was observed in any species. Conclusions: It seems that oregano compounds can be used as a new antimicrobial compound to treat fungal infections. Therefore, it is recommended to study the MFC and MIC of each plant on the above-mentioned strains according to the acceptable results of this study. Finally, each studied plant's anti-candidate and antifungal effects on clinical drug-resistant strains should be investigated to develop novel natural antioxidant and anti-bacterial drugs.

P127

## Fabrication and characterization of liraglutide-loaded microneedle arrays

*Narsis Pouralifard [a], Vahid Alimardani [a], Samira Sadat Abolmaali [a], Gholamhossein Yousefi [b], and Ali Mohammad Tamaddon [a]*

[a] Department of pharmaceutical nanotechnology and Center for Nanotechnology in Drug Delivery, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[b] Department of Pharmaceutics, Shiraz School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding Author: Ali Mohammad Tamaddon

Corresponding author Email: amtamadon@gmail.com

Diabetes mellitus is a common metabolic disorder resulting in elevated blood glucose levels. It is the most common cause of cardiovascular diseases, strokes, kidney failure, blindness, and amputation. After oral glucose intake, incretins play an important role in controlling insulin and glucagon secretion, and 70-80% of insulin is secreted by the action of incretins. Liraglutide, also known as incretin mimetic, is an injectable glucagon-like peptide-1 receptor agonist (GLP-1 receptor agonist) indicated in diabetes mellitus type 2 and obesity that works by increasing insulin release from the pancreas. One of the main liraglutide issues is the daily injection that might be associated with pain at the injection site. Therefore, the use of noninvasive methods like microneedle patches could be a suitable solution to resolve the problems of daily injection and to provide a steady prolonged drug release profile. Here, to prepare microneedle patch matrix, a low critical solution temperature (LCST)

hydrogel was developed based on a graft copolymer of methoxy polyethylene glycol-chitosan-poly N isopropyl acrylamide. The synthesized copolymer was characterized using FTIR, H-NMR, tube-inversion, and oscillatory rheology methods. Next, different concentrations of the copolymer (2, 5, and 10%) were used to fabricate Liraglutide (0.3 mg)-loaded microneedle arrays by micro-molding technique. Mechanical properties of fabricated microneedle arrays were characterized using a texture analyzer in compression mode. Additionally, in-vitro Liraglutide release from the microneedle arrays were determined by reverse-phase high-performance liquid chromatography (RP-HPLC). The graft copolymer underwent sol-gel transition at a temperature around 37°C. Fabricated microneedle arrays exhibited acceptable stiffness and slow release of Liraglutide over a prolonged period. It was shown that the drug release was controlled by the copolymer concentration. Therefore, the engineered fabricated microneedle array could be used as a promising sustained release liraglutide formulation in diabetes.

## P128

## Synthesis and characterization of erythrocyte membrane-camouflaged silibinin-loaded mesoporous silica nanocomposites in treatment of liver fibrosis

*Vahid Tayyebi Khorrami*[1], *Mohammad Javad Raee*[1*], *Samira Sadat Abolmaali*[1, 2*], *Ali Mohammad Tamaddon*[1, 2]

[1]Center for Nanotechnology in Drug Delivery, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Department of Pharmaceutical Nanotechnology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding Authors: M.J. Raee , SS Abolmaali

Corresponding authors Email: raeem@sums.ac.ir, abolmaali@sums.ac.ir,

Introduction: Hepatic fibrosis can be caused by excessive accumulation of extracellular matrix in viral or autoimmune hepatitis, bile duct obstruction, excessive iron accumulation, non-alcoholic fatty liver, , and alcohol-induced liver disease. (1) Silibinin has been used as herbal medicine for centuries to treat a variety of liver diseases such as hepatic fibrosis. (2) Various methods have been used for the delivery of silibinin, including micro- and nanoparticles. Mesoporous silica nanocomposites (3) coated with erythrocyte cell membranes could mimic the structure and function of biological systems such as longevity in the blood stream and silibinin delivery to the liver stellate cells (4).Material and methods: Nanocomposites comprised of mesoporous silica and poly(alkyl methacrylate) were synthesized by free radical polymerization and sol-gel reaction in an emulsion system that were loaded with silibinin by solid dispersion method. Then, red blood cells were collected from rat blood lysis in the hypotonic medium. Prepared RBC membrane vesicles were combined with mesoporous silica nanocomposites using bath sonication followed by lyophilization. The particles were characterized by zeta sizer, DLS and TEM microscopy. Drug loading and release in phosphate buffer (pH 7.4) were also studied by ultraviolet spectroscopy and dialysis methods.Results: Fabricated mesoporous silica nanocomposites were confirmed by SEM microscopy. Loading and release studies indicated the successful silibinin loading and prolonged drug release from the nanoparticles. TEM microscopy demonstrated the coating of drug-laden nanoparticles with RBC membrane-derived vesicles.Conclusion:The silibinin-laden particles could be useful in the treatment of liver fibrosis and other disorders, but they must be tested in an animal model.

## P129

## Quantitative determination of phenobarbital in pharmaceutical and biological samples using voltammetric techniques

*Saeid Ahmadzadeh*[1, 2], and *Zeinab Nejati*[3]

[1]Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran.

[2]Department of Medicinal Chemistry, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran.

[3]Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Corresponding author: Zeinab Nejati

Corresponding author Email: nejati2021.zeinab@gmail.com

Introduction: Phenobarbital, also known as phenobarbitone or phenobarb is a medication of the barbiturate type. It is recommended by the World Health Organization (WHO) for the treatment of certain types of epilepsy in developing countries. It may be used intravenously, injected into a muscle, or taken by mouth (1). The injectable form may be used to treat status epilepticus. Phenobarbital is occasionally used to treat trouble sleeping, anxiety, and drug withdrawal and to help with surgery. Side effects include a decreased level of consciousness along with a decreased effort to breathe. There is concern about both abuse and withdrawal following long-term use. It may also increase the risk of suicide (2, 3). Given the above-mentioned information about the importance of the phenobarbital, the development of a sensitive, accurate, selective and reliable method for its measurement in very low concentrations in pharmaceutical and biological samples is of great importance. Electrochemical methods in compare to other analysis strategies received more interest because the instrumental techniques mostly involve expensive instruments, lengthy sample preparation and complicated analysis procedures which has limited their application in the rapid and quantitative analysis of electroactive compounds. On the other hand, electrochemical sensors as an efficient approach offering advantages such as low cost, fast analysis, high sensitivity and selectivity (4, 5).Material and methods: Voltammetric measurements were performed on a Autolab PGSTAT204-Metrohm potentiostat/galvanostat programmed and controlled by NOVA 1.11 software and equipped with FRA module for electrochemical impedance spectroscopy studies. A three-electrode system was employed with a modified or unmodified carbon paste electrode as working electrode, a Pt wire as counter electrode, and a $Ag/AgCl/KCl_{saturated}$ electrode as reference electrode. Microstructure and surface morphology of nanoparticles were identified by a scanning electron microscope (SEM, Philips). Results: The proposed sensor showed good electrocatalytic activity towards the electro-oxidation response of phenobarbital with the enhancement of the electro-oxidation signal. The $ZnFe_2O_4$/NPs/IL/CPE exhibited a wide linear range of 5.0-250 µM and low detection limit of 2.24 µM for the determination of phenobarbital at pH 7.0 phosphate buffer (0.1 M). The excellent properties of the $ZnFe_2O_4$/NPs/IL/CPE make them promising for application to real sample analysis. The diffusion coefficient (D) of phenobarbital and the electron transfer coefficient (α) at the surface of $ZnFe_2O_4$/NPs/IL/CPE estimated to be $3.23\times10^{-4}$ cm $s^{-1}$ and 0.72.Discussion: This work demonstrated the application of a

$ZnFe_2O_4$/NPs and 1-butyl-3-methylimidazolium tetrafluoroborate as a modifier in carbon paste matrix for the determination of phenobarbital. The developed modified carbon paste electrode showed a considerable improvement in the kinetics of the electron transfer with an excellent reproducible analytical performance which indicated that the proposed sensor could be applied successfully for routine analysis.Conclusions: The proposed sensor as a promising and low-cost method successfully applied for determination of phenobarbital in pharmaceutical and biological samples

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## Preparation of niosomal gel containing olive (Olea sp.) extract in the tragacanth hydrogel base and evaluation of its wound healing effect

*Zahra Eghbali[1], Payam khazaeli[2], Fariba Sharififar[3],Somayyeh Karami-Mohajeri[4]*

[1]Student Research Committee , Pharmacy faculty, Kerman University of Medical Science, Kerman, Iran.

[2]Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Science, Kerman, Iran.

[3]Herbal and Traditional Medicines Research Center, Department of Pharmacognosy, Faculty of Pharmacy Kerman University of Medical Sciences, Haft Bagh-e Alavi Blvd, Kerman, Iran.

[4]Department of Toxicology and Pharmacology, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran.

Corresponding author: Payam khazaeli

Corresponding author Email: Khazaeli.payam@gmail.com

Introduction:Skin is the largest organ of the body and has a critical role in maintaining body homeostasis.Wound healing is a dynamic, interactive process initiated in response to injury that restores the function and integrity of damaged tissues. Healing of a wound is a complex and protracted process of tissue repair and remodeling in response to injury. Various plant products have been used in treatment of wounds over the years. Wound healing herbal extracts promote blood clotting, fight infection, and accelerate the healing of wounds.(1)Leaves and fruits of Olea sp. (Olive) have been used externally as emollient for skin ulcers, and healing of inflammatory wounds(2) and has been introduced as a potential therapeutic in wound healing owing to combined antioxidant and antimicrobial activity(3)Furthermore Iranian Gum Tragacanth (IGT) is the most common natural polymers which has found with lots of applications recently, and has attractive characteristic like nontoxic nature, biodegradability, higher resistance, antibacterial and good biological properties to bacterial attacks(4). Niosomes are vesicular, novel drug delivery system, which can be used for the controlled as well as targeted delivery of drugs. Niosomes can be used to encapsulate both hydrophilic as well as hydrophobic drugs(5).Gels are very popular due to their ease of use and improved skin absorption Also, the gel-based niosomes are more stable due to their fusion(6).Due to the anti-inflammatory and wound healing effects of olive extract and tragacanth gel, in this study, in order to facilitate the use and greater efficiency of the olive gel formulation, the neosomal formulation was prepared by tragacanth hydrogel and examined in the wound model of rats.If we see acceptable effects, we will test the formulation in clinical.Material and methods:

1. Preparation of olive leaf extract by warm maceration method
2. Standardization of plant extracts
3. Preparation of niosomes from standardized plant extracts
4. Formulation of olive niosomal gel based on tragacanth hydrogel
5. The effect of the formulation on the wound created in the rat

Results: According to tests, olive leaves contained tannins, steroids, terpenoids and flavonoids. The results of the current study indicated that the treatment of wounds with this formulation reduced infiltration of cells into incision sites, as well as helped wounds heal more quickly, when compared to the control group on day 3 post-incision.The histological examinations showed advanced reepithelialization and regeneration in the experimental group on day 7 post-incision. On day 7, the progression of wound healing was obvious when compared to the control group.Discussion: The experimental studies revealed that niosomal gel containing olive extract in the tragacanth hydrogel formulation displays remarkable wound healing activity. To be acting on the different stages of wound healing process could be considered as a beneficial effect of the formulation for the treatment of wound.Conclusions: Much remains to be learned about the effects of olive extract and tragacanth gel on wound healing and its mechanism of action. Based on the findings of this study, one possible mechanism of action may well be the anti-inflammatory and antioxidative properties of this phenolic compound.

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## Operational parameters effects on the removal of aspirin from pharmaceutical wastewater using electrocoagulation process

*Saeed Ahmadzadeh[1], Parsa Anjomshoa[2], Maryam Dolatabadi[3]*

[1]Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
[2]Pharmaceutical Sciences and Cosmetic Products Research Center, Kerman University of Medical Sciences, Kerman, Iran
[3]Environmental Science and Technology Research Center, Department of Environmental Health Engineering, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
Corresponding author: Saeed Ahmadzadeh
Corresponding author Email: Chem_ahmadzadeh@yahoo.com

Introduction: The increasing production and consumption of pharmaceutical products inevitably results in the release of a wide variety of synthetic organic compounds into the environment. Among the medicaments consumption, aspirin C9H8O4 (acetylsalicylic acid) is one of the important pharmaceutical compounds. Aspirin is a nonsteroidal anti-inflammatory drug (NSAID) and works similarly to other NSAIDs but also suppresses the normal functioning of platelets. Aspirin is used to treat pain, and reduce fever or inflammation. It is sometimes used to treat or prevent heart attacks, strokes, and chest pain (1, 2). Due to the harmful effects of the aspirin exposure such as irritation of the stomach or intestines, nausea, vomiting, heartburn, stomach cramps, stomach bleeding, worsening asthma, an effective and affordable treatment system should be under investigation (3, 4). During the last years, many methods have been applied to decrease the drug's effects including biological, chemical, and physical strategies, but certain green methods such as electrocoagulation have important role in sustainable chemistry (4, 5).Material and methods: The effect of operating parameters in the electrocoagulation (EC) process such as initial concentration of aspirin, pH solution, current density, inter electrode distance, and reaction time was investigated. Response surface methodology (RSM) under CCD category was used as a set of mathematical and statistical techniques for analysis and modeling the obtained results. The reactor setup equipped with two aluminum plate electrodes located in the center of the EC cell with immersed dimensions

of 4×2.5×0.1 cm. KNAUER Smartline HPLC (C18 column; 250×4.6×5 mm) with a UV detector at a wavelength of 235 nm was used for the quantitative determination of residual aspirin. The mobile phase consisted of acetonitrile and 10 mM and potassium phosphate buffer adjusted to pH 3.0 with phosphoric acid in the ratio 50:50 (v/v) (3).Results: The maximum removal rate of aspirin (99.1%) was achieved at pH 9.5, the current density of 6.0 mA cm-2, inter electrode distance of 2.5 cm, and initial concentration of 3.5 mg L-1 within the reaction time of 18.0 min. Analysis of variance (ANOVA) suggested that the effect of mentioned operating parameters was statistically significant on the aspirin removal. The obtained results revealed reasonable energy consumption of 0.315 kWh m-3. The obtained results from real sample analysis revealed that the initial aspirin concentration of 0.67±0.01 mg L-1 of pharmaceutical wastewater was found to reach zero after applying the optimal condition of the EC process.Discussion: It can be concluded that the adsorption of aspirin molecules on aluminum hydroxide and cationic hydroxides complexes (Aln(OH)3n) as main coagulants, which is known as sweep flocculation mechanism controlled the efficient removal of aspirin contaminant from pharmaceutical wastewater.Conclusions: The obtained results revealed that the EC process as a powerful and environmentally friendly emerging technique can be applied for efficient treatment of pharmaceutical wastewater sample in the current work.

## P132

## Evaluation of the Effectiveness of Cinnamon Oil Soft Capsule in Patients with Functional Dyspepsia: A Randomized Double-Blind Placebo-Controlled Clinical Trial

*Mohammad-Mehdi Gravandi[1], Mohammad-Hossein Farzaei[2], Mehdi Zobeiri[3]*

[1]Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

[2]Pharmaceutical Sciences Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

[3]Internal Medicine Department, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran

Corresponding author: Mohammad-Hossein Farzaei

Corresponding author Email: mh.farzaei@gmail.com

*Background*. Different effects of cinnamon and its oil in traditional medicine in the treatment of diseases, including gastrointestinal diseases, were reported. the aim of this study is to evaluate the efficacy and safety of cinnamon oil (*Cinnamomum zeylanicum*) in patients with functional dyspepsia in a double-blind, randomized placebo-controlled trial. *Methods*. Soft gelatin capsule was made using the rotary die process, and the final capsule was standardized based on its cinnamaldehyde amount and analyzed by high-performance liquid chromatography(HPLC) method. Sixty-four patients with symptomatic functional dyspepsia were randomized to receive cinnamon oil soft capsule ($n$= 29) or sesame oil soft capsule as placebo ($n$= 35) for 6 weeks. The primary efficacy variable was the sum score of the patient's gastrointestinal symptom (five-point scale). Secondary variables were the scores of each dyspeptic symptom including severity of vomiting, sickness, nausea, bloating, abdominal cramps, early satiety, acidic eructation/heartburn, loss of appetite, retrosternal discomfort, and epigastric pain/upper abdominal pain, as well as any reported adverse events.*Results:* the results showed that, after 6 weeks of treatment, the cinnamon oil and placebo groups significantly decreased the total dyspepsia score compared to the baseline at the endpoint ($P$ < 0.001). However, there was no significant difference between the cinnamon oil and placebo groups in terms of the baseline and endpoint values of the outcome variables ($P$ = 0.317 and $P$ = 0.174, respectively). Two patients in the cinnamon oil group complained of rashes, and three patients in the placebo group complained of nausea.*Conclusion*. this study showed significant improvements in gastrointestinal symptom score in both treatment and placebo groups. However, there was no significant difference between the cinnamon oil and sesame oil groups in terms of the baseline and endpoint values of the outcome variables.

## P133

## Evaluating the Analgesic Effects of Astaxanthin in Male Mice: The Role of L-arginine/cGMP/$K_{ATP}$ Channel Signaling Pathway

*Yasaman Ahmadpour[1], Hoda Rezaei[1], Samira Mohammadi[1], Mohammad Hosein Farzaei[2], Ahmad Mohammadi-Farani[2]* and *Sajad Fakhri[2]*

Student Research Committee, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

Pharmaceutical Sciences Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran

Corresponding author: Sajad Fakhri

Corresponding author Email: pharmacy.sajad@yahoo.com

Introduction: Pain is an unpleasant experience associated with potential tissue damages. Despite recent advances on pain studies, management of pain still faces many problems. Besides, the low efficacy of present drugs as well as the high incidence of related side effects, raise the needs to investigate novel drugs with relevant antinociceptive signaling pathway. Several mediators are involved in the antinociceptive signaling pathways such as L-arginine/nitric oxide (NO)/cyclic GMP (cGMP)/$K_{ATP}$. As a natural secondary metabolite, astaxanthin has shown anti-inflammatory, anti-apoptotic and anti-oxidant properties in several studies. According to these effects, in the present study, we investigated the antinociceptive effects of astaxanthin as well as the possible involvement of L-arginine/NO/cGMP/ $K_{ATP}$ in such effect.Material and methods: To assess the antinociceptive effects of the different doses of astaxanthin (5 mg/kg, 10 mg/kg, and 15 mg/kg), were examined in male NMRI mice (weighing 30 ± 3 g). Besides, to assess the involvement of NO in the antinociceptive effect of astaxanthin, mice were pretreated intraperitoneally with NO synthase inhibitor (L-NAME, 30 mg/kg), and NO donor (SNAP, 1 mg/kg). Beside, to evaluate the involvement of L-arginine, cGMP and $K_{ATP}$, L-arginine (as NO precursor, 100 mg/kg), sildenafil (5 mg/kg) and glibenclamide (10 mg/kg) were injected intraperitoneally respectively, 20 min before the administration of the most effective dose of astaxanthin. The formalin test (2%, 25µl i.pl.) was done 20 min after the administration of astaxanthin, and the antinociceptive effects of astaxanthin were investigated during the first acute phase and the second inflammatory phase for 5 and 15 min respectively.Results: The data of this study showed that 10 mg/kg dose of astaxanthin performed the best antinociceptive effects in the acute and chronic phases of formalin-induced pain. This effect was significantly enhanced by L-arginine, SNAP and sildenafil and also the antinociceptive effect of astaxanthin was significantly reduced by L-NAME and glibenclamide in early and late phases of formalin test. This results demonstrated the role of L-arginine/NO/cGMP/$K_{ATP}$ in the antinociceptive effects of astaxanthin.Discussion: Several studies have shown the role of NO, cGMP, and $K_{ATP}$ channel signaling pathway in modulation of pain. In this study, we investigated the analgesic effects of astaxanthin as a keto-carotenoid passing through NO, cGMP and $K_{ATP}$ channel by using formalin test in mice. In this regard, Kuedo *et al*. showed that astaxanthin isolated from Litopenaeus vannamei was able to increase the mechanical threshold for paw removal and reduce paw edema and lipid peroxidation products in the carrageenan induced pain model. In addition, they

showed that astaxanthin had a significant analgesic effect compared to indomethacin as a standard treatment to reduce the symptoms of inflammation.Conclusions: Based on the results, we concluded that the antinociceptive response of astaxanthin is interfered by L-arginine/NO/cGMP/$K_{ATP}$ pathway evaluated by formalin-induced pain in mice. Thus, astaxanthin could be a promising mediator in clinical applications.

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## Design and preparation of oral jelly candies of Ibuprofen and its nanoparticles

*Mohsen Sadeghi[1], Arvin Ardalan[2], Fereshteh Bagheri[3], Reza Tahvilian[4]*

Pharmaceutical Sciences Research Center, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran
Corresponding author: Reza Tahvilian
Corresponding author Email: rtahvilian@kums.ac.ir

Introduction: Nano drug delivery system is a relatively new but rapidly developing science where materials in the nanoscale range are employed to serve as means of diagnostic tools or to deliver therapeutic agents in a controlled manner. Ibuprofen as one of the most effective drugs for relieving fever and analgesic in treatment of mild to moderate pain in healthcare systems since many years ago. The aim of this study is to prepare a novel dosage form of Ibuprofen nanoparticles which are loaded on oral jelly candies that are suitable for children.Material and methods: Polyethylene glycol 6000 was dissolved in distilled water and then Ibuprofen powder was dissolved in ethanol and was added dropwise to the stirring solution of PEG. The nanoparticle solution then added to the solution of the jelly consist of gelatin, starch and sugar. The final solution stirred well and let to dry by itself in refrigerator temperature for 24houres. Characterization tests such as DSC, FT-IR spectroscopy, and TEM imaging, Entrapment efficiency and Release profiles of the nanoparticles and jelly candies were done.Results: The size of the synthesized nanoparticles was about 26-29 nm with a zeta potential of +11/6 mv. Cumulative drug release of the nanoparticles in jelly candies was about 82% after 24 hours and FT-IR results confirmed the formation of nanoparticles. Release profile of the nanoparticles obey the Higuchi model and the jelly candies show zero- order release profiles.Discussion: Studies have shown that the best nanoparticles in terms of size and zeta potential are obtained if the amount of polyethylene glycol polymer 1.33 g dissolved in 92 ml of distilled water and ibuprofen 1 g dissolved in 5 ml of ethanol and then The final volume of the mixture is 100 ml. In these values, the particle size is equal to 123 nm and the resulting zeta potential is equal to + 11.6 mV, which was smaller than previous studies. However, it should be noted that the size measured by the DLS device is actually equivalent to the hydrodynamic diameter of the nanoparticles and the average actual size of nanoparticles based on electron microscope findings is equal to 29 to 35 nm, which is quite suitable in terms of passing through the mucosal tissue of the gastrointestinal tract. The percentage of nanoparticles loading after calculations based on the amount of loaded and unloaded drug was estimated to be 20%, which is acceptable and the amount of unloaded drug is recyclable and the process can be performed on it again.Conclusions: It can be concluded that the oral jelly candies loaded by nanoparticles can be the next generation of novel dosage forms of Ibuprofen because of their ease of consumption and higher compliance of children than the conventional oral tablets.

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## Evaluation of anti-anxiety and analgesic effects of co-administration of *Achillea wilhelmsii* and *citrus aurantium* essential oil in rats

*Elnaz Moradi[1], Mohammad Bagher Majnooni[2], Sajad Fakhri[2], Mohammad Mehdi Gravandi[1], Mohammad Hosein Farzaei[2]*

[1]Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran.

[2]Pharmaceutical Sciences Research Center, Health Technology Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran.

Corresponding author: Elnaz Moradi1
Corresponding author Email: e.moradi998@gmail.com

Introduction:The use of medicinal herbs and natural compounds has always been one of the promising candidates for the treatment of psychiatric disorders and pain [1]. Therefore, in this study, the effects of co-administration of *Achillea wilhelmsii* and *citrus aurantium* essential oils, which are known in Iranian traditional medicine as sedative and analgesic herbs, have been investigated.Materials and methods:In this study, 30 rats were randomly divided into five groups. The hydrodistillation method and the Clevenger apparatus were used to prepare the essential oil. The studied groups were intraperitoneally injected a mixture of essential oils of *Achillea wilhelmsii* (A) and *citrus aurantium* (B) at doses of 0.5 and 1 mg/kg, including 0.5 (A) + 0.5 (B), 1 (A) + 0.5 (B), 0.5 (A)+ 1 (B), and 1 (A) + 1 (B), and the results were compared with the control group. The Teal Flick method was used to evaluate the analgesic effects and evaluate the anti-anxiety effect, Elevated Plus Maze, and Light/Dark box methods. The results were statistically analyzed using SPSS software (V = 11.5). Also, gas chromatography/mass spectroscopy (GC/MS) was used to analyze the essential oils.Results:The results of GC/MS analysis showed that p-ocimene (23%) and 1,8 cineole (20.8%) in *Achillea wilhelmsii* essential oil and linalool (8.01%) and limonene (57.57%) in *citrus aurantium* essential oil were the major compounds, respectively. Also, the results of co-administration of essential oils in all groups on reducing pain and anxiety were significant compared to the control group (P> 0.05). The results showed analgesic and anti-anxiety effects of the essential oil mixture in a dose-dependent manner.Discussion:The results of this study and its comparison with other results of similar studies showed that co-administration of *Achillea wilhelmsii* and *citrus aurantium* essential oils could reduce pain and anxiety more effectively in the studied groups[2, 3].Conclusion**:** The results obtained in this study can be used to produce a pre-formulation from the essential oils of both herbs and to perform pre-clinical and clinical studies.

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## Design, synthesis and in silico ADMET Prediction studies of 2-aryl-N-arylmethyl-1H-benzimidazole derivatives as potential inhibitors of platelet aggregation.

*Abolfazl Firouzbakht[1], Masoud Faghih Akhlaghi[2]*

[1]Guilan University of Medical Sciences, Rasht, Iran

[2]Department of Medicinal Chemistry, Guilan University of Medical Sciences, Rasht, Iran

Corresponding author: Masoud Faghih Akhlaghi
Corresponding author Email: mfakhlaghi@yahoo.com

Introduction: Cardiovascular disease are the leading cause of death worldwide and antiplatelete therapy is a main strategy in its prevention and treatment [1]. Different receptors and mechanisms are involved in the process of platelet aggregation including adenosine diphosphate (ADP) receptor. It has been proved that compounds with similar structure to purine base are competitive ADP receptor antagonists [2]. Benzimidazole is a well-known and safe purine analog which has been used in the structure of different drugs and endogen compounds. Therefore in the present study, a series of 2-aryl benzimidazole and 2-aryl-N-arylmethyl-1H-benzimidazole derivatives were synthesized as new potential antiplatelet agents, and their ADMET properties were predicted in silico.Material and methods: 2-aryl benzimidazole derivatives were synthetized by the reaction of orthophenylendiamine with appropriate aldehyde in acetonitrile and heated under reflux condition [3]. For synthesis of 2-aryl-N-arylmethyl-1H-benzimidazole derivatives, chlorosulfonic acid was added to the mixture of orthophenylendiamine and suitable aldehyde [4]. The reactions were monitored by TLC and after work up final products were recrystallized from proper solution (i. e. ethanol). The structure of compounds were analyzed using FTIR, GC-Mass, NMR and the ADMET properties of synthesized derivatives were evaluated in silico.Results: The results of FTIR, GC-Mass, NMR analysis confirmed synthesis of derivatives as potential antiplatelet agents.Discussion: In silico analysis of the physicochemical properties of compounds showed suitable ADMET properties. The molecular weight of compounds ranged from 194.2 to 374.4, the value of log P ranged from 2.9 to 5.2, the amount of H-bond donor (HBD) was 0 or 1 in all compounds, and the amount of H-bond acceptor (HBA) ranged from 1 to 5. The results showed that all derivatives met the Lipinski Rules of Five, have proper permeability and can be easily absorbed.Conclusions: Various 2-aryl benzimidazole and 2-aryl-N-arylmethyl-1H-benzimidazole derivatives were successfully synthesized with proper physicochemical properties, being potential candidates for *in vitro* and *in vivo* platelet aggregation studies.

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## Isolation,identification and characterization of some LTP antimicrobial peptides from Barberry(Berberis thunbergii)

*Mohsen Mohammadi[1],Nadia Gholamy[2]*

[1]Department of Biotechnology, Faculty of Pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran

[2]Student Research Committee, Faculty of Pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran

Corresponding author: Nadia Gholamy

Corresponding author Email: nadia.gholamy.daroo@gmail.com

Due to the increasing demand for new antimicrobial compounds in medicine, in recently research on Antimicrobial Peptides (AMP) for various reasons, including lack of resistance and broad spectrum action against different pathogens such as bacteria, viruses, fungi, cancer cells, etc significantly have increased. Plant antimicrobial peptides such as *Berberis Thunbergii* LTP peptides, which are naturally present in various plants, can be potential candidates to meet the medical needs of new antimicrobial compounds. this study identified the presence of different members of the LTP antimicrobial peptide gene family in the *Berberis Thunbergii* plant and the gene sequences of eight LTPs of *Berberis Thunbergii* by using various bioinformatics and laboratory methods for the first time.also their different structural and functional characteristics were determined. The overall results of this study showed that the LTP genes of the *Berberis Thunbergii* plant show similar structural and functional characteristics as other LTP peptides. The study also found that all *Berberis Thunbergii* LTP peptides have potential antimicrobial properties and may exhibit other activities. Due to these potential antimicrobial properties in *Berberis Thunbergii* LTP peptides, they can be used as new antimicrobial agents against human pathogens by extracting them from the plant or producing them in eukaryotic and prokaryotic expression systems.

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## Design and synthesize a number of new derivatives of 4- anilinoquinazoline and examining the interaction of the synthesized compounds with the epidermal growth factor receptor in a virtual form with the AutoDock software.

*Naser Seydbagian[1,2] , Rezvan Rezaeinasab[1], Fateme Ghaffary[1,2]*

[1]Department of Medicinal Chemistry, School of Pharmacy and Pharmaceutical Sciences, Lorestan University of Medical Sciences, Khorramabad, I.R. Iran

[2]Student research committee , School of Pharmacy and Pharmaceutical Sciences, Lorestan University of Medical Sciences, Khorramabad, I.R. Iran

Corresponding author: Rezvan Rezaeinasab

Corresponding author Email: rezaeepharm90@gmail.com

Introduction: With the increasing rate of cancer and the timing of the development of new drugs in laboratory methods, using a new method that has less cost and time, drugs with high effectiveness and fewer side effects can be achieved. The aim of this study was to introduce the tools for achieving new anti-cancer drugs and the benefits of pre-laboratory studies in reducing the cost of production of these drugs. In this study, computerized molecular docking method was used to investigate 4-anilinoquinazolin derivatives as potential epidermal growth factor receptor inhibitors. These compounds were synthesized after design and docking, which had good results.Material and methods: In this study, a number of 4-anilinoquinazolin derivatives were designed and synthesized. In order to investigate the binding of these compounds with the active position of epidermal growth factor receptor, the chemical structure of the compounds was initially drawn using Hyperchem software and then energy optimization was performed. Molecular docking studies were carried out by AutoDock4.2 software and in the final stage, the results were analyzed using AutoDockTools and DS Visualizer programs.Results: Among all the studied compounds, the best docking results were related to compound N-(4- nitrophenyl) 2 – phenylquinazolin-4-amine. This compound with the most negative binding energy level (-8.93 kcal/mol) is more willing to bind to key amino acids of the active position of epidermal growth factor receptor. The interaction location of this compound is similar to erlotinib. In this compound, nitrogen atom with two amino acids Lys721, Asp831, Met769 establishes the active position of hydrogen bonding receptor.Discussion: This should explore the significance of the results of the work, not repeat them.Conclusions: At the end, due to the high efficacy and docking results, it can be concluded that the combination of N-(4-nitrophenyl)-2-phenylquinazolin-4-amine can be considered as an epidermal growth factor receptor inhibitor.

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## Anti bacterial and molecular docking study of some 4-anilinoquinazoline derivatives

*Rezvan Rezaee Nasab*[1], *Soosan Abdollahi*[2], and *Esmail Dehghan Ghahfarokhi*[3]

[1]Department of Medicinal Chemistry, Faculty of pharmacy , Lorestan University of Medical Sciences, Khorramabad , Iran
[2]Department of Cosmetics and Toiletries Control, Faculty of pharmacy , Lorestan University of Medical Sciences, Khorramabad , Iran

[3]Student Research Committee, Faculty of pharmacy , Lorestan University of Medical Sciences, Khorramabad , Iran

Corresponding author: Rezvan Rezaee Nasab

Corresponding author Email: Rezaeepharm90@gmail.com

Introduction: Infectious diseases caused by bacteria affect millions of people around the world. Due to the growing human resistance to antibiotics, systematic programs for the discovery and development of new drugs have attracted much attention(1). DNA gyrase is one of the topoisomerase enzymes that catalyzes topological changes in DNA structure and is known as the target site of the drug in antimicrobial studies. Quinazoline derivatives are one of the compounds that have shown wide antimicrobial and antifungal effects in studies due to their different functional groups and are good candidates for the discovery and development of new antibiotic drugs(2). In studies, a number of synthesized quinazoline derivatives with various substitutions known as pharmacophores were tested, including 4-aniline quinazoline. In this research project, we will investigate the interaction of synthesized compounds with the active site of DNA gyrase enzyme by Autodac method. Also, due to the nature of quinazoline compounds as antimicrobial compounds, their antimicrobial effects on strains of gram-negative and gram-positive bacteria and fungi will be evaluated. Material and methods: In order to investigate the binding of these compounds with the active position of DNA gyrase, the chemical structure of the compounds was initially drawn using Hyperchem software and then energy optimization was performed. Molecular docking studies were carried out by AutoDock4.2 software and in the final stage, the results were analyzed using AutoDockTools and DS Visualizer programs. The biological activities were evaluated using minimum inhibitory concentration and minimum bactericidal concentration determined by microdilution Alamar Blue assay against gram-positive (S. aureus) and gram-negative (E. coli) bacteria which was compared with ciprofloxacin standard and one strain of fungi (Candida albicans) which was compared with nystatin standard.(3-4) Results: The results of molecular docking studies of compounds on DNA gyrase show the importance of the skeleton of dihydroquinazolinone compounds as well as substitutions on phenyl rings in establishing hydrogen bonds and hydrophobic interactions. 4-nitro aniline with the most negative binding energy level (-6.13 kcal/mol) is more willing to bind to key amino acids of the active position of epidermal growth factor receptor.The results showed that all tested compounds have mild to good antifungal antibacterial effects against candida albicans and both type of bacteria. Discussion: in this study the 4-quinazoline compounds showed better antibacterial effects against Gram negative bacteria in the broth media, but in the agar medium different factors were impacting the bacterial inhibition including the diffusion rate of quinqzoline solution and the growth rate of bacteria.(5)Conclusions: Due to the anti-bacterial effect of quinazoline derivatives , this compounds are good candidates for next studies to discovery and development new antibiotic drugs.

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## one-pot synthesis of dihydroquinazolinone derivatives and their in silico docking studies on EGFR1

*Keikhosravi Navid*[1], *Rezvan Rezaee-Nasab*[2]

[1]Student research committee , School of Pharmacy and Pharmaceutical Sciences, Lorestan University of Medical Sciences, Khorramabad, I.R. Iran
[2]Department of Medicinal Chemistry, School of Pharmacy and Pharmaceutical Sciences, Lorestan University of Medical Sciences, Khorramabad, I.R. Iran

Corresponding author:Rezvan Rezaee-Nasab

Corresponding author Email:Rezaeepharm90@gmail.com

Introduction: Quinazolinones are one of the important chemical heterocyclic compounds that have been used in the structure of many pharmaceutical compounds. These compounds have nitrogen atoms in their structure. These compounds have attracted much attention due to their wide range of pharmacological and therapeutic activities such as anti-cancer, anti-inflammatory, anti-diuretic, anti-fungal and anti-bacterial effects. Quinazolinones derivatives have been identified as inhibitors of epidermal growth factor receptors (EGFR). EGFR is a tyrosine kinase receptor that is overexpressed in human tumors. Therefore, EGFR inhibitors are expected to have great potential in the treatment of malignancies. Multi component reactions (MCRs) is a process in which three or more reactants combine together in a reaction container to synthesis a final product. Green synthesis is also the design, development and implementation of chemical reactions that reduce or eliminate the use and production of substances hazardous to human health and the environment. One of the methods of designing medicine using computer is molecular docking. Molecular docking with software such as Autodock is a molecular modeling technique that is used to predict how a protein (enzyme) interacts with small molecules (ligands).Material and methods: In this study, a number of compounds were synthesized based on one-pot and multi-component reactions via a three component of isatoic anhydride, Urea, and Benzaldehyde derivatives and using SnCl2.2H2O catalyst. by placing benzaldehyde substitutions in the position of 4 quinazolinones rings and their interaction with the active site of the EGFR receptor was investigated.Results: The results show that the desired products with high yield are synthesis at the suitable time. The products were identified by melting point measurements and FT-IR and 1HNMR spectra. The hit compounds identified were compound p4 with a binding affinity of − 6.87 kcal/mol. The shortest reaction time and the highest efficiency among the synthesized compounds is compound p6.Discussion: The results of molecular docking studies of compounds on EGFR show the importance of the skeleton of dihydroquinazolinone compounds as well as substitutions on phenyl rings in establishing hydrogen bonds and hydrophobic interactions. According to the results of docking studies, the most important bonds involved in drug-receptor binding are hydrogen bonds and hydrophobic bonds.Conclusions: In summary, we have described a successful strategy, an efficient and convenient synthesis for the preparation of 2,3-dihydroquinazolin-4(1H)-one derivatives via a three component of isatoic anhydride, Urea, and Benzaldehyde derivatives, using the inexpensive, non-toxic, and easily available SnCl2.2H2O catalyst. Molecular docking showed that most of the studied compounds have good performance and acceptable binding energy, so they can be studied in practical research as potential anti-cancer agents.

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## Preparation and characterization of a novel exosome_liposome hybrid nanoparticle incorporated with green tea's catechins

*Ronak sepahvand*[1,2], *mohmmadsadegh bazvand*[1,2], and *nooshin tasharrofi*[1]

[1]Department of pharmaceutics, Faculty of pharmacy, Lorestan university of medical Sciences, Khorramabad, Iran

[2]Student Research Committee, Lorestan University of Medical Sciences, Khorramabad, Iran

Corresponding author: Ronak sepahvand

Corresponding author Email:ronaksepahvand1380@gmail.com

Introduction:Regarding skin, topical nanocarriers have received a great deal of attention because of their versatility and high performance. Lipid nanoparticles, including liposomes, showed promising results in this field. Liposomes can be easily tailor-made to achieve the desired properties. Exosomes are bilayer membrane vesicles that are released from different cells and carry some biologicals; bearing some special proteins on their membrane, they can easily interact with the target cells and convey their payload to them (1). Because of the similarity of the liposomes and exosomes structures, they can easily be merged and take advantage of each other, i.e. stabilize exosomes and enhance cell permeability of liposomes (2). Green tea contains compounds, namely catechins, which can be advantageous for skin structure (3). Catechins are unstable molecules and in some undesirable conditions can be easily destroyed.In the present study, we attempted to produce a novel hybrid nanocarrier of a flexible liposome and human umbilical cord mesenchymal stem cell-derived exosome (hUCMSC-Exo), with optimized features for the delivery of green tea catechins to the skin.Material and methods: Mesenchymal stem cells isolated from the human umbilical cord were used as exosome-providing cells. They were cultured and their medium was collected. These media were centrifuged in several steps and exosomes were collected by ultracentrifugation and characterized. Liposomes were prepared using thin film hydration. Phosphatidylcholine and cholesterol were used as the main components of the liposome; besides tween 80 (a non-ionic surfactant) was used for making the liposome more flexible. Microwave-assisted extraction was used for preparing green tea extract and its catechins were extracted stepwise using chloroform and ethyl acetate (3). The liposomes and exosomes were merged by freeze and thaw and then loaded with the catechins (4); this hybrid carrier was characterized by DLS and SEM for their size, zeta potential, and morphology; the loading efficacy and release profile (in buffered isotonic saline at 32 ° C and pH= 5.5) were also assessed. The permeability test is not performed by now; if completed, the results will be reported later.Results:The hUCMSC-Exo with the mean diameter of 105 nm merged with 142 nm liposomes. The hybrid catechin-loaded nanocarrier showed a spherical shape and size of about 200 nm. The entrapment efficacy (%) of the optimized formulation was around 84 %. The release profile data is not analyzed yet and will be reported then.Discussion: In this study a novel hybrid liposomal formulation has been made and optimized. Using this method liposomes could effectively merge with exosomes to take advantage of the exosome's components and features. This hybrid carrier possessed suitable characteristics, like high %EE, reasonable size, and protecting unstable chatechines, which make it possible to be recruited as an applicable drug carrier.Conclusion: This drug delivery system showed promising results and after more complete in-vivo studies, it could be considered as an effective carrier for topical drug delivery.

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## Comparison of amantadine and dalfampridine efficacy in multiple sclerosis patients with fatigue Abstract

*Yasaman Sadeghi*[1],*Monireh Ghazaeian*[2], and Mohammad Baghbanian[3]

[1]Pharmacy Student, Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[2]Department of Clinical Pharmacy, Faculty of Pharmacy, Mazandaran Univesity of Medical Sciences, Iran

[3]Clinical Research Development Unit of Bou Ali Sina Hospital, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: mohammadbaghbanian@gmail.com

Corresponding author Email: Mohammad Baghbanian

Introduction:Fatigue is a common symptom of Multiple Sclerosis (MS) that cause significant distress and have detrimental effects on daily living function. The aim of this study was to compare the efficacy of dalfampridine and amantadine in relieving fatigue in patients with MS.Material and methods:This is a prospective, randomized, double-blind clinical study performed at the MS Clinic of Ibn-e- Sina Hospital. The primary outcome of the study was improvement of fatigue score according to modified fatigue impact scale (MFIS). Secondary outcome was quality life changes regarding 36-Item Short Form Survey(SF36). All changes were evaluated at baseline and monthly intervals for two months, and any possible side effects were recorded during the study. Results:Between July 2019 and October 2020, total of 120 MS patients with complain of fatigue referred to clinic and 54 of them completed the study and analyzed. Baseline clinical characteristics and demographics were not significantly different. In patients who received amantadine, the mean MFIS index was 46.74 at the beginning of the study and reached 38.29 at the end of the study, and in patients who received dalfampridine it decreased from 47.22 to 34.26 . Both amantadine($p=0.01$) and dalfampridine ($p<0.01$) were able to effectively reduce the fatigue of MS patients but were not significantly different in intragroup comparison at the end of the second month, ($p=0.132$). The SF36 index in patients received amantadine averaged from 41.4 to 29.42 and in patients received dalfampridine increased from 22.42 to 44.44. According to the data, the trend of changes in both groups was almost similar and upward.Discussion : In most of the previous studies amantadin was choice to reducing fatigue of patients with MS and the results of our study show that dalfampiridine can be a suitable alternative for this issue. Also, the positive effect of dalfampiridine on gait disorders in patients with MS is one of its valuable benefit which can improve the quality of life and reduce the tiredness in patients.
It seems that if the statistical population under study was higher or they continued to take the drug for a longer period of time, dalfampiridine could be more effective in reducing fatigue in patients with MS.Conclusions:The results of this study showed that dalfampridine effect was not inferior to amantadine to improvement of fatigue index in patients with MS. Furthermore, safety profile of both drugs was well tolerated without any alarming sign.

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## Formulation and evaluation of lipogel containing hydro alcoholic extract of lavandula stoechas for burn wound healing in wistar rats

*Hossein Asgari Rad[1], Shervin AmirKhanloo[2], Melika Ahmadi[2], Bahare Sayyad[3], Hossein ebrahimi[3]*

[1]Associate Professor, Department of Pharmaceutics, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[2]Ph.D Student in Pharmaceutics, Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[3]Pharmacy Student, Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: bahare sayyad

Corresponding author Email: bh.sayad@gmail.com

Introduction: According to conducted studies, burns are the sixth leading cause of death among Iranians. Burns damage the body's most important defense barrier, the skin. In this research project, lavender plant which has numerous applications in traditional medicine, has been used. Studies reported that lavender could have been beneficial in treatment of epilepsy, melancholy, neurological and cardiac enhancement, sweating and burns. There are limited number of studies about efficacy of Lavender in the treatment of wounds and insect bites. According to these studies lavender could heal the condition by reducing pain, inflammation and redness. Therefore, this study was conducted to evaluate efficacy of lavender in histopathological aspect of burn wound healing.Material and methods: lavender plants were purchased from authentic apothecary in Sari and also collected from the southern regions of Gorgan. Herbarium sample of plants was prepared and approved by a pharmacognosy specialist and extracted by maceration method by ratio of 70:30 alcohol to water respectively and was standardized by amount of quercetin. For formulation of lipogel, different amounts of paraffin and polyethylene were mixed together to reach the highest quality in physicochemical properties. For in vivo study, size of burn wounds were measured during three weeks of observation in rats and tissues were prepared for further histopatholoical evaluations.Results: The lipogel is stored at three temperatures of 2±4 ° C, 2± 25 ° C and 2± 45° C for 28 days. Then the physicochemical parameters were determined at regular intervals with the performed measurements in terms of phase separation, spreadability, microbial and organoleptic properties. According to invivo results, the group of rat received lavender lipogel showed better wound healing condition compared to other groups which received placebo and positive controlled drug. Also histopathology analyses showed the higher re epithelization, collagen synthesis and papilla formation and dermal ridge in tissues under treatment by lavender lipogel compared to other groups.Discussion: Due to the antibacterial properties of lavender, it can be suggested as a potential herbal drug for treatment of burn wounds to reduce antibiotic resistance. Lipogel is a drug delivery system which helps the skin to save its moisture by its occlusive effect that helps to accelerate wound healing process. Lavander hydroalcoholic extract could heal burn wound by improvement of histological parameters involved in wound healing procces and its anti-inflammatory effects.Conclusions: formulation of lipogel for lavender could increase its pharmaceutical properties which showed improvement in collagen synthesis and histological parameters in burn wound healing process.

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## An eco-friendly and hopeful platform for delivering Vitamin A in topical administration for wound disorder: Vitamin A loaded niosome and solid lipid nanoparticle

*Mohammad Eghbali[1], Seyyed Mohammad Hassan Hashemi [2], Amirhossein Babaei [2], Majid Saeedi[2]*

[1]Student Research Committee, Faculty of pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[2]Department of Pharmaceutics, Faculty of pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: Mohammad Eghbali

Corresponding author Email: mohammadeghbali1996@gmail.com

Introduction: Wound healing mostly means healing of the skin. The present work designed to improve the skin delivery of Vit A niosome was prepared via an ultrasonic technique. The Vit A loaded niosome formulations were optimized by investigating the effects of the cholesterol: surfactants ratio.Material and methods: To characterize the morphology and solid-state of Vit A in niosome, differential scanning calorimetry, photon correlation spectroscopy, powder x-ray diffractometer, scanning electron microscopy (SEM), and attenuated total reflectance-Fourier transform infrared spectroscopy were utilized.Results: The findings indicated that adding cholesterol incremented the niosome's particle size. Further studies proved that the zeta potential and the size of niosome can be modulated by the alterations in the ratio of cholesterol: surfactant. When the cholesterol concentration was high in the formulation, the highest entrapment efficiency was found to be approximately 88 %. Solid-state analysis showed that Vit A in the niosome was in the amorphous state. The drug release test indicated that niosomal formulation had slow release during 24 h. In vivo efficacy of Vit A-niosome was evaluated using an excision wound model (murine model) in male Wistar rat.Discussion: Macroscopic studies showed that the wound closure in the Vit A niosome-treated group and Vit A SLN(solid lipid nanoparticle) was same to each other and higher than the other groups. Pathological studies described that the recovery wound in the Vit A-niosomal gel group was higher than the other groups. The formulations were examined in terms of skin irritation on Wistar rats, and non-irritancy of Vit A niosomal gels and Vit A–SLN was indicated.Conclusions: The results of this work discovered that the prepared Vit A-niosome and Vit A–SLN could be utilized as possible nano-vesicle for the Vit A topical delivery and might open new approaches for the treatment of wound disorder.

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## Preparation and evaluation of cumin essential oil nanoemulgel as a potential skin enhancer: *in vivo* animal study

*Mohammad Eghbali[1], Amirhossein Babaei [2], Seyyed Mohammad Hassan Hashemi [2], Majid Saeedi[2]*

[1]Student Research Committee, Faculty of pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[2]Department of Pharmaceutics, Faculty of pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: Mohammad Eghbali

Corresponding author Email: mohammadeghbali1996@gmail.com

Introduction: Cumin (*Cuminum cyminum* L.) is an aromatic herb *in* the Apiaceae family. In Iranian traditional medicine, it has traditionally been utilized to provide treatments for toothache and relieve painful and inflammatory conditions. Natural compounds from essential oils have been proposed as promising non-toxic transdermal permeation enhancers. Still, their use has been limited because of its low water

solubility. Use of nanotechnology-based strategies is one of the ways to overcome these limitations. This study aimed to examine the transdermal permeation enhancing the capability of Cumin essential oil in nanoemulgel system for diclofenac delivery and compare its effect with the marketed formulation.Material and methods: Gas chromatography-mass spectrometry was employed to identify and quantify the constituents of the cumin essential oil. The o/w cumin nanoemulsions were produced by high-pressure homogenization technique and optimized at hydrophilic lipophilic balance values range of 9.65-16.7 with different surfactant mixture (Tween 20, 80 and Span 80). Preparations were characterized by polydispersity index, droplet size, and zeta potential. cumin nanoemulsion was incorporated in Carbopol 940 gel matrix with concentrations 1, and 2% of the total nanoemulgel formulation and further evaluation for its permeation enhancing effect was performed through Franz diffusion cells. Antinociceptive activities have been measured in thermal (tail-flick test) and chemical (formalin test) models of nociception in mice.Results: The characterization evaluation exhibited an optimized formulation with hydrophilic lipophilic balance 9.65 promoted the smallest particle size formed with spherical shape for transdermal purpose. Among the formulation, the highest permeation amounts were obtained by cumin nanoemulgel 2% and 1% containing diclofenac 34.75 ± 1.07 and 28.39 ± 1.23 μg/cm$^2$ at 24 h respectively. However, the value of simple diclofenac gel and the marketed product was lower than the formulations containing cumin nanoemulsion. Formulations containing cumin nanoemulsion plus Diclofenac showed considerably more antinociceptive effects in both formalin and tail-flick tests than simple diclofenac gel and marketed formulation.Discussion: In tail flick test, the topical administration of cumin nanoemulgel containing Diclofenac exhibited a significantly extended period of responses towards the pain stimuli in comparison to marketed product, simple diclofenac gel, and plain gel (which has no effect) within a period of 60 minutes of operation ($p < 0.0001$). In formalin test, incorporation of cumin nanoemulsion into the simple diclofenac gel significantly affected the antinociceptive effect of Diclofenac in the early phase. Higher analgesic effects of cumin nanoemulgel 2% and 1% containing diclofenac were observed compared to simple diclofenac gel and marketed formulation in the early phase ($p < 0.0001$). The late phase of formalin test indicated that cumin essential oil significantly affected the antinociceptive activity of Diclofenac. The enhancing effects of cumin nanoemulgel containing diclofenac were observed in comparison to both diclofenac simple gel and marketed formulation ($p < 0.0001$) in the late phase of the formalin test. Conclusions: The study showed that cumin essential oil in the nanoemulsion system might prove a promising alternative for analgesic and permeation enhancers as an efficient transdermal nanocarrier.

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## Preparation of spironolactone nanostructured lipid carriers coated with chitosan 1% gel and its evaluation on mild to moderate acne

*Amin Goodarzi*[1]

Corresponding author: Amin Goodarzi
Corresponding author Email: amingoodarzi7575@gmail.com

Introduction: Acne vulgaris ia common skin disease that occurs at a younger age that causes psychological effects. Spironolactone is an antagonist of aldosterone and an antagonist of androgenic receptors used orally to treat diseases such as Acne. Nano structured Lipid Carriers (NLCs) are colloidal carrier systems composed of a high melting point solid lipid as a solid core and liquid lipid coated by surfactants. Distinct advantages of Nano structured Lipid Carriers include controlled release and protection of active substances. Chitosan is a biopolymer that used in this study to control the release of the drug from nanoparticles and increase the drug level in the skin. The purpose of this study is preparation of gel formulation of nanostructured lipid carriers of spironolactone coated with chitosan and its evaluation on mild to moderate acne.Method: NLCs have been prepared by ultrasonication method at above the melting point of lipid and with using of palmitic acid and oleic acid as carriers. aqueous phase containing surfactants and water was added to the lipid phase containing drug, lipid and surfactants that was melted and mixed on the stirer. The resulting mixture was sonicated by a sonication device without the presence of temperature and with 50% Am for 7.5 minutes, then was placed in the ice bath on the stirrer. optimum formulation was selected for chitosan coating. The chitosan was then dissolved in dilute acid and added to the suspension dropwise on the stirer. Then, the properties of nanoparticles, such as particle size, PDI, zeta potential, entrapment efficiency, release and skin absorption were investigated. Resulted formulation was incorporated in Carbopol 940 gel matrix to prepare the gel. This study was a randomized, double blind clinical trial on 40 participants with mild to moderate acne vulgaris divided in two groups. One group was received spironolactone nanostructured lipid carriers coated with chitosan 1% gel and another group was received placebo. also, both groups were received clindamycin 2% solution. After 8 weeks the Total Lesion Counts (TLC) and Acne Severity Index (ASI) was evaluated.Results: The coating of Spironolactone nanoparticles with chitosan increases the particle size and PDI, and the zeta potential changes from a negative sign to a number with a positive sign. The chitosan coated NLCs have a slow and controlled release. The clinical trial results indicate that both groups reduced Total Lesion Counts and Acne Severity Index and also showed more reduction in spironolactone group. The adverse effect evaluation not showed significant difference between two groups.Conclusion: the study showed that the spironolactone NLCs coated with chitosan 1% gel can effectively improve the mild to moderate acne vulgaris and can be used in topical combination therapy.

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## Formulation and evaluation of hydrophilic ointment containing ostrich oil for wound healing in wistar rats

*Hossein Asgari Rad*[1], *Shervin AmirKhanloo*[2], *Melika Ahmadi*[2], *Hossein ebrahimi*[3]

[1]Associate Professor, Department of Pharmaceutics, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[2]Ph.D. Student in Pharmaceutics, Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[3]Pharmacy Student, Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: hossein ebrahimi

Corresponding author Email: h_ebrahimi98@yahoo.com

Introduction: Millions of people every year develop scars in response to skin injuries after surgeries, trauma, or burns. Wound healing is a complex biological process which includes four steps of hemostasis, inflammation, proliferation, and remodeling. anti-inflammatory, antioxidant, antifungal, antiviral, antimicrobial, and analgesic properties show positive impacts on the wound healing process. Ostrich oil is mainly composed of triglycerides and essential fatty acids. It also consists of various compounds such as carotenoids, tocopherol, vitamins, and flavones. The ostrich oil is commonly used in traditiomal medicine as an anti-inflammatory in eczema and contact dermatitis. Ostrich oil has antimicrobial and antioxidant properties, which

antioxidant activities of ostrich oil might be due to their fatty acids, vitamins and amino acids which can be helpful for wound healing.Material and methods:Ostrich oil was obtained and various formulations of ostrich oil hydrophilic ointment were prepared and evaluated by different amount of surfactants. Physicochemical and stability evaluations were conducted to obtain optimum formulation. For in-vivo study, square-shaped cutaneous wounds were developed on the back of adult albino rats and they were separated into 4 groups. Size of wounds was measured during three weeks of observation and tissues were prepared for further histopathological evaluations.Results: hydrophilic ointment formulations showed various physicochemical properties in viscosity, spreadability and stability which F4 showed optimum results compared to others. Histopathology results indicated that the group under treatment of ostrich oil hydrophilic ointment showed significant improvements in collagen synthesis, epithelial hyperplasia and regeneration of hair follicles, papilla formation and dermal rigid.Discussion: Essential fatty acids in ostrich oil like omega-3 can reduce inflammation and muscular pain in addition to vitamin A has excellent antioxidants activities. So due to painkilling effect, antioxidant levels, antimicrobial, anti-inflammatory properties and ability of reaching into deep skin, ostrich oil can be suggested for small wounds, cuts and burns.Conclusions: formulation of hydrophilic ointment of Ostrich oil could increase its pharmaceutical properties such as better spreadability and compatibility for administration of oils on skin. This formulation showed significant improvement in collagen synthesis and histological parameters in the wound healing process.

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## Determination amount of caffeine, total phenol, and heavy metals (lead, cadmium, and chromium) in green and black tea collected from different regions of Guilan province (Iran) by spectroscopic method

*Mohammad Hossein Hosseinzadeh[1], Faezeh* Bodaghabadi1, Mansoure Boustani1, Mohammad Shokrzadeh2, and Emran Habibi3,4

[1]Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[2]Associated professor, Pharmaceutical Sciences Research Center, Department of Toxicology and Pharmacology, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[3]Assistant professor, Department of Pharmacognosy and Biotechnology, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

[4]Pharmaceutical Sciences Research Center, Hemoglobinopathy Institute, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: Emran Habibi

Corresponding author Email: emrapharm@yahoo.com

Introduction: Because of the stimulating and useful effects, tea is the most common beverage in the world after the water. These effects are due to the presence of caffeine and phenolic compounds in tea. Food pollution to the heavy metals is one of the most important problems. Also, most of the tea planted in Iran is in Guilan province. In this research, we measured the total phenolic content, caffeine, Lead, cadmium, and chromium in green and black tea of Guilan province.Material and methods: 10 samples of green and black tea were purchased from different regions of Guilan (Astaneh-ye Ashrafiyeh, Gurab, Soostan, Langarud, Kumeleh & Otaqvar, . Methanol and dichloromethane extracts were prepared. Total phenol content and caffeine were detected by spectrophotometer. Quantification of heavy metals was done by digestion methods and examined by atomic absorption spectrophotometer.Results: The average amount of total phenolic content, caffeine, lead, cadmium, and chromium in green tea of all regions was 27.13±1.54%, 3.20±0.01%, 0.81±0.66 ppm, 1.54±1.39 ppm, 0.28±0.20 ppm respectively and in black tea was 14.90±1.53%, 3.20±0.05%, 1.00±0.79 ppm, 1.65±0.93 ppm, and 0.24±0.15 ppm respectively. Also, the results of each region are evaluated separately and compared with other regions.Discussion: The amount of total phenolic content and lead in tea was significantly different in different regions of Guilan province. Green tea contains more phenolic compounds than black tea, but the amount of caffeine in green and black tea is almost equal. The amount of cadmium and chromium in some Guilan province areas is significantly higher than the standard level, which needs to be investigated.Conclusions: Green tea has more antioxidant value than black tea. The level of lead and chromium contamination in tea is higher than the standard level in some areas, and the use of tea in these areas should be done with more caution. It is suggested that more detailed studies be carried out on the water supply sources of tea plantations and factories that produce environmental pollutants.

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## Prevention of colistin induced nephrotoxicity: a review of preclinical and clinical data

*Fatemeh Jafari[1], Sepideh Elyasi[2]*

[1]School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[2]Department of Clinical Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding author: Sepideh Elyasi

Corresponding author Email: ElyasiS@mums.ac.ir

Introduction: The emergence of antimicrobial resistance in Gram-negative bacteria is a concerning challenge for health systems. Polymyxins, including colistin, are one of the limited available options for these pathogens management. Nephrotoxicity, beside neurotoxicity is the major dose-limiting adverse reaction of polymyxins, with an up to 60% prevalence. As oxidative stress, inflammatory pathways, and apoptosis are considered as the main mechanisms of colistin-induced kidney damage, various studies have evaluated antioxidant and/or antiapoptotic compounds for its prevention. In this article, we reviewed animal and human studies on these probable preventive measures. Area covered: PubMed, Scopus, and Google Scholar databases were searched using several combinations of 'colistin', 'polymyxin E', 'CMS', 'Colistimethate sodium', 'nephrotoxicity', 'kidney injury', 'kidney damage', 'renal injury', 'renal damage', 'nephroprotectants', 'renoprotective', 'nephroprotective', and 'prevention'. All eligible articles including animal and human studies up to the end of 2020 were included. Expert opinion: Most of the available studies are in vivo researches on anti-oxidant and anti-apoptotic agents like NAC, vitamin C and E, silymarin, and curcumin which mostly showed promising findings. However, limited human studies on NAC and vitamin C did not demonstrate considerable efficacy. So, before proposing these compounds, further well-designed randomized clinical trials are necessary.

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## The controversial role of visfatin in metastasis, recurrence and death of patients with colorectal cancer

*Sara naghipour[1],Raana raygani[1],Mahdi jannati yazdanabad[1],Amir Hooshang Mohammadpour[2],Sepideh Elyasi[2]*

[1] School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

[2] Department of Clinical Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

Corresponding author: Sepideh Elyasi

Corresponding author Email: ElyasiS@mums.ac.ir

**Introduction:** Colorectal cancer is the third most common cancer among women and the fourth most common cancer among men in the world. One of the current challenges is to quickly diagnose and find prognostic factors to avert disease progression. Visfatin is an adipocyte secreted peptide that has been suggested to play a role in the prevention of colorectal cancer and other cancers. In this study, we investigated the serum concentration of visfatin and its role in the prognosis of colorectal cancer.**Material and methods**: We investigated 69 colorectal patients in Mashhad Razavi Hospital that has been followed up for two years. Firstly, the patient's demographic characteristics and comprehensive history were registered. In addition, data related to the patient cancer status, including the primary tumor location, tumor size, histopathology, tumor differentiation, stage of TNM, metastasis or vascular and lymphatic invasion recorded, as well as treatment protocol options over 2 years, Disease status including recurrence, need for re-chemotherapy or patient survival were enrolled. Serum visfatin concentration was measured by ELISA kit and the relationship between serum visfatin concentration and colorectal cancer prognosis was investigated. The relationship between serum biomarker concentration and various prognostic factors of colorectal cancer was evaluated by statistical tests.**Results**: The results show that the visfatin had a small role in death, metastasis and recurrence. Also, according to Cox-regression results, there was no significant relationship with death, metastasis and recurrence and Visfatin concentration ($p > 0.05$). The results of survival analysis show that different concentrations of visfatin are not significantly associated with death, metastasis and recurrence in patients ($p > 0.05$).**Conclusions**: Based on the results, it was found that the concentration of visfatin was not significantly different between the gender ($p > 0.05$). Also, there was no significant relationship between different concentrations of visfatin with death, metastasis and recurrence of colorectal cancer ($p > 0.05$).

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## The effects of monotherapy with melatonin on myocardial ischemia-reperfusion injury

*Adeleh Jeddi[1]*

[1]Department of Clinical Pharmacy, School of Pharmacy; Pharmaceutical Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Corresponding author: Adeleh Jeddi

Corresponding author Email: jeddi.a7@gmail.com

One of the major causes of morbidity and mortality in the world is attributed to the acute myocardial infarction (AMI) and reperfusion strategy is the standard therapy for AMI.Melatonin prevents the production of harmful metabolites by free radical scavenging and also inducing antioxidant enzyme activities that enable melatonin to attenuate the tissue damages inflicted by reactive oxygen species. This review describes both animal studies as well as randomized control trials (RCTs) collected from the PubMed, Web of Science, Scopus and Science Direct. Previous studies have long shown the impacts of melatonin on Ischemic reperfusion injury (IRI) as ameliorated cardiac action, significant declined infarcted area, reduced myocardial perfusion damages and repaired blood flow. Considering melatonin protecting roles against oxidative stress and reducing inflammation in patients with myocardial ischemia, it may have a significant role to improve public health. Pretreatment with melatonin as a pharmacological agent is associated with reducing myocardial IRI. However, the timing of melatonin administration and its prescription dose are important. The impacts of physiological doses appear to be more effective than pharmacological doses. The results from this study indicated the need for well-designed RCTs and long-term pharmacological melatonin treatment to prove the pharmacotherapeutic effects of melatonin.

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## Double-blinded randomized clinical trial to evaluate the effect of licorice hydroalcoholic extract capsule in the treatment of outpatients with Covid-19

*Adeleh Jeddi1, Milad Iranshahi2, Amirhooshang Mohammadpour3*

[1]Department of Clinical Pharmacy, School of Pharmacy; Pharmaceutical Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

[2]Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran

[3]Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding author: Adeleh Jeddi

Corresponding author Email: jeddi.a7@gmail.com

Objective: On January 30, 2020, the World Health Organization officially declared the new coronavirus (SARS-CoV-2) epidemic of Covid-19 as an international crisis in public health. The disease, which can cause acute respiratory conditions in infected people, is increasingly showing a steady human-to-human transmission around the world, with a mortality rate of about 3.4%. There is currently no definitive cure for the disease, and the antiviral drugs used in severe cases are mainly related to the treatment of other known viruses, including HIV and influenza. However, their clear therapeutic effects has not been reported. On the other hand, in mild cases that do not require hospitalization, there is a possibility of disease progression. There are various reports that plant extracts can have antibacterial, antiviral and antiparasitic effects. One of these plants is licorice. In this study, the effectiveness of a constant dose of licorice extract (glycyrrhizin) in patients with Covid-19 is investigated.Methods & Materials: Patients who complete the inclusion and exclusion criteria were treated as standard according to the Covid-19 national protocol. Then they were randomly and unknowingly divided between two groups of drugs and placebo (20 people in each group). One group was given hydroalcoholic extract of licorice at a total dose of 250 mg/day for 2 weeks and the other group was given a placebo similar to the other group 3 times a day for 2 weeks. Before starting the medication regimen and on days 3, 7 and 14, blood samples were taken from patients to measure laboratory parameters such as quantitative CRP, WBCs, lymphocytes and neutrophils. Also, all clinical symptoms of patients were recorded separately. Finally, the severity and frequency of each these symptoms and parameters in the two groups were compared statistically.Results: The results of this study showed that licorice extract improved the parameter of cough on the 7th day, dyspenea and nausea on the 3th day and also significantly improved the level of blood oxygen saturation on all days in the drug group compared

to the placebo group.(P-value<0.05)Conclusion: In general, in patients with Covid-19, the use of licorice extract improves some clinical symptoms such as cough, dyspenea, nausea and increased oxygen saturation. Although the results of this study showed that the extract of this plant has no positive effect on laboratory parameters and the time interval between recovery of lymphopenia and CRP, however, the use of licorice extract in the early stages of the Covid-19 disease seems beneficial. Reach and help reduce the number of critically ill patients and reduce the pressure on the health care system.

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## Evaluation of medication admixture and administration process via injectable solutions in emergency settings at Ghaem, Imam Reza and Shahid Kamyab hospitals, Mashhad, Iran

*Sara Rahsepar[1], Mohaddeseh Fayyazi[1], Sepideh Elyasi [2], Nasser Vahdati-Mashhadian[3]*

[1]School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.
[2]Department of Clinical Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.
[3]Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Sepideh Elyasi
Corresponding author Email: ElyasiS@mums.ac.ir

Introduction: Correct administration of injectable medicines is important for achieving therapeutic response and therefore treating the patients. Inappropriate medication administration results in complications like drug interactions or adverse reactions. Therefore, the present paper will evaluate the current status of injectable drugs admixture and administration in emergency settings of three educational hospitals affiliated to Mashhad University of Medical Sciences. Material and methods: In the present study, the emergency wards of Ghaem, Imam Reza and Kamyab hospitals evaluated and total number of 1000 medical records were randomly reviewed during 7 months. The researcher collected information about drugs' name, administration root and rate, and also the type and volume of diluting solution. Then, this information was assessed based on available scientific guidelines. Results: Among 1000 medical records which were evaluated during a seven months period, approximately 85.1% of cases were confirmed to be used appropriately. The most common bulk solution used for drug administration was normal saline (66.3%). the most common errors were seen in administration rate and choosing the wrong administration root as intramuscular.Conclusions: According to our results, more than 80% of injectable drugs in emergency settings of these 3 hospitals in Mashhad are being administered in an appropriate manner according to available guidelines. While the most errors are seen in rate of infusion, it is recommended to plan clinical lessons in order to reeducate the medical staff about administration and preparation of injectable medicines to reduce the rate of unwanted complications.

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## The therapeutic role of Rho kinase inhibitor, fasudil, on pulmonary hypertension; a systematic review and meta-analysis

*Farshad Abedi[1], Seyed-Navid Omidkhoda[2], Omid Arasteh[3], Vahid Ghavami[4], Hossein Hosseinzadeh[5]*

[1]Department of Clinical Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[2]Department of Biostatistics, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran
[3]Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Hossein Hosseinzadeh
Corresponding author Email: HosseinzadehH@mums.ac.ir

*Background:* Pulmonary hypertension (PH) is a pathophysiological disorder, which involves multiple clinical conditions. The upregulation of the Rho/ROCK signaling pathway was found to be related to the pathogenic mechanisms of PH development. Interestingly, fasudil as a Rho kinase inhibitor has been revealed efficacy in the treatment of PH. *Objectives:* The present systematic review and meta-analysis aimed to evaluate the human clinical trials regarding the efficacy and safety of fasudil in the management of PH. *Methods:* Databases were searched with pre-defined search terms, from inception up to April 2021. Efficacy measures were mean pulmonary arterial pressure (mPAP), systolic PAP (sPAP), pulmonary vascular resistance (PVR), systolic vascular resistance (SVR), right atrial pressure (RAP), systemic arterial pressure (SAP), cardiac index (CI), and arterial oxygen saturation ($SaO_2$). Adverse effects and safety were also assessed. *Results:* A total of 12 studies involving 578 PH patients were included in our study. Among them, five before-after studies, including 174 PH patients were analyzed. Compared with the pretreatment condition, the meta-analysis showed significant improvement of mPAP, sPAP, PVR, SVR, RAP, and CI. But effects on SAP and $SaO_2$ were insignificant. Also, subgroup analyses between 30 and 60 mg doses of fasudil were not in correlation with the significant difference in pulmonary hemodynamic outcomes. *Conclusion:* Fasudil therapy is safe and efficacious in the improvement of some hemodynamics in PH patients. However, long-term randomized controlled trials comparing fasudil with placebo and other treatments are warranted for confirmation of these benefits.

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## A clinical trial on hypnotic effects of an intranasal compound containing saffron, lettuce seeds and sweet violet on patients with primary chronic insomnia

*Reza Abdolahzadeh[1], Hossein Khaluyan[2], and Behjat Javadi[3]*

[1]Department of Pharmaceutics, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[2]Student Research Committee, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[3]Department of Traditional Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Behjat Javadi
Corresponding author Email: javadib@mums.ac.ir

Introduction: Insomnia is one of the most common sleep disorders affecting the quality of life and is characterized by the inability to sleep or reduction in sleep time. Many studies demonstrated insomnia prevalence to be 35-50 percent of adults. In modern medicine, pharmacotherapy and cognitive-behavioral methods have been used for

insomnia. Persian medicine (PM) refers to the hypnotic effects of many herbal medications including a compound intranasal preparation containing Viola odorata L. (sweet violet) flowers, Crocus sativa L. (saffron) stigma and Lactuca sativa L. (lettuce) seeds. In the present double-blinded, controlled clinical trial, we studied the hypnotic effects of oily extract of saffron stigma, viola flowers and lettuce seeds in chronic insomniac patients.Material and methods: 50 patients with sleep disorder divided into two groups: intervention group receiving the oily extract of saffron, lettuce seeds and viola, (2 drops to each nostril 2 times daily for 8 weeks); and Placebo group receiving sesame oil. The patients' sleep quality was assessed at the end of the first week and end of the study by the Pittsburgh sleep quality index (PSQI) questionnaire and insomnia severity index (ISI) questionnaire and results were analyzed.Results: Data analyzing results revealed the questionnaires' scores of both groups were decreased and the intervention medication showed more decline in scores than the placebo group at the end of the treatment.Discussion: Analyzing the PSQI questionnaire's data demonstrated that the intervention could decrease in dosage of co-administered hypnotic medicines significantly after 8 weeks. In addition, sleep delay reduced significantly in the intervention group and their mental quality of sleep increased more than the placebo group. In addition, sleep efficiency in both groups improved significantly.Conclusions: The intranasal application of PM compound preparation could improve sleep disorders in insomniac patients. Although, the data showed a modification in insomnia factors.

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## Bispecific antibody treatment for hematological malignancies

*Seyedeh Mona Haghi[1], Negar Yeganeh Khorasani[2]*

[1]Student Research Committee, Faculty of Pharmacy, Mashhad University of Medical Science, Mashhad, Iran
[2]Student Research Committee, Faculty of Pharmacy, Mashhad University of Medical Science, Mashhad, Iran
Corresponding author: Seyedeh Mona Haghi
Corresponding author Email: HaghiM971@mums.ac.ir

Introduction:Anti-tumor monoclonal antibodies (mAbs) that are clinically effective; usually target the immune system Cells with the Fc receptor (FcR) through the fixed fragment (Fc) and connect them to the tumor. Since T cells are FcR negative, these important cells are not involved. Unlike mAbs, bispecific antibodies (BsAbs) can be designed to interact with T cells. BsAbs are synthetic molecules designed to bind to two different antigens simultaneously, one to a tumor cell, the other to an immune-like cell such as CD3 in T cells. Patients with recurring and/or refractory hematological malignancies need better treatments than the ones we currently use. Immunotherapy has the potential to satisfy this demand. Redirecting T lymphocytes to hematological malignancies with bispecific antibodies (BsAbs) is an appealing method among the several types of immunotherapy. Material and methods:Here are the relevant articles from PubMed and Web of Science database from 2017 to 2021. A total number of 69 articles were resulted based on the search strategy and after excluding duplicate or irrelevant subjects based on their title or text, 24 articles were included.Results: Immunotherapy is an important technique in cancer treatment today, and it's a rapidly expanding field. To date, Bispecific antibody treatments have many potentials to cure hematological malignancies and the successful experience of blinatumomab brought a lot of attention to this matter and many researchers are dedicating their experiments to this subject. The use of BsAb constructs to target hematologic malignancies has had mixed results. The desire for discovering and deploying new constructions to solve engineering and clinical application hurdles for hematologic cancers remains high. But there are many challenges like resistance to treatment and the fact that these antibodies must be designed specifically for each patient's immune cells and surface proteins. According to articles that investigated solutions, there are many ways to improve the efficacy of bispecific antibodies and the future of this treatment is very bright. Discussion: Bispecific antibodies are monoclonal antibodies with two antigen-binding sites, one targeting a receptor that activates cytotoxic cells and the other targeting a specific antigen produced by tumor cells.Resistance is still a problem, and investigations of patients receiving bispecific antibodies will likely guide future breakthroughs in reducing the prevalence of resistance.Some of the resistance mechanisms:1.High disease burden2. High frequency of circulating regulatory T cells 3. Concurrent or prior history of extramedullary disease Examples of How to improve the efficacy of bispecific antibodies:1.Humanized mAbs or mAbs generated from phage display libraries based on human sequences will minimize the probability of Human anti-mouse antibody (HAMA) reactions dramatically.2. The generation of a tri-specific mAb or the infusion of two bispecific antibodies targeting two different surface antigens (e.g. CD19 and CD22) on the malignant cells. Conclusions:According to these studies, bsAb is a possible solution for hematological malignancies that current treatments are not sufficient for them. There are many challenges left unresolved but new studies have shown a promising future for this treatment as they have suggested many possible solutions.

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## Synthesis of therapeutic amphiphilic copolymer via raft polymerization for preparation of peptomicelles of SN38 prodrug for fighting against colon adenocarcinoma

*Mahboobe Ram*, Maryam Babaei, Reza Zolfaghari, Mohammad Ramezani, Mona Alibolandi**

Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author:Mahboobe Ram
Corresponding author Email: mahboobram@ymail.com

Introduction:Colorectal cancer (CRC) is the most prevalent and deadly form of cancer in the world [1]. To increase the efficacy of chemotherapy while reducing its side effects, self-assembly of polymer-drug conjugates can minimize systemic toxicity while enhancing therapeutic efficiency[2, 3]. Material and methods:In the present study, polyglutamic acid (PGA) was used to prepare the conjugate of hydrophobic anti-cancer agent, SN38, by forming ester bond between hydroxyl group of SN38 with activated carboxylic acid of PGA. Then, polyhydroxypropylmethacrylamide (PHPMA) block was synthesized started from the end of PGA chain via “grafting from” approach implementing reversible addition-fragmentation chain transfer (RAFT) polymerization. The synthesized diblock copolymer could freely self-assemble to form peptomicelle(polypeptide-based micellar structures) structures. Then, the prepared SN38-conjugated PGA-PHPMA peptomicelles was tagged with AS1411 aptamer in order to provide guided drug delivery to colon adenocarcinoma. Results: The synthesis of the therapeutic diblock copolymer was confirmed by 1H-NMR. The DLS analysis showed the size of 61.44 and 59.10nm with PDI of 0.44 and 0.32 for targeted and non-targeted peptomicelles, respectively. In vitro drug release experiments of the prepared system showed a controlled release profile, which was significantly accelerated in citrate buffer pH 5.4 in comparison with that of phosphate-buffered-saline (PBS pH 7.4). In vitro cytotoxicity experiment, MTT, illustrated a higher cytotoxicity for aptamer-targeted peptomicelles in comparison with that of non-targeted one against H29 and C26, as nucleolin-positive cell lines

which was statistically significant, while no difference was found between the toxicity of both targeted and non-targeted systems against CHO, as a nucleolin-negative cell line (p> 0.05). In vivo study on C26 tumor bearing mice confirmed superior therapeutic index of the aptamer-targeted peptomicelles in comparison with non-targeted peptomicelles in terms of tumor growth suppression and survival rate.Conclusions:Poly-peptide-based self-assembled therapeutic structures as an innovative platform could serve as a versatile approach for fighting against cancer.

## P158

## The effect of Caveolin-1 Neuron-Targeted gene therapy in the treatment of Alzheimer's (AD)

*Negar Yeganeh Khorasani[1], Mona Haghi[2]*

[1]Student Research Committee, Faculty of Pharmacy, Mashhad University of Medical Science, Mashhad , Iran

[2]Student Research Committee, Faculty of Pharmacy, Mashhad University of Medical Science, Mashhad , Iran

Corresponding author: Negar Yeganeh Khorasani

Corresponding author Email: Yeganehn972@mums.ac.ir

Introduction: Introduction: Introduction: Alzheimer's disease (AD) is one of the most common neurodegenerative diseases and accounts for more than 80% of dementias worldwide in the elderly. The basis of the pathogenicity of AD and the resulting cognitive impairments is the destruction of Synapse and disturbance of signaling .Amyloid precursor proteins and beta-amyloid molecules are involved in the physiological functions of the nervous system such as nerve cell growth, nerve survival and nerve damage. Studies have shown that there is a strong interaction between amyloid-beta and tao proteins, which causes amyloid-beta and tao accumulations inside and outside neurons, leading to dendritic spines and synapse destruction. At present, existing treatment strategies only relieve symptoms, while the removal of toxic amyloid species alone is not sufficient to reverse a functional defect in the AD patient's brain. Caveolin-1 (Cav-1) is a membrane-bound protein scaffold or lipid (MLRs) that organizes signaling complexes and can enhance neural and synaptic flexibility. Therefore, the purpose of this article is to investigate the effects of genes. Caveolin-1 Neuron-Targeted Therapy as New Targets for Alzheimer's Treatment.Methods: In this review, we include an article that discusses young blood plasma on Brain tissue rejuvenation. All articles were published between 2000_2020 and have ethical considerations. We searched PubMed and Google Scholar search engine with Caveolin- 1 OR cav-1 protein AND Alzheimer's disease, keywords were. Initially, 28 articles were found using this method. Then we excluded 18 articles from the study by considering the abstract and used 10 articles in this review.Results: An article on the possible neuroprotective effects of Caveolin 1, curcumin, and vitamin B12 inhibitors on Alzheimer's disease in rats shows Curcumin, Folic Acid, and Vitamin B12 can decrease the GSK/3ß activity & Tau hyperphosphorylation in STZ induced AD which may be associated with improvement of memory deficits in rats. Another 7 articles show that the loss of Cav-1 accelerates nerve damage and aging. The results showed that Cav-1 represents a novel control point for healthy neuronal aging and loss of Cav-1 represents a non-mutational model for Alzheimer's disease. One study showed a direct or indirect cav-1/sorLA interaction could modify the trafficking and sorting functions of sorLA in glia and its proposed neuroprotective role in AD. Another study showed miR-12-3p directly targeted Caveolin-1; miR-124-3p inhibited abnormal hyperphosphorylation of Tau by regulating Caveolin-1-PI3K/Akt/GSK3β pathway in AD, which may provide new ideas and therapeutic targets for AD.Discussion: Studies to date have shown that Caveolin-1 Neuron-Targeted gene therapy maintains cognitive function and synaptic flexibility in a model of Alzheimer's disease (AD) mice. Therefore, Caveolin-1 Neuron-Targeted gene therapy can be used as target of New gene therapy to be considered. Conclusions: Recently, significant efforts have been made to find new genes that are effective in the mechanism of Alzheimer's pathogenesis, as the identification of these genes can be used as gene therapy targets to treat AD patients. Despite these early stages, there is a long way to go from experimental studies to clinical application.

## P159

## The effect of Otostegia persica on fertility indices in female mice

*Aida Namdari[1], Moein masjedi[2] , Reza Heidari[3] , Mahmoodreza Moein[4]*

[1]Department of Traditional Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

2Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

[3]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

[4]Department of Pharmacognosy, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Aida Namdari

Corresponding author Email: aida.namdari1995@gmail.com

Introduction: Nowadays, infertility is one of the most serious medical problems which many couples encounter with. Any factor that upsets the balance of sex hormones can be caused by a disorder in the female reproductive system. One of the organs of the female reproductive system is the ovary, which is responsible for the growth and development and, ultimately, the release of the oocyte. Oxidative stress caused by free radicals is one of the major causes of infertility in women. Administration of antioxidants is one of the most important ways to reduce oxidative stress. Since some plants are rich in compounds with strong antioxidant activity, the medicinal plants are widely used for the treatment of infertility and induction of ovulation. In this study, Otostegia persica was used due to its antioxidant compounds. This study aimed to evaluate the effect of Otostegia persica extract on infertility in female mice.Material and methods:The aqueous extract of Otostegia persica was prepared and dried in rotary evaporator. The extract then standardized using high performance liquid chromatography technique based on caffeic acid content. Mice were divided into four groups (n=7). The control group received 0.5 ml of distilled water daily. The three experimental groups received the plant extract in three doses (50, 100 and 150mg) dissolved in 0.5 ml of distilled water daily (36 days) by gavage. After treatment, the serum levels of sex hormones in rats were measured by Linked Enzyme Fluorescent Assay (ELFA). Ovarian tissue was stained with the hematoxylin-eosin method to count every type of follicles.Results: The results of the study did not show any significant change in the number of pre-antral, antral follicles and corpus luteum. Still, the number of cystic follicles in the 150 mg/ml dose group compared to the control group showed a significant increase ($p<0.05$). Also, serum levels of estrogen, progesterone, and LH in the group receiving a high dose (150 mg/ml) showed a significant dose-dependent increase compared to the control group. Serum prolactin and testosterone levels also showed a significant decrease in the groups receiving doses of 100 and 150 mg/ml compared to the control group. However, no significant changes were observed in the serum level of FSH. Based on the results, it is possible that the extract of Otostegia persica in doses of and 100 mg due to its potent antioxidant properties has no toxic effect on ovarian follicles, and also due to the content of mineral substances such as calcium and magnesium, which affect the hypothalamic-pituitary axis, have been able to significantly increase the levels of progesterone, estrogen, and LH, which play a crucial role in fertility.Discussion and Conclusions: To sum up, it can be concluded that Otostegia persica

extract probably has no toxic effect on the number of ovarian follicles and has ability to increase fertility rate by affecting the serum concentration of sex hormone.

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## Cardioprotective effect of alpha-mangostin on doxorubicin-induced cardiotoxicity in rats

*Farhad Eisvand, Mahboobeh Ghasemzadeh Rahbardar, Mohsen Imenshahidi, Abbas Tabatabaei Yazdi, Bibi Marjan Razavi, Hossein Hosseinzadeh[a,b*]*

Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University
Corresponding author: Farhad Eisvand
Corresponding author Email: eisvandf951@mums.ac.ir

The main doxorubicin adverse effect is cardiotoxicity. Oxidative stress and apoptosis induction have been suggested as mechanisms involved in its cardiotoxicity. In this study, cardioprotective effects of alpha-mangostin, purified from the mangosteen fruit, against doxorubicin-induced cardiotoxicity in rats have been investigated. Rats were divided as follows: Control, doxorubicin (2 mg/kg every 48 hours), alpha-mangostin (200 mg/kg), alpha-mangostin (50, 100, 200 mg/kg) + doxorubicin (2 mg/kg every 48 hours) and vitamin E (200 IU/kg, every 48 hours) + doxorubicin (2 mg/kg every 48 hours). Alpha-mangostin was administered by gavage for 19 days while doxorubicin (12 days) and vitamin E (19 days) were injected intraperitoneally. Doxorubicin decreased heart rate, increased RRI, QTI, STI, and QRS duration and reduced systolic and diastolic arterial blood pressure, and caused histological damage in rat hearts. Doxorubicin decreased heart weight and heart/body weight ratio as well as elevated CK-MB and LDH. Doxorubicin increased MDA, TNF-α, IL1-β, Bax/bcl2, caspase 3 and 9 and decreased GSH content in heart tissue but co-administration of alpha-mangostin restored all doxorubicin toxic effects. Results show that alpha-mangostin has protective effects against doxorubicin-induced cardiotoxicity by antioxidant, anti-inflammatory and anti-apoptotic effects that may ameliorate doxorubicin cardiotoxicity in human chemotherapy without reduction in its anticancer effect.

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## Effects of natural products and bioactive compounds on attenuation of cyclophosphamide-induced cardiotoxicity

*Amirhossein Ajzashokouhi[1]*

[1]School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Amirhossein Ajzashokouhi
Corresponding author Email: shokouhi.ah@gmail.com

Introduction: Cyclophosphamide (CP), also known as cytophosphane, is an antineoplastic and immunosuppressor medication. As a chemotherapy agent, it is used in lymphoma, multiple myeloma, leukemia, ovarian, and some other kinds of cancer treatment. The major limitation of CP therapy is cardiotoxicity. It is proposed that a combination of medicinal herbs or some bioactive compounds attenuate this important side effect.Method: In this review, following scientific databases PubMed, Scopus, ScienceDirect, and Web of Science were searched for relevant articles in English published between 2000 and February 2021, with different keywords including “cyclophosphamide”, “cardiotoxicity”, “natural products”, “bioactive compound”, “herbal preparation” either in the title, the abstracts or the text.Results: We have collected the information of eighteen natural products and bioactive compounds (nicorandil, ellagic acid, kolaviron, mangiferin, gallic acid, silymarin, curcumin, selenium, taurine, N-acetylcysteine, anthocyanin, quercetin, probucol, thymoquinone, lipoic acid, lupeol linoleate, squalene, and hesperidin), which have a protective effect against CP-induced cardiotoxicity. This effect is exerted via multiple mechanisms including activation of antioxidant enzymes (GPx, CAT, and SOD), increasing the ratio of ATP to ADP in the myocardial cells, inhibition of ROS generation, apoptosis, NF-kB, p53, and DNA damage. Besides the cardioprotective effects, they tend to confer some synergistic effects with CP and therefore have the potential to be used as an adjunct.Conclusions: The present review demonstrates that natural products have pivotal roles in cardiotoxicity amelioration in cells and animal models, their therapeutic potentials for clinical needs further investigation.

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## Intraperitoneal lavage with Crocus sativus prevents postoperative-induced peritoneal adhesion in a Rat Model: Evidence from animal and cellular studies

*Pouria Rahmanian[1], Vafa Baradaran-Rahimi[2], Vahidreza Askari[3], Hasan Rakhshandeh[4]*

Corresponding author: Pouria Rahmanian
Corresponding author Email: rahmanianDP971@mums.ac.ir

Post-operative peritoneal adhesions are considered the major complication following abdominal surgeries. The primary clinical complications of peritoneal adhesion are intestinal obstruction, infertility, pelvic pain and post-operative mortality. In this study, regarding the anti-inflammatory and anti-oxidant activities of Crocus sativus, we aimed to evaluate the effects of Crocus sativus on the prevention of postsurgical-induced peritoneal adhesion. Male Wistar-Albino rats were used to investigate the preventive effects of pirfenidone (PFD, 7.5 % w/v) and C. sativus extract (0.5%, 0.25% and 0.125% w/v) against postsurgical-induced peritoneal adhesion. The levels of oxidative, anti-oxidative, inflammatory and anti-inflammatory biomarkers, fibrosis and angiogenesis biomarkers. We also investigated the protective effects of PFD (100 □g/ml) and C. sativus extract (100, 200, 400 □g/ml) in TGF-□1-induced fibrotic macrophage polarisation. The levels of cell proliferation, oxidative, anti-oxidative, inflammatory and anti-inflammatory, fibrosis and angiogenesis biomarkers were evaluated. C. sativus extract ameliorates post-operational-induced peritoneal adhesion development through attenuating oxidative stress (MDA), inflammatory mediators (IL-6, TNF-□, and PGE2), fibrosis (TGF-□1, and IL-4, and PAI) and angiogenesis (VEGF) markers, whilst propagating anti-oxidant (GSH), anti-inflammatory (IL-10), and fibrinolytic (tPA) markers and tPA/PAI ratio. In a cellular model, we revealed that the extract, without any toxicity, modulated the levels of cell proliferation and inflammatory (TNF-□), angiogenesis (VEGF), anti-inflammatory (IL-10), M1 (iNOS) and M2 (Arg-1) biomarkers, and iNOS/Arg-1 ratio towards anti-fibrotic M1 phenotype of macrophage, in a concentration-dependent manner. Taken together, the current study indicated that C. sativus reduces peritoneal adhesion formation by modulating the macrophage polarisation from M2 towards M1 cells.

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## Efficient pyran derivatives synthesis in DES medium and their antimicrobial evaluation as inhibitors of mycobacterium bovis (BCG)

*Saber HakimiNasab[1], Azizollah Habibi[1]*, Seyyed Mohammad Shahcheragh[1,2], Yekta Farahani[2], Soroush Sardari[2], Hadi Dolati[1], Seyedeh Mahbobeh Mahdavi[1], Maysam Habibi[1]*

[1]Faculty of Chemistry, Kharazmi University, No. 43, P. Code 15719-14911; Mofatteh Street, Enghelab Ave.; Tehran, Iran.
[1]Drug Design and Bioinformatics Unit, Medical Biotechnology Department, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran.
Corresponding author: Azizollah Habibi
Corresponding author Email: habibi@khu.ac.ir

An ecofriendly one-pot three-component reaction of 1,3-dicarbonyl compounds, aromatic aldehydes and malononitrile was carried out in deep eutectic solvent (DES) based on choline chloride, to synthesize highly functionalized pyran derivatives under moderate conditions. The main advantages of this approach are mild reaction conditions, high yields, relaxed workup without chromatographic purification steps or extraction and easily reusable of DES's. Then, these compounds were evaluated for anti-mycobacterium activity against Mycobacterium bovis (Bacillus Calmette–Guerin). The preliminary results indicated that most of the tested compounds showed relatively good activity against the test organism. The compounds 4a, 4c, 4e, 4n demonstrated the high activities against Mycobacterium (0.044–0.084 μM/mL) and 4k showed highest activity (0.033 μM/mL). The commonalities of these compounds are having a chlorine atom on the ring which is located on position 4 of the 4H-pyran structures.

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## In silico study of five SARS CoV-2 target proteins on known drugs

*Zahra Jamshidi[1]*

[1]School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Zahra Jamshidi
Corresponding author Email: JamshidiZ981@mums.ac.ir

Introduction: After severe acute respiratory syndrome (SARS) in 2003 and Middle East Respiratory Syndrome (MERS) in 2012, coronavirus (2019-nCoV or SARS CoV-2), a new member of the family Coronaviridae was reported in Wuhan, China in late 2019 (1-4). Fever, dry cough, fatigue, anorexia, myalgia, and dyspnea are common clinical symptoms of COVID-19 (5,6). Despite the efforts of scientists to discover anti-viral drugs for prevention or treatment of SARS CoV-2, there have not been significant successes so far since discovering drugs for a novel virus might take several years and need high cost to complete (7-9) Thus, finding a treatment for this unknown disease is very necessary. In this research, we used a Virtual Screening (VS), a technique used for analyzing huge databases and discovering lead compounds, to find potential drugs among 2701 FDA approved drugs for the treatment of coronavirus (10).Material and methods: In the current study, VS was used as a screening tool for predicting the efficacy of clinically approved drugs taken from the https://www.selleckchem.com/screening/fda-approved-drug-library.html, consisting of 2701 approved drugs with (SDF) format.The Amber10: EHT Force Field and the default docking setting of the Molecular Operating Environment (MOE) software was used. Five crystal structures of the SARS CoV-2 downloaded from RCSB PDB database (www.rcsb.org/structure ), included (5R7Y), (5R81), (5R82), (6YI3) and (7BTF).Results: The screening result for 5R7Y protease is shown Lypressin acetate had the highest score among the listed drugs. Lypressin acetate is a hormone nonapeptide, so it is a substrate for protease (11). Evenif it bound to the target, it would be immediately cleaved by the target itself, so it is not an appropriate drug for SARS Cov-2 main protease. Delamanid is an anti-tuberculosis agent derived from the nitro dihydroimidazooxazole class of compounds that are used to treat multidrug-resistant tuberculosis (12)Tannins, naturally or synthetically gained noticeable effectiveness against a huge range of viruses including herpes simplex and hepatitis C, human immunodeficiency, adenoviruses, and influenza virus A. In vitro study also exhibited antioxidant properties Tannins bound to virus-specific proteins and they work as competitors for glycosaminoglycans in the treatment of herpes simplex infections (13).Discussion: Among the drugs checked out, tannic acid and delamanid may have the potential to be used for the treatment of coronavirus disease.Conclusions: The study suggested that tannic acid and cobicistat might be potent drugs for wet-lab studies in the treatment of COVID-19. Tannic acid was effective on four SARS-CoV-2 target proteins (PDB codes: 5R7Y, 7BTF, 6YI3, 5R81). Cobicistat, used in the treatment of virus infection (HIV/AIDS),was predicted to be effective on two SARS-CoV-2 target proteins (7BTF, 5R82). Further studies for investigating the clinical efficacy of these two drugs are highly recommended.

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## Synthesis, characterization and in vitro study of PH sensitive hyaluronic-adipic acid dihydrazide conjugate for targeted delivery of epirubicin to cancer cell with MUC-1 aptamer

*Reza Dehghan[1], Mojgan Nejabat[2], Farzin Hadizadeh[2,4], Khalil Abnous[2,5] and Seyed Mohammad Taghdisi[3,6]*

[1]Student Research Committee, Faculty of pharmacy, Mashhad University of medical sciences, Mashhad, Iran
[2]Department of medicinal chemistry, Faculty of pharmacy, Mashhad University of medical sciences, Mashhad, Iran
[3]Department of pharmaceutical biotechnology, Faculty of pharmacy, Mashhad University of medical sciences, Mashhad, Iran
[4]Biotechnology research Center, Pharmaceutical technology institute, Mashhad University of medical sciences, Mashhad, Iran
[5]Pharmaceutical research Center, Pharmaceutical technology institute, Mashhad University of medical sciences, Mashhad, Iran
[6]Targeted drug delivery research Center, Pharmaceutical technology institute, Mashhad University of medical sciences, Mashhad, Iran
Corresponding author: Reza Dehghan
Corresponding author Email: Dehghanr941@mums.ac.ir

Introduction: Epirubicin (Ep) is an anti-cancer drug. It is usually applied in combination with other anti-cancer drugs in breast cancer. Bone marrow suppression is the most important acute dose-limiting adverse effect of Ep. Cardiac toxicity is another important adverse effect of Ep that limits cumulative dose (1). Hyaluronic acid (HA) is a non-toxic, biodegradable, biocompatible, hydrophilic and non-immunogenic glycosaminoglycan polymer that is a part of extra cellular matrix. HA has some overexpressed receptors on cancer cells (2, 3). Aptamer is a single stranded oligonucleotide. Mucin-1 (MUC-1) aptamer was developed to target MUC-1 transmembrane glycoprotein that is overexpressed in various cancer cells (4, 5). In this study, we focus on

MUC-1 aptamer and HA for dual targeted drug delivery of Ep to reduce its adverse effect. Material and methods: Adipic acid dihydrazide was used as a linker to conjugate Ep and MUC-1 aptamer to HA. HA-EP-MUC-1 aptamer synthesis was confirmed by proton nuclear magnetic resonance (1H NMR), infrared spectroscopy (IR) and agarose gel electrophoresis. Ep loading efficiency and loading content were determined by fluorescence spectroscopy. Particle size of formulation and release profile were determined by dynamic light scattering and dialysis bag respectively. Cytotoxic activity was investigated during in vitro study.Results: In 1H NMR spectra, chemical shifts at 2.14, 2.31, 1.51 and 1.56 ppm were corresponded to 8 protons of hydrazide linker and 5.38, 7.40, 7.54 and 7.67 ppm were corresponded to 4 protons of Ep. In IR spectra, band around 1296 cm-1 was assigned to N-N stretching of linker. HA-EP-MUC-1 aptamer showed a different band to free MUC-1 aptamer in agarose gel electrophoresis. Ep loading content and loading efficiency were estimated as 1.1% w/w and 6.25% respectively. Particle size of formulation was 81 nm. Cumulative release ratio percentage of Ep from formulation was estimated as 27%, 71% and 100% at PH of 7.4, 6 and 5 respectively. Discussion: HA-EP-MUC-1 aptamer released more Ep at acidic PH due to PH sensitive bound between Ep and linker. HA-EP-MUC-1 aptamer showed a greater cytotoxic effect than Ep on colon-26 carcinoma and Michigan cancer foundation-7 cell lines ($p < 0.05$) and fluorescence imaging and flow cytometry demonstrated that HA-EP-MUC-1 aptamer resulted in a greater internalization than Ep into these cell lines ($p < 0.05$). However, cytotoxic effect did not differ significantly between HA-EP-MUC-1 aptamer and Ep in Chinese hamster ovary cell line. Also HA-EP-MUC-1 aptamer internalized less than Ep into this cell line due to very low expression of MUC-1 in this cell line. HA and HA-MUC-1 aptamer showed no significant toxicity on all cell lines due to their biocompatibility.Conclusions: Ep has adverse effects that limit its administrable dose and harm to the patient. HA and MUC-1 can be used to form Targeted drug delivery system of Ep. This system selectively concentrate Ep in acidic tissue like tumor and internalize Ep in cancer cells that overexpress some receptors. In conclusion, this system can deliver Ep selectively to tumor and reduce Ep distribution in other tissues and therefore it reduces Ep adverse effect.

## P166

## 6Design and Synthesis of New Carbamates as Inhibitors for Fatty Acid Amide Hydrolase and Cholinesterases: Molecular Dynamic, In vitro and In vivo Studies

*Mahdi Faal Maleki[a], Hamid Nadri[b] , Mostafa Kianfar[c] , Najmeh Edraki[d], Farhad Eisvand[c], Razieh Ghodsi[a,e] , Seyed Ahmad Mohajeri[c], Farzin Hadizadeh[a,e] **

[a]Department of Medicinal Chemistry, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[b]Department of Medicinal Chemistry, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[c]Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[d]Medicinal and Natural Products Chemistry Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[e]Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding authors: Farzin Hadizadeh
Corresponding author Email: hadizadehf@mums.ac.ir

As anandamide (N-arachidonoylethanolamine, AEA) shows neuroprotective effects, the inhibition of its degradative enzyme, fatty acid amide hydrolase (FAAH) has been considered as a hopeful avenue for the treatment of neurodegenerative diseases, like Alzheimer's disease (AD). Memory loss, cognitive impairment and diminution ofthe cholinergic tone, due to the dying cholinergic neurons in the basal forebrain, are common hallmarks in patients with AD. By taking advantage of cholinesterase inhibitors (ChEIs), the degradation of acetylcholine (ACh) is decreased leading to enhanced cholinergic neurotransmission in the aforementioned region and ultimately improves the clinical condition of AD patients. In this work, new carbamates were designed as inhibitors of FAAH and cholinestrases (ChEs) (acetylcholinestrase (AChE), butyrylcholinestrase (BuChE)) inspired by the structure of the native substrates, structure of active sites and the SARs of the well-known inhibitors of these enzymes. All the designed compounds were synthesized using different reactions. All the target compounds were tested for their inhibitory activity against FAAH and ChEs by employing the Cayman assay kit and Elman method respectively. Generally, compounds possessing aminomethyl phenyl linker was more potent compared to their corresponding compounds possessing piperazinyl ethyl linker. The inhibitory potential of the compounds 3a-q extended from $0.83 \pm 0.03$ μM (3i) to >100 μM (3a) for FAAH, $0.39 \pm 0.02$ μM (3i) to 24% inhibition in $113 \pm 4.8$ μM (3b) for AChE, and $1.8 \pm 3.2$ μM (3i) to $23.2 \pm 0.2$ μM (3b) for BuChE.Compound 3i a heptyl carbamate analog possessing 2-oxo-1,2-dihydroquinolin ring and aminomethyl phenyl linker showed the most inhibitory activity against three enzymes. Also, compound 3i was investigated for memory improvement using the Morris water maze test in which the compound showed better memory improvement at 10 mg/kg compared to reference drug rivastigmine at 2.5 mg/kg. Molecular docking and molecular dynamic studies of compound 3i into the enzymes displayed the possible interactions of key residues of the active sites with compound 3i. Finally, kinetic study indicated that 3i inhibits AChE through the mixed-mode mechanism and non-competitive inhibition mechanism was revealed for BuChE.

## P167

## Organocatalytic ring-opening polymerization of PCL-PEG-PCL and preparation of porous scaffolds containing dexamethasone using supercritical CO2 gas foaming

*Seyed-Hasan Mahmoudihashemi[1]*

Corresponding authors: Seyed-Hasan Mahmoudihashemi
Corresponding author Email: mahmoudih931@mums.ac.ir

Triblock copolymers of PCL-PEG-PCL were fabricated using ring opening polymerization (ROP) of ε-caprolactone using organocatalyst DBU. 1H NMR, FTIR, and GPC spectra of the triblock were used to confirm the structure and determine the molecular weight. To construct the scaffols, triblock powder was mixed with dexamethasone (DXMT) and then compressed applying a hydraulic pressure of $9 \times 10$ -2 MPa, which resulted in the formation of disc-like tablets. Following that, the scaffolds with tablet shape were placed into the scCO2 gas foaming apparatus. Central composite design (CCD) was used to obtain the maximum porosity % with the scCO2 variables of soaking time (ts), pressure (P), temperature (T), and time required to depressurize (td). The PDI and synthesis temperature of triblock using organocatalyst DBU was lower compared with than Tin(II) octoate. At the maximum porosity % (55.58 %), P, T, Ts, and Td were 198 bar, 50 °C, 2.0 h, and 28 min, respectively. Cumulative in-vitro drug release assay revealed that at post-scCO2 treatment, the scaffolds delivered an almost complete release ($83.74 \pm 1.54$ %) while at pre-scCO2 treatment, release percentage was $52.24 \pm 2.03$ % after 30 days. This confirmed suitable

release time and properties for controlled delivery of the dexamethasone loaded in PCL-PEG-PCL triblock copolymer-based scaffolds. So, using the scCO2 gas foaming method provides the possibility to construct morphologically and structurally adjustable porous PCL-PEG-PCL scaffolds.

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## Synthesis, optimization, and evaluation of ibuprofen-hydroxypropyl-beta-cyclodextrin inclusion complex: An in vitro and in silico study

*Mostafa Amirinejad[1], Omid rajabi[2], Mozhgan Nejabat[3], Atoosa Haghizadeh[4]*

[1]Student research committee , Faculty of pharmacy , Mashhad university of medical scince , Mashhad , Iran

[2]Department of Drug control , Faculty of Pharmacy , Mashhad university of medical science , Masshad , Iran

[3]Department of Medicinal Chemistry, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[4]Research and Development Department, Dr. Rajabi Pharmaceutical Company, Mashhad, Iran

Corresponding authors: Omid Rajabi

Corresponding author Email: RajabiO@mums.ac.ir

Introduction: Ibuprofen is a widely-used non-steroidal anti-inflammatory drug, which is a BCS II class drug with low aqueous solubility that its prescription is limited by its low dissolution rate. A growing body of research has studied inclusion complex as a considerable method to overcome the problem. Cyclodextrins and especially hydroxypropyl-beta-cyclodextrin have been reported to be able to inrease solubility of hydrophobe drugs. The aim of this study is development and optimization of ibuprofen-hydroxypropyl-beta-cyclodextrin inclusion complex.Material and methods: Complex of ibuprofen and hydroxypropyl-beta-cyclodextrin was prepared by co-evaporation with different ratio of solvents (methanol, ethanol and distilled water were used as solvents). In aim to find out the optimum solvent ratio, molecular dynamics simulations were done by Maestro and NAMD. In addition, differential scanning calorimetry was applied to assess the complexes crystinallity and thermal behaviours and Fourier transform infrared was applicated to monitor structural changes. Furthermore, solubility and dissolution profile of the complexes were evaluated and compared.Results and discussion: Complexation with hydroxypropyl-beta-cyclodextrin was reported to be able to reduce crystinallity and improve thermal stability, water solubility and dissolution profile of all the produced complexes. When ethanol and water were used as solvents in ratio of 9:1 and 3:1, aqueous solubility of ibuprofen was increased by 1216% and 921%. Using co-evaporation with ethanol and water solvents in the mentioned ratios were considered as optimum method for the complexation.Conclusions:Ibuprofen-hydroxypropyl-beta-cyclodextrin inclusion complexes especially using ethanol and distilled water in the mentioned ratios was demonstrated to be able to increase stability and absorption rate of ibuprofen.

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## Synthesis and characterization of chromium (III)-metformin complex in chitosan matrix and comparison of its properties with metformin

*Samin khabbazian[1], Mina Borhani[1] , Atoosa Haghighizadeh[2], Omid Rajabi[3]*

[1]Student research committee , Faculty of pharmacy , Mashhad university of medical scince , Mashhad , Iran

[2]Department of polymer chemistry, kish International Campus, University of Tehran, Tehran, Iran

[3]Department of Drug control , Faculty of Pharmacy , Mashhad university of medical science , Masshad , Iran

Corresponding author: Omid Rajabi

Corresponding author Email: Rajabio@mums.ac.ir

The aim of this study was to investigate the effect of the complex chromium (III) with metformin on the chitosan matrix as a new alternative to metformin hydrochloride (Mfn.HCl). In this regard, different ratios of drug to metal ion and following up the complex loading on chitosan matrix with different concentration were studied to obtain the optimal formulation. The infrared spectroscopic data in the comparison between free Mfn.HCl and Mfn-HCl-chromium (III)-chitosan complex proved that metformin hydrochloride react with the metal as a bidentate ligand through its imino groups. Shifting the peaks gives the result that the metal ions strongly complexed to the amino groups of chitosan. Moreover the complex was thermally more stable than free Mfn.HCl.Introduction : Recently, some metal complexes or organic compounds have been used in drug formulation to improve the drug performance. Chromium III supplements are complexed with metformin due to its role in glucose metabolism. Today polysaccharides such as chitosan are widely used in formulations to control drug release due to their stability, maximum load capacity, and biodegradability. In addition to these benefits, chitosan is used as dietary fiber to control the body fat, increase cholesterol, weight gain, hypo insulinemia and tissue regeneration. Mfn.HCl has short half-life that is needed more prescriptions to keep blood sugar levels low. So a new formulation is required to improve the drug performance and lower the oral dosage.Method : Mfn.HCl (2 mmol) is dissolved in 25 ml of methanol and then mixed with chromium solution (1 mmol) CrCl3.6H2O in a 1: 2 molar ratio. The mixture will be heated under reflux for 3 hours. Then the mixture is left overnight at room temperature to precipitate. The resulting precipitate is filtered and washed with diethyl ether then dried. 5 mg of chitosan will be dissolved in an aqueous solution of 10% V/V HCl with vigorous stirring to obtain a solution containing a concentration of 5%. Different ratios of complex and chitosan in 60 ml of 0.1 M HCl dissolved at 60 °C for 2 hours until the complex is complete, a homogeneous solution of the metal complex and chitosan is added dropwise to a solution of 0.5 ml of NaOH. The resulting complex will be filtered, washed several times with distilled water and air dried for 48 hours.Result : The elemental analysis showed that Mfn.HCl/Cr2O3+chitosan complexes with metformin in 1:2 ratio is more racial. The most significant difference in the IR spectrum of the ligand and the complex was the shift (C=N) stretching frequencies to lower frequencies due to metal-ligand coordination which takes place through the imine nitrogen. Six membered ring formation possibilities also exist from coordination involving amino nitrogen. SEM and DSC analysis showed that the metal ions strongly complexed to the amino groups of chitosan and resulted a smooth surface product, amorphous phase, thermally more stable and high electrical conductivity than other complexes.Conclusion : The prepared complexes in chitosan matrix have shown significant increase in hypoglycemic activity when compared to pure drug.

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## Preparation and characterization of budesonide liqui-Pellet as a strategy for enhancement of drug dissolution rate

*Fatemeh Soltani.[2], Fatemeh Sadeghi[1,2], Hadi Afrasiabi Garekani[3,2], Abbas Akhgari[1,2], Hosain Kamali[1,2] and Ali Nokhodchi[4]*

[1]Targeted Drug Delivery Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran.
[2]Department of Pharmaceutics, School of Pharmacy, Mashhad University of Medical Sciences. Mashhad, Iran.
[3]Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran.
[4]Pharmaceutics Research Laboratory, Arundel Building, School of Life Sciences, University of Sussex, Brighton, UK
Corresponding author: Fatemeh Soltani
Corresponding author Email: soltanift971@mums.ac.ir

Introduction: Budesonide is a practically insoluble at physiological pH in the intestinal region. The low solubility could lead to limited dissolution and decreased therapeutic potential of this drug. Several approaches have been used to increase the solubility or dissolution rate of poorly soluble drugs. Among these approaches liquid-solid technology has attracted much attention and recently liqui-pellets have been introduced as a next generation of solid oral dosage form. In this novel method a high amount of liquid medication could be mixed with excipients which are referred to as carriers and coating materials and then incorporated into the pellet formulation. Microcrystalline cellulose (Avicel), could be used as carriers, whereas silicon dioxide (Aerosil) could be used as coating materials. The aim of the present study was to evaluate the liqui-pellet of Budesonide as a means to enhance dissolution rate of this drug.Material and methods: To choose the best liquid vehicle, solubility studies of budesonide were conducted in different solvents (PEG 400, propylene glycol, Tween 80 and glycerol). For preparation of liqui-pellets, the effect of two key parameters i.e. carrier type and liquid load factor (the weight ratio of the liquid medicine to carrier (Lf)) were investigated on characteristics of pellets. To formulate liqui-pellets, the drug was dispersed in PEG 400 along with PVP K30. This mixture was adsorbed onto carrier (Avicel PH 102 or Avicel: lactose at different ratios) and then coated with Aerosil 300 and turned to pellets by extrusion spheronization technique using water as granulating liquid. Ordinary pellets were also prepared using the mixture of drug, PVP K30, Avicel and lactose for comparison purposes. The pellets were evaluated for their particle size and shape (stereoscope), hardness (material testing machine), flowability (Carr's index) and dissolution rate (dissolution test).Results: Solubility studies indicated that the best liquid vehicle was PEG 400. Liqui-pellets showed higher dissolution rate than ordinary pellets. In liqui-pellets increase in the Lf (from 0.3 to 1), increased the size of pellets and the amount of drug release during 2h (from 60% to 80%) while decreased the crushing strength of pellets (from 7.03±0.95 to 0.65±0.1 N). However, formulations cannot successfully spheronized into pellets with further increase of Lf to 1.2. Changes in Avicel: lactose ratio (from 1:0 to 3:1) increased the size and decreased elastic modulus of the pellets (from 72.01±3 to 3.33±1.68 Mpa) but it did not have a significant effect on dissolution profile of drug (similarity factor: 82.75). Formulation with Lf equal to 1 and ratio of Avicel: lactose 1:0 was found to be the best among others. Theses pellets showed smooth surfaces and narrow size distribution, were resistant to friability, with excellent flow (Carr's index is 5.25 ± 0.86%).Discussion: The increase in dissolution rate of drug in the form of liqui-pellets could be due to dissolution or dispersion of drug in liquid vehicle which could either provide the drug immediately available for release or to increase the wettability and effective surface area for dissolution. Nevertheless with higher amount of liquid vehicle, the extrudate is prone to the leakage of the vehicle and agglomeration. Increase in lactose ratio reduced the hardness and resulted in a change of pellet characteristics from brittle to plastic.Conclusions: Liqui-pellet showed an enhanced dissolution rate and the capacity for high liquid load factor whilst maintaining excellent flow ability, so it can be anticipated as a highly commercially feasible product.

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## Production of lycopene pellet by extrusion-spheronization technique from tomato extract

*Reza Abdolahzadeh[1], Mehrdad Iranshahi[2], Abbas Akhgari[3,4], Hossein Shahdadi Sardo[3,4], and Milad Iranshahy[2]*

[1]Department of Pharmaceutics, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Pharmacognosy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[3]Targeted Drug Delivery Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
[4]Department of Pharmaceutics, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Milad Iranshahy
Corresponding author Email: iranshahiml@mums.ac.ir

Introduction: Lycopene, a natural red carotenoid pigment is found in tomato, pink grapefruit, watermelon, papaya, guava, and other fruits, shows favorable pharmacological properties including antioxidant, anti-inflammatory and anticancer. Nevertheless, due to very high lipophilicity, it has a limited systemic absorption, following oral administration. This study was designed to produce a pellet formulation for lycopene to improve its characteristics.Material and methods: For preparing the lycopene extract different solvents have been tested and the best solvent was chosen based on the extraction yield. The tomato paste, which has the most amount of lycopene among tomato products, was used as the raw material. The extraction process was carried out at 40 °C for 5 hours. The extrusion-spheronization was used as the pelletization technique. Our best formulation (containing microcrystalline cellulose and polyvinylpyrrolidone as excipients were added to the concentrated extract) was chosen for film coating to protect the lycopene from oxidation and gastric acid pH. These pellets were encapsulated in hard gelatin capsules and tested for their characteristics.Results: Examining six different solvents for extracting tomato, including acetone, ethyl acetate, n-hexane, petroleum ether, sesame oil, and olive oil displayed that the extraction percentage is higher by using the mixture of ethyl acetate and acetone (1:1) at 40 °C for 5 hours (0.1%). UV spectrophotometer analysis showed that each 700 mg tomato extract capsule contains 4.2 ± 0.07 mg of lycopene.According to scanning electron microscopy (SEM) pictures, all pellets showed nearly the same surface texture. The porosity and the sphericity of the pellets were acceptable and providing satisfactory conditions for releasing lycopene in the gastrointestinal tract. The percentage released was less than 10% in 2 hours in 0.1N HCl media (pH 1.2) and higher than 80% in 4 hours using phosphate buffer media (pH 6.8).Discussion: The data revealed that the extraction method with the highest percentage of lycopene content could provide a suitable formulation as pellets. The release percentage supplies a significant estimation for lycopene release in the gastrointestinal tract, meaning that the Eudragit L 100-55 coated pellets are protected from gastric acid. The formulation may also be resistant to oxidation and sunlight.Conclusions: These data suggest that the pelletizing strategy made it possible to achieve the desired stable lycopene formulation and generates perspectives for the potential further use of the lycopene pellets as a solid dosage form for prostate cancer treatment and other chronic diseases, including metabolic syndrome.

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## Preparation of porous PEG-PCL-PEG scaffolds with supercritical CO2 for controlled delivery of dexamethasone.

*Samir Hossein-Nejad[1], Hossein Kamali[2], Elham Khodaverdi[3], Farzin Hadizadeh[4]*

University of Medical Sciences, Mashhad, Iran
Corresponding author:Farzin Hadizadeh
Corresponding author Email: hadizadehf@mums.ac.ir

Objective: Tissue engineering, by applying the principles and methods of engineering and biological sciences, seeks to develop appropriate biological alternatives to repair, survive or improve tissue function. Scaffolds, as one of the key factors in the field of tissue engineering, provide a suitable substrate with the composition and biomechanical characteristics of the extracellular matrix (ECM). 3D scaffolds affect the growth and differentiation of stem cells And in terms of origin, they are divided into two categories, natural and synthetic.Scaffolds are made in different ways to facilitate the distribution of cells and guide their growth in the three-dimensional space. Scaffolding fabrication methods include cryopreservation, electrospinning, gas foaming, 3D printing, salt washing, and fuzzy separation. According to research, in the synthesis methods used to produce scaffolds, low biodegradability, production of toxic chemicals, adhesion and improper cell proliferation limit the use of any method.The use of supercritical carbon dioxide solves this problem. The pore size in this method is 1.9 µm and the scaffold structure has about 11% porosity. Due to the non-use of any organic solvent in the construction of scaffolding, this construction method is a safe method .In this study, PEG-PCL-PEG scaffolds were loaded with dexamethasone as an active ingredient that is widely used as an anti-inflammatory and immunosuppressive drug, as well as to enhance Stem cell differentiation is used, prepared.Methods & Materials: Reagents (caprolactone, polyethylene glycol, methoxy polyethylene glycol and catalyst) depending on the type of reaction are first added to the polymerization cell after cleaning and drying, then using a pump HPLC to which the circulator (gas-to-liquid) cooler is connected, the system pressure reaches a critical high pressure (73.8 bar), then by means of an oven and with the help of a carbon dioxide preheater to a super-critical high temperature (31.1 ° C) After the polymerization process is completed, the valve is opened and carbon dioxide gas is released and the synthesized co-polymer is obtained. For purification, the synthesized copolymer is dissolved in dichloromethane and cold diethyl ether is added at a ratio of 10 times the dichloromethane. During this process, the synthesized copolymer precipitates and is easily separated from the unreacted material. Independent variables in the supercritical fluid co-polymerization process include temperature, pressure and time. The response surface optimization method is used to obtain the optimal conditions of temperature, pressure and time. After the process, 1H-NMR and FTIR are used to determine the structure and GPC is used to determine the molecular mass. Also, the melting temperature Tm and the glazing temperature of Tg copolymers of DSC are used.Results: Synthesis of PEGCL tri-block copolymer was performed with 83.5% efficiency. The effect of different variables on scaffold morphology was investigated. Increasing the pressure reduces the pore size and increases the density. In the first region of temperature rise (40-49 ° C), the CO2 emission velocity overlaps with supercritical CO2 density up to 49 ° C, where maximum porosity is achieved. Above 49 ° C, the effect of reducing CO2 density dominates the increase in emission rate. Shorter wetting times typically result in larger pores with fewer pores and longer soaking times resulting in smaller pores with more pores in the scCO2 flooring process. The pore size increases with increasing pressure reduction time. A rapid decrease in pressure leads to an increase in the level of higher CO2 saturation, a decrease in the nucleus and consequently smaller pores. And rapid nucleation and rapid CO2 emission limit pore growth and the resulting pores appear more homogeneous. Drug loading in the microspheres decreased shortly after scCO2 use, which is predictable, indicating that DXMT enters the supercritical phase during the scCO2 process.Cumulative data from in vitro drug release show that the experimental data fit well with the Higuchi model. This result shows that the main diffusion mechanism follows the Higuchi (Diffusion) model.

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## Preparation and characterization of lip cosmetic product based on the recommendations of traditional medicine containing nanoemulsions of vitamin D

*Elnaz Piramoon[1], Shiva Golmohammadzadeh[2], Zahra Sobhani[3], Hossein Kamali[4], Vahid Soheili[5], Seyed-Ahmad Emami[6]*

University of Medical Sciences, Mashhad, Iran
Corresponding author:Shiva Golmohammadzadeh
Corresponding author Email: golmohamadzadehsh@mums.ac.ir

Objective: Vitamin D is a fat-soluble micronutrient that plays an important role in calcium homeostasis and bone health in humans. Since 1921, this vitamin has been researched. Vitamin D deficiency has now become a pandemic, and it is linked to a variety of disorders, including certain tumors, skin diseases like vitiligo, cardiovascular diseases, viral infections like COVID_ 19, and so on. In the other side, due to the carcinogenicity of direct sun exposure on the skin, vitamin D supply through sun exposure has recently been debated, resulting in several studies on systemic drug distribution of vitamin D in different forms. Translabial drug delivery is one of the new methods of drug delivery to reduce systemic complications, the possibility of long-term drug delivery, elimination of the first hepatic passage and removal of the stratum corneum of the skin against the penetration of drugs. Translabial drug delivery is a novel way of drug delivery that reduces systemic risks, allows for long-term drug delivery, eliminates the first hepatic passage, and eliminates the skin's stratum corneum, which protects drugs from penetration. The aim of this research was to create and test the properties of a lip cosmetic product based on conventional medicine guidelines that included nanoemulsions containing vitamin D.Methods & Materials: Liquid lipstick was produced in this analysis using an appropriate emulsion base containing vitamin D nanoemulsion. To make a vitamin D nanoemulsion using the HPH process, combine two aqueous phases of 2% tween 80, 0.1% methyl paraben (preservative), and deionized water, and a lipid phase of 5% olive oil (lipid carrier), 0.1 percent vitamin E (antioxidant), 1% phenoxyethanol, and 0.02% propyl paraben. Prepared nanoemulsion in terms of size, polydispersity index (PDI), zeta potential and physical stability were assessed. In order to prepare the emulsion base, the ingredients used were beeswax, candelila and carnuba waxes, castor oil, dimethicone, cetyl alcohol, isopropyl myristate, shea butter, edible red and beetroot dye, vitamin E and butyl hydroxy toluene (BHT) As antioxidants, tween 80 and span 20 as surfuctant and methyl paraben, propyl paraben and phenoxyethanol as preservative. For this purpose, 7 formulations were designed that in formulations F01 to F03, the main part of the aqueous phase was water, but in formulations F04 to F07, the nanoemulsion itself was used as the main part of the aqueous phase. Two percent, 65% and 75% of the nanoemulsion were prepared from the F07 formulation. The physico_chemical properties of liquid lipstick were investigated and dialysis bag and HPLC were used to

evaluate the release of vitamin D. Also, the effectiveness of protective materials was examined in 3 different levels by testing the effectiveness of protective materials and microbial limitations.Results: Among the liquid lipstick formulations, F07 formulation was selected as the optimal formulation both in terms of physico-chemical properties such as pH and viscosity and the ability to accept an acceptable amount of nanoemulsion. For nanomulsion formulated, particle size in the range of (149.7 ± 16.8)_(157.7 ± 12.4) nm, zeta potential in the range of (-17.7 ± 3.5)_(-22.5 ± 1.5) and PDI in the range of (0.127 ± 0.012)_(0.177 ± 0.021) were reported. All 3 parameters are in the ideal range. The results of the release test showed that vitamin D was released slowly and the percentage released from our formulation within 24 hours in the 65%sample was equal to 59.24 ±0.87% and in the 75% sample was equal to 66.16 ± 0.91% which is an acceptable release.Conclusion: In general, all the results confirm that the nanoemulsion system is a suitable system for translabial drug delivery of vitamin D, and the liquid lipstick base along with the natural color of beetroot extract is a suitable base for lip delivery and has the necessary safety to use on the lip skin. Finally, clinical trials are needed to confirm formulation efficacy.

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## Pharmacokinetic, Biodistribution and systematic cytotoxicity evaluation of the PLGA nanoparticles co-loaded with doxorubicin (Dox) and superparamagnetic iron oxide (SPION) as a theranostic platform in MRI of rabbit

*Faeze Nazeran*, Hosein Kamali,Farhad Isvand ,Zahra Jafari,Hanie Rezaei and Jafar Mosafer**

[1]Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

[2]Research Center of Advanced Technologies in Medicine, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

Corresponding author: Faeze Nazeran

Corresponding author Email: faezenazeran@gmail.com

Introduction: Doxurubicin is derived by chemical semisynthesis from a bacterial species (wild type strains of Streptomyces) and wieldy used as chemotherapeutic agent(1). As a DNA intercalating agent, DOX could effectively treat various types of cancers including hematological malignancies (like leukemia, blood cancers, and lymphoma), and several types of soft tissue sarcomas and carcinoma (solid tumors)(2). The clinical application of DOX-HCl can be restricted due to its side effects, namely cardiotoxicity, myelotoxicity, nephrotoxicity and massive reactive oxygen species (ROS) generation. Encapsulation of DOX into the hydrophobic polymers such as PLGA(poly lactic-co-glycolic acid) improves the chemotherapy outcome by enabling the safe dosing of DOX to overcome issues like rapid systemic clearance, cytotoxic effects or poor local distribution(3). Nanoparticle-based delivery systems are playing a crucial role to the treatment of cancers via a synchronous delivery of chemotherapeutic and diagnostic agents to the malignant cells. The challenge lies in synthesis of new biocompatible and biodegradable nanocarriers which are capable of co-encapsulating nanoparticle-based contrast agents and chemotherapeutic drugs targeted with specific ligands in order to improve efficacy and tumor targeting properties(4,5).Material and methods : Theranostics nanoparticles were synthesized via co-encapsulation of a chemotherapeutic drug (Doxorubicin) and a MRI(Magnetic resonance imaging) contrast agents (SPION(Superparamagnetic Iron Oxide Nanoparticles)) into a biocompatible and biodegradable polymer (PLGA-PEG) via emulsification method and called SPION/DOX-NPs. The physic chemical properties of these nanoparticles including the particle size, morphology, release pattern, magnetic properties and cytotoxicity were investigated and followed by its of in-vivo evaluation of them in rabbit. The pharmacokinetic studies were conducted at the sera of rabbit injected intravenously (IV) with Free-DOX and SPION/DOX-NPs. Also, the images of rabbit organs were depicted via MRI and fluorescent techniques.Results: The mean size of SPION/DOX-NPs (Nano Particles) was 209 nm with a narrow particle size distribution and DOX loading of 1.33%. An acceptable magnetic property including a sufficient saturation magnetization value of 1.6 emu/g was obtained and analyzed using vibration simple magnetometer analysis. The best release profile from NPs was observed in PBS at pH 7.4, in which very low burst release was observed. The loading of DOX into the PLGA nanoparticles enhanced cellular uptake of DOX in NIH/3T3 normal cells; therefore, enhanced the cytotoxicity effect of encapsulated DOX compared to the Free-DOX solution. Furthermore, SPION/DOX-NPs enhanced the contrast of magnetic resonance images in rabbit organs, especially in liver and spleen duo to the EPR effect. The organs florescent images of SPION/DOX-NPs-injected rabbits showed a red color related to the accumulation of DOX in liver, kidney. These results showed that the NPs have no cytotoxicity effect on heart. Calculating the main pharmacokinetic parameters relating to the serum DOX concentrations revealed that the NP could enhance the DOX retention in serum. Altogether, the prepared NPs could be considered as a powerful delivery system for their potential as dual therapeutic and diagnostic applications.Conclusions: The prepared SPION/DOX-NPs could be considered as a powerful delivery system for their potential as dual therapeutic and diagnostic applications in many diseases.

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## preparation and evaluation mucoadhesive scaffold formulation contain phenytoin in wound healing

*Soheil Tafazzoli-Mehrjardi [1,2], , Vahid Ramezani [1*], Hamid Reza Jamshidi Solukloei[1]*

[1]Department of Pharmaceutics, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

[2]Department of Pharmaceutics, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding author : Vahid ramezani,

Corresponding author Email: vramezani@razi.tums.ac.ir

Introduction:Skin wounds annually cost a lot to the health system of different countries. Accelerating wound healing is considered as a principle in treatment, which aims to increase the rate of healing, improve healing chronic wounds. Increasing the quality of wound healing, such as scarring reduction, has always been emphasized by the researchers. According to Winterer's theory, the wound's envirment moisture is an effective factor in wound healing, leading to attempts to reach modern wound dressing. wound dressing that can absorb excess moisture as well as retain moisture in the wounds. One of these new wound dressing is porous drug delivery systems (WAFERs). Wafers have certain properties, such as the ability to load high amounts of the drug, the ability to absorb additional wound moisture, and the creation of a pseudo-skeleton structure that makes them a wound-like system for drug delivery. The phenytoin is also used as an anti-epileptic drug that can cause gingival hyperplasia in nearly half of its users by the accumulation of large extracellular matrix molecules in gingival connective tissue. The phenytoin sodium ointment is also used as a treatment for Bedsore injuries. The goal of this study was to provide an optimal formulation of the wafer containing phenytoin sodium. To achieve this goal, the organoleptic characteristics mucoadhesivity test, and the rate of drug release was calculated. Another goal of this study

was to evaluate the wafers constructed on the wound healing of mice, in which factors such as the rate of wound healing were measured.
Methods:In this study, twelve formulations of Alginate, Chitosan, and HydroxyPropyl methyl Cellulose Polymers were made. Wafers from these twelve formulations were then constructed with the help of the Freeze Dryer. Initially, the organoleptic characteristics of the wafers, such as flexibility and homogeneity, were studied, which separated the four formulations. In the next step, evaluations such as drug release rate and mucoadhesive formulation were performed. To better evaluate the isolated wafer, tests such as surface imaging were performed by electron microscopy and differential scanning calorimetry. Finally, a selected and measured formulation evaluated in the wound healing of mice. During the wound healing process, an image and tissue samples were obtained from the wounds.Results:In the construction phase of the wafer, the results of superficial electron microscopy showed that the alginate can produce plate cavities, and wafers containing alginate / chitosan / hydroxyl propyl methylcellulose / propylene glycol form porous cavities. Also, Drug release results showed that hydroxypropyl methylcellulose polymer could reduce the rate of drug release, and alginate/chitosan polymers have a low ability to release drugs. Compared to the ointment with a wafer containing phenytoin, the wafer containing phenytoin can further increase the repair speed.Discussion:The wafers made from alginate/chitosan/hydroxyl propyl methylcellulose/propylene glycol can release the appropriate phenytoin sodium for at least forty-eight hours. The wafer mucoadhesivity and pseudo-skeleton structure can also increase cell proliferation. These proper characteristics have led to an increase in the speed of wound healing compared with phenytoin ointment.

## P176

## نانوامولسیون گیاهی موضعی برای درمان ریزش مو براساس توصیه های طب سنتی

*Fatemeh Jahanpak[1], Zahra Sobhani[2]*

[1]University of Medical Sciences, Mashhad, Iran
[2]Department of Traditional Pharmacy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author:Zahra Sobhani
Corresponding author Email: SobhaniZ@mums.ac.ir

Introduction: The aim of this research is to develop and characterize a novel and transparent oil in water (O/W) herbal nanoemulsion containing amla, mazu and myrtle extract (Phyllanthus emblica, Quercus infectoria galls, Myrtus communis L.) aiming pharmaceutical and cosmetic applications.Material and methods: The emulsifier and co-emulsifier were selected according to the solubility of the extract in them. Oil-in-water nanoemulsions were prepared by the low energy method with various proportions of surfactant/co-surfactant as 4:1, 3:1, 2:1, and 1:1. The water titration method was used to make the pseudoternary phase diagrams of nanoemulsions and optimize the prescription composition. Formulations were evaluated regarding their appearance, droplet size, polydispersity index, zeta potential, viscosity, and pH. Total phenolic contents in free herbal extracts and extract loaded nanoemulsions were determined spectrophotometrically. In addition, the physical and chemical stability of formulations at various temperatures (-20°C, 4°C, 25°C and 40°C) were also evaluated. Then, in vitro permeation study of optimal formulation was performed using Franz diffusion cell.Results: Herbal nanoemulsions showed significant concentrations of phenolics. Tween 80 as surfactant and glycerol as co-surfactant were selected to plot pseudo ternary phase diagram. Maximum nanoemulsion region was obtained in pseudo-ternary phase diagrams with surfactant to co-surfactant ratio (Smix) of 3:1. So, the optimal formulation of herbal nanoemulsions contained tween 80 as an emulsifier, glycerol as a co-emulsifier, mazu and myrtle oil as oil phase, and their proportion was 27:9:1, respectively. Colloidal dispersions exhibited transparent appearance with a mean particle size around 20 nm, particle size distribution between 0.161- 0.327 and zeta potential of -2.99 to -3.86. Viscosity range was 0.024 - 0.191 Pa.s and pH was about 4.14 - 4.18. Stability studies showed that the 1 : 9 (oil : Smix) nanoemulsions had better stability under different conditions and were stable over 28 days of storage at room and refrigerator temperature. And it showed 57.423% retention into the rat skin in Franz diffusion cell. Discussion: These results confirm the formation of oil in water nanoemulsion due to small particle size (< 100 nm) and noticeable retention into the skin, which enables drug delivery to the hair follicles. Also, physicochemical properties of the nanoemulsion samples showed appropriate stability according to a monodisperse size distribution, negative zeta potential result, and no significant differences in pH and viscosity during 60 days of storage at room and refrigerator temperature. Conclusions: This study demonstrated that nanoemulsions containing amla, mazu and myrtle extract can be successfully produced and are stable at room and refrigerator temperatures. As a result, this herbal nanoemulsion might be a potential candidate for a novel hairloss therapy.

## P177

## Protective effects of Urtica dioica (nettle) and its constituent Carvacrol against natural or chemical toxicities

*Bahareh Samakar [1], Soghra Mehri[2, 3], and Hossein Hosseinzadeh[2, 3]*

[1]School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
[2]Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran
[3]Department of Pharmacodynamics and Toxicology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Bahareh Samakar
Corresponding author Email:baharehsamakar@yahoo.com

Introduction:There has been increasing popularity in treatment with traditional medicine in the past few years due to their positive features such as easy accessibility, relative low cost, low side effects and technological input. Urtica dioica L., from Urticace family and commonly known as ‘stinging nettle’, has been known as a medicinal herb for many years across the world. This perennial herb is widely used in south Asian countries and Indian subcontinent due to its various chemical compounds such as tannins, flavonoids, saponins, phytosterols, proteins and amino acids. U. dioica has traditionally been used in various disorders such as cardiovascular diseases especially hypertension. Numerous studies have established that nettle and its active compound carvacrol, have beneficial effects towards many toxic elements in various organs.This review aims to demonstrate the effects of U. dioica as a medicinal plant and carvacrol, one of its biologically active constituents, on chemical and natural organ toxicities.Material and methods: In this review article, different electronic databases such as Pubmed, Scopus, and Google Scholar have been used to search with the following keywords: U. dioica, nettle, carvacrol, antidote, toxicity, protective effects, chemical toxin and natural toxin. We collected all published in vitro, in vivo, and clinical studies investigating the possible protective effects of U. dioica and carvacrol, against natural or chemical toxicities. The most relevant articles were included without publication time limitation.Results: The protective effects of carvacrol against natural toxins such as various fungal (Cryptococcus, Malassezia, Aspergillus, albicans and non-albicans Candidas), bacterial (Salmonella, Klebsiella, Staphylococcus, Clostridium, Escherichia coli and Vibrio cholerae) or viral (HIV, CMV, Coronavirus) infections and chemical

toxicities such as metals (Cadmium and lead), carbon tetrachloride and several anticancers (Cyclophosphamide, Doxorubicin, Cisplatin, Methotrexate) have been observed in numerous investigations.Discussion and conclusions: It has been concluded that nettle could ameliorate toxicity of natural and chemical toxins in heart, lungs, kidneys, liver, neurons and testis. Its constituent, carvacrol could be a promising natural agent in reversing the toxic effects of various toxins in several organs. However, more researches are needed to be accomplished in order to identify the mechanisms underlying these effects. Also, it is suggested to verify these effects on human in more clinical trials.

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## A mechanistic insight into the biological activities of urolithins as gut microbial metabolites of ellagitannins

*Seyyed Hossein Hasheminezhad*[1], *Motahareh Boozari*[1], *Mehrdad Iranshahi*[2], *Omid Yazarlu*[3], *Amirhossein Sahebkar*[2], *Maede Hasanpour*[2] *and Milad Iranshahy*[1]

[1]Department of Pharmacognosy, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

[2]Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran.

[3]Department of General Surgery, Mashhad University of Medical Sciences, Mashhad, Iran.

Corresponding author: Milad Iranshahy, Maede Hasanpour
Corresponding author Email: IranshahiML@mums.ac.ir , Hasanpourmm963@mums.ac.ir

Introduction: Urolithins are the gut metabolites produced from ellagitannin-rich foods such as pomegranates, tea, walnuts, as well as strawberries, raspberries, blackberries, and cloudberries. Urolithins are of growing interest due to their various biological activities including cardiovascular protection, nephroprotection, neuroprotection, anti-inflammatory activity, anticancer properties, antidiabetic activity, antioxidant and antibacterial properties.Material and methods: Here, we comprehensively review the potential role of urolithins as new therapeutic agents and investigate the molecular pathways have been involved in their biological effects.Results: Several studies mostly based on in vitro and in vivo experiments have investigated the potential mechanisms of urolithins which support the beneficial effects of urolithins in the treatment of several diseases such as Alzheimer's disease, type 2 diabetes mellitus, liver disease, cardiovascular disease and various cancers. UroA has an exceptionally high potential for use in clinical trials of aging-associated diseases including muscle atrophy (sarcopenia), Alzheimer's disease and atherosclerosis due to its unique mitopaghy activating mechanism, since it has acceptable safety profile in human. Anticancer activity of UroA is much more related to p53 activation and deserves special attention for treatment of cancers with mutations in MDM2 as an important negative regulator of p53. UroB has valuable effects against cardiovascular disorders and may be used in the future studies, albeit its safety is not properly proved in previous studies.Discussion and Conclusions: Several lines of evidence indicate that urolithins possess unique mechanisms of action and may be harnessed as pharmacological agents to protect against range of disorders including cancer, neurodegeneration, obesity and atherosclerosis.

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## Quantification of main compounds in the essential oil of Zataria multiflora Boiss. and Foeniculum vulgare Mill. plants, and their medicinal products using qH-NMR methods in comparison with GC-MS.

*Yekta reyhani*[1], *Faegheh farhadi*[2], *Dr Mehrdad Iranshahi**

[1]Pharmacognosy, Pharmacy, Mashhad university of medical science, Mashhad , Iran

[2]Student Research Committee, Pharmacy, Mashhad university of medical science, Mashhad , Iran

[3]Research Center, Mashhad university of medical science, Mashhad , Iran

Corresponding author: Yekta Reyhani
Corresponding author Email: yekta.reyhani220@gmail.com

Introduction: The use of appropriate methods of standardization, submitted to a strict quality control for the quantification of commercial essential oils and their products available in market, seems very necessary. since their chemical composition may vary according to the source, storage conditions and adulteration, applying fast and reliable standardization methods is one of the basic needs in the field of medicinal plant research.Sweet Fennel is one of the oldest herbaceous and aromatic species of the Umbelliferae family that grows widely in the Mediterranean region.Shirazi Thyme is a fragrant species of the mint family and grows only in Iran, Afghanistan and Pakistan. This type of thyme is traditionally used in the medical, cosmetic and food industries.The aim of this study was to provide a rapid and reliable method of evaluating and determining the amount of anethole and thymol samples in both plants and their products available in the market using qH-NMR and GC-MS methods.Material and methods: First, essential oils were extracted from selected plant species by water distillation method. Also, available medicinal products were prepared from each species. Quantitative analysis of essential oils, pure compounds and products was performed by GC-MS and qH-NMR methods. Also, tests related to the linearity, stability and reproducibility of qH-NMR were performed.Results and Discussion: Validation tests were performed on the qH-NMR method and the RSD results of reproducibility, linearity, stability and response of the device to the change of parameters, confirmed the qH-NMR method. LOD and LOQ values were determined to be 0.210 and 0.66 mg/ml for thymol composition, respectively. That is, in 35 mg of thyme essential oil, the detectable thymol content should be at least 0.6% and the measurable thymol content should be 1.7%. Also, in the case of anethole, LOD and LOQ values were 0.52 and 1.59 mg/ml, respectively. That is, in 40 mg of fennel essential oil, the minimum detectable amount is 1.3% and the minimum measurable amount is 3.9%.Also, the amount of anethole and thymol in the two products that were selected in this study, were less than what is mentioned in the product description Conclusions Using GC-MS approach the content of anethole and thymol compounds in essential oil and product samples was higher than qH-NMR method, but the important point is the very small difference between these values. Accordingly, the use of qH-NMR method can be considered as an alternative to the conventional GC-MS method. The qH-NMR method is also a valid method for investigating adulterant and quality of natural products.

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## بررسی اثر تیموکینون بر فرایند تمایز به آدیپوسیت در سلولهای بنیادی مشتق از بافت چربی

*Seyed Ahmad Emami, Zahra Tayarani-Najaran, Zahra Salmasi, Elham Nikkhah, Monire shahbodi*

Pharmacy faculty of Medical scince of Mashhad university of Iran
Corresponding author: Monire Shahbodi
Corresponding author Email: Shahbodim2@mums.ac.ir

Introduction: The bone marrow compartment contains several cell populations, including mesenchymal stem cells (MSCs) that are capable of differentiating into adipogenic, osteogenic, chondrogenic, and myogenic cells.State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.Material and methods: Provide sufficient details to allow the work to be reproduced by an other independent researcher. Methods should For this study, lipid samples from liposuction surgery patients aged 38-45 years were transferred to the laboratory in sterile conditions. After washing with PBS, the fat samples were exposed to collagenase enzyme and after enzymatic digestion, cells were incubated in a flask at 37 ° C and 5% CO2. After the third passage, the cells were cultured in 24-well plates, and after reaching 70-80% density The extracts cytotoxicity on ADSCs was measured , they were subjected to induction of differentiation into fat in the presence of thymoquinone. Cell culture medium was changed every 2 days, and after 21 days of adipocytes culture, differentiation were assessed by Oil Red staining and expression of PPARγ( Peroxisome proliferator-activated receptor γ )and FAS( Fatty Acid Synthetase) proteins using Western blotting technique be summarized.Results: Thymoquinone at concentrations of 100 µM ($p<0.05$), 150 and 200 ($p<0.001$) decreased the viability of mesenchymal stem cells, but at concentrations lower than 100 µM thymoquinone had no significant effect compared to the control group. Then in Oil Red test it was observed that thymoquinone with concentrations of 12.5 µM ($p<0.01$) and 25 ($p< 0.001$) significantly reduced the differentiation of stem cells into adipocytes compared to the positive control group that decrease of differentiation was dose-depended. On the other hand, qualitative examination of cells in the Oil Red test also showed that the highest amount of fat vacuoles is seen in the concentration of 6.25 Mµ.Finally, the results of Western blot showed that thymoquinone at concentrations of 12.5 µM ($p <0.05$) and 25 µM ($p <0.01$) reduced the FAS / β-actin ratio compared to the positive control group. Also, thymoquinone at concentrations of 6.25 µM ($p <0.01$) reduced the amount of PPARγ protein compared to the positive control group.Results should be clear and concise.Discussion: In the present study demonstrated that Thymoquinon had anti-adipogenic effect by reduction of FAS expression. Our finding suggest that Thymoquinon may serve as a promising natural product for treatment or prevention of obesity and metabolic disorders in human.This should explore the significance of the results of the work, not repeat them.Conclusions: This study showed that thymoquinone reduces the process of differentiation of fat stem cells into fat cells and can be considered as an anti-obesity compound. The main conclusions of the study should be noted clearly.

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## Coumarin derivatives as anti-PqsR agents against Pseudomonas aeruginosa PAO1 reduce the production of biofilm and virulence factors

*Amineh Sadat Tajani[a], Arianoush PourMohammad[a], Armin PourMohammad[a], Vahid Soheili[a*], Bibi Sedigheh Fazli Bazzaz[a*]*

[a]Department of Pharmaceutical Control, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Vahid Soheili
Corresponding author Email: soheiliV@mums.ac.ir

Antibiotic resistance is a global threat that has caused lots of difficulties in treating microbial infections. The discovery and development of new strategies are needed to address this problem. The bacterial quorum sensing system (QS) is a promising target for treating and managing clinical infections. Recent studies have revealed the potential role of coumarins, small natural molecules, in blocking QS signaling systems and suppressing biofilm formation in clinical pathogens. In addition to human infections, coumarin derivatives effectively control plant pathogens, aquatic infectious microorganisms, food spoilage bacteria, and other industries. The biofilm inhibition effect of some coumarin derivatives (Umbelliprenin, 4-Farnesyloxycoumarin, Gummosin, Samarcandin, Farnesifrol A, B, C, and Auraptan) was assessed through a colorimetric method in Pseudomonas aeruginosa PAO1. Moreover, their impact on virulence factors production was also measured via the light absorption of pigments by ELISA reader. The synergistic effect of coumarin compounds with tobramycin and the molecular interaction of coumarins and PqsR protein was also studied. Finally, the expression of PqsR protein genes in the presence of selected compounds was investigated by RT-qPCR.According to the results, the compounds 4-Farnesyloxycoumarin, Gummosin, and Farnesifrol A, B, and C have reduced biofilm formation and virulence factors (pyocyanin, pyoverdin, and protease) production and increase penetration and efficiency of tobramycin. 4-Farnesyloxycoumarin has demonstrated a significant decrease in the relative expression of the PqsR gene. Finally, These compounds may be effective in inhibiting biofilm production and reducing the pathogenicity of P. aeruginosa.

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## Targeted Star-Shaped Copolymeric Micelles for Hydrophobic Agents Drug Delivery

*Mehrdad Sahranavard[1, 2, 3], Mahsa Shahriari[1, 2, 4], Khalil Abnous[1, 5], Farzin Hadizadeh[6], Seyed Mohammad Taghdisi[7], Reza Zolfaghari[1], Mohammad Ramezani[1, 2*], Mona Alibolandi[1, 2*]*

[1]Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

[2]Department of Pharmaceutical Biotechnology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[3]Student Research Committee, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[4]Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Zabol University of
Medical Sciences, Zabol, Iran

[5]Department of Medicinal Chemistry, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

[6]Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

[7]Targeted Drug Delivery Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding author: Dr. Mona Alibolandi, Prof. Mohammad Ramezani
Corresponding author Email: alibolandim@mums.ac.ir, ramezanim@mums.ac.ir

Introduction: The use of the potent antineoplastic agent, camptothecin, for the third common cancer type in the world, colorectal cancer, has been limited due to instability and low solubility of active form accompanied by severe adverse effects. Targeted star-shaped micelles can target tumor cells and provide an efficient drug delivery system with low critical micelle concentration and high thermodynamic stability to avoid hydrophobic agents, including camptothecin, drug delivery drawbacks. Herein we synthesized and characterized epithelial cell adhesion molecule (EpCAM) targeted star-shaped polylactic acid (PLA)-polyethylene glycol (PEG) copolymer to deliver camptothecin to colorectal tumor cells. Also, we performed in vivo and in vitro assessments of the formulation.Material and methods: 3-azido-2,2-bis(azidomethyl)propan-1-ol was synthesized and used as the initiator of PLA synthesis through ring-opening polymerization. Three PLA molecules were conjugated with 1,3,5-benzenetricarbonyl trichloride, and three alkyne-PEG-maleimide molecules were conjugated to the end of each PLA using click reaction. Maleimide terminal of PEG was used for EpCAM targeting aptamer conjugation. 1H nuclear magnetic resonance, gel permeation chromatography and differential scanning calorimetry were used to confirm synthesis steps. Loading and release profiles, size distribution and shape of camptothecin-loaded copolymeric micelles were studied using dynamic light scattering and scanning and transmission electron microscopy. Also, in vitro studies on C26, HT29 and CHO cell lines were performed followed by in vivo tumor suppression efficacy, biodistribution and histopathological evaluation.Results: Analysis showed proper copolymer synthesis. Targeted camptothecin-containing micelles were Spherical and 192 nm in diameter. Size distribution polydispersity index was 0.2 and Zeta potential was found to be -17.3 mV. Camptothecin loading content was 3.7±0.4 and encapsulation efficiency (EE%) was 73.7±8.2. In vitro assays showed significantly higher dose-dependent cytotoxicity respectively in targeted and non-targeted formulations than free drug on C26 and HT29 cell lines, while no significant difference was found on CHO cell line. Observed in in vivo studies, targeted camptothecin copolymeric micelles showed better efficiency than other formulations and then non-targeted camptothecin copolymeric micelles and the free drug showed better efficiency, respectively. Biodistribution studies showed significantly higher entrance of non-targeted formulation into the tumor after 6 hours, while it showed significantly higher entrance of targeted formulation into the tumor after 18 hours. Discussion: A size lower than 200 nm makes the nanoparticle perfect for the enhanced permeability and retention (EPR) effect. It seems that EpCAM targeting aptamer is the reason for the higher cytotoxicity of targeted micelles in cancer cell lines, while receptor-mediated endocytosis is the reason for higher cytotoxicity of non-targeted micelles in the cancer cell lines. Moreover, no significant difference in cytotoxicity in normal cell line indicates efficient targeted drug delivery. Also, higher distribution of non-targeted formulation in tumor tissue after 6 hours seems to be due to the EPR effect, while the higher distribution of targeted formulation in tumor tissue after 18 hours could be due to the EpCAM targetingConclusions: Appropriate results of analysis of the present nano drug delivery system make it a good candidate for targeted drug delivery of hydrophobic agents and raises hope for overcome camptothecin clinical drawbacks.

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## Silybin Liposome protects against Acetaminophen-induced liver toxicity

*Samin Khabbazian[1] , Seyedeh Hoda Alavizadeh[2] , Fatemeh Gheybi[3], Mahmoud Reza Jaafari[2]*

[1]Student Research Center, Faculty of Pharmacy, Mashhad University of Medical Science, Mashhad , Iran
[2]Department of Pharmaceutical Nanotechnology, School of Pharmacy, Mashhad University of Medical Sciences , Mashhad , Iran
[3]Department of Medical Biotechnology and Nanotechnology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
Corresponding author: Seyedeh Hoda Alavizadeh
Corresponding author Email: AlavizadehH@mums.ac.ir

Introduction**:** In large doses, the commonly used analgesic Acetaminophen (Act) induce a centrilobular hepatic necrosis in human and experimental animals. Currently, N-acetylcysteine (NAC) a glutathione precursor is used as an antidote for Act overdose. However, NAC is effective only if used within hours of an acute overdose. Thus, searching for alternative detoxifying modalities are required. Silymarin, a natural compound derived from species Silybum Marianum or milk thistle, and its major active component silybin (SLB) are used in the treatment of various liver disease. However, poor aqueous solubility and low bioavailability restricted their parenteral use. The main objective of the present work was to formulate, characterize and evaluate liposomal silybin (Lip-SLB) and investigate its hepatoprotective potential.Methods**:** SLB liposomes (Lip-SLB) were successfully synthesized by a novel remote-loading method. After characterization of liposomes, mice were randomly divided into 6 groups containing 10 animals each. To induce hepatotoxicity, Act was injected i.p. at 400 mg/kg, and mice were administered with two times (15 mg/kg iv or i.p.) at 2 and 8 h after Act dosing. Control animals received either Act (400 mg/kg, i.p.), Dextrose 5%, Lip-SLB alone (15 mg/kg, iv) and free liposomes (iv). 24 h after dosing, mice were sacrificed, blood was collected and serum analysis was performed to measure ALT (alanine transaminase), AST (aspartate transaminase) and ALP (Alkaline Phosphatase). Liver tissues were fixed in 10% aqueous formalin for pathology (HEstaining). Results**:** Liposomes of 150 nm in diameter and uniform dispersity showed a high entrapment efficiency of SLB (2.5 mg/ml) using spectrophotometry analysis. The liposome features made them suitable for parenteral administration. With regard to Act-induced liver injury, i.p. administration of Lip-SLB significantly attenuated the serum levels of ALT, AST and ALP, biomarkers of liver disease. On the contrary, iv administration of Lip-SLB did not results in a remarkable decrease in the level of enzymes. Pathological analysis of liver tissues indicated severe fatty degeneration of liver in control animals, while SLB liposomes succeed in reversing these changes following i.p administration.Conclusion **:** It is concluded that SLB liposomes in rational pharmaceutical design are not only suitable for parenteral administration, but also could reverse Act-induced hepatotoxicity. Despite promising results with i.p. administration of SLB liposomes, intravenous injection of these carrier did not work as expected. The high efficiency of SLB loading in liposomes using the novel method could deliver the right doses of SLB to the liver presumably if liposomes of larger sizes are applied. Since liposomes of larger size tend to be captured by the cells of reticuloendothelial systems including Kupffer cells. The in vitro tests regarding intracellular GSH levels and flow cytometry of HepG2 cells are in progress to show the mechanisms involved in hepato-protective effects. Collectively, our promising in vivo finding suggest that the parenteral formulation of SLB liposomes has potential against Act toxicity and merit further investigation.

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## The effect of Caveolin-1 Neuron-Targeted gene therapy in the treatment of Alzheimer's (AD)

*Negar Yeganeh Khorasani[1], Mona Haghi[2]*

[1]Student Research Committee, Faculty of Pharmacy, Mashhad University of Medical Science, Mashhad , Iran

[2]Student Research Committee, Faculty of Pharmacy, Mashhad University of Medical Science, Mashhad , Iran

Corresponding author: Negar Yeganeh Khorasani

Corresponding author Email: Yeganehn972@mums.ac.ir

Introduction: Introduction: Introduction: Alzheimer's disease (AD) is one of the most common neurodegenerative diseases and accounts for more than 80% of dementias worldwide in the elderly. The basis of the pathogenicity of AD and the resulting cognitive impairments is the destruction of Synapse and disturbance of signaling .Amyloid precursor proteins and beta-amyloid molecules are involved in the physiological functions of the nervous system such as nerve cell growth, nerve survival and nerve damage. Studies have shown that there is a strong interaction between amyloid-beta and tao proteins, which causes amyloid-beta and tao accumulations inside and outside neurons, leading to dendritic spines and synapse destruction. At present, existing treatment strategies only relieve symptoms, while the removal of toxic amyloid species alone is not sufficient to reverse a functional defect in the AD patient's brain. Caveolin-1 (Cav-1) is a membrane-bound protein scaffold or lipid (MLRs) that organizes signaling complexes and can enhance neural and synaptic flexibility. Therefore, the purpose of this article is to investigate the effects of genes. Caveolin-1 Neuron-Targeted Therapy as New Targets for Alzheimer's Treatment.Methods: In this review, we include an article that discusses young blood plasma on Brain tissue rejuvenation. All articles were published between 2000_2020 and have ethical considerations. We searched PubMed and Google Scholar search engine with Caveolin- 1 OR cav-1 protein AND Alzheimer's disease, keywords were. Initially, 28 articles were found using this method. Then we excluded 18 articles from the study by considering the abstract and used 10 articles in this review.Results: An article on the possible neuroprotective effects of Caveolin 1, curcumin, and vitamin B12 inhibitors on Alzheimer's disease in rats shows Curcumin, Folic Acid, and Vitamin B12 can decrease the GSK/3ß activity & Tau hyperphosphorylation in STZ induced AD which may be associated with improvement of memory deficits in rats. Another 7 articles show that the loss of Cav-1 accelerates nerve damage and aging. The results showed that Cav-1 represents a novel control point for healthy neuronal aging and loss of Cav-1 represents a non-mutational model for Alzheimer's disease. One study showed a direct or indirect cav-1/sorLA interaction could modify the trafficking and sorting functions of sorLA in glia and its proposed neuroprotective role in AD. Another study showed miR-12-3p directly targeted Caveolin-1; miR-124-3p inhibited abnormal hyperphosphorylation of Tau by regulating Caveolin-1-PI3K/Akt/GSK3β pathway in AD, which may provide new ideas and therapeutic targets for AD.Discussion: Studies to date have shown that Caveolin-1 Neuron-Targeted gene therapy maintains cognitive function and synaptic flexibility in a model of Alzheimer's disease (AD) mice. Therefore, Caveolin-1 Neuron-Targeted gene therapy can be used as target of New gene therapy to be considered.Conclusions: Recently, significant efforts have been made to find new genes that are effective in the mechanism of Alzheimer's pathogenesis, as the identification of these genes can be used as gene therapy targets to treat AD patients. Despite these early stages, there is a long way to go from experimental studies to clinical application.

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## Preparation and evaluation in vitro of PLGA nanoparticles containing doxorubicin and iron oxide superparamagnetic nanoparticles (SPIONs) with simultaneous treatment and detection capability in magnetic resonance imaging (MRI) technique

*Hanieh Rezaee[2], Hosein Kamali[2], Zahra salmasi[2], Zahra jafari[2], Faeze Nazeran[2] and Jafar Mosafer[1,2*]*

[1]Research Center of Advanced Technologies in Medicine, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

[2]Pharmaceutical Research Center, Pharmaceutical Tehnology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

Corresponding author: Jafar Mosafer

Corresponding author Email: mosaferj901@gmail.com

Introduction: Despite decades of basic and clinical research and trials of promising new therapies, cancer remains a major cause of morbidity and mortality (1). Functional nanoparticles used in the treatment of cancer attract extensive attention due to their intrinsic physical properties, long blood circulation time, specific targeting capability, enhanced intracellular uptake, and manipulation of molecular behavior on the nanometer scale (2). The aim of this study was to develop a novel multifunctional nanoparticle, which encapsulates SPIONs (superparamagnetic iron oxide nanoparticles) and DOX (Doxorubicin) in PLGA (poly(lactide-co-glycolide)-b-poly(ethylene glycol)-carboxylic acid) to form a multifunctional drug delivery system for therapeutic and diagnostic purposes.Material and methods: SPIONs were synthesized using a co-precipitation method. Theranostics nanoparticles were synthesized via co-encapsulation of a DOX and SPIONs into the PLGA polymer via the double emulsion method (W1/O/W2). Hydrodynamic diameter, Poly Disparity Index (PDI), zeta potential, and size distribution profile of nanoparticles were obtained with the dynamic light scattering method. The size and shape of the nanoparticles were resolved by Scanning electron microscopy (SEM). The particle size and morphology of the magnetic nanoparticles were observed by transmission electron microscopy (TEM). Magnetic measurement of NPs was obtained using A vibration sample magnetometer (VSM). Loading and encapsulation efficiency of DOX was determined by using a UV-Vis spectrophotometer. Evaluation of drug release from nanoparticle formulation was performed using PBS buffer at pH 7.4 and acetate buffer at pH 5.5. Finally, a cytotoxicity test by the Alamar Blue method was used to compare the drug concentration of each formulation that can kill 50% of the cell population (IC50).Results: The mean size of SPION/DOX-NPs was 209 nm with a DOX loading of 1.33%. An acceptable magnetic value of 1.6 emu/g was obtained and analyzed using a vibration sample magnetometer. The Dox-loaded NPs exhibited a similar release pattern in both acidic and neutral media, except that the NPs in the acidic media released higher amounts of Dox. A nearly three-fold higher cumulative Dox release was observed in acetate buffer (pH 5.5) than in PBS (pH 7.4), The loading of DOX into the PLGA nanoparticles enhanced cellular uptake of DOX in NIH/3T3 normal cells.Discussion: The results of this study showed that by using the dual emulsion method of solvent evaporation, simultaneously the highly hydrophilic drug doxorubicin and the highly hydrophobic nanoparticles SPION coated with oleic acid Enclose within the PLGA polymer matrix and finally achieve the formulation of nanoparticles with suitable physicochemical properties in terms of particle size, particle size distribution, optimum magnetic properties as well as appropriate and simultaneous encapsulation of doxorubicin and SPION nanoparticles. Since the pH of cellular organelles such as endosomes is about 5.5, the relatively high release of Dox in acidic media would be beneficial for increasing the cytotoxicity effect of Dox inside the cells while the low release of Dox at neutral pH implies the limitation of Dox release in blood circulation.Conclusions: The prepared SPION/DOX-NPs could be considered as a powerful delivery system for their potential as dual therapeutic and diagnostic applications in many diseases.

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## Synthesis of chimeric peptosomes hybridized with gold nano-rod for doxorubicin delivery to metastatic breast cancer

*Malihe Hassannia[1], Mohammad Ramezani[2*], Mona Alibolandi[2*]*

[1]Department of Pharmaceutical Nanotechnology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

[2]Department of Pharmaceutical Biotechnology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

Crresponding author:Mona Alibolandi

Corresponding author Email: alibolandim@mums.ac.ir or ramezanim@mums.ac.ir

Introduction: Polymersomes are more promising nanocarriers that can be formed via amphiphilic block copolymers with various molecular weights and structures. These nanoparticles can be loaded with hydrophilic drugs in their aqueous interior and hydrophobic drugs in their bilayer shell [1]. Recently polypeptide-based block copolymers have been used to the formation of vesicular nanoparticles called peptosome. Peptosomes have more advantages compared to conventional polymersomes including precise secondary conformations, excellent biodegradability, and biocompatibility .[2] According to clinical studies, poly (ethylene glycol)-b-poly (amino acid) based micelles encapsulated with paclitaxel, SN-38, doxorubicin, or cisplatin have increased antitumor efficacy with reduced side effects [3]. Nanoplatin™ (NC-6004) is a cisplatin-loaded methoxypoly(ethylene glycol)-block-poly(L-glutamic acid) (mPEG-b-PLG) that was evaluated in the Phase I/II/III clinical trial [4]. In this research, we successfully synthesized a poly(ethylene glycol)-b-poly(γ-benzyl L-glutamate) (PEG-b-PBLG) based peptosome and was applied for co-encapsulation of hydrophobic gold nanorod (as computed tomography (CT) contrast agent) and hydrophilic doxorubicin (as anti-cancer agent) via double emulsion method.Material and methods: The small gold nanorod (GNR) was synthesized through seed-mediated growth method and was hydrophobic via ligand exchange method with 11-mercaptoundecanoic acid. In the next step, poly (g-benzyl-Lglutamate) (PBLG) was successfully prepared by the ring-opening polymerization of γ-Benzyl-L-glutamate-N-carboxyanhydride (BLG-NCA) using n-hexylamine as the initiator and conjugated to maleimide polyethylene glycol carboxylic acid (Mal-PEG-COOH). Hydrophobic GNR and hydrophilic DOX were loaded in PEG-PBLG peptosome through double emulsion method. Results: The hydrophobic PBLG was prepared and characterized via 1H-NMR, FTIR and GPC chromatogram. GPC of the PBLG indicated low polydispersity and the molecular weight 11662 g/mol. The size of PEG-PBLG@DOX-GNR was 176nm with PDI of 0.06. The encapsulation efficiency of DOX in PEG-PBLG@DOX-GNR was %42 ± 2.5.Discussion: Cellular cytotoxicity and cellular uptake analysis in murine 4T1 and human MCF-7 cancer cell lines indicated acceptable drug delivery of the system in vitro.Conclusions: It could be concluded that the PEG-PBLG@DOX-GNR is a promising nano-platform for further investigation toward diagnosis and treatment in preclinical stage.

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## نانو الیاف پلی ساکارید محلول در آب سویا حاوی سوماتریپتان

*Sina Majidi[1]*

[1]Mashhad University of Medical Sciences, Mashhad, Iran.

Corresponding author:Sina Majidi

Corresponding author Email: majidis941@mums.ac.ir

Objective: The incidence of migraine headaches is associated with a decrease in the quality of life of patients. Triptans and Sumatriptan are among the medications used to relieve these headaches. One of the parameters that is important in the efficacy of these drugs to relieve headaches is the initiation of their therapeutic effect. The oral form of Sumatriptan is less effective than its injectable form due to the onset of delayed effect. One of the ways to improve the onset of drug efficacy is the use of new drug delivery systems. In this study, the retractable shape of Sumatriptan mouth made of nanofibers containing soy solution polysaccharide has been investigated and tested. The reason for the use of soy solution polysaccharide is its pharmaceutic benefits as well as the inexpensiveness of this material.Methods and Materials: Due to the characteristics of soy solution polysaccharide and Sumatriptan succinate, first, the formulation containing Sumatriptan was prepared with concentrations of 0.15%, 0.5% and 1% and was spliced by electrospinning device for the production of nanofibers. The properties of polymeric solution such as viscosity, pH and electrical conductivity were investigated. Nanofiber diameter, morphology and fiber diameter distribution were investigated using SEM method. XRD, DSC and FTIR tests were used to evaluate crystalline properties and material interference. The characteristics of this drug delivery system such as tensile strength, loading rate and drug release profile as well as cytotoxicity of nanofiber membranes were evaluated.Results: Nanofibers were prepared using electrospinning method and the mean fiber diameters were 31 nm ± 313, 29 ± 373, 37 ± 412 and 42 ± 453 for Blank fibers, 0.15% SS, 0.5% SS and 1% SS, respectively. By adding Sumatriptan succinate to the soluble viscosity polymer, electrical conductivity and tensile strength in fibers increased, but pH decreased. The percentage of drug loading for SSPS-Sumatriptan was 0.15%, 0.5% and 1%, respectively. Analysis of FT-IR, DSC and XRD confirmed the absence of interactions between drugs and extensions in polymer membranes. Drug release profile analysis showed that nanofibers containing Sumatriptan release the drug faster than Sumatriptan powder alone.Conclusion: According to the studies, it can be concluded that Sumatriptan can be loaded well in soy solution polysaccharide nanofibers and released more quickly in oral space. It is predicted that this increase in drug release rate will be effective in improving the onset of therapeutic effects and reducing migraine headaches.

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## Identifying new non-psychiatric drugs for treatment of mood disorders based on blood biomarkers: A review article

*Sara Tavakoli[1], Maryam Tivay[2], Maryam Babaee[3], Reza Haghshenas Hafshejani[4],Zahra Etemadi[5], Alireza Keshavarzian[6], Fatemeh Hendijani[7]*

[1]Student Research Committee, Faculty of Pharmacy, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

[2]Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

Corresponding author:Fatemeh Hendijani

Corresponding author Email: hendijani@hotmail.com

Introduction: According to the World Health Organization, Depression is a prevalent mental disorder which affects more than 264 million people globally. Bipolar disorder is another disabling mental illness

(consisting of mania and depression episodes) with a worldwide prevalence of about 45 million people. Unfortunately, misdiagnosis risk of mood disorders is high which results in inappropriate treatment. In this review article, we focused on diagnostic blood biomarkers and potential candidate non-psychiatric drugs with antidepressant effects.Material and methods: The PubMed, Scopus, Web of Science and Google Scholar databases were searched for studies published in English over the past 20 years (March 2001–March 2021) using relevant search terms (depression; bipolar disorder, mood disorder, diagnostic blood biomarkers, depression-related molecular mechanisms and pathways). Finally, 56 articles about potential role of blood gene expression biomarkers in diagnosis and treatment of mood disorders were reviewed.Results: Le-Niculescu et al suggested a novel approach for predicting, diagnosing and treating mood disorders (depression and bipolar disorder) using blood gene expression biomarkers. After discovery, prioritization, and validation of these blood biomarkers, their molecular pathways, biological and pharmacological effects were analyzed. Blood biomarkers associated with depression included NRG1(Neuregulin), PRPS1(phosphoribosyl pyrophosphate synthetase1), GLS(glutaminase), DOCK10(dedicator of cytokinesis10), TMEM161B (transmembrane protein161B), SLC6A4(Solute Carrier Family6 Member4), GLO1(glyoxalas1), HNRNPDL (heterogeneous nuclear ribonucleoprotein D like), CD47(CD47molecule), SMAD7(SMAD family member7), OLFM1(olfactomedin1) and FANCF (fibroblast growth factor receptor1). Among them, the first six items were involved in diagnosis of both depression and bipolar disorder, but the last six were specifically used in diagnosis of depression. Biomarkers with the potential of being psychiatric and non-psychiatric drugs targets were evaluated.Discussion: Based on connectivity map analysis, some non-psychiatric agents with potential antidepressant effects were identified. Chlorogenic acid is a natural polyphenol which exhibits antidepressant effects through developing expression of synapsin I and increasing 5-HT release, in vivo and in vitro. Asiaticoside is a triterpenoid component which is observed to have antidepressant like effects by different mechanisms, such as modulation of inflammatory cytokines and activating cAMP/protein kinase A signaling pathway. Adding pindolol, the beta-blocker and 5-HT1A/1B receptor ligand to venlafaxine, a serotonin-norepinephrine reuptake inhibitor, has improved its antidepressant clinical effects through inhibiting 5-HT1A receptor in dorsal raphe nucleus neurons. Pindolol has also been reported to accelerate and enhance antidepressant effects of selective serotonin reuptake inhibitors. Pioglitazone is a thiazolidinedione antidiabetic agent which is shown to have anti-inflammatory and antidepressant effects by peroxisome proliferator-activated receptor γ-mediated mechanisms. The other suggested potential therapeutics for depression are the peroxisome proliferator-activated receptor-α (PPARα) agonist ciprofibrate and antispasmodic adiphenine.Conclusions: Screening blood biomarkers provides physicians a new and promising strategy to diagnose and predict the future risk of mood disorders, which can significantly lead to enhance response outcomes. It can also be a helpful approach for drug discovery and repurposing, revealing potential candidate drugs for treatment of mood disorders. Combination therapy with these suggested therapeutics can be a promising strategy to ameliorate efficacy of antidepressant drugs.

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# Design, synthesis and biological evaluation of anticholinesterase peptides: Fragment-based vs. template-based peptide design

*Elahe Tahmasebi[1], Dara Dastan[2*], Ahmad Ebadi[1*]*

[1]Department of Medicinal Chemistry, School of Pharmacy, Medicinal Plants and Natural Products Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
[2]Department of Pharmacognosy, School of Pharmacy, Medicinal Plants and Natural Products Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
Corresponding author:Ahmad Ebadi
Corresponding author Email: a.ebadi@umsha.ac.ir

The prevalence of Alzheimer's disease (AD) has become a substantial global concern. Approved AChE inhibitors have been used for symptomatic treatment of AD. Binding of amyloid β (Aβ) to the peripheral anionic site of AChE facilitates the formation of Aβ plaques. Blocking this proposed protein–protein interaction by inhibition of the peripheral anionic site of AChE, in addition to increasing the level of ACh, reduces the Aβ aggregation and might qualify to slow down the progression of disease besides the palliative treatment. Targeting protein–protein interactions consider as one of the most challenging issues in the realm of drug design in which peptides have potentials to excel in. In the present study, we applied two virtual fragment-based and template-based approaches to design peptidic inhibitors of the PAS of AChE. Based on the in silico studies, high scored peptides p2 (WTWYGYWVW) and p10 (NHRMLTRRY) obtained from fragment-based and template-based design respectively. Regarding in vitro results, p2 (IC50 = 16 ± 3.2 μM) and p10 (IC50 = 23.6 ± 4.9 μM) showed significant AChE inhibitory effects. The molecular mechanism of inhibition studied by Lineweaver-Burk plots was mixed inhibition for both peptides. The in vitro results conformed to the in silico results and showed that both peptides occupied the CAS and PAS of AChE. The comparison of two peptide-design approaches revealed that the fragment-based design had more chemical diversity and showed priority to the template-based design. According to the obtained results, peptidic inhibitors of AChE designed by the proposed fragment-based approach might be more efficient in comparison to traditional approaches.

## P190

# Ketamine as a new treatment protocol for treatment-resistant major depressive disorder

*Atena FallahTafti[1], Seyed Mojtaba Yassini[2], Yekta Rameshi[3], Fatemeh Saghafi[4], Mahmoud Vakili[5], Hossein Jafari[6], Reza Bidaki[7]*

Corresponding author:Reza Bidaki
Corresponding author Email: reza.bidaki111@gamil.com

Introduction: Major depressive disorder (MDD) has destructive effects on patient's quality of life (QOL). It seems that the use of ketamine in the treatment of MDD is an easy and less invasive technique compared with invasive methods such as Electroconvulsive therapy (ECT). The current study aimed to evaluate the therapeutic effect of injected ketamine on patients with treatment-resistant MDD.Material and methods: In this pre- and post-clinical trial, 18 patients with a diagnosis of MDD based on Diagnostic and Statistical Manual of Mental Disorders (5e) text revision Adapted from American Psychiatric Association (DSM-V) aged 18-70 years, and without histories of physical and mental comorbidity were eligible to participate. After taking The Hamilton Rating Scale for Depression (HRSD) score, patients received 0.5 mg/kg ketamine infusion over 40 minutes with vital signs monitoring. After 2.5 hours of infusion, the HRSD score was repeated and patients who responded to treatment (≥50% reduction in HRSD score), the infusion repeated on days 3, 5, 7, 9, and 11 after the start of the study. Patients were re-evaluated after the last dose of ketamine.Results: 13 of 18 (72%)

responded to treatment after the first ketamine infusion. A significant decrease was seen between the mean depression score before (21.6 ± 8.5) and 2.5 hours after the first injection (9.7 ± 4.8) in responded patient (p<0.001), as well as a significant decrease was seen in all of 13 patients who continued ketamine until the 11th day (6.3 ± 4.0) compared with before intervention (p<0.001).Discussion: Our study revealed a better response to ketamine treatment. Theoretically and according to practical results, it seems that ketamine could play an important role in treating treatment-resistant depression.Conclusions: Findings suggest that ketamine injection is efficacious in reducing the severity of depression in patients with MDD. Due to the decrease in the average of HRSD score and the absence of significant side effects, a combination of ketamine and conventional maintenance treatments can be offered as a new treatment protocol for TRD.

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## Effects of donepezil and medroxyprogesterone versus placebo on weaning in adult patients with non-pulmonary etiologies receiving invasive mechanical ventilation: A triple-blind randomized clinical trial.

*Zahra Alizadeh[1], Navid Hadadzadegan[2], Adeleh Sahebnasagh[3], Farhad Mohammadi[4], Fatemeh Saghafi[5]*

Corresponding author:Zahra Alizadeh
Corresponding author Email: zahraalizade1996@gmail.com

Background: Medroxyprogesterone and donepezil could be used as respiratory stimulants in ventilated patients. However, no randomized placebo-controlled trial is available to confirm this approach and compare these drugs. The aim of the current study was to evaluate the effects of donepezil or medroxyprogesterone compared to the placebo in improvement in respiratory status and weaning facilitation in critically ill adult patients receiving mechanical ventilation.Material and Methods: This randomized, triple-blind trial was conducted on 78 ventilated patients in intensive care units (ICU). Patients who were intubated due to pulmonary disorders were ruled out. Patients were randomized in a 1:1:1 ratio to receive 5 milligram (mg) donepezil (n =23) or 5 mg medroxyprogesterone (n = 26), or placebo (n = 24) twice a day until weaning (maximum 10 days). The primary endpoints were weaning duration, and duration of invasive mechanical ventilation. Secondary endpoints included rate of successful weaning, changes in arterial blood gas (ABG) parameters, GCS and sequential organ failure assessment (SOFA) score, hemoglobin (Hgb), ICU-mortality, and duration of ICU stay, were measured before and after the intervention and if successful weaning was recorded.Results: Of 78 studied patients who were randomized, 59 weaned successfully. 87% patients in donepezil and 88.5% patients in medroxyprogesterone groups were successfully weaned compared to 66.7% patients in the placebo group. However, this difference was not statistically significant (P-Value=0.111). Changes in pH, mean duration of intubation, and weaning duration were statistically different in donepezil compared with the control group (P-value < 0.05). No significant difference in ABG, Hgb, GCS and SOFA score, and duration of intubation were seen in the medroxyprogesterone group, but weaning duration was significantly reduced to 1.429 days compared with the control group (P-Value =0.038).Conclusion: The results of this clinical trial have demonstrated that the administered dose of medroxyprogesterone and donepezil can expedite the weaning process by reducing the weaning the total duration of invasive ventilation was duration compared to placebo. Furthermore, significantly lower in the donepezil group compared to the control group. Future clinical trials with a larger sample size will determine the exact role of medroxyprogesterone and donepezil in mechanically ventilated patients.

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## Drug utilization evaluation of antibiotics in burn patients at a referral teaching hospital of Isfahan, Iran

*Shabnam Sajjadi[1], Rasool Soltani[2], Kiana Shirani[3], Mohsen minaiyan[4], Fatemeh Saghafi[5,*]*

[1]Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[2]Department of Clinical Pharmacy and Pharmacy Practice, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran
[3]Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
[4]Department of Pharmacology, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran
[5]Department of Clinical Pharmacy, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
Corresponding author: Fatemeh Saghafi
Corresponding author Email: f.saghafi@ssu.ac.ir

Introduction: Nowadays, due to the irrational and excessive use of antibiotics, antimicrobial resistance has become one of the main concerns of the medical community (1). Patients with burns are more prone to infections due to the loss of the skin's defense barrier as well as a weakened immune system. Therefore, proper antibiotic treatment is very important in these patients (2). Drug utilization evaluation (DUE) is a type of study evaluating the usage of drugs regarding different aspects to detect errors in their prescriptions. The main purpose of these studies is to ensure the rationality and appropriateness of drug use, as well as cost control in the health care system (3). The present study aimed to evaluate the pattern of antibiotic consumption in Imam Mousa Kazem Burn Hospital in Isfahan, Iran.Material and methods: This prospective cross-sectional descriptive study was performed on 102 patients hospitalized at Imam Mousa Kazem Hospital over a 9-month period (2019-2020). Adult burn patients who received at least one antibiotic were included in the study. All required information including demographic data, the prescribed antibiotic, basis of administration (empiric vs. culture-based), dose and duration of use, microbial culture test, and treatment outcome were recorded in the data collection form by referring to patients' medical profile and the hospital computer system. Judgments about the accuracy of the indication, dose, and duration of treatment, as well as the need for dose adjustment in renal or hepatic impairment were made by an infectious diseases specialist and a clinical pharmacist based on the current guidelines.Results: Among the 196 antibiotic prescriptions, cefepime (40.3%) was the most frequently used antibiotic, followed by vancomycin (17.9%) and meropenem (16.8%). The most prescriptions were empirical, while the antibiotics were administered based on the microbial culture results only in three cases (1.5%). The indication of use was correct in 52.6% of prescriptions (n = 103), of which 74.8% (n = 77) had correct dose. Also, in 47 cases (45.6%), the duration of treatment by antibiotic was correct.Discussion: According to the results of this study, antibiotics are widely used in our burn center, while there is high rate of incorrect prescriptions. Furthermore, microbial culture and susceptibility testing are performed in very few cases. Therefore, new strategies including educational programs should be implemented to improve the pattern of antibiotic use in this referral center.Conclusions: Prescribing antibiotics in Imam Mousa Kazem Hospital is associated with many errors in various aspects, including indication, dose, de-escalation, and duration of treatment.

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## Evaluation of the effect of thymol nanoparticles and nanoliposomes on Trichomonas vaginalis In-Vitro

*Solaleh sadat Jalili[1], Farzaneh Mirzaei[2], Vahid Ramezani[3], Mina Jabbari[1], Mohsen Zabihi[1*]*

[1]Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[2]Department of Parasitology and Mycology, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[3]Department of Pharmaceutics, School of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
Corresponding author: Mohsen Zabihi
Corresponding author Email: mzabihi@ssu.ac.ir

Introduction: Trichomonas vaginalis is a flagellate protozoan that causes a relatively common infection in the genitourinary tract. Metronidazole, as an effective drug against this infection, has been shown to be carcinogenic in animals and has been reported to develop resistance. Phenolic compounds such as thymol and its isomer carvacrol have antibacterial, antifungal, and antioxidant properties that their various drug forms can be a good alternative against Trichomonas vaginalis. This study aimed to evaluate the effect of thymol and its nanoparticle and liposome forms on Trichomonas vaginalis.Material and methods: In this study, which is an experimental study, thymol and nanoparticle forms (using glycerol monostearate, Tefose, Labrafil and stearic acid fats) and liposomal form in different concentrations (0.5-25 $\mu$g/ml) was prepared. The prepared drug forms were qualitatively evaluated and the two superior formulations, as well as metronidazole, were challenged with Trichomonas vaginalis in TYI-S33-culture medium. Then, at 24, 48 and 72 hours, live parasites were counted by the hemocytometer method and the growth inhibition rate of Trichomonas vaginalis was assessed using statistical tests.Results: Thymol and its nanostructure forms, including nanoparticles and nanoliposomes, within different periods as well as different concentrations were able to remove Trichomonas vaginalis cells after 24, 48, and 72 hours as metronidazole (65 ug/ml) do.Discussion: The limitation of the study was the preparation of liposomal and nanoparticle forms and the measurement of their size due to the conditions of their submission and the resulting costs. It seems that the preparation of these forms, despite their useful properties, has no effect on the lethality of the parasite and preparing nanoparticles and liposomal forms are not cost effective. Extensive studies may be helpful.Conclusions: The percentage of growth inhibition of Trichomonas vaginalis by nanoparticles and liposomal forms of thymol depended on the passage of time and thymol concentration. Thymol and its nano liposome showed a lower IC50 than the nanoparticles in growth inhibition after 24 and 48 hours. Still, the efficacy of all three forms did not significantly differ following 72 hours of exposure.

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## Study of the effects of co-administration of erythropoietin and VEGF on the BAX and Bcl-2 genes expression levels in hypoxic H9c2 cells

*Shahrzad mazaheri[1], Dr.Fatemeh tavakoli[2], and Ahmad reza eider[3]*

[1]Pharmacology, Pharmacy, Shahid Sdughi , Yazd , Iran
[2]Pharmacology & Pharmacognosy, Pharmacy, Shahid Sdughi, yazd , Iran
[3]Pharmacology, shahid sadughi, Yazd , Iran
Corresponding author: shahrzad Mazaheri
Corresponding author Email: shahrzad.mazaheri@gmail.com

Introduction: Heart failure is one of the most common diseases of the cardiovascular system that causes high annual mortality worldwide. One of the most important etiological factors of congestive heart fail-ure is myocardial infarction. Myocardial infarction MI is caused by an imbalance between the coronary blood source and the myocardial need for blood, and eventually leads to myocardial ne-crosis. Ischemic heart failure is characterized by a decrease in the number of cardiomyocytes after a sudden decrease in heart rate.Apoptosis (programmed cell death) is a physiological process that participates in most heart dis-orders and reduces the number of cardiomyocytes. . Apoptosis has two internal and external path-ways.Erythropoietin (EPO) is a glycoprotein cytokine that is made in the liver during pregnancy and in the kidneys in adulthood and is known as a hematopoietic growth factor that stimulates the prolif-eration and differentiation of erythroid progenitor cells. In addition to this known role, expression of EPO receptors outside the hematopoietic system, including endothelial cells, cardiomyocytes, and neurons, suggests greater potential effects for EPO. With tissue oxygen depletion, EPO pro-duction in the kidneys, liver and brain increases. A specific critical role for EPO and EPO receptors in hypoxia has been demonstrated in neuronal and erythrocyte culture. Stimulation of the two in hypoxia has led to EPO being proposed as a treatment for ischemia or hypoxia-damaged tissues in the central nervous system.Vascular endothelial growth factor (VEGF) is a family of glycoprotein dimers that are involved in the growth and homeostasis of blood vessels and the formation of lymph vessels. VEGF-A, a major member of this family, plays a key role in angiogenesis. Angiogenesis is a physiological or patho-logical process in which new small vessels germinate and deform from previous vessels. VEGF is produced by a variety of cells, including macrophages, endothelial cells, and tumor cells. The VEGF and VEGF-R signaling pathways (VEGF receptors) are one of the three main pathways that are activated in hypoxic conditions and prevent inflammation and tissue damage due to hypoxia.The internal pathway of apoptosis is regulated by members of the Bcl-2 family. Anti-apoptotic proteins of this family, such as Bcl-2, inhibit apoptosis while pro-apoptotic organs, including BAX, activate the secretion of caspases.Material and methods: H9c2 cells were cultured in culture medium containing DMEM, 10% FBS, 100 U / ml penicillin and 100 µg / ml streptomycin at 37 ° C and 5% CO2 pressure.To induce hypoxia, we used a combination of cobalt 2 hexa chloride (COCl2. 6H2O, MW = 23709).The effect of erythropoietin with a concentration of 40 units per ml and VEGF with a concentra-tion of 0.05 micrograms per ml each on the survival rate of H9c2 cells under normal and hypoxic conditions was evaluated by MTT assay.The expression levels of BAX and Bcl-2 genes were also measured in each of the above conditions using Real Time – PCR . Results: Our results also showed that the use of erythropoietin and VEGF decreased BAX gene expression, but this reduction was significant only for VEGF. Also, concomitant use of erythropoietin and VEGF in hypoxic conditions could significantly reduce BAX expression. However, unlike the BAX gene, the use of erythropoietin and VEGF in the study of Bcl-2 gene expression, either alone or in combination, could not significantly increase the expression of this gene.Therefore, we conclude that the effect of erythropoietin and VEGF on the survival of H9c2 cells is more through reducing the expression of proapoptotic BAX gene. VEGF was also more efficient in this regard.Discussion: In this study, the results of BAX and Bcl-2 expression showed that the induction of hypoxic con-ditions on H9c2 cells increased the expression of BAX proapoptotic gene and decreased the ex-pression of Bcl-2 anti-apoptotic gene significantly. This phenomenon indicates the role of hypoxia in activating the apoptotic process.Conclusions:

Concomitant use of VEGF and erythropoietin has a greater effect on the response of H9c2 cells to hypoxic conditions than either alone. And these two effects are mostly exerted by inhibiting BAX gene expression and thus reducing the ratio of BAX to Bcl-2..

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## Evaluation of the effect of erythropoietin in reducing the complications of heart failure in diabetic rats

Alireza Eslamie, Fateme Fadavi, Fatemeh Tavakoli*

[1]Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.Student Research Committee, Faculty, University, City , Country
[2]Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.Student Research Committee, Faculty, University, City , Country
Corresponding author: Fatemeh Tavakoli
Corresponding author Email: fateme.t1358@gmail.com

Introduction: Heart failure is one of the most common types of heart disease and a major public health problem in the world. The disease has a high mortality rate and is a major cause of hospitalization. One of the major causes of heart failure is diabetes. This means that the two diseases are often associated with each other. Erythropoietin can be used by various mechanisms to make the heart resistant to heart failure and also improve the damaged heart. In this study, we investigated the effect of erythropoietin in reducing the effects of heart failure in diabetic rats.Material and methods: First, induction of diabetes by streptozotocin was performed in 36 male Wistar rats. After induction of diabetes, the animals were randomly divided into 6 groups of 6 and the interventions were performed for 2 weeks as follows: Group 1: Diabetic rats receiving only erythropoietin and doxorubicin. Group 2: Diabetic rats receiving doxorubicin and erythropoietin carriers. Group 3: Diabetic rats receiving erythropoietin 3000 U / kg and doxorubicin carrier. Erythropoietin 1000 group: Diabetic rats receiving doxorubicin and erythropoietin 1000 U / kg. Erythropoietin 3000 group: Diabetic rats receiving doxorubicin and erythropoietin 3000 U / kg. Erythropoietin 5000 group: Diabetic rats receiving doxorubicin and erythropoietin 5000 U / kg. Doxorubicin was used to induce heart failure. At the end of the test period, blood serum and heart tissue were prepared from the studied mice. The levels of CAT, GSH and MDA enzymes were examined. The results were statistically analyzed using SPSS V21. Results: The highest and lowest MDA levels were in the doxorubicin group with a mean of 25.64 and standard deviation of 14.70 and the control group with an average of 8.62 and standard deviation of 1.60. The level of MDA in the doxorubicin group was higher than the other groups and there was a statistically significant difference between the control and doxorubicin-treated groups in terms of mean MDA level ($p< 0.05$). The amount of glutathione in the group of doxorubicin + erythropoietin 5000 u / kg with an average of 0.63 and a standard 2. deviation of 0.08 has the highest level of GSH. Therefore, there was a statistically significant difference between Dox + Epo 5000 group and other treated groups as well as the control group in terms of mean GSH level ($p< 0.05$). There was no statistically significant difference between the control and treatment groups with erythropoietin and doxorubicin in terms of mean catalase level ($p< 0.05$).Discussion: Erythropoietin could reduce the cardiac toxicity of doxorubicin by reducing oxidative stress in a dose-dependent manner.Conclusions: In the end, we concluded that the use of erythropoietin had positive effects on samples with diabetes and CHF and had significant effects on reducing the amount of MDA factor, however, it did not reduce the level of CAT. It seems that erythropoietin can be used and effective in reducing the damage caused by CHF in patients with diabetes.

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## Evaluating the effect of carvacrol on Leishmania major in vitro

*Mahsa sadat Sadat[1], Eftekhar Morabbi[2], and Mohsen Zabihi[3*]*

[1]Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd , Iran
[2]Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd , Iran
[3]Department of Pharmacology, School of Pharmacy and Pharmaceutical Sciences, Shahid Sadoughi University of Medical Sciences, Yazd , Iran*
Corresponding author*: Mohsen Zabihi
Corresponding author Email: mzabihi100@gmail.com

Introduction: Leishmania major is the causative agent of cutaneous leishmaniasis in rural areas of Iran. Carvacrol is one of the main constituents of thyme essential oil. As the antibiotic, antifungal, antiinflammatory and antioxidant effects of carvacrol have been proven, the aim of this research was evaluation of the growth inhibitory effect of carvacrol on promastigote form of leishmania major and comparison of its efficacy with amphotericin B in-vitro.Material and methods: Different concentrations of carvacrol were prepared. The parasites were grown in the culture medium. Then, promastigotes were exposed to carvacrol. Number of promastigotes were counted after 24, 48 and 72 hours. Then, the average percentage of growth inhibition was calculated at different concentrations 24, 48, and 72 hours after the exposure. The findings were compared with negative control using analysis of variance.Results:in the logarithmic phase of Leishmania major growth, the percentage of growth inhibition by carvacrol improved both with time and with increasing concentration of carvacrol. Similar findings were observed for amphotericin B at the concentration of 0.1 µg/ml. After 72 hours, the growth inhibition increased to 100% following exposure to carvacrol at the concentration of 3.125 ng / ml or higher and to amphotericin B at the concentration of 0.1 µg/ml. After 48 hours, the growth inhibition percentage reached 100% using carvacrol at the concentration of 3.125 ng-/-ml, but the growth inhibition percentage was 87.4% following exposure to amphotericin at the concentration of 0.1 µg/ml. According to our findings, the concentration of 3.125 ng/ml was significantly more effective within 48 and 72 hours than the lower concentrations ($P < 0.01$). Moreover, after 24 hours, carvacrol at the concentrations of 3.125 ng/ml and 6.25 ng/ml and amphotericin at the concentrations of 0.1 µg/ml inhibited parasite growth by 2.94.8%, 100% and 63.1%, respectively. In addition, we found that the concentration of 6.25 ng/ml within 24 hours was significantly more efficient in controlling Leishmania promastigotes than the lower concentrations ($p < 0.01$). Discussion: The study of Bagherian et al. In 2018 was conducted to investigate the effect of thyme in comparison with amphotericin B on Leishmania major amastigote in vitro. The results showed that the concentration of 250 µg / ml of control drug had a better effect on amastigotes than other concentrations and the mean light absorption in the studied groups was significantly different and the four essential oils of thyme had an anti-leishmaniasis effect compared to the control drug. A study by Dr. Mirzaei et al. In 2015 showed that the hydroalcoholic extract of savory and bitterness can be effective in the treatment of Leishmania major because carvacrol is one of the effective ingredients of savory and can increase the growth inhibition of promastigotes to 100%.Conclusions: The results showed that carvacrol had good anti-leishmaniasis activity. We also found that the percentage of inhibition of growth of Leishmania promastigotes by carvacrol in logarithmic phase of growth depends on carvacrol concentration and time. As a result, carvacrol can be used as an adjunct in the treatment of leishmaniasis.

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## Design, synthesis and evaluation of some novel pyrazole-ferulic acid derivatives as LOX inhibitors

*Samane Shaban[1], Alireza Moradi[2], Amir Hossein Karimi[3]*

[1]Department of Medicinal Chemistry, School of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

[2]Department of Medicinal Chemistry, School of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

[3]Department of Medicinal Chemistry, School of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Corresponding author: Alireza Moradi

Corresponding author Email: alirezamrp@gmail.com

Introduction: The lipoxygenase metabolism pathway of arachidonic acid (AA) provides the most potent pro-inflammatory mediators. One of the other factors that causes inflammation is Reactive oxygen species (ROS) implicate in a variety of inflammatory diseases .

4,5-Dihydropyrazole derivatives have been received significant attention due to their excellent effectiveness as anti-inflammatory, antioxidant and antitumor agents. Ferulic acid (FA) has exhibited as potential anti-inflammatory agents for the treatment of inflammatory diseases. With due attention to the importance of these biological activities have reported up to now, we designed a series of pyrazole-ferulic acid hybrid compounds as LOX inhibitor and antioxidant agents and report here synthesis and biological activity of them. Material and methods: A novel series of pyrazoline-ferulic acid derivatives (5a-j) was designed and synthesized. The synthesis of chalcone (3a-j) was carried out by the Claisen-Schmidt condensation reaction. Then they were refluxed with hydrazine hydrate in absolute ethanol to get pyrazole (4a-j). Finally, they were added to a solution of ferulic acid and DCC (N,N-Dicyclohexylcarbodiimide) in the mixture of DCM (Dichloromethane) and DMF (N,N-Dimethylformamide) to get desired products. The compounds were characterized by spectral data (1H NMR and IR) and all of that gave desired data by following their structures. Results: The synthesized compounds were tested in vitro for their inhibitory properties against the soybean lipoxygenase enzyme. The data acquired showed that all the compounds were less active in comparison with quercetin used as the reference standard compound (IC50=5.87 µM). Compounds 5a, 5b, and 5e were the least active compounds as lipoxygenase enzyme inhibitor by 22-41 percent of inhibition at 200 µM concentration. All the synthesized derivatives have been tested for their antioxidant activity by DPPH assay and their inhibition constant (IC50) was calculated. Discussion: Therefore, replacing amide groups with ester groups that would be able to donate more protons to DPPH can lead to an increment in antioxidant activity of the compound. Such pattern can be used to improve the antioxidant effects of other components in future studies.Conclusions: The activity of a novel series of pyrazole-ferulic acid derivatives was synthesized against soybean lipoxygenase and their antioxidant activity was studied. Although the synthesized compounds showed less activity than standard, concerning for to their novel structure these compounds can be used as a base compound for the synthesis of strong lipoxygenase inhibitors and antioxidant agents in the future.

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## Homology modeling, Molecular Dynamics Simulation and Docking studies of formyl peptide receptor like 1

*Bahar Pakseresht[1], Dr.Hamid Nadri[2], Dr. Amirhosein Sakhteman[3], Dr. Alireza Moradi[4] and AhmadReza Eider[5]*

[1]Medical Chemistry , Pharmacy School, Shahid Sadoughi, Yazd , Iran

[2]Medical Chemistry, Pharmacy School, Shahid Sadoughi, Yazd , Iran

[3]Faculty of Pharmacy, Shahid Sadoughi university of medical Science ,Yazd ,Iran

Corresponding author: Bahar Pakseresht

Corresponding author Email: bahar.pakseresh@gmail.com

Introduction: FPRL-1 is a GPCR receptor, class A. This receptor is known to play an important role in Alzheimer's Disease (AD). Since the 3D structure of this protein is not fully understood yet, finding it's 3D structure is favored. Predicting the 3D structure of this receptor based on information prepared by different databases can help us gain more knowledge towards the antagonists which can be designed to inhibit this receptor and therefore be a solution to treat AD.Material and methods: with the aid of templates retrieved from I-TASSER server, we were able to perform homology modeling studies. In order to check the validity of the final model, Ramachandran plot was sketched by RAMPAGE server. The final model was embedded into a DPPC membrane system and subjected to a 100ns molecular dynamics simulation afterwards. Using Root Mean Square Deviation (RMSD) of $C\alpha$ atoms, the final trajectories of simulation were clustered. Then 8 known ligands of FPRL-1 were docked using Autodock4.2, into frames inside each cluster.Results: The best model was built by modeler 9v12. ROC value of this receptor was 0.9 which indicates the high quality of the best model. As retrieved by the results of this study the best frame extracted was frame 169.Discussion: After finishing the simulation of FPRL-1 in a bilayer lipid membrane and achieving the most stable frame of this receptor (frame 169) with the known ligands, the 3D structure of this protein has been modeled and docked for the first time. Based on ROC values and validations conducted by PROCHECK server we concluded that this model is energetically stable and favored and it is very much like to be similar to the real receptor. Binding energy obtained at last was -195.905 which indicates a perfectly stable system. Since the 3D structure of receptor are vital to design ligands relatively effective in altering the cellular response, we did our best to predict the 3D structure of receptor perfectly. This research may lead to further studies regarding the effectiveness of designed antagonists against FPRL-1 in the treatment of Alzheimer's Disease.Conclusions: After finishing the simulation of FPRL-1 in a bilayer lipid membrane and achieving the most stable frame of this receptor (frame 169) with the known ligands, the 3D structure of this protein has been modeled and docked for the first time. Based on ROC values and validations conducted by PROCHECK server we concluded that this model is energetically stable and favored and it is very much like to be similar to the real receptor.

# سخنرانی های صنفی

1

## Startup-Based Learning as an Innovative Method for Pharmacy Education Medicinal Plants Course Model

*Ehsan Amiri-Ardekani[1], Mohamad Hasan Keshavarzi[1], Seyed Aliakbar Faghihi[1], Parmis Badr[1], Mohammad M. Zarshenas[1], Zohreh Abolhassanzadeh[1], Abdolali Mohagheghzadeh[1]*

[1] Shiraz University of Medical Sciences

Corresponding author: Abdolali Mohagheghzadeh

Corresponding author Email: mohaghegh@sums

Introduction: Familiarizing students with knowledge-based business is one of the goals emphasized in the developed educational systems worldwide. In this study, we aimed to design Startup-based learning model (SBL)Material and methods: As a qualitative research study, startup teams were formed by Shiraz University of Medical Sciences pharmacy students in 2020. This model was used to train 120 students as pharmaceutical entrepreneurs through related lectures, simulations, and field activities. We used this model for students to become familiar with the various stages of examining market needs, Knowledge-based company registration, intellectual property, logo design, and even pharmaceutical product development. Students' feedback was assessed using a questionnaire designed by the team of researchers, and its results were used to analyze the course and improve the quality of the proposed model.Results: Most of the studied indices show that students rated this model as good or excellent. Satisfaction with more important indices includes Student creativity and ideation in educational activity(60.7%), attractive presentation(60.4%), teamwork among learners(62.2%), appropriateness of evaluation method(65.4%), understanding how to make herbal remedies(49.1%), learner participation in the educational activity (74.8%), entrepreneurial motivation(60.7%), applicability(64.4%).Discussion and Conclusions: We found this model effective in boosting students' satisfaction, creativity, and entrepreneurial spirit. Also, lecturers play a facilitator role in addition to specialized training. So, in this model, both lecturers and students can grow more and make education more attractive. This study, for the first time, demonstrated that SBL can be used in education systems and providing students more interest in educational content, and help students to prepare for the job market.

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## Knowledge,Attitude and Practice of Tehran Community Pharmacists about Evidence-Based Medicine

*Mahsa Torkaman[1], Sadaf Ehdai Vand[1], Hadi Esmail[1]*

[1]Shahid Beheshti University of Medical Sciences

Corresponding author: Hadi Esmail

Corresponding author Email: esmaily_hadi@sbmu.ac.ir

Introduction: Pharmacotherapy of common disorders, monitoring, and control of adverse events are among the pharmacist's services(1). In this regard, university education in this field also changed based on the patient-centered attitude(2). The present study was designed and conducted to evaluate the knowledge, attitude, and practice of pharmacists working in urban pharmacies in Tehran about evidence-based medicine (EBM).Material and methods: For this purpose, a questionnaire was designed including background information, knowledge, and attitude. The validity of the questionnaires was reviewed and confirmed by an expert panel. The internal consistency of the questionnaire was verified by Cronbach's alpha method. The questionnaire was completed by 200 pharmacists and the simulated patient method was used to determine their practice. Statistical analysis of the collected data was performed using SPSS 26.0 software and appropriate statistical tests.

Results: The participated pharmacists include 68 men (34%) and 132 women (66%), the mean score of knowledge was 38.07 and the mean score of practice was 50.34 (out of a total score of 100). Pharmacist's attitudes toward the necessity of applying evidence-based medicine were positive in 99.5% of cases, however only 29.5% of them have reviewed resources in their real practice, and 78.5% of pharmacists agreed to increase patient satisfaction if EBM were utilized. 86.5% of pharmacists agreed that it is not possible to search for resources when the pharmacy is busy, and 65.5% agreed that when referring to resources, patient's mentality towards pharmacist's knowledge will be changed to negative.Discussion: The results obtained in the present study indicate the poor knowledge and average practice scores of pharmacists in the field of EBM. Barriers such as lack of enough time, credible evidence, and lack of investment and support of officials have caused this matter.Conclusions: In this regard, most participants agreed with the need for EBM. Necessary planning needs to be done to create various processes to improve the performance of pharmacists in the field of EBM.

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## شناسایی خطاهای بالقوه فرآیندهای دارویی با استفاده از روش تحلیل حالات و اثرات خطا (Failure Mode and Effect Analysis) در کلیه بخش های ICU بیمارستان شهید رحیمی خرم آباد ۱۳۹۹

*هادی حیاتی آب باریک[1]، محمد شفیعی[1و2]، عارفه خانی[1و2]*

[1] دپارتمان مدیریت و اقتصاد دارو، دانشکده داروسازی، دانشگاه علوم پزشکی لرستان، خرم آباد، ایران

[2] کمیته تحقیقات دانشجویی، دانشکده داروسازی، دانشگاه علوم پزشکی لرستان، خرم آباد، ایران

نویسنده مسئول: هادی حیاتی آب باریک

ایمیل نویسنده مسئول: hadihayati88@gmail.com

مقدمه: خطاهای دارویی از عوامل تهدید کننده حیات بیماران است که تلاش برای شناسایی آن در سال‌های اخیر بیشتر مورد توجه قرار گرفته است. این مطالعه با هدف شناسایی و تحلیل خطاهای فرایندهای دارویی در بخش ICU (Intensive Care Unit) بیمارستان شهید رحیمی خرم آباد با استفاده از روش تحلیل حالات و اثرات خطا (Failure Mode and Effect Analysis) به عنوان یکی از تکنیک‌های مدیریت ریسک انجام گرفت.مواد و روش‌ها: این مطالعه از نوع توصیفی-مقطعی است که به صورت ترکیب کمی-کیفی، حالات و اثرات خطا را با روش تحلیل حالات و اثرات خطا، در بخش ICU بیمارستان شهید رحیمی خرم آباد در سال ۱۳۹۹ مورد ارزیابی و تحلیل قرار داده است. برای جمع آوری داده‌ها از کاربرگ استاندارد و تکنیک تحلیل حالات خطا و اثرات ناشی از آن و نمونه-گیری مبتنی بر هدف استفاده شد. در این روش به هر یک از خطاها بر اساس شدت خطا، میزان وقوع خطا و احتمال

کشف خطا نمره ای بین 1 تا 5 تعلق گرفته که از حاصلضرب این سه شاخص، نمره عدد اولویت ریسک (Risk Priority Number) به دست می‌آید. جهت تحلیل داده ها از نرم افزار SPSSv21 استفاده گردید و داده ها بر اساس فرمول RPN = S × O × D محاسبه و رتبه‌بندی گردید.نتایج: این مطالعه بر روی کلیه پرستاران در ۵ بخش ICU انجام شد. به کمک روش FMEA (Failure Modes and Effect Analysis)، 35 حالت خطای بالقوه در 9 حیطه منتخب فرایندهای دارویی شناسایی و ارزیابی و نمره RPN هر یک محاسبه گردید و میانگین نمرات RPN هر حیطه به دست آورده‌شد. نمره کل ICU برابر ۱۸/۸۶ محاسبه شد و ICU اورژانس بیشترین نمره ۲۲/۷۱ و کمترین نمره مربوط ICU داخلی ۱۴/۴۶ بود. بحث: با توجه به یافته‌های فوق، به منظور کاهش احتمال وقوع خطاهای بررسی شده در بیمارستان‌ها، می-توان از دوره‌های بازآموزی، تدوین مقررات و رهنمودها و رویه‌های اجرایی مستند برای فرایندهای دارویی، برقراری هماهنگی بین پرستاران و پزشکان و برقراری هماهنگی و ارتباطات بین بخشی استفاده کرد.نتیجه‌گیری: با توجه به اهمیت اورژانس و حساسیت کار در این بخش و احتمال رخداد بیشتر خطا لزوم بازنگری در فرایندهای کاری ضروری بنظر می رسد.

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## Impact of COVID-19 on the pharmacy students and their Education System in Eastern Meditation Region

*Melika Maleki*[1]

[1]Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.

Corresponding author: Melika Maleki

Corresponding author Email: melika.pharma@gmail.com

Introduction: This study was intended to examine the effect of COVID-19 on pharmacy students and their education in EMR (Eastern Mediterranean Region) by IPSF- EMRO (International Pharmacy Students Federation Eastern Mediterranean Regional Office) in October 2020 and is guided by the following objectives; to evaluate the EMRO pharmacy students and recent graduates' situation in COVID-19, to examine the impact of COVID-19 on education in EMRO. Material and methods: This study was an educational intervention in September 2020. The inclusion criteria were being a pharmacy student or recent graduate, having enough time, and completing the questionnaire. In this study, using a researcher-made questionnaire, EMRO pharmacy students and recent graduates' situation in COVID-19, to examine the impact of COVID-19 on education were measured. The obtained data were categorized and analyzed by SPSS V.22 software using descriptive statistics and paired t-test. The significance level in this study was considered 0.05.Results: The COVID-19 has affected worldwide education sectors by shutting down many institutes and temporarily pushing the majority of pharmacy students out of faculty. Most countries have temporarily closed their educational institutions to control the COVID-19 pandemic and are using online platforms to deliver education during the pandemic. A total of 147 pharmacy students and recent graduates from 15 different countries are members of this study. Based on our study, personal discipline/motivation to study are included in: 12% Very good, 21%Good, and 12% same as always 36.1% Bad, 15% Very bad and 15% Non-existent. 91.7 % of them have University Online Education, and 4.5 % have Non-Formal Education. The two most common methodologies for their education are PowerPoints and materials shared by 80.5% and Online lectures by 77.4% the highest rate of satisfaction based on our form related to PowerPoints and materials shared. 51.0% of them mentioned their universities use a platform that is specific. All items of the questionnaire improved significantly (p = 0.001).Discussion & Conclusions: Results of this study revealed that technicalities are needed to run the education system smoothly besides this pandemic situation accordingly. According to the results In the Eastern Mediterranean Regional Office, efforts will be made to provide members with the needed knowledge to build their local/national activities, a drive folder was created with all the needed materials, documents, resources, and up to date information of the COVID-19 outbreak and E-Learning. We also want to organize more projects to improve our members' mental health and also by providing scientific sessions and make them more knowledgeable.

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## Knowledge, attitude and acceptance of COVID-19 vaccine among Iranian medical students in Iran

*Seyyed Mohammad Moein Mohseni [1], Kimia Masoumi [2], Dorsa Bahrami Zanjanbar[3] , , Hasti Khalili [4], Alireza Haji Abbas Shirazi[5], Ramin Abdi Dezfouli[6] , Shadi Sarahroodi[7]**

[1]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran Iran.
[2]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
[3]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
[4]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
[5]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.
[6]PharmD student, Faculty of pharmacy and pharmacutical sciences - Tehran medical sciences-Islamic azad university-Tehran-Iran.
[7]Department of Pharmacology &Toxicology, School of Pharmacy, Tehran Medical sciences Islamic Azad University*.
Corresponding author: : Shadi Sarahroodi
Corresponding author Email: sarahroodi@iautmu.ac.ir

Introduction: COVID-19, which was appeared in China, Wuhan in 2019 affected many countries and territories. Up to November 4, 2021 about 248 million cases have been infected and approximately 5 million individuals have died because of that. In Iran more than 5.9 million cases have been recognized since its beginning and sadly, about 126000 of them died. In February 2021, a limited number of Russian Sputnik V COVID-19 vaccines were distributed to Iranian residents. only less than 10% of Iranians are vaccinated and most of them only received their first dose(1)(2). Like other vaccines different kinds of COVID-19 vaccines showed some side effects which has been reported and they are not more than other usual vaccines, but rumors about them are much more than the fact. It's obvious around us that individuals even among treatment staff (physicians,pharmacists, nurses and …) refuse taking the vaccine based on fictions rather than facts. So we decided to investigate the acceptability of COVID-19 vaccines and its predictors as well as the attitudes towards these vaccines among medical students in a survey.Material and methods: Data of this survey has been collected by two questionnaire .In the first questionnaire from Jun 12th to Jun 21th 2021 , 532 medical students whom study medicine, pharmacy as well as

paramedicine sciences has been questioned through an online survey (18 questions) from Jun 12th to Jun 21th 2021 and in the second questionnaire from Sep 19th to Sep 30th 2021 , 445 medical students has been surveyed. The analysis was carried out using the Statistical Package for Social Sciences (SPSS) using Chi-square test and a P-value of less than 0.05 was considered significant.Results: In this survey 17% of students have known the type of vaccines. Also 44% of them have been aware of warning signs of AstraZeneca vaccine (coagulation). Students were asked to choose their favorite vaccine for injection and the results in descending order were: Sputnik-V(49.8%), Astrazeneca(16.5%) and Sinopharm(12%). Also 10% of participants chose COVIran Barakat vaccine, while 2% of participants chose Covopars (another Iranian vaccine).Our study revealed that 8.6% of medical students chose not to be vaccinated. Other part of our results showed that Although that 70% of participants had been asked about the Corona vaccines, but 61% of them notified us that they have never participated in any workshop, seminar or webinar about COVID-19 and they have not read any article about that. In this study, about 50% of students chose the Sputnik as their favorite vaccine to inject, while more than 80% of them didn't know the basic information about this vaccine as well as its type.Discussion: This study revealed a high vaccine acceptance rate of 90.1% . Differences in acceptance rates in other studies ranged from almost 93% (in Tonga) to 89.4% (in India) and less than 43% (in Egypt), which shows Iranian medical students have a good rate of acceptance among our treatment staff. (3), (4), (5).Conclusions: According to the mentioned points and statistics, the necessity of coordinated academic education to increase the awareness and information of medical students is crucial cause the controversial and unreliable news about COVID-19 vaccination specially in social media has caused so much confusion among public. educated medical students can play a key roll as a reliable reference for public and increase the level of public awareness as well as acceptance of COVID-19 vaccine.

# پوسترهای صنفی

1

## Addictovigilance Network System: A Preventive Mechanism against Substance Abuse in Iran

*Sarah Yousefi*[1], *Zahra Sadat Mehrabi*[2], and *Sanaz Omidi*[3], *Sepideh Arbabi Bidgoli*[*]

[1]Pharmacy student, IAUPS, Tehran, Iran

[2]Pharmacy student, IAUPS, Tehran, Iran

[3]Pharmacy student, IAUPS, Tehran, Iran

*Prof. of Toxicology - Pharmacology-Pharmaceutical Ethics, Department of Toxicology and Pharmacology, Department of Medical Ethics and Legal Medicine

Corresponding author: *Sepideh Arbabi Bidgoli*

Corresponding author Email: sepideharbabi@yahoo.com

Introduction: Social and clinical evidence show that the prevalence of substance abuse, addictive behaviors in low and middle income countries such as Iran is growing and governmental and non-governmental organizations with preventive programs against these behaviors in Iran are rare. We aimed in this study to recognized and evaluate the preventive mechanisms for substance abuse worldwide and suggest a good template for starting some national activities through private or governmental systems.Material and Methods: To specify our focus on the role of preventive or monitoring systems against substance abuse, all available first hand original articles in PubMed, Scopus, Google Scholar, Sid.ir and Magiran databases were considered using addictovigilance system as the main key word and all other synonyms . Results: Out of 43 original papers with desired keywords and abstracts, the French addictovigilance system was detected as a unique monitoring system. It relies on a network of 13 regional centers called addictovigilance network system (FAN), which collects information from broadening sources including health professional, health records, police and justice, prescription forms, analytical laboratories, international scientific literature and users in direct contact, prison, web and social media. Detecting signs and signals are the cornerstone of addictovigilance actors in this system. Signs may refer to products such as new psychoactive substances, to adverse effects such as deaths, pathological signs, or to practice such as new administration route or new context of use. We have many similar conditions and different background factors in Iran e.g. geographical location , individual, family, friends, school, and community reasons ,high prevalence of self-medication, meaningful rate of non-regulated prescription drugs with abuse potentials , misuse and abuse of drugs in athletes, high rate of mortality even in addiction treatment programs. Other than to the above evidence, some pharmacies and groceries sell them without any prescription. Moreover, there are several reports on falsified prescriptions to convince pharmacies to sell them. Discussion: Abusing and misusing drugs are two big challenges for all societies. The countries devised some plans to deal with these problems but the success rate of the countries is different. The government should consider some approaches such as prevention and treatment programs. Related policies also must be taken into account. The implement of the addictovigilance system was an adequate response to issues including false prescriptions, drug abuse, etc. in France, and as we're encountering similar obstacles in Iran, a monitoring system for prescription drugs with abuse potential appears to be a proper solution.Conclusion: As the problems related to drug abuse grow in every aspect of society, an addictovigilance system, as implemented in France, has to be set up to monitor the process. The regulatory affairs of potent drugs for abuse must be checked more than before. The more this system is comprehensive, the less socio-economic burden will be imposed on the government. Since the COVID-19 pandemic emerged, the necessity for this monitoring system is touchable.

2

## بررسی تطبیقی کوریکولوم آموزش داروسازی مصوب وزارت بهداشت، درمان و آموزش پزشکی ایران در مقایسه با دانشگاه های برتر جهان

*Sogand Amiri*[1] *, Seyed Mohammad Iman Moezzi*[1] *, Navid Ravan*[2] *, Sadra Nadimi \ Porshokoohi*[2]

[1]Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

[2]Center for Strategic Pharmaceutical Studies, Shiraz University of Medical Sciences, Shiraz, Iran

Corresponding author: Navid Ravan

Corresponding author Email: navidravan1998@gmail.com

مقدمه:برنامه ریزی و محتوای آموزشی باید منطبق بر وظایف و مسئولیت های آتی فارغ التحصیلان در جامعه باشد. داروسازان در فضای گسترده ای، از داروخانه گرفته تا صنایع داروسازی، فعالیت می کنند. این گستردگی مسئولیت های ممکن داروسازان، این پرسش را برمی انگیزد که چه میزان از دروس ارائه شده در کوریکولوم آموزش دکتری عمومی داروسازی، دانشجوی داروسازی را برای هر یک از فعالیت ها و مسئولیت

ترکیبی، در کنار آموزش به بیمار بوده است. در حال حاضر، داروساز خدمات متعددی را ارائه می کند. در کشور ایران، علی رغم ابلاغ " سند جامع خدمات سلامت در داروخانه های ایران" ، هنوز بستر مناسبی برای ارائه این خدمات فراهم نشده است. تجربه پاندمی کرونا نشان داد که داروخانه ها، چه در کشور های با سرانه درآمد بالا و چه در کشورهای با سرانه درآمد پائین، جبهه اول مواجهه با بیماری هستند و هرچه خدمات بیشتری ارائه دهند، منفعت بیشتری نصیب مردم می شود(1,2).روش کار: مقاله حاضر یک مطالعه توصیفی- تطبیقی است. در بخش اول، با بررسی سند فوق ، ۱۰ فعالیت بیمار-محور شامل: اندازه گیری قند خون، مدیریت دیابت، اندازه گیری فشار خون، مدیریت پرفشاری خون، مدیریت کلسترول، مدیریت وزن، مدیریت آسم ، واکسیناسیون، مدیریت ناخوشی های جزئی و انجام تست تشخیصی سریع انتخاب شد و ارائه این خدمات در ۲۴ کشور اتحادیه اروپا، ایالت متحده ی آمریکا، کانادا، استرالیا، مالزی، هنگ کنگ و امارات متحده ی عربی بررسی شد . در بخش دوم، با استفاده از کلمات کلیدی" Community pharmacy "، " Roles "، " Services "در پایگاه های Pubmed، Google Scholar و Scopus مقالات مرتبط جست و جو و استخراج شدند.نتایج: در بخش دوم این پژوهش، ۱۷۸ مقاله در ابتدا یافت شد و پس از بررسی عنوان و چکیده، ۲۶ مقاله، مورد استفاده قرار گرفت. مدیریت ناخوشی های جزئی در ۹۶/۷٪ از کشورهای مورد بررسی توسط داروسازان انجام می گرفت. به همین ترتیب، اندازه گیری فشار خون در ۸۳/۳ % ،اندازه گیری قند خون در ۸۰٪ ، مدیریت وزن در ۸۰٪ ، مدیریت کلسترول در ۷۳/۳٪ ، مدیریت دیابت در ۶۶/۷٪ ، مدیریت آسم در ۶۳/۳٪ ، مدیریت فشار خون در ۶۰٪ ، تست تشخیصی سریع در ۴۶/۶٪ و واکسیناسیون در ۴۳/۳٪ از کشورهای مورد بررسی توسط داروسازان انجام می گرفت.بحث و نتیجه گیری: نتایج به دست آمده نشان می دهد که فعالیت های انتخاب شده از سند جامع خدمات سلامت در حال حاضر در کشور های مختلفی در حال اجرا است و اختلاف درصد انجام این خدمات ، احتمالاً ناشی از عوامل متعددی مانند پرداخت هزینه توسط سازمان های بیمه گر ، آموزش های مهارتی داروسازان، قوانین موجود و امکانات داروخانه ها می باشد. علاوه بر فعالیت های بررسی شده در این مطالعه، خدمات متعدد دیگری نیز توسط داروخانه های شهری در کشور های مختلف انجام می شود؛ از جمله این خدمات می توان به: خدمات ترک سیگار، مدیریت داروهای ضد انعقاد، تلفیق دارویی، تکرار نسخه، ارائه مراقبت در منزل، مدیریت درد، خدمات مرتبط با مواد مخدر( تعویض سرنگ و تحویل اوپیوئید جایگزین) اشاره کرد. (3,4) از سوی دیگر، با توجه به پیر شدن جمعیت، خدمات مرتبط با این جمعیت نیز باید در نظر گرفته شود. داروخانه های شهری می توانند یک جایگاه قابل توجه خدمت رسانی به این جمعیت را داشته باشند.(5) خدمت-محور کردن فعالیت های داروخانه ها، همچنین می تواند باعث ایجاد پایگاه های قابل اطمینان جهت ارائه خدمات در شرایط بحران های طبیعی و غیرطبیعی شود.

## 4

# Preparation of a medication manual for patient with HIV: As a pharmaceutical service

*Mina Dashti[1], Parisa Sarkoohi[1]*

[1]Student Research Committee,Faculty of pharmacy,Hormozgan University of Medical Sciences,BandarAbbas,Iran

های آینده او آماده می کند. آموزش داروسازی و کوریکولوم آموزش داروسازی به عنوان محور آن، این وظیفه را برعهده دارد تا نیروی انسانی کارآمد و حرفه ای را متناسب با نیازهای جامعه و مسئولیت های داروساز در جامعه تربیت کند. مقایسه برنامه آموزش داروسازی ایران با کشورهای پیشرفته جهان، موجب شکل گیری چشم اندازی برای تغییرات لازم در آموزش و به تبع آن فعالیت های حرفه ای داروسازان می شود. روش اجرا:در راستای اهداف ذکر شده، دانشگاه های "آکسفورد" انگلستان، "موناش" استرالیا، "هاروارد" آمریکا، "تورنتو" کانادا، "لایدن" هلند، "دانشگاه ملی سنگاپور" و "دانشگاه توکیو" ژاپن به عنوان نمونه ای از دانشگاه های برتر با پراکندگی جغرافیایی مناسب و دارای برنامه آموزش دکتری داروسازی، برای مقایسه با برنامه آموزش داروسازی ایران انتخاب شد. دانشگاه های نام برده بر اساسQuacquarelli Symonds World University Rankingsدر سال 2021، به ترتیب رتبه 1، 2، 3، 10، 11، 12 و 13 را کسب نموده اند. سپس کوریکولوم آن ها از سایت رسمیشان استخراج گردید و این کوریکولوم ها با کوریکولوم آموزش داروسازی عمومی ایران به روش تحلیل محتوا (Content analysis)و بر مبنای سهم دروس مرتبط با هر شاخه از داروسازی مقایسه و نتایج حاصل در یک پنل خبرگان متشکل از اعضای هیئت علمی دانشکده داروسازی و متخصصین آموزش پزشکی به بحث و بررسی گذاشته شد.بحث و نتیجه گیری:به نظر می رسد آموزش داروسازی در ایران، نیازمند انطباق بیشتر بر اصول جهانی و نگرش های نوین به آموزش در عین توجه به شرایط، اولویت ها و نیازهای داخلی است. لازم است تا علاوه بر نیازهای کشور، آموزش مبتنی بر شایستگی (Competency-based) نیز مد نظر قرار گیرد، تا شاهد تربیت نیروی انسانی موثر و کارآمد باشیم. تعریف سازمان بهداشت جهانی از داروساز ایده آل (داروساز هفت ستاره)، داروسازی است که دارای ویژگی های مراقبت کننده، تصمیم ساز، ارتباط گیرنده، رهبر، مدیر، معلم و فراگیر مادام العمر باشد. برنامه آموزشی کشورهای پیشرفته در راستای ایجاد این ویژگی ها در دانش آموختگان جهتدهی شده است. همانطور که ذکر شد، علاوه بر اینکه کوریکولوم باید بر اساس نیاز های کشور باشد، باید بر اساس توانمندی های مورد نیاز دانشجو در بازار کار آینده فرد هم باشد به این معنا که لازم است چشم اندازها و اهداف کشور را در نظر گرفته و مطابق با آن، کوریکولوم ایده آل و کارآمد را وضع کرد. علاوه بر این، با توجه به کوریکولوم کشورهای مبدا مقایسه به نظر می رسد، افزودن یک درس در ترم اول دوره جهت آشنایی با فضای کار، مهارت های مورد نیاز و وظایفِ مورد توقع از داروساز می تواند باعث ایجاد دید صحیح و واقع گرایانه دانشجو از آینده خود شود. همچنین در این دانشگاه ها اولویت و هدف گذاری به سمت آموزش برای مراقبت دارویی، براساس دید بالینی و نگاه بیمار- محور رفته است.جمع بندی:به نظر می رسد تغییرات موثری در برنامه آموزش داروسازی در ایران نیاز است تا به آموزش ایده آل در دنیا نزدیک شود.

## 3

# بررسی تطبیقی فعالیت‌های بیمار-محور سند جامع خدمات سلامت در داروخانه‌های ایران با سایر کشورها

*محمدرضا حیدری[2] ، مهدی محمدی[1]*

[1] گروه داروسازی بالینی، دانشکده داروسازی، دانشگاه علوم پزشکی البرز،کرج، ایران
[2] کمیته تحقیقات دانشجویی ، دانشکده داروسازی، دانشگاه علوم پزشکی البرز،کرج، ایران
نویسنده مسئول: مهدی محمدی
ایمیل نویسنده مسئول: m.mohammadi@abzums.ac.ir

مقدمه و پیشینه اطلاعاتی : داروخانه، موسسه پزشکی است که محل عرضه فرآورده های سلامت- محور، ارائه خدمات دارویی و مراقبت های مشاوره ای است. نقش سنتی داروساز، مهیا کردن نسخه و تهیه کردن دارو های

Corresponding author: Parisa Sarkoohi
Corresponding author Email: psarkoohi@hums.ac.ir

Introduction: AIDS (Acquired immunodeficiency syndrome) is the final stage of HIV (Human Immunodeficiency Virus) infection.The virus causes various opportunistic infections, Opportunistic malignancy and deaths by killing immune system cells. According to World Health Organization report, in 2019, the virus is the ninth leading cause of death in low-income countries. Drugs used in treatment change the progression of the disease, improve the patient's quality of life, and reduce the incidence of opportunistic infections. In addition to choosing the best treatment regimen for patients, monitoring the following points can improve the response to treatment in patients: 1- Recognizing the interactions of these drugs with other drugs consumed by the patient and food, 2- Proper use of drugs, 3- Recognizing the common side effects of drugs. Lack of attention to the above points can lead to treatment failure. Therefore, pharmacists have an important role in completing the treatment process of patients with appropriate intervention. Our goal in this project is to provide a medication manual for patients with the HIV virus.Material and methods: After collecting information from reputable scientific sources including the Uptodate website and the book Martindale: The Complete Drug Reference 38thedition and the book Applied Therapeutics 11th edition 2018 and categorizing the obtained data, All data is presented in the form of text and tables. This information is written for the patient information in a simple and understandable language and will be in the form of a booklet as well as a brief pamphlet.Results: This booklet will address the following:

• Recognize the disease and express its different stages

• Provide information to motivate patients to follow instructions

• Preparation of medication list of prescription drugs for these patients

• Provide information on the best time to take medication

• Provide information on the time interval between taking medications and meals for oral medication forms

• Provide common and important side effects of drugs and how to deal with them in case of occurrence

• Provide important drug interactions regarding possible medications used by the patient and provide appropriate solutions

•Provide solutions to socio-cultural problems

Discussion: A clinical study evaluating the improvement in clinical willingness and achievement due to HIV pharmacist interventions; the important effect of the pharmacist in reducing the number and frequency of pills, increasing adherence to the drug and improving clinical outcomes has been confirmed. Also based on a systematic review study, which evaluated the effect of an HIV clinical pharmacist on HIV treatment outcomes, many studies have emphasized the positive effect of pharmacist interventions on the willingness to treat and control HIV. In line with the above studies, hope that the development of this booklet, will increase adherence to treatment and improve treatment response in patients with HIV.Conclusions: Developing a medication manual by a pharmacist increases a person's knowledge and awareness about her/his disease and it can increase the patient's cooperation in the drug treatment process as well as improve the response to treatment in patients with AIDS .

5

## How the Future Pharmacists are Aware of the New Career Opportunities; A Cross-Sectional Survey

*Mojtaba Rajabi Aslani[1], Alireza Maboudi[2], and Seyed hossein Hajimiri[3]*

[1]Pharmacy faculty, Zanjan University of Medical Sciences , Zanjan, Iran

[2]Pharmacy faculty, Zanjan University of Medical Sciences , Zanjan , Iran

[3]Pharmacoenomics and pharmaceutical administration Department, Tehran University of Medical Sciences, Tehran , Iran

Corresponding author: Mojtaba Rajabi Aslani

Corresponding author Email: mrajabirx@gmail.com

Introduction: Considering more than 1,000 new entries to the pharmacy schools in Iran annually, more pharmacists are graduating than ever. Through saturation of the conventional job positions of pharmacists, finding a full-time job could become soon a big challenge. On the other side, extensive career opportunities are still neglected and have a great potential for development. This study aims to examine the level of students' familiarity with the neglected career opportunities for pharmacists in Iran.Material and methods: A list of pharmacist-related job positions following a search into the recruitment websites was extracted. After checking with subject matter experts, a questionnaire-based online survey was designed to evaluate the level of students' familiarity with 11 common careers in the field of pharmacy. The survey was conveyed to pharmacy students within an online platform between 21th August and 1st October in 2020.Results: Followed by a pilot study (n= 140), the main study was conducted with 427 participants. Most of them were in the 2nd or 3rd year of study. Among the suggested careers, Home care pharmacist (28.6%) and Managed care pharmacist (18.6%) were considered as the most and the least familiar ones, respectively.Discussion: though no previous research conducted so far, this study reveals that the role of pharmacists in Iran is not diverse and recognized as much as many other countries. Pharmacy students require more focus on the patient –centered jobs of pharmacists as well as the technology-based positions. This study can be useful for health policymakers to provide opportunities to create these jobs so that a better employment situation for Iranian pharmacists in the future could be provided.Conclusions: The results demonstrate a very limited level of familiarity with newer job opportunities between pharmacy students. Systematic development of these jobs in the coming years would help the employment status of pharmacists get rid of the current concerns. Encouraging students to focus on acquiring related skills could be a strategic approach to looking at the job outlook for pharmacists.

6

## Assessing the Knowledge, awareness and recommendations associated with COVID-19 among Medical and Pharmacy students in Iran

*Mahdie Ghadrshenas[1], Hanieh Jalalian targhi[2], Saba Shojaan[3], Shadi Sarahroodi[4]*

[1,2,3]Pharmaceutical Sciences, Tehran Medical sciences Islamic Azad University (IAUPS), Tehran, Iran

[4]Department of Pharmacology&Toxicology, Pharmaceutical Sciences, Tehran Medical sciences Islamic Azad University (IAUPS), Tehran, Iran

Corresponding author: Shadi Sarahroodi

Corresponding author Email: sarahroodi@yahoo.com

Introduction: The COVID-19 pandemic has become a significant challenge to public health, and has impacted every single one of societies lifestyle. The accurate knowledge and ability to obtain it is crucial in this era and in the sometimes the amount of fake news around us are countless. In this situation usually physicians and pharmacists are great sources of information and valuable treasures for the public. Last year students of Medicine and Pharmacy are also great and usually update source of knowledge and people ask them regarding COVID-19. primary objective of this study is to assess the knowledge of final year medical and pharmacy students in Iran toward COVID-19 pandemic. Material and methods: The cross-sectional study was carried out in June 2021, with an online questionnaire form. A 28-item survey regarding Knowledge, awareness and recommendations associated with COVID-19 was developed and randomly distributed among the pharmacy and medicine students of Islamic Azad Medical University. Descriptive statistical analysis was used to summarize data.Results: A total of 67 questionnaires were completed. 65.7% of the participants were pharmacy and the rest of them medical students. 66.7% of participants mentioned that they receive lots of question regarding COVID-19 from public. Only 18.2% of them received classified information about COVID-19 in their universities, while 54.5% of them mentioned that they receive and update their information regarding this condition from social media and 36.4% from academic websites or published articles. Also, 81.8% of them mentioned that they use their knowledge regarding COVID-19 in their own life and they mostly had a very good knowledge regarding usual medications used in COVID-19. Discussion: Medical and pharmacy students in Iran are a great source of knowledge and our study showed they have a very strong knowledge about COVID-19 and its possible treatments. But unfortunately they have never received official and academic education and information about this condition.Conclusions: Iranian medical and pharmacy students have sufficient knowledge of COVID-19 and might be a large source for health care response when the need arises.

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## Invaluable Role of Pharmacists in Controlling Hypertension: A Medication Preparation Pamphlet

*Fatemeh Shojaei[1], Parisa Sarkoohi[1]*

[1]Student Research Committee,Faculty of pharmacy, Hormozgan University of Medical Sciences,BandarAbbas,Iran
[2] Department of Pharmacology and Toxicology, Faculty of Pharmacy, Hormozgan University of Medical Sciences, Bandar Abbas, Iran*
Corresponding author: Parisa Sarkoohi
Corresponding author Email: psarkoohi@hums.ac.ir

Introduction: Hypertension is defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. Untreated hypertension is one of the most important cardiovascular disorders that may result in some cardiovascular diseases such as cerebral hemorrhage, kidney failure, myocardial infarction or thrombotic stroke. According to WHO statistics, in 2019, the mortality rate from hypertension increased from number-18 to number-9 ranking and the prevalence of hypertension in cardiovascular patients in Iran is currently high. The goal of hypertension treatment is to reduce its complications and mortality rates associated with it, achieve a medication regimen that reduce cardiovascular events and improve a person's lifestyle. Besides choosing the best medicinal regimen, identification of the interaction of hypertension medicines with other drugs or foods, correct administration of medicines and recognition of their side effects can improve treatment responses. Therefore, pharmacists play significant roles in completing patients' therapy by identifying the aforementioned points, taking appropriate interventions and making necessary recommendations. In this regard, we decided to prepare a medication manual for patients with hypertensionMaterial and methods: After confirming the importance of the role of the pharmacist through studies obtained from systematic search with the following keywords: "interventions by pharmacists and hypertension" and "pharmacists and hypertension" in PubMed , Google Scholar, between 2005-2021, we started to prepare a medication manual for patients with hypertension in the form of a pamphlet in a simple language using the following resources:

Martindale: The Complete Drug Reference 38th edition, Applied Therapeutics 11th edition and Uptodate website 2018 and the data obtained were categorized.Results:In general, articles showed the important impact of the pharmacist on improving the status of patients with hypertension directly or indirectly. The following detailed information was also summarized in the prepared pamphlet: a list of drugs used in hypertension, their side effects and interactions with foods and other drugs as well as the best time to take medications and the appropriate interval between medications to help the patient learn more about the disease and the correct use of medications.Discussion: In line with previous studies, the role of pharmacist intervention in patients taking multiple medications or suffering from chronic diseases was identified. The results also showed that improper use and overuse of drugs can lead to various types of negative clinical outcomes for patients and health care providers. The available data also indicate that pharmacists can be effective through a variety of interventions such as reducing the number of drugs and doses used, improving the patient's quality of life, reducing treatment costs and preventing drug side effects.Conclusion: Based on the results, the pharmacist's relationship with the patient with hypertension could affect the health status of patient with hypertension through the correct method of taking the most appropriate antihypertensive drugs. In this regard, developing a medication manual by a pharmacist and his/her effective intervention can increase adherence to drug therapy and improve response to treatment in patients with hypertension as well as reducing treatment costs and preventing drug side effects and interactions.

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## Evaluating the health status and health services of pharmacies in Tehran from the perspective of community pharmacists during the Corona pandemic in 1400

*Fateme Safari[1], Ali Ferdosi[1], Leyla Dadashi[2]*

[1]student of the Faculty of Pharmacy , Tehran Medical Sciences , Islamic Azad University , Tehran , Iran
[2] senior expert of medical education and management, Ardabil Medical Science University,Ardabil,Iran
Corresponding author: Leyla Dadashi
Corresponding author Email: f_safari1377@yahoo.com

Introduction: : During the current COVID-19 pandemic, it has been recognized that public pharmacies are often the first point of contact with the health care system for people with COVID-19-related health concerns or people who need reliable information and advice.Observance of hygienic items in the pharmacy is essential to maintain the health of clients and pharmacy staff. Also, with the correct guidance of the pharmacist present in the pharmacy, patients' visits to more infected medical centers will be significantly reduced. Therefore, hygienic cases should be observed in pharmacies to an acceptable level

to be a safe environment for service recipients so that they can attend the pharmacy with less concern.The purpose of this study is to investigate the health status and services of pharmacies in Tehran in Corona pandemic.Material and metod: This cross-sectional descriptive study was performed on 88 pharmacies from different parts of Tehran in 1400, which were selected by stratified random sampling method. To collect information, a self-made questionnaire including 11 questions about pharmacy environmental health, 11 questions about maintaining the health of staff and pharmacists and 3 questions about the service and role of pharmacies and pharmacists during the Corona pandemic were used. A total of 25 questions were used. They were designed with the help of the CDC guideline. In this study, concurrent validity methods and heuristic and confirmatory factor analysis were used to evaluate the construct validity and Cronbach's alpha method was used to evaluate the reliability (alpha = 0.75). Data analysis was performed using SPSS 16 software.Results: The average level of environmental hygiene in pharmacies was 65.18% and the average level of health in terms of health of people in pharmacies (both employees and customers) was 76.04%. Also, 77.27% of pharmacists believed that their referral for medical advice in pandemic conditions has increased. In addition, 96.59% of pharmacists believed that all the potential of pharmacies was not used in a pandemic situation, but only in 20.45% of pharmacies, the pharmacist was always available for consultation.Discussion: By examining the health status of pharmacies during the corona pandemic, it is possible to make this frequented environment safer by improving the health practices. Visiting patients with minor problems and outpatient and screening patients, which of course requires providing a hygienic and safe environment in the pharmacy.Conclusions: Based on the findings of this study, the environmental health of the pharmacy and the health of the staff and those who refer to the pharmacy are properly observed. The number of requests for pharmaceutical consultations in the pharmacy has increased, which indicates the man's trust in this group. It is expected that a pharmacist is always available in the pharmacy, but only in a limited number of these pharmacies, the pharmacist was always present. Pharmacists, on the other hand, strongly believed that the potential of pharmacies was not used in a pandemic.

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## Investigating the role of pharmacy students to improve public knowledge about COVID-19:review of current evidence

*Fateme Safari[1], Sarvin Salamat[1], Amir Rezazadeh[2]*

[1]student of the Faculty of Pharmacy , Tehran Medical Sciences , Islamic Azad University , Tehran , Iran

[2] Department of Clinical Pharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: Amir Rezazadeh

Corresponding author Email: amirrezazadeh86@yahoo.com

Introduction: Coronavirus (COVID-19) was declared a public health emergency and international concern in January 2020. This pandemic has greatly impacted healthcare services around the world. Due to the emergence of this disease and lack of public information about it, people with insufficient knowledge may be exposed to serious injuries especially people who live in poor and developing areas. Health care students, including pharmacists, can act as providers of reliable and credible information .These students are future pharmacists ; therefore, it is necessary to ensure that they have a good knowledge of COVID-19 or any other pandemic that may occur in the future .Without a prepared pharmacy workforce and pharmacy involvement in disaster management, critical skill and service gaps in disasters may negatively impact patients .The aim of this study was to investigate the role of pharmacy students to inform the public about coronavirus.Material and methods: In this systematic review which was done in 2021 May, four medical databases including PubMed , Google Scholar ,Cochrane Library and Scopus were searched from 2010 to the 4 May 2021 with keywords based on MeSh database .Search terms revolved around the role of pharmacist students in the corona pandemic, as well as the role of health providers such as pharmacy students in various pandemics that have occurred around the world .Search words were: “pharmacy students”,”COVID-19”,”inform”,” Public health education”. Related articles were included after the screening and their data was extracted.Results: Based on methods and resources utilized ,four key focus areas were identified to provide the conditions for employing pharmacy students as providers of credible and important information in the community, as follows: 1.Adequate awareness and knowledge 2.Organizing a skilled workforce 3.Identify target groups 4. Evaluation, research, and dissemination for impact and outcomes.Discussion: Pharmacy students can play an important role in raising awareness in the community .Yet, challenges remain, such as limited availability of personal protective equipment, high risk of infectious exposures inherent in healthcare professions, obstacles to organizing and using trained students and creating a platform for proper education of students. Also for better preparation, pharmacy students should further integrate with interdisciplinary public health teams.Conclusions: Due to the rapid spread of the corona virus and its frequent mutations, and in order to prevent the spread of the disease and maintain the health of people in the community (especially high-risk groups), it is necessary to improve knowledge and beliefs among the people. Otherwise, people will be easily exposed to this dangerous virus due to lack of awareness. Pharmacy students with an academic background and a basic understanding of COVID-19 can play an important role by making people aware of the seriousness of this pandemic .They need to increase their knowledge about COVID-19.

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## Investigating the effect of using web-based application for prescription reading and multimedia database of Iranian generic drugs on learning and motivation of internship course for general pharmacy students

*Zhila Taher Zadeh[1], Setareh Emadzadeh[2],Hanieh mastoor[3], Yamin Hejazi[4], Sajjad Azad[5]*

Pharmacology, Faculty of Pharmacy, Mashhad medical science, Mashhad , Iran

Pharmacy student, Faculty of pharmacy, Mashhad medical science, Mashhad , Iran

Medical education, Faculty of medicine, Mashhad medical science, Mashhad , Iran

M.S of Medical Informatics , Azad university, Mashhad , Iran

Pharmacy student, Faculty of pharmacy, Mashhad medical science, Mashhad , Iran

Corresponding author: Setareh Emadzadeh

Corresponding author Email:emadzadehsetareh@gmail.com

Introduction: The internship course of pharmacy in the general pharmacy with the aim of empowering students to work in the real environment with emphasis on controlling and prescribing and providing medication

advice to patients and the correct acceptance of insurance prescriptions, is included in the curriculum. At present, this course is taught electronically in Mashhad School of Pharmacy by placing the educational content on the learning management system of the university, which due to the practical and skillful nature of the course, challenges this method of teaching learning. On the other hand, one of the problems related to this course is the limited variety of versions offered that the student can see and have the opportunity to learn through them. While using applications, it is possible to solve this problem and gain more learning experiences for students. The purpose of this study is to investigate the effect of web application software for teaching prescription reading and multimedia database of generic Iranian drugs on learning and motivation of internship students in pharmacy . Material and methods: This study was a quasi-experimental study and all students who had chosen the internship course in urban pharmacy in the second semester of the academic year 1300-1400, were included in the study and were divided into two groups of intervention and control. Thematic tests and the Motivational Learning Strategies Questionnaire (MSLQ). Teaching method in the control group was the common teaching method and in the intervention group was the common teaching with working with software. After the intervention, students' learning was assessed using the scores of learning tests and their motivation was assessed using the MSLQ questionnaire.Results: In the field of learning, it was found that the score of students in the intervention group was significantly higher than the score of students in the control group and the use of the application increased scores and learning ($p < 0.05$). But in terms of motivation, students' scores in the intervention group were not significantly different from their scores in the control group ($p > 0.05$).Discussion: The results showed that students who used this application in addition to the usual method, learning to read prescriptions, drugs related to a disease, familiarity with drug forms and correct dosing of drugs compared to the group that was only trained in the common method. They were in a better situation. Although the results of this study did not show a significant difference in the motivation of students in the two groups, but the opinions of a number of students who had used the application, showed their greater interest in learning about the internship course of urban pharmacy.Conclusions: In general, it can be concluded that the use of new technologies to educate students of the current generation can at least have a significant impact on improving the quality of their learning, and of course, according to the characteristics and interests of these students, their interest in using Technology in learning should be emphasized by the educational system and respected professors.

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## Iranian pharmacists attitudes, awareness and suggestion towards the use of herbs in COVID-19

*Maryam Fadaie Fathabadi*[1], *shadi sarahroodi*[2]

[1] Faculty of Pharmacy,Tehran Medical sciences Islamic Azad University, Tehran , Iran
[2]Department of pharmacology and toxicology, Faculty of Pharmacy, Tehran Medical sciences Islamic Azad University , Tehran , Iran
Corresponding author :shadi sarahroodi
Corresponding author Email: Sarahroodi@imutmu.ac.ir

Introduction:Since first days of the novel Coronavirus (COVID-19) outbreak in 2019, pharmacists all around the globe played a key role adopting innovative strategies to minimize the adverse impact of the pandemic.COVID-19 has caused many concerns around the world, as people are more vulnerable in front of an infection (COVID-19) without any specific cure and makes them to seek unlabeled and non-official agents to fight with this condition .One of the most favorable agents as main or complimentary medicine among patients are herbals and pharmacists are one of the most reliable experts that can help patients in this regard.Material and methods:A web-based cross sectional survey was conducted during June and Julu 2021. A 21-item survey was developed and randomly distributed among the pharmacists. Descriptive statistics was applied to represent participant characteristics and Chi-square test was used to evaluate the level of association among variables with a significance level of $p < 0.05$. Results:Iranian pharmacists (n=86), mostly (92.9%.) didn't have any interest to recommend herbal drugs for COVID_19 prophylaxis. Most of them (62.7%)mentioned they are not comfortable to recommend herbals as they believe herbs are not effective and options fors COVID-19 prophylaxis and there is no significant difference between male or female pharmacist ($P>0.05$). 62.7% of pharmacists mentioned that they studied about herbal medicines role in COVID-19, while the main source for their study about COVID-19 were published articles (37.5%) and international guidelines (39.6% 54.8% of our vrespondents mentioned that they would refer any suspicious case to a doctor while 20.2% mentioned that they would recommend some chemical drugs and 3.6%would suggest herbals drugs and 21.4% would suggest combination of chemical and herbal drugs to their patients, and there was no significant difference between the genders of our respondents ($P>0.05$). most of pharmacists in our study (54.8%) believed that herbal drugs are not effective agents as official mecicationsin treatment of mild symptoms of covid 19, while (16.1%) believe that herbal drugs are expensive and 25.8% believe that patients don't accept herbal drugs.In the other part of our study, we asked about the most requested medication and the most medication that pharmacist suggest regarding COVID-19. the most requested medications were Hydroxychloroquine (26.3%) as well as Famotidine (25 %) while the most suggested medication by pharmacists were famotidine (21.5%) and supplements (18.5%).Discussion: Our findings showed that Iranian pharmacists rarly recommend herbals in COVID-19, which is against finding in other countries like China and other East Asian nations. Also, the main requested medication by patients is Famotidine and Hydroxychloroquine, which shows they are under influence of fake news of media.Conclusions:According to this study, pharmacists in Iran rarely recommend herbal medicines to patients. For COVID-19prevention or treatment and as herbals can be good complementary medications in COVID-19, some continued medical education (CME) in this field can be helpful for society .

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## Undergraduate Pharmacy Students' Future Career Perceptions and Plans, A preliminary Study

*Mojtaba Rajabi Aslani* , *Alireza Maboudi* and *Seyed hossein Hajimiri*

[1]Zanjan school of pharmacy, Zanjan University of Medical Sciences , Zanjan, Iran
[2]Zanjan school of pharmacy, Zanjan University of Medical Sciences , Zanjan , Iran
[3]Pharmacoenomics and pharmaceutical administration Department, Tehran University of Medical Sciences, Tehran , Iran
Corresponding author: Alireza Maboudi

Corresponding author Email: Alireza.maboudi77@yahoo.com
Introduction: Many important changes have occurred in pharmacist roles. Naturally, these new roles need new skills which means education plays an important rule in preparing student for future. So far lacking in the scientific literature, in this research, Iranian pharmacy students were asked about their perception about how much they are prepared and interested for their future career. The aim of this study is to investigate pharmacy student's viewpoint about their future career and which of career paths is more desired.Material and methods: A cross-sectional, questionnaire-based survey was conducted. An online questionnaire was designed under supervision of subject matter experts and delivered to pharmacy students through instagram ,following a pilot study. The survey included 10 items evaluating the perception of students on future career and their belief about pharmacist jobs.Results:In total, 564 pharmacy students (137 and 427 in the pilot and main studies, respectively) from 17 universities completed the survey.Around 60% of the respondents were studying in the first three year of university. About 87% believed that at university, they don't obtain enough skills they will need in the future. It is also demonstrated that most of the students (85%) don't prefer to work all their career in drugstore. 42% of student believed that social position is biggest disadvantage to work in drugstore. In addition, about half of the students (52%) didn't want to continue studying in PhD field. Pharmaceutical industry and hospital were among the most interesting setting to be chosen for the future professional life (33% and 19%, respectively). While only 12% prefer drugstore as the favorite place for future career. 45% of them believe that being hired in industry is biggest disadvantage of industry job opportunities.Discussion:Iranian pharmacy students who are potentially the pharmacists of future have few interest to have a career in drugstores because of the hurdles in the establishment of a drugstore and also the lack of a strong social position. Students prefer to enter other pharmacy job field. However, they mostly assume they are not enough skillful and their entry to other fields might be difficult. Hence pharmacy students have to overcome many barriers to get their favorite and satisfactory job.Conclusions: Pharmacy curriculum should strategically be changed to make the students prepared in such a way to bridge the gaps of the job market demand. Moreover, a long term planning should be in place to encourage pharmacy students for developing new paradigms in many fields of a professional pharmacist career opportunities. Future research is needed to deepen such results.

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## The cost-effectiveness of pharmacist-led medication reconciliation in the hospital: Systematic review and meta-analysis

*Mohammad Amin Manavi*[1*], *Mohammad Hossein fathian nasab*[1],

[1]Department of pharmacotherapy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
Corresponding author: Mohammad Amin Manavi
Corresponding author Email: ma-manavi@student.tums.ac.ir
Introduction: Adverse drug events (ADEs) impose a major clinical and cost burden on acute hospital services. It has been reported that medicines reconciliation provided by pharmacists is effective in minimizing the chances of hospital admissions related to adverse drug events. We systematically review the literature to evaluate intervention effectiveness in terms of discrepancy identification and resolution, clinical relevance of resolved discrepancies and healthcare utilization, including readmission rates, emergency department attendance and primary care workload.Material and methods: five major online databases were sifted up to 30 April 2021, without inception date (Embase, PubMed, Embase, google scholar, Web of Science and Scopus) to assess the effect of pharmacist-led interventions on medication discrepancies, preventable adverse drug events, potential adverse drug events and healthcare utilization. The Cochrane tool was applied to evaluate the chances of bias. Meta-analysis was carried out using a random effects model. Results: From 107 articles identified on initial searching, 18 RCTs (6,038 patients) were included. In the next step, 52 study was included and 55 study excluded. after examining the abstract 35 studies confirmed to final analysis. Controlled studies evaluating pharmacist-led medication reconciliation in the community after hospital discharge were included. Study quality was appraised using the Critical Appraisal Skills Programmed Evidence was assessed through meta-analysis of readmission rates. Discussion: Pharmacists-led interventions led to an important decrease in favor of the intervention group, with a pooled risk ratio of 42% RR 0.58 (95% CI 0.49 to 0.67) P<0.00001 in medication discrepancy. Reductions in healthcare utilization by 22% RR 0.78 (95% CI 0.61 to 1.00) P = 0.05, potential ADEs by10% RR 0.90 (95% CI 0.78 to 1.03) P = 0.65 and preventable ADEs by 27% RR 0.73 (0.22 to 2.40) P = 0.60 were not considerable. Conclusions: Pharmacists-led interventions were effective in reducing medication discrepancies. However, these interventions did not lead to a significant reduction in potential and preventable ADEs and healthcare utilization. Future research should examine the clinical relevance of discrepancies and potential benefits on reducing healthcare team workload. Pharmacists can identify and resolve discrepancies when completing medication reconciliation after hospital discharge, but patient outcome or care workload improvements were not consistently seen.

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## بررسی دیدگاه دانشجویان داروسازی سراسر کشور نسبت به کیفیت ارائه دروس فارماکوگنوزی، فارماسیوتیکس، شیمی دارویی و دارودرمان بیماریها

*شایان طهماسبی*[1]، *پریسا الهی*[1]، *لیلا کوتی*[2]

[1] دانشجوی دکتری عمومی داروسازی، دانشکده داروسازی، دانشگاه علوم پزشکی جندی شاپور اهواز، اهواز، ایران
[2] متخصص داروسازی بالینی، استادیار گروه داروسازی بالینی، دانشکده داروسازی، دانشگاه علوم پزشکی جندی شاپور اهواز، اهواز، ایران
نویسنده مسئول :شایان طهماسبی
ایمیل نویسنده مسئول: shayan.tahmasebi76@gmail.com

مقدمه: رشته داروسازی در سالیان اخیر و پس از عدم بازنگری طولانی مدت در کوریکولوم درسی دانشجویان، دچار مشکلات متعددی شده بود که در نهایت شورای آموزش داروسازی و تخصصی وزارت بهداشت، بر آن شد تا تغییری در این وضعیت ایجادکند. با قطعی شدن برگزاری آزمون جامع داروسازی، نگرانی ها و دغدغه های تازه ای به ویژه برای دانشجویان بوجود آمد؛ از جمله آنکه عدم بازنگری وزارت بهداشت در کوریکولوم داروسازی، توام با عدم سنجش کیفیت ارائه دروس این رشته بوده است و با وجود روش های قدیمی تدریس و عدم استفاده صحیح از شیوه های متناسب با نیازهای روز جامعه داروسازی، دانشجویان مجبورند برای تسلط به دروس اختصاصی خود، به منظور گذراندن آزمون جامع داروسازی، همت دو چندان بورزند. با توجه به موارد فوق، در پی آنیم که در این مطالعه کیفیت ارائه دروس اصلی رشته داروسازی را که بیشترین سهم را از نظر تعداد سوال در آزمون جامع 180 واحدی دارند، از دید دانشجویان بسنجیم؛ همچنین طبق بررسیهای صورت گرفته، مطالعه حاضر، اولین مطالعه کیفیت سنجی ارائه دروس داروسازی در

ایران است که با توجه به برگزاری آزمون جامع 180 واحدی داروسازی از سال 99، لازم می نماید.روش کار: در این مطالعه، 465 نفر از دانشجویان داروسازی کشور از ورودیهای 92 به بعد که واحدهای فارماسیوتیکس، فارماکوگنوزی، شیمی دارویی و داروردرمانی بیماریها را گذرانده بودند و رضایت به شرکت در نظرسنجی داشتند، در مطالعه شرکت کردند. ابزار جمع آوری اطلاعات، ترجمه پرسشنامه ای از دانشگاه Wisconsin Madison آمریکا بود که پایایی آن با ضریب آلفا کرانباخ 0.88 و روایی آن به روش cvi تایید شد و به صورت پرسشنامه آنلاین طراحی گردید. این پرسشنامه در دو مرحله برای نمایندگان ورودیهای 92 به بعد تمامی دانشگاه های علوم پزشکی کشور ارسال شد. در هر مرحله 2 درس از 4 درس مورد مطالعه، گنجانده شد و معیارهای ورود به مطالعه صراحتا در پرسشنامه ذکر گردید؛ بنابراین دانشجویانی که واجد معیارهای ورود بودند، در مطالعه شرکت نمودند. در این پرسشنامه چهار حیطه مطالب آموزشی، مشارکت دانشجویان، ساختار دوره و نمای کلی با مقیاس لیکرت مورد سوال قرار گرفت.نتایج: داده های جمع آوری شده، با نرم افزار spssنسخه 26 تحلیل شد. میانگین نمره درس فارماکوگنوزی 42.53، فارماسیوتیکس 53.13، شیمی دارویی 55.85 و داروردرمان 63.33 بود.بحث: با استفاده از آزمون تحلیل واریانس، فرض برابری میانگین 4 گروه رد شد، سپس آزمون شفه نمایان کرد که بین گروه های داروردرمان و شیمی دارویی همچنین شیمی دارویی و فارماسیوتیکس تفاوت معناداری وجود ندارد اما بین داروردرمان و فارماکوگنوزی، داروردرمان و فارماسیوتیکس، شیمی دارویی و فارماکوگنوزی و فارماکوگنوزی و فارماسیوتیکس تفاوت معناداری مشاهده می شود. داروردرمان دارای بالاترین میانگین و فارماکوگنوزی دارای پایینترین میانگین می باشد.نتیجه گیری: تحلیل نمرات دروس در هریک از حیطه های مورد سوال پرسشنامه، همچنین انجام مقایسه بین نمرات دانشگاه های تیپ 1، 2 و 3 که در مقاله اصلی ارائه خواهد شد، ابزاری راهبردی و مفید برای شناسایی نقاط ضعف دروس مختلف و نحوه ارائه آنها، همچنین زمینه ساز رفع نواقص و ارتقاء سطح کیفی دروس مورد مطالعه خواهد بود.

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# Assessment of self-medication practices in the context of the COVID-19 in the adult population of the northern parts of Iran

*Mona Rastad*[1] ,and Shadi Sarahroodi[2*]

[1]Pharmaceutical Sciences Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

[2*]Department of Pharmacology&Toxicology, School of Pharmacy, Tehran Medical sciences Islamic Azad University

Corresponding author: Shadi Sarahroodi

Corresponding author Email: sarahroodi@yahoo.com

Introduction: Self-medication is a term to explain the use of medications for treatment of self-diagnosed disorders. This practice is common among Iranian patients, and involves lots of inappropriate use of medicines by patients. As there is no approved medication to control mild and moderate COVID-19 treatment , self medication is significantly high in the first days of the disease. This practice might be harmful and delays the time to reach medical centers and achieving the right treatment in the proper time.Material and methods: A randomized, cross sectional online survey was conducted on 130 adult citizens by structured questionnaires during COVID-19 outbreak in July 2021, in Lahijan city, to observe the pattern, prevalence and sources of self-medication among the respondents. Data was analyzed using SPSS version 23, and analysis was conducted with descriptive analysis procedures.Results: A total of 130 participants (78.5 % women) were included in our study. While they were mostly (76.2%) between 20-40 years of old and had academic education(86.9%).The overall prevalence of self-medication to prevent COVID-19 was 25.7%, while the prevalence of self-medication of the respondents were 78.5% for other conditions. The most commonly used products as self-medication were vitamins (32.7%) and herbals (30.6%), which were mainly obtained from pharmacies (58.8%).Discussion: Due to self-medication knowledge and awareness of society, we see a high level of self-medication for various conditions but in COVID-19 cases, this practice significantly diminishes which reveals that people are alert about COVID-19 and its dangers and its golden time to treat as well as the necessity of visiting physicians or reaching to the hospital and receiving proper health services .Conclusions: We see the lowest amount of self-medication in COVID-19 which shows people are alert about COVID-19 dangers and we can use the same systems of information for other aspects of self-medication.