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The evaluation of Anti-cancer effects of Silibinin nano-micelles in B16 melanoma cells

Ashkan Hassankhani Rad*, Ommoleila Molavi

P1

Authors' Affiliations:
Tabriz University of medical science

Abstract Presenter:
Ashkan Hassankhani Rad

****Correspondance:***
Ashkan Hassankhani Rad

Coauthors:
Ommoleila Molavi

Abstract:

Silibinin is a natural non-toxic compound with several known beneficial effects for prevention and treatment of several human diseases including cancer. A major limitation to the clinical use of silibinin is its poor water solubility which compromises its bioavailability and subsequently its therapeutic effects. In this research, we have evaluated the potential of poly (ethylene glycol)-poly(ε-caprolactone) (PEG-PCL) based copolymeric micelles for solubilization and targeted delivery of silibinin. Encapsulation of silibinin in the micelles made with different derivatives of PEG-PCL polymers by co-solvent evaporation method, resulted in micelles less than 98 nm in size. Among PEG-PCL based micelles, the one with poly(-α-benzyl-ε-caprolactone) core (PEG-PBCL) was found to encapsulate silibinin with the highest encapsulation efficiency being 98%. The water solubility of silibinin increased from 0.092 mg/mL in the absence of PEG-PBCL polymer to 1 mg/mL comparing with silibinin encapsulated in PEG-PBCL micelles. Assessing the drug release profile of PEG-PBCL micellar formulation of silibinin using dialysis bag method, showed that PEG-PBCL micelles can provide a controlled release of silibinin from their micelles, which was indicated with less than 30% release of silibinin leaded to micelles in 24 hours. Functional analysis showed that PEG-PBCL micelles can effectively deliver drug to B16 melanoma cancer cells resulting in a growth inhibitory effects which was found to be significantly higher from what observed with free drug. Our findings showed a potential for PEG-PBCL micelles as a vehicle for solublized and targeted delivery of silibinin.

Keywords: Polimeric micelles, Silibinin, Nano-particles, Nano-particles

Evaluation of increase in dissolution rate of simvastatin from pellets preparedby extrusion-spheronization containing PEGs with different molecular weights

Seyyede Fateme Aftabi*, Fateme Sadeghi, Hadi Afrasiabi

P2

Authors' Affiliations:
Mashhad University of Medical Science, Iran.

Abstract Presenter:
Seyyede Fateme Aftabi

****Correspondance:***
Seyyede Fateme Aftabi

Coauthors:
Fateme Sadeghi
Hadi Afrasiabi

Introduction:

Simvastatin is a Cholesterol lowering agent, which prevents cholesterol biosynthesis by inhibiting the HMG-CoA reductase enzyme. Simvastatin is a poorly water soluble drug with slow absorbtion rate through gastrointestinal tract and therefore insufficient oral bioavailability. The aim of this study investigate the possibility of increasing the dissolution rate of simvastatin by preparing pellet formulation and evaluating the effect of polyethylene glycols (PEGs) with different molecular weights in mechanical and dissolution characteristics of pellets.

Methods:

In this study, pellets containing simvastatin, Avicel, PVP and different percentages of PEG (20, 30 and 40%) with different molecular weights (400, 600, and 1500) were prepared by extrusion- spheronization technique. Also the effect of granulation liquid type (water or water/ ethanol mixture) was investigated on characteristics of selected pellets (pellets containing 30% PEG). The properties of prepared pellets such as yield of production, shape, surface charactersitices, sphericity, particle size, crushing strength, elastic modulus, and also drug release were evaluated.

Results:

Addition of PEG up to 20% to the formulation was performed with no problem in the pelletization process; however, further enhancement in the percentage of PEG to 30% made the process of extrusion and spheronization more difficult, so that appropriate pellets could not be prepared from formulations with more than 30% of PEG. The results of pellet analysis revealed that inclusion of PEG up to 20% increased the yield of production of pellets but further increase in percentage of PEG resulted in decreasing in the yield of production. The mean particle size of pellets was dependent on the type and percent of PEG in formulation. The hardness and elastic modulus of pellets decreased upon inclusion of PEG in pellet formulation. However, pellets containing PEG1500 were harder than pellets containing PEG with lower molecular weights. The result of dissolution test indicated that addition of PEG and increasing in the amount of it, considerably increased the dissolution rate of drug. Formulations with 30% PEG showed the highest dissolution rate. The dissolution rate of drug was independent of molecular weight of PEG. The use of water/ethanol mixture as granulation liquid increased the dissolution rate of drug briefly but did not have any considerable effect on mechanical properties of pellets.

Conclusion:

Generally, the results indicated that substitution of Avicel with PEG in simvastatin pellets is possible up to 30% PEG inclusion. With this replacement not only pellets with appropriate mean particle size and physicomechanical properties were obtained, but also considerable increasing in dissolution rate of simvastatin was observed. Despite this outcome, dissolution of just 50% of drug after 90 minutes for the best formulation highlighted the necessity of more attempt in order to increase the dissolution rate of drug.

Keywords: Simvastatin, Pellet, Extrusion-spheronization, Polyethylene glycol, Dissolution rate

Thermal stabilization of medicinal urate oxidase enzyme by trehalose: in silico and in vitro study

Zahra Taherimehr, Maryam Zaboli, Masoud Torkzadeh-Mahani*

P3

Authors' Affiliations:
Graduate University of Advanced Technology, Iran.

Abstract Presenter:
Zahra Taherimehr

****Correspondance:***
Masoud Torkzadeh-Mahani

Coauthors:
Maryam Zaboli
Masoud Torkzadeh-Mahani

Abstract

Introduction:

Urate oxidase (UOX) is an important medicinal enzyme, which is clinically used to diagnose and treat gout, hyperuricemia and tumor lysis syndrome. One of the problems with using proteins, such as drug enzymes, is their low stability. Various methods including the use of additives are used to stabilize proteins. Osmolytes like trehalose are small organic compounds naturally found in living cells that protect cells against osmotic stresses [1]. It is evident that osmolytes stabilize protein structures and protect them from unfolding. Despite the importance of UOX therapeutic enzyme, there is lack of enough data on the effect of osmolytes on its thermal stability, activity, and function. In this work trehalose was examined as support to increase the UOX stability.

Methods and Results:

The recombinant protein was expressed and then purified by Ni–NTA agarose affinity chromatography. After purification, the UOX was treated using different trehalose concentrations. The obtained results showed 1.5 M of trehalose had the most stabilization effect on the UOX. The optimum temperature and pH were 20º and 9, respectively for both free and treated enzyme. The results of MD simulation showed that the hydrophobic and also, hydrogen bonding interactions were involved in the interaction between trehalose and UOX. Also, the RMSD, RMSF and secondary structure analysis indicated that the trehalose protects the enzyme conformation. The activity of enzyme was increased more than two times in the presence of trehalose. The half-life of enzyme in the free and treated states were 7.9 and 11.7 minutes, respectively (at 30º).

Conclusions:

Additives like trehalose protects the UOX conformation, increases its activity and also, improves its stability at high temperatures. So, trehalose is a suitable additive for stabilization of the UOX.

Key Words: Urate oxidase, Trehalose, Thermal stability, Hyperuricemia therapy, Molecular dynamics simulation

Preparation and characterization of methotrexate deformable nanoliposomes for the transepidermal delivery to treat psoriasis

Maryam Bahrami Zade*, Shiva Golmohammadzadeh, Mehdi Hatamipour, Mahmood Reza Jaafari

P4

Authors' Affiliations:
School of pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Maryam Bahrami Zade

****Correspondance:***
Maryam Bahrami Zade

Coauthors:
Shiva Golmohammadzadeh
Mehdi Hatamipour
Mahmood Reza Jaafari

Introduction:

The objectives were preparation of nano-liposomes containing methotrexate and studying the effects of material variables on the preparation and properties of these nanoparticles.

Material and methods:

Preparation of nano-liposomes containing different percentages of methotrexate (0.5%, 1.0%, 0.25% and 0.5%) was carried out by Soya PC, cholesterol, oleic acid, methyl paraben and propyl paraben as lipid phase and water as aqueous phase. Due to the high solubility of methotrexate in water, the drug was dissolved in the aqueous phase. The fusion method was used for preparation. The Ultra Turrax device was used with a high shear technology to reduce the size of the particles. To determine the size and zeta potential of the nano-liposomes, the particle size analyzer was used. The ultrafiltration Falcon (cut off 10 kD, centrifugation at 4000 g for 30 min) was used to calculate the encapsulation percentage. Determination of methotrexate was done by HPLC (pharmacopoeia method). Nano-liposomal formulations containing methotrexate were stored at room temperature, 4 degrees and 40 degrees for 6 months and their stability was investigated. Also, the drug release from formulations was performed in vitro by the method of Cell Diffusion in both inflammatory and non-inflammatory skin of Balb / C mouse with two different values of drug loading. The inflammation produced at this stage by topical application of the drug is made to create similarity to the inflammation in psoriasis.

Results:

The particle size and PDI of all liposomes were up to 170 nm and 0.5, respectively with a mean zeta potential of -72.87 mV. The encapsulation percentage in nanoparticles was more than 85%. Formulation of 0.25% and 0.5% showed good stability for 6 months.

Conclusion:

Methotrexate-containing nano-liposomes prepared in this study, have good physicochemical properties, high encapsulation percentage and good dermal penetration ability. The penetration of MTX was increased in the inflammatory conditions. Topical nano-liposomal MTX can provide an opportunity for modern drug delivery in the treatment of psoriasis.

Keywords: nanoliposome, methotrexate, psoriasis

Preparation of lipid nanoparticle of voriconazole

Somayyeh Ebrahimi, Tayebeh Toliyat*

P5

Authors' Affiliations:
Tehran University of Medical Sciences. Tehran, Iran ,

Abstract Presenter:
Somayyeh Ebrahimi

Correspondance:
Tayebeh Toliyat

Introduction:

Among the various antifungal drugs, voriconazole is a newer member of the triazolegroup that has higher efficacy and safety profiles as compared to other members. Voriconazole(VRC) is active against all Candida species that have acquired resistance to fluconazole and is currently used to treat aspergillosis and candidiasis infections. Solid lipid-based particulate systems have several desirable features such as low toxicity of constituents, the ability to protect the incorporated drug from degradation by immobilization in the solid particle matrix, and the ability to release loaded molecules in a controlled manner.

Method:

Solid Lipid Nanoparticle was prepared by emulsification process. Oily phase was prepared using acid palmitic, glycerol monostearate and lecithin. The aqueous phase was prepared using tween 80. Both phases were put in water bath at 65◦ C. Aqueous phase was added to oily phase under hemogenizer. Then probsonicator was used. The mixture was added to Poly Vinyl Alcohol (PVA) solution (0.2% w/v in water), and homogenized at 26,000 rpm using a high-speed homogenizer

Result and discussion:

According to the Table, multiple formulations were used in different hemogenizer round and time, But the size of nanoparticle was not changed significantly. Different manner of hemogenizer 1 and 2 had no important effect in size. It seems that using probsonicator in final stage of formulation reduced the size more than aqueous sonicator. According to the data, it appears that both of the factors (Using probsonicator in the final stage of formulation and ratio of Palmitic acid and glycerol mono stearate of 70:30) are effective in reducing the particle size.

Conclusion:

It seems that a certain proportion of palmiticacid and glycerol Monoestearate and using probsonicator have the most important role in reducing the particle size of solid lipid nanoparticles.

Key Words: Voriconazole ,Solid lipid nanoparticle ,Particle size ,Drug delivery.

Self-nanoemulsifying drug delivery systems of Gentamicin

Shahrzad Mohammadi, Zahra Jafariazar, Tayebeh Toliyat*

P6

Authors' Affiliations:
Department of Pharmaceutics, Faculty of Pharmacy, Tehran University of Medical Sciences.

Abstract Presenter:
Shahrzad Mohammadi

***Correspondance:**
Tayebeh Toliyat

Coauthors:
Zahra Jafariazar
Tayebeh Toliyat

Abstract:
Gentamicin is an important antibacterial agent for treatment of microbial infections. There are two dosage forms of Gentamicin in market, parenteral solution and topical cream. Oral delivery is the most acceptable route for drug delivery. Because of hydrophilic nature of Gentamicin, its oral absorption is poor. Self nano-emulsifying drug delivery system (SNEDDs), are isotropic and clear mixture of oil, surfactant, co surfactant and drug. This system causes increase in solubility of lipid soluble drugs and increase in absorption of water soluble drugs. In this study, we use sorbitan mono oleate (span 80) and sorbitan mono stearate (span 60) as surfactant, propylene glycol and Polyethylene glycol 400 as co-surfactant and oleic acid and sesame oil as lipid phase. Results show that the formulation consists of Span 80, PG (6 to 1) and oleic acid was suitable. Optimum particle size was 295 nm, zeta potential was determined and more than 80 percent of drug was released in 30 min.

Key Words: Gentamicin, Self nano emulsifying drug delivery system (SNEDDs), Dissolution, Solubility.

Preparation and evaluation of topical formulation of Adapalene loaded in NLCs for epidermal targeted drug delivery

Faezeh Kuhestani*, Saman Ahmad Nasrollahi, Alireza Vatan Ara , Atefe Naimifar

P7

Authors' Affiliations:
Nanodermatology Unit, Center for Research & Training in Skin Diseases & Leprosy, Tehran University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Faezeh Kuhestani

****Correspondance:***
Faezeh Kuhestani

Coauthors:
Saman Ahmad Nasrollahi
Alireza Vatan Ara
Atefe Naimifar

Introduction:

Adapalene is one of the topical treatments used commonly in comedon predominant acne patients, whereas topical application results in skin irritation, reddish and scaling that diminishes patient compliance. NLCs have been developed as an effective carrier system with some advantages such as increased solubility, drug targeting, controlled-drug release and stability of Adapalene. This study was targeted to obtain the formulation which had a fine drug carrier, solubility, nanoparticle size, high drug loading and drug release.

Methods:

In this study, NLCs were formulated with probe sonication method. For all formulations, Adapalene was dispersed in lipid phase on a magnetic hot plate at 10℃ above lipid phase`s melting point and a premix emulsion was formed by high pressure homogenizer. Then emulsion was sonicated by using a probe sonicator to fabricate nano-sized particles. The z-average, Zp and PDI was analyzed by Malvern Zetasizer ZEN 3600.

Results:

The NLC formulation has a spherical shape and round edge corresponded to TEM thermograph and its size and Zp was in a nano range. This formulation has a great EE corresponded to DSC results. Release results illustrated controlled and approximately completed drug release profile.

Conclusion:

Preparation of nano-structured lipid carrier of Adapalene with the novel pharmaceutical formulation by using ultrasonic method was carried out. The results e proved the appropriate physicochemical property and solubility, high EE and drug release. In addition, this method is reproducible and convenient to use in a large scale.

Key Words: NLC, Adapalene, Probe sonication, Zeta sizer, TEM thermograph

Preparation and in vitro Evaluation of bi-layered floating tablets of isosorbide dinitrates

Maryam Jalali*, Mitra Jelvehgari

P8

Authors' Affiliations:
Student Research Committee, Tabriz Univers, iRAN.

Abstract Presenter:
Maryam Jalali

****Correspondance:***
Maryam Jalali

Coauthors:
Mitra Jelvehgari

Introduction:

Isosorbide di-nitrate (ISD) is used as a vasodilator in patients with angina pectoris. Recently, efforts have been made to reach a long retention time in the upper parts of the gastrointestinal tract using floating bi-layer systems.

Objective: This study was performed to design bilayer floating tablets of ISD to give immediate release and sustained release effects. Bilayer floating tablets comprised two layers, i.e immediate release and controlled release layers.

Method:

Bilayer floating systems of ISD were prepared using hydroxypropylmethyl cellulose (HPMC K4M), polyvinyl pyrolidone (PVP K 30), and microcrystaline cellulose, which could increase the residence time in the gastrointestinal tract. Direct compression method was used for formulation of tablets. The immediate release layer is comprised sodium starch glycolate as a superdisintegrant, the sustained release layer is comprised HPMC K4M as the release retarding polymer and microcrystalin cellulose as diluent. Sodium bicarbonate was used as a gas generating agent. Floating tablets were evaluated for hardness, friability, weight variation, drug content, floating properties and in vitro release pattern.

Results:

Formulations of fast-release as I1 (containing 8 mg sodium starch glycolate and 2 mg polyvinyl pyrrolidone) and release-controlled as C9 (containing 5 mg of citric acid, 3.5 mg of polyvinyl pyrrolidone and 25 mg of ethyl cellulose) showed the best results. The optimized formulation (I1+C9) was found to be buoyant for 8 h in stomach. The results of release showed that I1 formulation and ISD® tablet (immediate release) had 82.77% and 96.92% drug release after 5 min, respectively ($p>0.05$). C9 formulation and ISD tablet® (controlled release) showed 82.47% and 81.34%, drug release after 2 hours, respectively ($p>0.05$). The drug release in the bi-layer floating tablet was found to be 30.73%, 89.46% and 99.81% within 5 minutes, 2 and 8 hours, respectively. Polyvinyl pyrrolidone and ethyl cellulose sustained the release of ISD from the controlled release layer for more than 8 hours in the stomach.

Conclusion:

Optimum floating tablet may improve the bioavailability of the drug by increasing patient compliance, reducing the frequency of drug use and prolonging the presence time of the drug in the stomach.

Key Words: Isosorbide dinitrate, orally tablet, Controlled-release, Fast-release, Bi-layer floating.

In vivo evaluation of dexamethasone-loaded polymeric micelles for ocular

Mohammad Javad Hassani*, Behzad Sharif Makhmal Zadeh, Anayat Salimi, Mustafa Feghhi

P9

Authors' Affiliations:
Ahvaz Jundishapur University of Medical Sciences, Iran.

Abstract Presenter:
Mohammad Javad Hassani

****Correspondance:***
Mohammad Javad Hassani

Coauthors:
Behzad Sharif Makhmal Zadeh
Anayat Salimi
Mustafa Feghhi

Abstract:

A drawback of traditional ocular dosage forms is dilution of drug by tear and it's rapidly drained away from pre-corneal cavity by tear flow and lacrimo-nasal drainage. Prolongation of residence time with different strategies such as mucoadhesive vehicle will help to have continuous drug delivery to the eyes. The present study emphasizes the preparation and evaluation of polymeric micellar formulation on in vivo rabbit corneal permeation like dexamethasone as relatively lipophilic drug model. Drug release data were fitted by higuchi model. Significant correlation type of polymer and drug released after 25 hours was between 18-65% that indicates slow releasing pattern. Polymeric micelle formulations improved dexamethasone permeation through rabbit cornea. It seems that the effect of micellar formulations is not due to mucoadhesive and film forming properties and mainly is controlled by drug releasing rate.

Keywords: Ocular drug delivery, ocular permeability, polymeric micelle, mucoadhesive, dexamethasone,

Synthesis of thermo-sensitive boronated chitosan-poly (N-isopropylacrylamide) NPs to use in BNCT

Monireh Soleiman Beigi*, Farshid Hassanzadeh, Mahboubeh Rostami, Yaser Kasesaz

P10

Authors' Affiliations:
Master of Science student of Medicinal Chemistry, Department of Medicinal Chemistry, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Science, Isfahan, Iran

Abstract Presenter:
Monireh Soleiman Beigi

****Correspondance:***
Monireh Soleiman Beigi

Coauthors:
Farshid Hassanzadeh
Mahboubeh Rostami
Yaser Kasesaz

Introduction:

Glioma stem cells in the quiescent state are resistant to clinical forms of therapy. An almost inevitable glioma recurrence is due to the persistence of these cells. The high linear energy transfer associated with BNCT could kill quiescent and proliferative cells [1].BNCT is a targeted therapy in which cancer cells accumulate boron and are subsequently irradiated with neutrons.During this process in which 4He and 7Li are emitted when 10B reacts with thermal neutrons releasing energy. In order to be successful, a sufficient amount of 10B must be selectively delivered to the tumor [2, 3].The most important purpose of the study is to synthesize boronated CS-NPs which can deliver a high boron payload to the tumors.

Methods:

At the first to improve the thermos responsivity of chitosan, poly (N-isopropylacrylamide) was applied to modification. In the second step, to modify the water solubility, Succinic acid moieties were grafted onto the CS. To make the targeted system, BPA was attached to the main body of the CS. BPA loaded CS-NPs were prepared by a simple dialysis method by TPP crosslinking. The release profile of BPA from the prepared nanoparticles at temperatures ranging from 37 to 42 ºC. The size and zeta potential of prepared nanoparticles were studied by direct light scattering instrument.

Results & Discussion:

The FT-IR and NMR spectra confirmed the structure of modified systems. The quantity of BPA loaded in NPs was about 88 %. About of 81% of loaded BPA was released at 39 ºC after 24h. It seems that release follows a swelling-controlled mechanism. Our preliminary study thus providing clear evidence for the successful preparation of BPA loaded with novel thermo-sensitive chitosan-poly(N-isopropylacrylamide) NPs. The results of this study are promising to introduce a novel formulation of a highly stable boronated nanocarrier of BPA with extensive physico chemical characterization to BNCT studies.

Keywords: Chitosan, Thermo-Sensitive, nanoparticles(NPs),boron neutron capture therapy, BNCT

Controlled Release and in Vitro Efficient Delivery of Salicylate/GrO

Arash Iranmanesh, Mehdi Ranjbar*

P11

Authors' Affiliations:
Student research committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Arash Iranmanesh

Correspondance:
Mehdi Ranjbar

Introduction:

The development of new and effective drug delivery systems with the ability to improve the therapeutic profile and efficacy of therapeutic agents is one of the key issues faced by modern medicine. Advances in nanoscience and nanotechnology, enabling the synthesis of new nanomaterials, have led to the development of a number of new drug delivery systems [1]. The recent discovery of graphene has been accompanied by increasing research attention to explore this new material for drug delivery applications [2]. Graphene, a single layer of sp2-hybridized carbon atoms arranged in a honeycomb two-dimensional (2-D) crystal lattice, has evoked enormous interest throughout the scientific community since its first appearance. Due to its unique structure and geometry, graphene possesses remarkable physical–chemical properties, including a high Young's modulus, high fracture strength, excellent electrical and thermal conductivity, fast mobility of charge carriers, large specific surface area and biocompatibility [3].

Methods and Results:

100 mg of carriers (Clin, GO and GrO (R)) were impregnated in 20 mL of doxorubicin (50 ppm) in water under constant stirring at room temperature for 24 h. Samples were taken out at given time intervals and the solution was centrifuged at 1500 rpm for 5 min and then filtered to remove the carrier particles completely. The supernatantwas collected and analyzed with a Shimadzu UV-240 spectrophotometer at 485 nm (λmax of DOX). After a certain adsorption time, there were no further changes in the concentration of Salicylate in the liquid phase, and it was assumed that the loading capacity of the particles had been reached.

Conclusions:

In this paper we have introduced Salicylate/GrO nanocomposite as a new drug carrier with high loading capacity. It was synthesized using two different methods, microwave assisted hydrothermal method and reflux method. The nanocomposite synthesized using reflux method was homogeneous and stable so it was used as carrier. Moreover, Salicylate /GrO nanocomposite exhibited no toxic effect to cells especially at concentrations below 160 mg/mL. Loading capacity of Salicylate, GrO and Salicylate /GO nanocomposites for DOX are respectively, 70% in 120 min, 80% in 30 min and 90% in 30 min.

Keywords: Efficient Delivery, Salicylate, Nanostructures, Nanocomposites

In- vitro anticancer activity of pH-Triggered Biocompatible Polymeric Micelles for Targeted Anti-Tumor Drug Delivery

Moloud Kazemi*, Jaber Emami

P12

Authors' Affiliations:
Department of Pharmaceutics, Novel Drug Delivery Systems Research Center, Faculty of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract Presenter:
Moloud Kazemi

****Correspondance:***
Moloud Kazemi

Coauthors:
Jaber Emami

Introduction:

Docetaxel(DTX)is used in the treatment of breast cancer. To overcome the DTX problems?? in chemotherapy such as inappropriate solubility, low tumor selectivity, and inadequate intra-cellular drug release, novel heparin-based pH-triggered polymeric nanoparticles were developed. The aim of this study is to develop In- vitro cell cytotoxicity evaluation of biocompatible nanoparticles composed of alpha-tocopherol and natural Polysaccharide, heparin, (Hep-AC-Toc) with antitumor activities featuring pH- sensitivity to the tumor micro environment for (1-3) targeted drug delivery.

Method:

The amphiphilic copolymer(Hep-AC-Toc) which could self-assemble into sphere micelle in water was synthesized by grafting alpha- tocopherol into the hydroxyl group of heparin via aconitic bond as pH sensitive spacer. DTX loaded Hep-AC-Toc nanoparticles were prepared via a dialysis method. MTT assays was used to determine the in vitro cytotoxicity of free DTX, DTX-loaded Hep-AC-Toc and blank micelles on Human breast cancer cells, MCF-7 and murine breast cancer cells, 4T1 after 48 h of incubation. The cellular uptake study of coumarin-6 loaded Hep-AC-Toc nanoparticles were investigated by using fluorescence microscope and flow cytometry.

Results and discussion:

for both MCF-7 and 4T1 cells treated with Hep-AC-Toc nanoparticles, more than 90% cells remained viable even at a high concentration (2000 nM), Indicates low toxicity and desirable safety of Hep-AC-Toc nanoparticles. In contrast, DTX/ Hep-AC-Toc and free DTX exhibited dose-dependent cytotoxicity at DTX concentration 0.5-2000 nM. Compared to the free drug, DTX/Hep-AC-Toc micelles were showed more cell cytotoxicity and less IC50. These results can be due to nanoparticle's response to the low pH in MCF-7 and 4T1 cells resulting in a rapid drug release and increasing in anti-cancer activity. According to the fluorescence images and flow cytometry histograms, fluorescence intensity of coumarin-6 increased as incubation time increased, suggesting time-dependent endocytosis internalization of nanoparticles.

Conclusion:

In both cell lines, DTX-loaded micelles exhibit lower IC50 than free drug and blank micelles, significantly. Although, Hep-AC-Toc nanoparticles could be effectively up taken by cancerous cells. Briefly, this self-assemble heparin-based drug nanocarrier with multifunctional activity and pH-sensitive drug release have great potential for intracellular delivery of DTX and anti-cancer therapy. Furthermore, indicated heparin is a versatile compound for design of smart drug carrier.

Keywords: Docetaxel, pH-triggered, Nanocarrier, Heparin, Cell cytotoxicity.

Formulation and evaluation of in-situ gel chitosan nanoparticles containing acyclovir for ocular drug delivery

Zahra Mansouri, Mohammadmehdi Mahboobian*

P13

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran

Abstract Presenter:
Zahra Mansouri

****Correspondance:***
Mohammadmehdi Mahboobian

Introduction:

Ocular Herpes simplex infection is a major cause of visual morbidity in developed countries. Anti-viral drugs, such as acyclovir (ACV), are used to treat this disease. ACV ocular ointment (ZOVIRAX®) is the only available ocular dosage form, because of its low ocular bioavailability it must be administrated every 4 hours. The aim of this study is preparation of in situ gel nanoparticles (NPs) of ACV as a novel ocular drug delivery system.

Methods:

Ionic gelation method was employed to prepare NPs of ACV based on chitosan (CS) and sodium alginate (Alg) polymers. NPs with different weight ratios of CS/Alg were constructed. Different volumes of Alg solution were added drop-wise under continuous stirring to prepare poly-cationic CS solution. Physiochemical properties like particle size, poly-dispersity index (PDI), Zeta-potential, entrapment efficacy (EE %) and loading efficacy (LC%) of NPs were measured. According to physiochemical investigations, the optimum formulation was selected for in-situ gelling process. After freeze-drying of formulation, different concentrations of carbopol934 as pH sensitive gelling agent were used to prepare pH trigged in-situ gel. In vitro release study and other investigations such as pH, refractive index (RI), viscosity and osmolality of optimum in-situ gel NPs formulation were performed. Accelerated stability testes were also investigated. Modified Draize and HET-CAM test were used to evaluate ocular irritation of optimum formulation.

Results:

The optimum in-situ-gel NPs formulation showed the sustained release pattern compared with control solution. Particle size analysis illustrated that the optimum formulation was in Nano metric scale (164±6.52) with suitable PDI, zeta potential, EE% and LC%. Other physiochemical investigations such as pH, viscosity, refractive index(RI) and osmolality showed that the optimum in-situ-gel NPs formulation was acceptable for ocular administration. No physical instabilities were observed during stability studies. Draize and HET-CAM test proved that formulation had no ocular irritation and could be tolerated by eye.

Conclusion:

Our results showed that the developed formulations with sustained release properties could be employed to improve the ocular bioavailability. And according to the results of cytotoxicity and irritancy tests this formulation could be used for ocular application.

Keywords: nano particle, in-situ-gel, ocular drug delivery, Acyclovir

Formulation and Characterization of Dihydroxyacetone Nanoparticles Based Nano Emulsions: Artificial Tanning Effects Study

Aida Sinaee, Payam Khazaeli, Mehdi Ranjbar*

P14

Authors' Affiliations:
Pharmacy Student; Department of Pharmaceutics, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran

Abstract Presenter:
Aida Sinaee

***Correspondance:**
Mehdi Ranjbar

Coauthors:
Payam Khazaeli

Introduction:

The Maillard reaction produces browning of compounds due to the initial condensation between a non-protonated amino group of aminoacids, peptides or proteins and a carbonyl group, usually a reducing sugar residue, to form a Schiff base. This definition clearly includes many types of structures, whether human made or nature. Nanomaterials are called nanoscale materials. Nanostructured matter refers to any material with at least one of its dimensions on a nanometer scale (below 100 nanometers). (. same as above) From the medical point of view, nanoparticles have found many uses, for example, silver and gold nanoparticles are known as antimicrobial and anti-inflammatory agents, respectively [1]. In this study, using the dihydroxy stearate emulsion nanostructures, we will examine the effect and effectiveness of the reaction of Millard. Dihydroxytene attaches to the proteins found in the horny layer of the skin and creates a non-toxic bronzing color [2]. These pigments are called melanocytes or brown chromophers. Dihydroxysteone acts as an active ingredient in sunflower lotions of the sun with amino acid groups to create a brown colored compound, since 1980, due to increased dihydroxy stearate sources and its refined production, improved tanning formulations Non-solar (synthetic) batteries are available. Today, dihydroxytene is the active ingredient in most sunscreens to protect the skin [3].

Methods and Results:

In the first step 50mg/l of oleic acid and 30mg/l of sodium dodecyl sulfate were solved in 20 ml distilled water and 100 µL surfactant added drop by drop to above solution then solution placed under vigorous stirring at 50 oC for 120min and in final pH adjusted to 7.5–8 with 5ml NaOH 2M. For the second stage, solutions were kept at room temperature, in the next section 100 mg/L of carbomer weighed and solved in ratio 3:1 ml distilled water/chloroform, then pH adjusted between 6 and 7.5 with digital pH meter under vigorous stirring at 50 oC. For creating a suitable substrate 20 mg/L of polylactic acid as biodegradable copolymer was solved in 20 ml of distilled water in ratio 1:1 ml distilled water/chloroform and then added to carbomer solution.

Conclusions:

Investigating the effect of the size and morphology of the prepared nanostructures showed that these compounds are synthesized in a uniform and uniform dispersion between 89-112 nm. To investigate the effects of tanning with Millard's reaction will be examined. The results indicate that optimized nanostructures exhibit better tanning effects in terms of shape and size.

Key Words: Dihydroxyacetone, Millard reaction, Artificial Tanning, Nanostructures.

Preparation and evaluation of cell viability of triacetin based brinzolamide nanoemulsions

Seyedeh Negin Kassaee, Mohammad Mehdi Mahboobian*

P15

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran.

Abstract Presenter:
Seyedeh Negin Kassaee

***Correspondance:**
Mohammad Mehdi Mahboobian

Introduction:

Brinzolamide is a topical carbonic anhydrase inhibitor used as first or second-line medication for treatment of glaucoma. The aim of the present study was to prepare triacetin based nanoemulsions (NEs) containing brinzolamide and evaluate their cytotoxicity for ophthalmic use.

Methods:

Based on partial pseudo ternary phase diagrams, seven NEs formulations composed of Triacetin or Capryol 90 as oils, various surfactants such as Tyloxapol, Cremophor® RH 40, Labrasole and Brij 35, Transcutol P as a co-surfactant and water at different surfactant/co-surfactant weight ratios (1:1, 2:1) were prepared by the spontaneous emulsification method. To confirm the safety of the formulations for ocular use, preparations were examined for potential ocular irritancy using a cell viability assay on retinal cells. Also the half maximal inhibitory concentration (IC50) values of various surfactants and oils determined using the sulforhodamine B cell viability assay on retinal cells.

Results:

According to the results, Tyloxapol and Cremophor RH40 showed significantly lower toxicity than other excipients after 1 h. On the other hand, Capryol 90 and Brij 35 showed high cytotoxicity, with their IC50 values determined to be less than 0.5 mg/mL after 1 h of incubation. Among all samples with suitable physicochemical properties, the formulation containing Triacetin, Tyloxapol, Transcutol P at different concentrations of 0.1, 0.5 and 1% v/v showed no cytotoxic effects.

Discussion and Conclusion:

Our findings confirmed that Transcutol P, Cremophor RH40 and Triacetin were the least toxic excipients and may be safely used in the eye at various concentrations. On the other hand, the concentrations of some oils and surfactants such as Capryol 90, Brij 35 and Labrasol must be restricted to avoid ocular irritation. Although a number of NEs exhibited some degree of cytotoxicity, two NE formulations were considered safe for ocular use.

Keywords: Nanoemulsions, Brinzolamide, Cell viability, Ocular delivery.

Design and optimization of topical gabapentin loaded niosomes for enhanced management in patients with neuropathic pain: Application of 2-levels factorial design

Sara Masoumi*, Payam Khazaeli, Mostafa Pournamdari, Abbas Pardakhty

P16

Authors' Affiliations:
Department of Pharmaceutics, Kerman University of Medical Sciences, Kerman, Iran

Abstract Presenter:
Sara Masoumi

****Correspondance:***
Sara Masoumi

Coauthors:
Payam Khazaeli
Mostafa Pournamdari
Abbas Pardakhty

Abstract:

Gabapentin (GBP), a GABA analogue, is orally used for the treatment of partial epilepsy and has useful effects on controlling neuropathic pain by inhibiting calcium channel α2δ subunit. Due to its low bioavailability at higher oral doses and the relevant side effects, topical formulations are recommended recently. In the current study, a novel topical niosomal gel with potential effects on neuropathic pain by experimental design was prepared. Niosomal formulations were produced by thin film hydration method in which several combinations of Spans and Tweens were used together with cholesterol. In experimental design, optimization of gabapentin niosomal formulations were evaluated considering 3 response including minimum niosomal size, maximum percentage of entrapment efficiency and maximum cumulative drug release. The effects of amount of lipid (150-300 µmole), percentage of cholesterol (30-50%) and hydration time (30-60 minute) were assessed on the above-mentioned responses. Mean particle size of niosomes was measured using laser light scattering method and the release of GBP from Carbomer-PEG niosomal gel was evaluated by Franz diffusion cell. The encapsulation efficiency percentage (EE%) of the formulations were determined following centrifugation and the stability profile of the optimized formulation was then assessed for 6 months. GBP was quantified by a developed and validated reversed phase HPLC method carried out on a C8 column and using acetonitrile/phosphate buffer pH 6.9 as mobile phase in an isocratic elution mode with UV detection at 210 nm.
The results showed that the optimal experimental condition is 300 µmole lipid containing 50% cholesterol in a 60-minute hydration time. The release profile was best fitted with diffusion-based kinetic model and the EE% was 97%. Mean particle size of optimized niosomal formulation was found about 8.10 µm and no significant changes (P value>0.05) in vesicle size was observed. The validation parameters of HPLC method were good enough to reliably determine the drug in the prepared dosage forms.
The optimized formulation showed to be a suitable topical dosage form appropriate for clinical studies on treatingpatients with chronic neuropathic pain.

Key Words: Gabapentin, Niosomal gel, Chronic Neuropathic Pain, Optimization.

Development and characterization of lipid based nanoparticles for efavirenz oral administration

Somayeh Taymouri, A. Alizadeh, J.Varshosaz

P17

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy and Novel Drug Delivery Systems Research Centre, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract Presenter:
Somayeh Taymouri

****Correspondance:***
Somayeh Taymouri

Coauthors:
A. Alizadeh
J.Varshosaz

Introduction:

Present investigation aimed to prepare, optimise, and characterise lipid nanocapsules (LNCs) for improving the solubility and bioavailability of efavirenz (EFV). The human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) is a global health problem and one of the most destructive epidemics. High dose of highly active antiretroviral therapy, complex administration schedules, drug side effects, reduced patient compliance, and high cost of treatment have led to a failure of HIV/AIDS therapy (1). EFV is as the first-line therapy for children HIV infection. The low aqueous solubility and extensive first pass metabolism of EFV leads to low (40–45%) oral bioavailability and high inter-individual (55–58%) and intra-individual (19–24%) variability in its absorption (2). High dose and frequent administration of EFV led to several serious side effects including neuropsychiatric disturbances, hepatotoxicity, and metabolic alterations. In this study, aiming to increase water solubility and oral absorption of EFV, EFV-loaded LNCs were developed by the phase inversion method.

Methods and Results:

EFV-loaded LNCs were prepared by the phase-inversion temperature method and the influence of various formulation variables was assessed using Box–Behnken design. Then, it was subjected to ex-vivo permeation using rat intestine. EFV-loaded LNCs were found to be spherical shape in the range of 20–100 nm with EE of 82–97%. The best results obtained from LNCs prepared by 17.5% labrafac and 10% solutol HS15 when the volume ratio of the diluting aqueous phase to the initial emulsion was 3.5. The mean particle size, zeta potential, PdI, EE, drug loading%, and RE during 144 h of optimised formulation were confirmed to 60.71 nm, -35.93 mV, 0.09, 92.60, 7.39 and 55.96%, respectively. Optimised LNCs increased the ex vivo intestinal permeation of EFV when compared with drug suspension.

Conclusions:

It has been clarified that the incorporation of EFV into LNCs had succeeded to sustain the drug release and increase the ex-vivo intestinal permeation. These results suggested that LNCs could be promising for improved oral delivery of EFV.

Keywords: HIV, LNCs, efavirenz, ex-vivo permeation

Preparation and in vitro characterization of perphenazine–containing solid lipid nanoparticles

Parisa Abbasi, Reza Mahjub, Mohammad Mehdi Mahboobian*

P18

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Hamadan University of Medical Sciences, Iran.

Abstract Presenter:
Parisa Abbasi

***Correspondance:**
Mohammad Mehdi Mahboobian

Coauthors:
Reza Mahjub

Abstract:

Schizophrenia is a chronic psychotic disorder that disrupts social skills and personal performance of patients. Therefore, one of the preferred medications for the treatment of this mental illness is a typical antipsychotic drug known as perphenazine (PPZ) which is reported to be as much effective as atypical medications. PPZ has a lipophilic nature that is associated with blood-brain barrier penetration restriction and poor bioavailability (40%) due to its intensive first-pass metabolism following oral administration. To minimize all these limitations, in the present study perphenazine-loaded solid lipid nanoparticle (PPZ-SLNs) drug delivery system was developed. PPZ-SLNs have been prepared by solvent emulsification/evaporation method, utilizing lipids such as soy bean Lecitin, glycerol monostearate (GMS) and Tween 80 as a surfactant. Experimental design and Box-Behnkenanalysis was employed for optimizing the solid lipid nanoparticles. Minimum particle size, maximum entrapment efficiency and suitable zeta potential were main criteria to achieve optimized formulation. In addition to these parameters, Optimized SLNs were evaluated for surface morphology and in vitro release. Results indicated that the mean particle size, zetapotential and entrapment efficiency of optimized PPZ-SLN was 104±3.92 nm, -28±2.28 mV and 83%±1.29 respectively. The in vitro release study showed that PPZ-SLN achieved a sustained-release up to 24 h. Based on appropriate characteristics of developed nanoparticles, PPZ-SLNs can make a promising formulation in order to modify disadvantages of perphenazine oral administration.

Keywords: solid lipid nanoparticle, perphenazine, oral delivery.

Formulation and physicochemical characterization of solid lipid nanoparticles of Dimethyl Fumarate and its cytotoxic effects

Mohammad Mahdi Poustchin, Jamaleddin Mousavi, Mahdieh Soltani, Saleheh Sabouri, Gholmreza Asadi, Mehdi Ansari*

P19

Authors' Affiliations:
Deputy of Research, Kerman University of Medical Sciences, Kerman, Iran

Abstract Presenter:
Mohammad Mahdi Poustchin

****Correspondance:***
Mehdi Ansari

Coauthors:
Jamaleddin Mousavi
Mahdieh Soltani
Saleheh Sabouri
Gholmreza Asadi

Introduction:

Multiple sclerosis is an autoimmune disease in which T-cells attack against neuron's myelin and the efficiency of nervous system is decreased over time [1]. One of the newest oral medicines for MS is Dimethyl Fumarate (DMF) that treats relapsing-remitting MS. DMF has several adverse effects like abdominal pain, diarrhea, nausea, and flushing. Also, DMF passing from blood brain barrier is difficult and it has low permanency in nervous system. One of the new drug-delivery systems are solid lipid nanoparticles that can compensate the adverse effects of DMF and allow for its passage from blood brain barrier [2].

Methods:

In this study, DMF was determined by UV spectrophotometry at λmax of 212.94 nm. Several formulations of DMF loaded SLN were prepared using high-shear homogenization and ultrasonic method. SLNs were developed by Witepsol®-H35, Tween® 80, Tween® 20, and Span® 80. Particle size, release rate, and physical stability of the formulation at refrigerator, room, and oven temperature were investigated. Its effects on some cancerous cell lines were also studied.

Results:

Results showed that the size of nanoparticles in the selected formulation was around 57 nm. Encapsulation efficiency of the loaded DMF was found to be 55.7% and the release studies by Franz diffusion cell through Cellophane membrane showed that 7% and 22% of the loaded DMF was released after 60 and 240 min, respectively, compared to 19% from the solution of DMF in just 60 min. It can be concluded that the formulation was slow released. Results depicted that the formulation was stable for more than 6 months at refrigerator and room temperature. Loaded SLNs also showed a significant effect on the cells compared to the normal formulation.

Conclusion:

Packing DMF into the SLN changed significantly its physical, release and cytotoxic effects.

Keywords: Dimethyl Fumarate, Solid Lipid Nanoparticle, physicochemical characterization, Cytotoxic effects

Biocompatible nanofibers of Muscari neglectum and investigation of antifungal and antitoxicity effects

Hadis Zarafshani, Fereshteh Bagheri , Pouran Moradipour,
Mahdi Mojarrab, Elham Arkan*

P20

Authors' Affiliations:
Student Research Committee, Kermanshah University of Medical Science, Kermanshah, Iran

Abstract Presenter:
Hadis Zarafshani

***Correspondance:**
Elham Arkan

Coauthors:
Fereshteh Bagheri
Pouran Moradipour
Mahdi Mojarrab

Introduction:

Muscari neglectum belongs to Liliaceace family and is used for different purposes. It is traditionally used for the treatment of rheumatism in Turkey. The root of Muscari neglectum has pectoral stimulatory effects, including anti-inflammatory, anti-allergic, and aphrodisiac effects. The approach of using plants for synthesis of nanofiber is quite novel and an example of green chemistry, which provide advancement over chemical and physical methods. The mentioned method is cost effective, environment friendly, easily scaled up for large scale synthesis, and there is no need to use high pressure, energy, temperature, and toxic chemicals. In the present study, the aqueous extract of Muscari neglectum was used for the first time as NDDS. Then, the obtained fibers of Muscari neglectum were optimized and their cytotoxicity effect were investigated.

Methods:

Muscari neglectum was collected from Kermanshah province, pharmacy faculty, Iran and authenticated under number 9296 in RANK. The extract of Muscari neglectum via water and some other solvents was obtained. Afterward Muscari neglectum nanofibers were prepard by electrospining method. Chemical and physical characterization were carried out through FTIR, XRD, SEM, UV-Vis, and TG-DTA. Also, cellular toxicity of the nanofibers was studied on fibroblasts cell line and their antifungal effect was assessed using candida albicans and aspergillus niger.

Results:

Diameter of nanofiber was in the range of nanometer (80-120 nm). XRD results demonstrated that extracts of Muscari neglectum were semi crystal and amorphous. The aqueous extracts from M. neglectum bulbs had the highest DPPH (2,2-Diphenyl-1-picrylhydrazyl) and ABTS (2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) radical scavenging activity, respectively. The results showed that aqueous extracts obtained from bulbs and herba didnot show any cytotoxicity effect against cell lines.

Discussion and Conclusion:

The findings indicated that the nanofibers of extract Muscari neglectum have high mechanical strength and without any cytotoxicity and lead to more patient compatibility. Finally, the fiber was selected as NDDS. Based on our preliminary studies, we predict that muscari neglectum can be used as a synergistic agent with other antibacterial medicines.

Keywords: Muscari neglectum, extract, Nanofiber

Preparation & evaluation of sustained drug delivery systems for Growth Hormone by injectable, thermo –sensitive, in-situ forming hydrogels using PCL-PEG-PCL

Khadijeh Delroba*, Farzin Hadizadeh, Elham Khodaverdi, Bahmane Khamene

P21

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Khadijeh Delroba

***Correspondance:**
Khadijeh Delroba

Coauthors:
Farzin Hadizadeh
Elham Khodaverdi
Bahmane Khamene

Abstract:

Recently, thermosensitive polymers-based injectable in situ forming hydrogels have received increasing attention as controlled drug carriers because of their many advantages, such as the convenience of application, sustained drug release behaviors, less systemic toxicity, and etc.

Human growth hormone (hGH) is widely used for treatment of growth hormone deficiency. Besides many advantages of hGH, it has some limitations, such as short in vivo half-life and instabilities.

The study aimed to design biodegradable and injectable in situ gel-forming controlled drug delivery system for hGH using triblock copolymer poly(ε-caprolactone)-poly (ethylene glycol)-poly(ε-caprolactone) (PCEC). A series of PCEC copolymers were successfully synthesized by ring-opening copolymerization using microwave, and characterized by H-NMR and DSC. The critical micelle concentration (CMC) of the copolymer solutions was determined by spectrophotometry. Thermosensitivity of the PCEC copolymers was tested using the tube inversion method. The surface morphology of the hydrogel and copolymer was studied by Scanning Electron Microscope (SEM). Rheological properties and in situ gel forming were investigated to achieve an injectable controlled-release drug delivery system.

Also drug formulations were prepared by adding hGH into 30% (wt) aqueous solution of triblock copolymer. hGH concentrations in the released samples were determined using standard MicroBCA method and FPLC. At the end, CD spectrum and SDS-PAGE test were investigated to approve hGH structural and conformational stability.

The results indicated that synthesis of copolymer using microwave is fast and effective. Aqueous solutions of PCEC copolymers underwent thermosensitive sol–gel–sol transition as temperature increases when the concentration was above corresponding critical gel concentration (CGC). The formation of hydrogel was confirmed by the result of SEM and DSC. Also, rheographs indicated that these hydrogels have pseudoplastic behavior but their tixotropic behavior is not significant. Results showed that aqueous solutions of the synthesized PCEC copolymers can form in situ gel rapidly after injection under physiological conditions.

In vitro release studies demonstrated that there were no initial burst of hGH from formulations containing dose (0.42%, w/v) of hGH. Also, the triblock copolymer used in this study was able to control the release of the incorporated hGH in vitro for longer duration.

Keywords: controlled drug delivery system, sustained release, in situ gelling system

Decomposed of diclofenac from pharmaceutical wastewater using electro Fenton process: A new technique of treatment

Alireza Zeinadini Meymand, Maryam Dolatabadi, Saeid Ahmadzadeh*

P22

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Alireza Zeinadini Meymand

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi

Introduction:

Diclofenac (DCF) is a non-steroidal anti-inflammatory drug, used as an analgesic to reduce inflammation in arthritis, rheumatic conditions, and even to ease menstrual pain (1, 2). DCF is one of the pharmaceuticals most detected in water sources, which can be detected in influents and effluents from water treatment plants at concentrations up to µg L-1 level. Biological treatments seem to be inefficient on the degradation of this compound, the study of new technologies such as advance oxidation processes (AOPs), avoiding the contamination of pharmaceutical wastewater, is necessary (3).

Methods and Results:

The current work aimed to evaluate the efficiency of photo electro Fenton process for removal of DCF from the water. The effects of five operating parameters, including initial DCF concentration, pH solution, the dosage of H2O2, the irradiance of UV, and reaction time were evaluated by applying response surface methodology (RSM) using the central composite design (CCD). Optimization results showed 97.4% DCF was removed in the optimum removal efficiency, including initial DCF concentration of 10 mg L-1, H2O2 dose of 520 µL L-1, the current density of 6.5 mA cm-2, and electrolytic time of 6 min. the optimum molar ratio of H2O2/Fe2+ was 1.5. Analysis of variance displayed the non-significant lack of fit value (0.091), whereas, the predicted correlation coefficient values (R2=0.937) were reasonably in agreement with the adjusted value (R2=0.950), demonstrating a highly significant model for DCF removal.

Conclusions:

This process produces the highly oxidizing species, the hydroxyl radical (•OH), which is mainly responsible for the oxidative degradation of DCF. Kinetic analysis showed that the removal of DCF by Advanced electrochemical oxidation followed a first-order kinetic model.

Keywords: Electro Fenton process, Diclofenac, Decomposed, Pharmaceutical wastewater

Advanced treatment of pharmaceutical wastewater using new bipolar electrocoagulation process

Fateme Maghfory, Maryam Dolatabadi, Saeid Ahmadzadeh*

P23

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Fateme Maghfory

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi

Introduction:

Cefixime (CFX), a third-generation cephalosporin, is an important prescribed antibiotic. This drug is chemically unstable and poorly soluble in water, and thus possesses a low bioavailability of 40-50%. (1, 2) CFX covers a wide range of diseases, related to infections caused by bacteria, such as pneumonia, bronchitis, syphilis and gonorrhea, and ear, throat, lung, and urinary tract infections. Moreover, the presence of antibiotics in effluents has also increased in the environment and their abatement will be a challenge in the near future.

Methods and Results:

The electrocoagulation (EC) set up was consisted of two aluminum plate electrodes immersed in the 250 mL of wastewater sample using Plexiglas with dimensions of 12×5×5 cm. All experiments were conducted in batch mode. The experimental design was carried out based on the central composite design with response surface methodology (3). The effect of various variables, including pH solution, current density, initial CFX concentration on CFX removal efficiency from pharmaceutical wastewater was investigated using EC process. EC process was applied successfully with removal efficiency of 100 % under the optimal operating condition of 8.5 pH, 13.5 mA cm-2 current density, 16 mg L-1 initial CFX concentration, and reaction time of 14 min, which is in adequate agreement with the predicted model using ANOVA. Under the optimal conditions of the EC process, electrode consumption and electrical energy consumption were found to be 0.071 g during a single run and 0.957 kWh m-3, respectively.

Conclusions:

The predicted removal efficiency by Design Expert 7 software and obtained experimental value revealed that there is a satisfactory agreement between the CFX removal efficiency obtained from the experiment and the estimated value by the suggested model. The obtained results revealed that the EC process was able to eliminate antibiotic CFX effectively.

Keywords: Cefixime, Electrocoagulation Proces, Pharmaceutical Wastewater, Treatment

Development and performance evaluation of the electro-Fenton process for degradation of ampicillin from pharmaceutical wastewater

Fateme Maghfory, Maryam Dolatabadi, Saeid Ahmadzadeh*

P24

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Fateme Maghfory

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi

Introduction:

Antibiotics are designed specifically as a drug to treat or prevent infective diseases in human or animal body. For preventing or treating infections in humans or animals, only some parts of the antibiotics given dose are metabolized and the rest is excreted still as active compound. Ampicillin is a beta-lactam that has been used extensively to treat infections caused by both gram-positive and gram-negative bacteria. Ampicillin is against microorganisms by inhibiting the synthesis of cell wall during active multiplication (1, 2). Residues from human environments, medical wastes, pharmaceutical, and hospitals sewage may contain various antibiotics and antibiotic resistance genes that can contaminate natural environments. Therefore, this study aimed to determine the efficiency of the electro-Fenton (EF) process for removing ampicillin from pharmaceutical wastewater (3).

Methods and Results:

Experimental design using response surface methodology was applied to enhance the removal efficiency of the EF process by optimizing the effects of main variables and their interactions and minimizing the imprecision of experiments. In the current work, experimental studies were done by a plexiglass reactor in laboratory scale using Fe electrodes. The effect of various variables including; type of electrolyte, pH solution, H2O2 dosage, current density, initial Ampicillin concentration on Ampicillin removal efficiency was investigated. The best removal efficiency of 95.4% has been achieved under the optimal experimental condition including initial pH 3, H2O2 dosage 170 µL L-1, ampicillin concentration 6.5 mg L-1, and current density 6.2 mA cm-2 during the reaction time of 11 min. The predicted removal efficiency of 94.0% was in satisfactory agreement with the obtained experimental removal efficiency of 95.4%.

Conclusions:

Using ordinary radical scavengers revealed that degradation as the main mechanism of ampicillin removal controlled under hydroxyl free radicals produced throughout the EF process. Kinetics of degradation process followed first-order kinetics model with rate constants (Kapp) of 0.674 min^{-1}.

Keywords: Ampicillin, Electro-Fenton process, Degradation, Experimental design, Pharmaceutical wastewater,

Advanced electrochemical oxidation process for mineralization of acetaminophen from hospital wastewater

Alireza Zeinadini Meymand, Maryam Dolatabadi, Saeid Ahmadzadeh*

P25

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Alireza Zeinadini

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi

Introduction:

Acetaminophen (ACT), a type of analgesic and an antipyretic drug commonly used as a fever reducer and pain reliever, is generally safe at therapeutic dosage but acute overdose causes potentially fatal liver damage (1). ACT is absorbed around 5–15% by the body, and the remaining portion is excreted in the urine as unaltered ACT (4%) and intermediate compounds (96%). Because of high consumption worldwide, it is one of the most frequently detected drugs in bodies of water (2). This drug has been found in European Sewage Treatment Plant (STP) effluents with a concentration of 6–11 ppb. Therefore, its removal from water sources as an emerging contaminant is greatly desired.

Methods and Results:

In the current work the reactor setup was equipped with two iron plate electrodes located in the center of the electrochemical cell with immersed dimensions of 7×2×0.2 cm. Response surface methodology (RSM) under CCD category was used as a set of mathematical and statistical techniques for analysis and modeling the obtained results Experiments were done under five levels of various operational parameters (3). Mineralization yield of 99.5 % was obtained under optimal experimental conditions, namely 5.75 mg L-1 initial AC concentration, 2.75 pH solution, 122.5 µL L-1 H2O2, 8 mA cm-2 current density at equilibrium time of 8 min. The predicted removal efficiency of 99.4% was in satisfactory agreement with the obtained experimental removal efficiency of 98.7%. Using ordinary radical scavengers demonstrated that hydroxyl radical (•OH) was the main oxidant species contributed to degradation of AC under the EF process.

Conclusions:

The excess iron (II) scavenged the active radicals and diminished the concentration of •OH available to react with AC. The obtained results demonstrated a satisfactory correlation between experimental removal efficiency of 98.7% and predicted removal efficiency of 99.4% with the correlation coefficient of 0.9545.

Keywords: Acetaminophen, Mineralization, Advanced oxidation process, Response surface methodology

The Influence of Pluronic F68 on Physicochemical Properties of Milled Carvedilol

Mina Shafiee, Panah Darabad, Noushin Bolourchian*

P26

Authors' Affiliations:
Department of Pharmaceutics and Pharmaceutical Nanotechnology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Mina Shafiee
Panah Darabad

***Correspondance:**
Noushin Bolourchian

Introduction:

Milling, as a mechanical process, is widely used to reduce the particle size of drug crystals, in order to improve the dissolution rate and hence the bioavailability of poorly-soluble compounds (1). The aim of the present study was to investigate the effect of pluronic F68 (F), a hydrophilic carrier, on physicochemical properties and dissolution behavior of carvedilol (CAR) after wet milling process (2). CAR, which is commonly used in the treatment of hypertension and heart failure, is a poorly water-soluble drug with low oral bioavailability (3).

Method:

Drug suspensions were prepared using pluronic F68 containing aqueous solutions with different CAR-F ratios of 1:0.25 to 1:1. After wet milling, the obtained samples were freeze dried and studied for their dissolution and particle size. Infrared spectrophotometry (IR) and differential scanning calorimetry (DSC) were also performed on the best samples.

Results:

According to the results, all wet milled samples improved CAR dissolution significantly (P 0.05). Decreasing the CAR: F ratio resulted in higher dissolution efficiencies (DE). The best result was obtained for the ratio of 1:1 with DE= 63.03 % compared with the intact CAR (12.11 %), related physical mixture (39.20 %) as well as wet milled drug in the absence of F (45.67 %). In fact, the DE was more than 5 times improved for the best sample in comparison with CAR. This could be due to the presence of hydrophilic carrier and decreased particle size after milling process (D0.9= 86.3 and 38.2 µm for CAR and the best sample, respectively). IR and DSC analysis ruled out any chemical reactions between the ingredients during wet milling process.

Conclusion:

The presence of pluronic F68 as a hydrophilic carrier has a positive influence on wet milled CAR dissolution.

Keywords: Carvedilol, Dissolution, Pluronic F68, Wet milling

Comparison of dissolution profiles of ibuprofen-phospholipid pellets

Javid Davoodi*, Mostafa Amirinejad, Mohammad Reza Abbaspour, Ali Badiee

P27

Authors' Affiliations:
Student Research Committee, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract Presenter:
Javid Davoodi

Correspondance:
Javid Davoodi

Coauthors:
Mostafa Amirinejad
Mohammad Reza Abbaspour
Ali Badiee

Introduction:

In vitro dissolution has been recognized for six decades as an important element and used both in drug development and quality of assessment, especially for poor soluble drugs. Ibuprofen is known as a poorly water soluble NSAID and causes gastrointestinal (GI) irritation. It was shown that a promising approach to increase dissolution rate and bioavailability and reduce GI toxicity of NSAIDs is associated with phospholipid. The association has a viscose and semi-solid nature which is hard to administration. In this work we studied the physicomechanical properties of PA pellets and its effects on release profiles, comparing with ibuprofen pellet.

Methods:

Ibuprofen pellets and ibuprofen-phospholipid association (PA) pellets in four drug contents (20%, 30%, 40% and 50%) were prepared by extrusion-spheronization. Mechanical strength of pellets was tested by material testing. Morphology of pellets, shape factors, and their surface characteristic were investigated by image analysis and electronic microscope images before and after dissolution. Dissolution test also was conducted in a USP Method 1 (rotating basket) apparatus in phosphate buffer (pH 7.2), phosphate buffer (pH 7.2) + 2% SDS, and HCl 0.1 N.

Results:

The results showed that using suitable composition of solid components and granulation fluid, pellets with desirable size, shape, and sphericity could be produces. The PA-pellet formulation had faster drug release compared with ibuprofen pellets and the PAs ratio had considerable effect on their dissolution profiles.

Discussion and Conclusion:

This study shows that phospholipid- association improves dissolution rate of ibuprofen pellets via increasing ibuprofen solubility by reducing crystallinity in solid state or micelle formation in dissolution media. Overall results revealed the feasibility of preparing desirable pellets containing ibuprofen-phospholipid associated with improved release properties which can be administered as hard gelatin capsules.

Keywords: Ibuprofen, Phospholipid-association, Pellet, Dissolution

Evaluation of toxic effects of polyethylene glycol derivative surfactants from brij ether on the biological membrane using Red Blood Cell model

Maryam Alaei, Masih Hasani, Payam Khazaeli*

P28

Authors' Affiliations:
Pharmaceutics Research Center, Neuropharmacology Institute, Kerman University of Medical Sciences, Iran.

Abstract Presenter:
Maryam Alaei

****Correspondance:***
Payam Khazaeli

Coauthors:
Masih Hasani

Introduction:

Surface active agents have been used in pharmaceutical formulations for several aims, so the study of the effect of these agents on biological membranes is necessary. The aim of this study is the evaluation of the effect of a group of surfactants including polyoxyethylenealkylether (brijs: 35, 52,56,58,72 and 92) on red blood cells (RBC) as a model for biological membranes. Also in this study some physicochemical properties including Emulsification index (E24), Foam producing activity (Fh), and Critical Micelle Concentration (cmc) were studied.

Method:

In this study the hemolytic effect of six non-ionic surfactants from brij category were evaluated. Surfactants solutions were mixed with 0.2 ml of surfactants' solution incubated in two different temperatures for three different times. The absorbance of the samples were determined by UV spectrophotometer. Each test was done 3 times. The results were shown by mean± SD. Fh and cmc were also determined for each surfactant solution.

Results:

All of the surfactants solutions showed hemolysis. In concentration less than cmc, the hemolysis was lower than the concentration above the cmc. Comparing the six studied surfactants, brij 56 has the highest hemolytic effect and the brij 72 has the lowest one. The values of E24 and Fh have good correlation with hydrophilic-lipophilic balance (HLB) values. Increasing in HLB value leads to increase the studied.

Conclusion:

According to the results of this study we shall use brijs at concentrations lower cmc in parenteral formulations. On the basis of our results, the use of brijs with low hemolytic effect such as brij 72 is preferred in pharmaceutical preparations. Because of more interaction of some brijs like as brij 56 with biological membranes, we can use these agents as penetration enhancer in some new drug delivery system like noisome.

Keywords: brij, biological membrane, hemolysis

Microwave Generated Solid Dispersions Containing Carvedilol-PEG 6000

Maedeh Barati, Noushin Bolourchian*

P29

Authors' Affiliations:
Department of Pharmaceutics and Pharmaceutical Nanotechnology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Maedeh Barati

Correspondance:
Noushin Bolourchian

Introduction:

Carvedilol, used in the treatment of hypertension and congestive heart failure, belongs to BCS (Biopharmaceutical Classification System) class-II drugs, with a poor water solubility and dissolution rate. Solid dispersion is one of the methods which is widely used to improve the dissolution rate of poorly soluble compounds. Microwave (MW) irradiation is a well-known technique for heating, drying, and melting. In comparison with conventional heating, MW irradiation is a rapid and energy-saving method with no overheating at the surface.

The purpose of this study was to improve the dissolution rate of carvedilol by the solid dispersion technique using MW irradiation in the presence of polyethylene glycol (PEG) 6000.

Methods and Results:

Different drug-polymer ratios were mixed and irradiated for 2 and 10 minutes (MW-2 and MW-10). Dissolution studies were conducted on the prepared samples using the USP apparatus II (paddle) in phosphate buffer solution (pH= 6.8). The solubility and dissolution efficiency (DE %) were calculated and compared to the pure drug and the related physical mixture (PM). The samples were also characterized using differential scanning calorimetry (DSC) and infrared spectroscopy (IR).

Based on the results, in all of the irradiated samples the dissolution of carvedilol improved significantly ($P < 0.001$). The best result was obtained for MW-2 (drug: polymer ratio of 1:5) with approximately two folds increase in dissolution efficiency (DE120 = 62.8 %) compared with the carvedilol (DE120 = 31.2 %) and the related physical mixture (DE120= 43.1 %). The solubility of above mentioned sample was also improved significantly ($P < 0.001$) in comparison with the intact drug. According to the DSC and IR analysis, there was no chemical reaction between ingredients during the preparation method.

Conclusions:

MW irradiation method provides a promising way to enhance the dissolution rate of carvedilol by solid dispersion technique in the presence of PEG 6000 as a hydrophilic carrier.

Keywords: Carvedilol, Dissolution, Microwave, Polyethylene glycol, Solid dispersion

Controlled Release Behavior of Novel Particle-Like Structural of Ibuprofen-Intercalated Ca/Al- LDHs and Antioxidant Study

Amir Mohammad Bagheri, Mehdi Ranjbar*

P30

Authors' Affiliations:
Student research committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Amir Mohammad Bagheri

***Correspondance:**
Mehdi Ranjbar

Abstract:

The control of the drug release from drug carriers, embodying control of both the release rate of a drug and the delivery of this drug to a specific organ or location in the body (i.e., targeting), has been a major goal in drug delivery research over the last two decades.1,2 Magnetic nanoparticles have, thus, received much more attention for biomedical applications, meeting the demand of versatile, high-performance controlled release systems. Recently, Sokolova and Epple reviewed inorganic nanoparticles as carriers of nucleic acids into cells.13 One class of inorganic nanoparticles, layered nanoparticles, especially the layered double hydroxides (LDH), have attracted considerable interest as effective drug release systems. In this regard, the application of suitable (e.g., biocompatible, biodegradable with low or null toxicity) nano particles in drug delivery is very important on account of their small size, customized surface, improved solubility, and multi-functionality and is expected to exhibit maximum therapeutic efficacy, when compared to the conventional drugs. Hence, pertinent to this area, a plethora of nanoparticles, e.g., polymeric

0.495 Ca(NO3)2·6H2O and 0.165 (M) Al(NO3)3·9H2Owere dissolved in 250ml of water to synthesize Ca\Al LDH with Mg: Al ratio of 3:1. To maintain the pH of the mixed precursor solution at 8, ammonia was dropwise added to it with constant stirring for 24 h. The appearance of a white gelatinous precipitate indicated the formation of Ca/Al-LDH. The precipitate was collected by centrifugation and repeatedly washed by redispersing it in water followed by centrifugation (at 3000 rpm for 5 mins) to remove excess nitrate anions. The washed LDH precipitate was then oven dried at 100C to get Ca/Al-LDH nanopowder.

In the present study salicylate intercalated Ca/Al-LDH nano hybrid were synthesized using the co-precipitation method. Successful intercalation of Ibuprofen in the interlayer space of Ca/Al-LDH was confirmed by XRD data and FTIR Spectroscopy of the intercalated nano hybrid. Ibuprofen was loaded to the extent of 30wt.% in the LDH Ibuprofen formulation. The cumulative release profile of Salicylate in PBS (pH = 7.4) medium revealed nearly 80% release in 24 h at 37 °C, and the entire drug was released over a period of 48 h. First order release kinetics model was fitted very well with release behavior of salicylate in pH = 7.4, revealing the fact that the salicylate release was primarily through a combination of Ibuprofen drug diffusion and nano LDH dissolution mechanism. This work supports that Ca/AL-LDH nano powder can be a very effective carrier for controlled and sustained release of Ibuprofen under physiological conditions.

Keywords: Drug delivery, Ca/Al-LDH, Nanocomposites, Nanostructures.

Formulation and Charactrization of Zr/Al-LDHs as Minoxidil in Vitro Efficient Delivery

Elnaz Tavakoli Nejad, Mehdi Rezaeifar, Mehdi Ranjbar*

P31

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Elnaz Tavakoli Nejad

****Correspondance:***
Mehdi Ranjbar

Coauthors:
Mehdi Rezaeifar

Abstract:

In the past two decades' scientists have attention to layered double hydroxides (LDHs) as cost effective, environmentally friendly adsorbents [1] and new diagnostic systems that are effective in the targets, detection and recognition and specialized treatment of diseases [2]. Nanotechnology with the important strategy in preparation of the new structures such as LDHs exhibited diagnosis possible at the cellular which this may significantly improve the diagnosis different concentrations of drugs. The chemical composition of LDH is generally expressed as [M(II)1-xM(III)x(OH)2]. Y-. zH2O, where M(II) is divalent metal cation, M(III) is trivalent metal cation, 'Y' is interlayer anionic species, 'n' is charge on interlayer anion, 'x' and 'y' are fraction constants. By virtue of this unique structure, LDHs have been widely explored as inorganic composite materials for drug/gene delivery, demonstrating controllable drug release and excellent biocompatibility. Compared with bulk LDHs, monolayer LDH (MLDH) nanosheets exhibit much higher specific surface and more combinative sites, leading to greatly enhanced surface activity for drug loading.

Layered double hydroxides (LDHs), have been known for many decades as catalyst and ceramic precursors, traps for anionic pollutants, and additives for polymers. Recently, their successful synthesis on the nanometer scale opened up a whole new field for their application in nanomedicine. Here we report the efficacy of Zr- xAlx (NO3) x (OH)2 LDH nanoparticles as a carrier and for controlled release of one of the non-steroidal anti-inflammatory drugs (NSAID), sodium Minoxidil. Zr- xAlx (NO3) x (OH)2. nH2O nanoparticles were synthesized using coprecipitation method froman aqueous solution of Zr(NO3)2.6H2O and Al(NO3)3.9H2O. Minoxidil was intercalated in the interlayer space of Zr- Al LDH after suspending nanoparticles in 0.0025(M) HNO3 and 0.75 (M) NaNO3 solution and using anion exchange method under N2 atmosphere.

In the present study salicylate intercalated Zr/Al-LDH nano hybrid were synthesized using the co-precipitationmethod. Successful intercalation of Minoxidil in the interlayer space of Zr/Al-LDH was confirmed by XRD data and FTIR Spectroscopy of the intercalated nano hybrid. Minoxidil was loaded to the extent of 30wt.% in the LDH Minoxidil formulation. The cumulative release profile of Minoxidil in PBS (pH = 7.4) medium revealed nearly 80% release in 24 h at 37 °C, and the entire drug was released over a period of 48 h.

Keywords: Minoxidil, Zr/Al-LDHs, Antioxidant, Drug delivery

Development and evaluation of ibuprofen-phospholipid association aimed for improved bioavailability

Mostafa Amirinejad*, Javid Davoudi , Ali Badiee, Mohammad Reza Abbaspour

P32

Authors' Affiliations:
Student Research Committee, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Mostafa Amirinejad

****Correspondance:***
Mostafa Amirinejad

Coauthors:
Javid Davoudi
Ali Badiee
Mohammad Reza Abbaspour

Introduction:
Prescription of ibuprofen, one of the most widely used non-steroidal anti-inflammatory drugs (NSAIDs), is limited by relatively insolubility in water and gastrointestinal side effects. In the current paper, association of ibuprofen with phosphatidylcholine is studied.
Methods:
Ibuprofen-Phosphatidylcholine association were prepared (in 1:0.25, 1:0.5 and 1:1 molar ratios) in the presence of ethanol. Drug content, nuclear magnetic resonance (NMR), Fourier-transform infrared spectroscopy (FT-IR), X-ray diffraction (XRD), differential scanning calorimetry (DSC), Photon Correlation Spectroscopy (PCS), saturated solubility and in vitro dissolution tests were applied for the IPAs and plain ibuprofen.
Results:
As IPA 1:0.25 was precipitated by evaporation stress, it was assumed that there were few chances of interaction between ibuprofen and phosphatidylcholine in this molar ratio and the obtained association would be less stable. Thus, it was removed from further steps of the experiment. Drug content in the IPA 1:1 and 1:0.5 was found to be 96.7±2.4% and 98.0±1.8%, respectively. DSC thermograms and FT-IR, NMR and XRD patterns confirmed the formation of the phosphatidylcholine association. PSC results demonstrated that mean particle size of IPA 1:1 and IPA 1:0.5 were 254.8±31.8 nm and 338.6±45.3 nm, respectively, and zeta potential of the IPAs was negative. IPA 1:1 and 1:0.5 showed 112% and 156% improvement in solubility in phosphate buffer pH 7.2 medium and 20% and 25% decrease in solubility in HCl pH 1.2. The IPAs dissolution rate was found to be increased at the end of 120 minutes of dissolution study in the simulated intestinal medium, whereas the dissolution rate of the IPAs was reduced at the end of 180 minutes of dissolution study in the simulated gastric medium.
Conclusion:
It is concluded that the phosphatidylcholine association of ibuprofen may be of potential use for improving the ibuprofen solubility and hence its bioavailability. Furthermore, considering the decrease of dissolution rate of ibuprofen in gastric simulated medium, it is predicted that the IPAs may also reduce gastrointestinal toxicity of ibuprofen. Comparing the types of IPAs, IPA 1:0.5 showed more improved characteristics and bioavailability.

Keywords: Ibuprofen, Bioavailability, Association, Phosphatidylcholine

Preparation and evaluation of vancomycin fusogenic Liposomes for broadening and potentiating its antibacterial efficacy

Azadeh Serri, Hamidreza Moghimi, Arash Mahboubi, Afshin Zarghi

P33

Authors' Affiliations:
Shahid beheshti university of pharmacy, faculty of pharmaceutics

Abstract Presenter:
Azadeh Serri

****Correspondance:***
Azadeh Serri

Coauthors:
Hamidreza Moghimi
Arash Mahboubi
Afshin Zarghi

Abstract:

Gram-negative bacteria are resistant to many antibiotics (like glycopeptide antibiotics such as vancomycin hydrochloride) because their outer membrane acts as a barrier which hinder drug entrance into the bacteria. In this investigation, we have investigated fusogenic liposomes to overcome bacterial resistance. This kind of liposomes may interact by bacterial lipidic outer membrane and hence introduce the antibiotic into the bacterial periplasmic space.

Lipid film hydration method and sonication method were used to prepare vancomycin liposomes from a phospholipid mixture composed of either DPPC: DOPE: Chol or DPPC: DOPE: CHEMS, both in 1: 0.5: 1 molar ratios. Broth microdilution method was used to evaluate antibacterial properties of prepared liposomes. As vancomycin is a very large hydrophilic molecule the encapsulation efficiency of liposomes, prepared by lipid film method was in a range of approximately 0.1 to 9 % for different formulations, whereas liposomes prepared by probe sonication had smaller size and were also more stable.

Vancomycin encapsulation in liposomes can be used to enhance antibiotic delivery into bacteria. We have previously described a novel, polymeric nanocarrier for vancomycin which shows better in vitro efficacy compared to free vancomycin, while vancomycin encapsulation in lipid nanocarriers conversely decreased antibacterial effects of vancomycin and caused enhancement in MIC values, compared to those of free vancomycin. The enhanced MIC values of vancomycin liposomes may be related to retardant effect of this nano carrier, which may have hindered vancomycin permeation and release into the bacterial inner space or may form carrier-drug complexation. Retardant effects of liposomes have been previously described in literature, however the results are very controversial. In order to establish the best suitable lipid mixture and liposomal formulation which potentiate antibiotic efficacy, further investigations are crucially needed.

Keywords: Fusogenic liposomes, Vancomycin hydrochloride, bacterial resistance

Preparation and physicochemical evaluation of thermosensitive chitosan-gelatin-glycerol phosphate hydrogel containing chitosan/chondroitin sulfate nanoparticles for delivery of rosuvastatin in bone ti

Zahra Ebrahimi*, Mahboubeh Rezazadeh, Vajihe Akbari

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P34

Authors' Affiliations:
School of Pharmacy and Pharmaceutical sciences, Isfahan University of Medeical Sciences, Iran.

Abstract Presenter:
Zahra Ebrahimi

****Correspondance:***
Zahra Ebrahimi

Coauthors:
Mahboubeh Rezazadeh
Vajihe Akbari

Introduction:

Bone loss diseases such as osteoporosis and bone defects have still remained a major clinical problem. It has been demonstrated statins have potential to simulate bone regeneration since they alter bone metabolism. Based on literature review, localized sustained administration of statins in bone sites would enhance their efficacy in bone reconstruction. The purpose of the current study was to develop a localized controlled delivery system from rosuvastatin (RSV) by incorporating RSV-loaded chitosan/chondroitin sulfate (CTS/CS) nanoparticles into thermosensitive Chitosan/Glycerophosphate/Gelatin (CTS/GP/G) hydrogel.

Methods:

The purpose of the current study was to develop an injectable carrier for localized controlled delivery of rosuvastatin (RSV) using a 2-level system: (i) incorporation of RSV within chitosan/chondroitin sulfate nanoparticles (NRSV) and (ii) inclusion of freeze-dried NRSV into chitosan (CTS)/glycerophosphate (GP)/gelatin (G) mixtures as thermally sensitive hydrogel. Both of the mixtures were embedded with 1.5 or 3 % w/v of NRS. The hydrogels loaded with NRSV were subjected to physico-mechanical and biological characterizations including rheological properties, dissolution tests, release rate of RSV, cell viability, alkaline phosphate activity, and cell calcification using human osteoblast-like MG-63 cells.

Results:

Mean particle size, zeta potential, entrapment efficiency, and mean release time of the optimized NRSV were confirmed 283.2 ± 16 nm, -31.2 ± 6.8 mV, 63.1 ± 4.2 %, and 6.14 ± 0.3h, respectively. The hydrogels containing 3 % w/v NRSV were solutions with low viscosities at 4 ˚C converted to a semisolid upon increasing the temperature to 33-36 ˚C. The release rates of RSV from the NRSV-embedded hydrogel were significantly slower than that of NRSV. As revealed by alkaline phosphatase and mineralization assays, NRSV-embedded in CTS/GP/G hydrogel had the most promotive effect on differentiation of osteoblasts among other mixtures.

Conclusion:

NRSV-embedded GTS/GP/G are predicted to have great potential in bone regeneration applications.

Keywords: Bone tissue engineering, Thermosensitive hydrogel, Chitosan/chondroitin sulfate nanoparticles, Rosuvastatin, Osteoblast-like MG-63 cells

Synthesis and characterization of magnetic graphene oxide nanosheets as dispersive solid phase extraction sorbent for determination of Allopurinol

Sam Talaei, Niloofar Jafari, Elham Asadian, Maryam Bavand Savadkouhi, Fatemeh Ghorbani Bidkorpeh*

P35

Authors' Affiliations:
School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Sam Talaei

****Correspondance:***
Fatemeh Ghorbani Bidkorpeh

Coauthors:
Niloofar Jafari
Elham Asadian
Maryam Bavand Savadkouhi

Introduction:

Most of pharmaceutical compounds, metabolized or not metabolized, enter to drinking water and biological fluids. One of the most important environmental complications is the determination of trace amounts of pharmaceuticals. Scientists try to find sensitive, accurate and precise methods of pharmaceutical determination. The objective of this study was the synthesis of magnetic graphene oxide (MGO) nanosheets using Hummers method and investing adsorption efficiency of trace amount of Allopurinol by solid phase extraction method from water samples.

Methods:

The nanomaterial was prepared using Hummers method and was magnetized by coprecipitation. Physical and structural characterization of the synthesized magnetic graphene oxide adsorbent nanosheets were analyzed using XRD, SEM, FT-IR, and UV spectrophotometry techniques. The studied API determined by validated HPLC and UV spectrophotometry methods. Furthermore, this study evaluated the influence of different parameters such as pH, time, different kinds of solvents and API concentrations in adsorption and desorption processes. The application of the nanosheets in microdispersive solid phase extraction of allopurinol from real samples was evaluated.

Results:

The SEM and X-ray image proved the morphology of magnetic graphene nanosheets and an average particle diameter of about 30 nm. Parameters were optimized for adsorption of allopurinol on MGO nanosheets as pH = 3 and the best adsorption time as 1 minute. The amount of adsorption decreased up to 60 minutes. Desorption studies showed that the best solvent for allopurinol was 0.1N HCL and desorption increased up to 60 minutes. adsorption isotherms on MGO followed the Temkin model proving allopurinol electrostatic bonding between positive and negative of MGO. The comparative study showed magnetic graphene oxide is a better absorbent compared to C18 for solid phase extraction of allopurinol.

Conclusion:

Considering the results of adsorption and desorption studies of Allopurinol on magnetic graphene oxide nanosheets, designing dispersive solid phase extraction utilizing magnetic graphene oxide for allopurinol is an easy and simple way of extraction from water or biologic sample

Keywords: Allopurinol, Magnetic Graphene Oxide Nanosheets, Solid Phase Extraction

Tetrac-decorated chitosan-coated PLGA nanoparticles as a new platform for targeted delivery of SN38

Mahsa Zahiri, Mohammad Ramezani, Mona Alibolandi*

P36

Authors' Affiliations:
Department of Pharmaceutical Nanotechnology, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Mahsa Zahiri

****Correspondance:***
Mona Alibolandi

Coauthors:
Mohammad Ramezani

Abstarct:

Colorectal cancer is the third most diagnosed cancer in both men and women worldwide and it is estimated that 135,430 new cases be diagnosed in 2017 in USA. Also, it was reported that about 50,260 people would die from colorectal cancer in 2017. One of the emerging targets for drug delivery is the Avb3- integrin expressed on the surface of endothelial cells and vascular smooth muscles which stimulation by thyroid hormones leading to induction of proliferation of tumour cells and angiogenesis. Tetrac (tetraiodothyroacetic acid) is a deaminated thyroid hormone analogue which specifically binds to Avb3 integrin overexpressed on tumour endothelial cells and inhibits the binding of its agonists which are thyroid hormones. It was demonstrated that L-thyroxine (T4) induces the proliferation of cancer cells by activation of MAPK (ERK1,2) signalling pathway. It was shown that tetrac downregulates the vascular supply to human tumour tissue by blocking the binding of T4 to Avb3 integrin or angiogenesis induced by vascular endothelial growth factor (VEGF). New integrin-targeted nanoparticles made of chitosan-stabilized PLGA matrix was developed to specifically target colon adenocarcinoma. To this aim, SN38-encapsulated chitosan-coated PLGA NPs were conjugated with tetrac for integrin receptor-guided delivery. To provide a sustained release pattern for SN38, it was loaded into nanoparticles using single emulsion method. The size of NPs were 174.23 ± 6.12 nm with drug encapsulation efficiency and loading content of 73.16 ± 11.15 and 4.45 ± 0.31, respectively. The in vitro results confirmed that the designed nanoplatform showed specific cellular uptake and cytotoxicity in integrin overexpressing cancer cells and provided a sustained release profile for SN38. Additionally, an increased therapeutic potency of targeted formulation over both nontargeted and free drug was shown in vivo

Keywords: chitosan-coated PLGA nanoparticles, Tetrac, targeted drug delivery

Chitosan- Alginate nanoparticles for Glaucoma treatment

Roya Ilka, Marzie Abnoos, Mojdeh Mohseni, Bita Mehravi*

P37

Authors' Affiliations:
Iran University of Medical Sciences, Teharn, Iran.

Abstract Presenter:
Roya Ilka

****Correspondance:***
Bita Mehravi

Coauthors:
Marzie Abnoos
Mojdeh Mohseni

Introduction:

Timolol-Malate is one of the most important drugs used to reduce intraocular pressure to treat glaucoma but approximately 5% of the drug penetrates into the target area and it is still effective. To solve this problem, use the carriers were produced by nanotechnology

Methods:

Biocompatible nanoparticles (Chitosan- Alginate nanoparticles) were designed and synthesized to delivery Timolol-Malate to treat glaucoma.

After synthesis of Chitosan- Alginate nanoparticles, physical and chemical properties were evaluated by FTIR, SEM, DLS and TEM. The percentage of drug loading in the nanoparticle has been investigated and the releasing rate of the drug from the nanoparticles determined by a dialysis bag in the external medium. Ex-vivo analysis performed on the rabbit's eye by using FRANZ diffusion cell and a fluorescence microscope.

Results:

Shape of Chitosan-alginate nanoparticles were spherical with dimensions of 80-100 nm. The nanoparticles remained stable in the phosphate buffer for up to 6 months (pH~7.4). The drug loading rate of these nanoparticles was %93. Releasing pattern was slow by a burst release about (%20) at first hour. Next, about %35 of drugs were released after 5 hours, then releasing pattern reached sustained, and after approximately 24 hours, about %45 of the drug has been released and transferred from the nanoparticles to the environment. The results of the ex-vivo studies indicated that nanoparticles penetrate to the cornea, and then to the posterior segments of the cornea.

Conclusions:

This study concludes that Chitosan- Alginate nanoparticles are suitable candidates for controlled delivery of Timolol. They also have ability to cross the cornea to treat glaucoma.

Keywords: Nanoparticles, Timolol, Ocular delivery, synthesis, characterization

Formulation and evaluation of Polylactic Acid/Calcium Oxide Nanocomposites for Antibactrial Study

Zahra Zeynalizadeh Rafsanjanipur, Mohammad hasan Moshafi, Mehdi Ranjbar*

P39

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Zahra Zeynalizadeh Rafsanjanipur

****Correspondance:***
Mehdi Ranjbar

Coauthors:
Mohammad hasan Moshafi

Abstract:

New drug deliveries include: Drug delivery at a single time and with controlled doses for specific drug targets. In this study at first along with the development of human life and the rapid and uncontrolled growth of microorganisms [1, 2], nanotechnology has provided opportunities for discovering the antibacterial effects of metal nanoparticles. In addition to the small size, nanoparticles have the large surface to volume ratio which provides a larger contact area with the ambient and thereby cause a considerable increase in antimicrobial properties [3]. In this study, a polylactic acid/calcium oxide (PLA/CaO) nanofilm was prepared using microwave-assisted and micellar methods. Physicochemical and microbiological properties of the nanofilms were investigated. Microwave micellization of CaO was done at 50° C and 600 Watt microwave power. PLA was prepared through the hydrothermal process in a stainless steel autoclave at 150° C and under pressure of 10 bar. For making the PLA/CaO nanofilms, different concentrations of CaO (0.25-1%) were placed on PLA with three concentrations (0.5-1%). Then, PLA/CaO nanofilms were prepared under 10 minutes pulsed microwave radiation. The on/off cycles were done with the ½ ratio. Particle size and morphology of PLA/CaO nanoparticles were investigated by XRD and SEM analysis. In this research, nanoparticles were first made in different sizes and stabilizing concentrations, and then microbiological culture media were prepared using MIC (Minimum Inhibitory Concentration) and several gram-negative bacteria were examined for several nanostructures. To prepare 100 cc of the medium, weigh the hinton broth 2.1 grams, and in another 500 ml, it dissolves. Then we make microbial leachate from the tested microorganisms and compare them with the half McFarland their turbidity, to the extent that they are half McFarland. The antimicrobial properties of PLA/CaO nanofilms were evaluated by MIC method in a Mueller Hinton culture medium using 4 gram-positive bacteria (Staphylococcus epidermidis -Bacillus cereus, ...) and 4 gram-negative bacteria (Klebsiella-Pseudomonas syringae, ...). The results show that the growth is inhibited in concentration range of 16-32 µg/ml for gram-positive bacteria and 32-64 µg/ml for gram-negative bacteria.

Keywords: Nanostructures, Polylactic Acid/Calcium Oxide, Gram Positive and Negative Bacteria, Antibactrial

Synthesis and optimization of fluorescent labeled chitosan nanoparticles specific for intestinal drug delivery

Golshan Karimi Zindashti, Fatemeh Rahbarizadeh, Sepide Khaleghi*

P40

Authors' Affiliations:
Tehran Medical Science Islamic Azad University, Tehran. Iran.

Abstract Presenter:
Golshan Karimi Zindashti

***Correspondance:**
Sepide Khaleghi

Coauthors:
Fatemeh Rahbarizadeh

Abstract:

Chitosan is a biodegradable, biocompatible polymer regarded as a safe substance for human dietary. Nanoparticles (NP) prepared with chitosan and chitosan derivatives typically possess a positive surface charge and mucoadhesive properties that can adhere to mucus membranes and release the drug payload in a sustained-release manner so it can be a suitable carrier for intestinal drug delivery, because of more absorption and basic environment. Current study is focused on preparing several kinds of chitosan formulations and different concentrations of cross linking agents in various conditions and characterization for achievement of most stable and biocompatible nanoparticle which labeled by FITC for in vitro and in vivo tracking. Preparation of chitosan nanoparticles is done by Ionotropic gelation method using different concentration of sodium tripolyphosphate (TPP) as cross-linking agent. Moreover, the synthesis of FITC-labeled chitosan was based on the reaction between the isothiocyanate group of FITC in different concentration and the primary amino group of chitosan. The combination of time, pH and salt concentration and the proteinase enzyme control system for chitosan nanoparticles were investigated in order to synthesize a special and perfect chitosan nanoparticle for especially intestine drug delivery. Physical characterizations of nanoparticles were estimated by DLS and TEM as well as conjugation and covalent links were confirmed by FITR. The stability of nanoparticles was confirmed by DLS. Chitosan nanoparticles' size was determined by Transmission electron microscopy (TEM). The particle size was determined to be about 100±20 nm. Hydrodynamic diameter was measured by DLS around 150±20 nm. In FTIR, according to different absorption peak or cross link, protein conjugation to the chitosan nanoparticles with control samples was confirmed. UV spectroscopy was used to determine the efficiency of conjugation which was over 70%. All of these findings favor the notion that the FITC conjugated chitosan nanoparticles produced in our work may offer promise for the development of an efficient therapeutic agent and diagnosis carrier for colon cancer in the future. However, further investigation is required to provide more evidence on different aspects of the targeting activity and stability of this nanoparticle in in vivo.

Keywords: Chitosan nanoparticle, FITC, Colon cancer, Intestine, Stability.

Formulation and Charactrization of Hydroquinone Nanoparticles Based Nano Emulsions: A Cosmetic Study

Mohammadhasan Yeganeh Dastgerdi, Payam Khazaeli, Mehdi Ranjbar*

P41

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Mohammadhasan Yeganeh Dastgerdi

Correspondance:
Mehdi Ranjbar

Coauthors:
Payam Khazaeli

Introduction:

Lipid nanoparticles with solid particle matrix are derived from o/w emulsions by simply replacing the liquid lipid (oil) by a solid lipid, i.e. being solid at body temperature. The first generation of solid lipid nanoparticles (SLN) was developed at the beginning of the nineties [1]. They were produced from a solid lipid only. In the second generation technology of the nanostructured lipid carriers (NLC), the particles are produced by using a blend of a solid lipid with a liquid lipid, this blend is also solid at body temperature [2]. The production process is identical for both SLN and NLC particles. The solid lipid or lipid blend is melted, the pharmaceutical or cosmetic active? Dissolved in the melted lipid phase which is subsequently dispersed by high speed stirring in a hot aqueous surfactant/stabilizer solution of equivalent temperature. The obtained pre-emulsion is homogenized in a high pressure homogenizer yielding a hot o/w nano emulsion [3].

Methods and Results:

In this study for the first step 60mg/l of oleic acid and 30mg/l of sodium dodecyl sulfate were solved in 20 ml distilled water and 100 µL surfactant added drop by drop to above solution then solution placed under vigorous stirring at 50 ° C for 120min and in final pH adjusted to 7.5–8 with 5ml NaOH 2M. For the second stage, solutions were kept at room temperature, in the next section 100 mg/L of carbomer weighed and solved in ratio 3:1 ml distilled water/chloroform, then pH adjusted between 6-7.5 with digital pH meter under vigorous stirring at 50 °C. For creating a suitable substrate 20 mg/L of polylactic acid as biodegradable copolymer was solved in 20 ml of distilled water in ratio of 1:1 ml distilled water/DMF and then added to carbomer solution. In the final steps hydroquinone stocks such as 5%, 10% and 15% were added to latter solution.

Conclusions:

This is one of the most effective ways to sustained drug release from a micellar delivery system. This approach typically involves forming a conjugate of the drug with the hydrophobic part of an amphiphilic polymer and then forming micelles out of this conjugate. Such a formulation will add two steps in the release of the drug. Polymers with very low CMC (0.1 µg/ml) can be used for prolonging the circulation time before the micelle degrades.

Keywords: Hydroquinon, Cosmetic, Nanoemultion, Nanostructures

Preparation and evaluation of electrospun nanofibrous scaffold of poly (lactic-co-glycolic acid)/phenytoin and polyvinyl alcohol/honey as a wound dressing for diabetic ulcer

Sahar Saebi, Sheida Shahverdi, Aliakbar Ghareaghaji, Rasoul Dinarvand*

P42

Authors' Affiliations:
Tehran University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Sahar Saebi

****Correspondance:***
Rasoul Dinarvand

Coauthors:
Sheida Shahverdi
Aliakbar Ghareaghaji

Introduction:

Diabetic and chronic ulcers can affect patients' quality of life, and bring major problems for patients and the health care systems. Modern bandage materials are made from electrospun biopolymers containing various active compounds that are beneficial to the healing of wounds. Honey has been an excellent adjuvant for accelerating wound healing over the past centuries. In addition, topical phenytoin is used to promote wound healing in a variety of chronic wounds. These two active compounds can be used as ingredients of scaffold for wound healing.

Methods:

In this study, hybrid electrospinning method was used to prepare a wound dressing scaffold using synthetic and biodegradable polymers, PVA (polyvinyl alcohol) and PLGA (poly (lactic-co-glycolic acid)). Thereafter, honey and phenytoin were loaded in PVA and PLGA, respectively. In order to confirm the mechanical properties of this hybrid nanofiber scaffold, we performed scanning electron microscopy (SEM), mechanical property, water uptake, and contact angle.

Results:

The optimum condition for electrospinning of PVA/honey was obtained at 7.5 Wt% with 80/20 ratio. PLGA solution was loaded by 3% phenytoin. Morphology of nanofibers was determined by SEM. The mean diameter of electrospunnanofibers was 210 nm for PLGA, 238 nm for PVA and 219 nm for the hybrid of PVA and PLGA. In mechanical property, tensile strength of PLGA was higher than PVA. Contact angle in PLGA was greater than PVA which represents higher hydrophobicity of PLGA. Thickness of scaffold was 50µm.

Conclusions:

According to the literature, PVA is a biodegradable, biocompatible, water soluble and non-expensive polymer, but does not hold enough strength to stand alone as a wound healing bandage. However, in this method, adding PLGA as a second part of hybrid scaffold increased tensile strength and contact angle and also decreased water uptake. Mats of electrospunnanofibers generally show very good adhesion to moist wounds. The porous structure of a nanofiber dressing is excellent for the respiration of cells which does not lead the wound to dry up. Nanofiber structure of scaffold promotes skin growth. Moreover, combining phenytoin and honey makes hybrid scaffold potentially applicable as a wound dressing material.

Keywords: electrospinning, wound dressing, polyvinyl alcohol

Sandwich like Polycaprolactone/Gelatin/Polycaprolactone Electrospun Mat for Controled Release of Ceftazidime and Ag nanoparticles

Fatemeh Bagrezaei, Ali Fattahi*

P43

Authors' Affiliations:
Pharmacy School of Kermanshah University of Medical Science, Kermanshah, Iran.

Abstract Presenter:
Fatemeh Bagrezaei

***Correspondance:**
Ali Fattahi

Abstract:
In the present work, sandwich-like polycaprolactone/gelatin/polycaprolactone (PCL/Ge/PCL) multi-layered mats were fabricated by electrospinning method. The sandwich structure membranes with a different thickness of polycaprolactone as the surface layers and gelatin or ceftazidime (CTZ) loaded gelatin as the core layer were electrospun [1]. The profile of drug release from the electrospunnanofibers with presence of polycaprolactone was compared to unmodified gelatine mat and cross-linked gelatine mat [2]. In order to create antibacterial activity in these nanofibers, Ag nanoparticles with concentration of 150 µg/mL was incorporated to each PCL layer. SEM images exhibited that the polycaprolactone and gelatin/ceftazidime nanofibers with an average diameter of 129±22nm and 84±13nm were formed, respectively. The obtained results showed that the drug release rate from ceftazidime loaded PCL/Ge/PCL sandwich like nanofiber mat was slower than the monolayer method [3]. The prepared sandwich structure-like nanofibers with appropriate physicochemical properties and improved potency against Pseudomonas aeruginosa and staphylococcus aureus were formed [4]. All steps in designing the electrospunnanofibers were monitored using different characterization techniques such as powder X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR) and in Vitro Cytotoxicity.

Keywords: PCL, electrospinning, nanofiber, sandwich, ceftazidime

Chitosan, active ingredient in cosmetic industry

Masoud Zare*, Eskandar Moghimipour

P44

Authors' Affiliations:
School of Pharmacy, Marine Pharmaceutical, Science Research Center Ahvaz JundiShapur University of Medical Sciences, Ahvaz, Iran

Abstract Presenter:
Masoud Zare

Correspondance:
Masoud Zare

Coauthors:
Eskandar Moghimipour

Introduction:

Marine organisms have diverse functional roles as a secondary metabolite and these properties can be applied to the developments of novel pharmaceuticals and cosmeceuticals. Cosmetic compounds derived from marine sources having activities with health benefits. Chitin and its deacetylated derivative chitosan are of great interest to the cosmeceutical industry due to their unique biological and technological properties. Their main functions are in skin protecting.

Methods and Results:

The shrimp shells were collected from local fish market 530 g, were washed with warm tap. The shells boiled in water was obtained 430 g, the dried shells were ground into a fine powder. Solid powder obtained from shrimp shell 100g with sodium hypochlorite was used for decolourisation was obtained 77g. To remove the calcium carbonate, the hydrochloric acid concentration 1 M that was obtained 34 g. Sodium hydroxide 1 M reflux for deproteination was obtained 29 g. sodium hydroxide, as deacetylation reagent (50% by weight) was mixed at fixed temperature 100 °C under constant stirring. After 5 h, the solid was filtered, washed with water and 80% (v/v) alcohol until the filtrate was neutral. Then it was oven-dried at 80 °C was obtained 16 g. At the end Chitosan was analyzed by IR test.

With respect to chitosan obtained from shrimp shell, we prepare 3 formulations Cream 1% by Fusion Method that active ingredient in 3 formulations is chitosan with variable ingredients 25 g, 50 g, 75 g and these formulations compare in PH, Viscosity, stability. In PH test was mentioned respectively F1:8/24, F2:8/23, F3:8/21. In viscosity test was mentioned respectively RPM: 5,10,20,25,30, F1: 13079,10493,6269,5639,5359 CP 11%,16%,20%,22%,25%shear stress; F2: 42739,22419,14669,13549,13377 CP 30%,37%,48%,50%,66% shear stress; F3: 28834,16596,8784,7274,6958 CP 21%,27%,28%,31%,34% shear stress.

Conclusions:

The fact that chitosan is one of the richest sources of known and novel bioactive compounds with wide pharmaceutical applications is unquestionable. chitosan is useful for welfare of mankind especially in delivery system, skin protecting, anti-bacterial. Advantage of chitosan as a skin protecting lies in the economy, chitosan have the potential for expanded utilization in cosmetics.

Keywords: marine-cosmetic compounds, chitosan, shrimp shell

Rapid investigation of some variables on dissolution rate of celecoxib

Fariba Hajifathaliha

P45

Authors' Affiliations:
Department of Pharmaceutics, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Fariba Hajifathaliha

****Correspondance:***
Fariba Hajifathaliha

Abstract:
Celecoxib (CXB) is a nonsteroidal anti-inflammatory drug (NSAID) and also a member of BCSII classification system which is characterized by low solubility and high permeability. Since low solubility is highly related to the low bioavailability of this class members, overcoming this issue is one of the greatest concern in pharmaceutical industries. Particle size reduction and adding co-solvent to the formulations, are known as two convenient strategies to improve drug solubility. In this study, we investigated the effect of different grinding times, co-solvent and surfactant presence on the dissolution rate of CXB by co-grinding of this drug with PVP (1:1) or with PVP/SLS (1:1:1) in ball mill apparatus, for different times of 5, 10 and 15 min. Dissolution test was carried out by apparatus II, paddle (50 rpm). According to the results, in unground-binary combination (CXB: PVP), the amount of dissolution within 60 min, reached to the highest level, in comparison with the other un-ground formulations; CXB and ternary combination, (70% vs. 35% and 32% respectively) (P0.05). Likewise, comparison of different formulations which were grounded for 5 min revealed that binary combination in comparison with CXB and ternary combination showed highest amount of dissolution within 60 min (62% vs. 20 and 32%, respectively) (P0.05). Increasing the grinding time, from 5 to 15 min, led to the lower amount of dissolution, as longer time of grinding may cause the formation of more surface charge and as a consequence, more particle agglomeration. Here we could conclude that, different factors such as grinding time and types of additives should be optimized for each drug formulation.

Keywords: Celecoxib, Ball mill, Co-grinding

Preparation and characterization of indomethacin polymeric and phospholipid/polymeric films as potential anti-adhesion barriers

Adrina Efatpanah, Rozhin Talimi, Shahram Rabbani, Seyed Alireza Mortazavi, Azadeh Haeri

P46

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Adrina Efatpanah

****Correspondance:***
Azadeh Haeri

Coauthors:
Rozhin Talimi
Shahram Rabbani
Seyed Alireza Mortazavi

Introduction:

Adhesion is one of the most clinically important postsurgical complications, occurring during healing process of the damaged tissues (1). Few effective treatments are currently available for prevention of adhesion. Polymeric anti-adhesion film could serve as an effective barrier to reduce adhesion. On the other hand, phospholipids (2) and NSAIDs (3) are capable to counterattack postoperative adhesion. For better management of postoperative complications and prevent adhesion, in this study, polymeric and polymeric/phospholipidic films containing an analgesic and inflammatory agent (indomethacin) were developed and characterized.

Methods:

Three polymeric films were prepared using polycaprolactone (PCL) at polymer to drug (P: D) weight ratios of 15, 30, and 45. Soya phospholipid/PCL hybrid films (six formulations) were prepared at same weight ratios (15, 30, and 45) with 30% and 50% lipid percentages. All thin film formulations were prepared using solution casting method. The thickness, drug content, and release profiles (up to 3 weeks) of various formulations were measured. The films were also characterized by scanning electron microscopy (SEM), atomic force microscopy (AFM), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), thermogravimetry analysis (TGA), mechanical strengths, and stability.

Results:

The obtained film formulations exhibited excellent uniformity and mechanical properties. The indomethacin release rate decreased by increasing P: D weight ratio (percentage of drug release after 2 weeks were 87% and 68% for films with 15 and 45 P: D weight ratios, respectively). Incorporation of 30% phospholipid into films increased release rate to 100% in two weeks. In vitro drug release profiles showed enhanced release rate by further increase of phospholipid content to 50% (> 75% drug release in 72 h). FTIR analysis of the thin films revealed no interaction between drug and polymer/phospholipid. SEM and AFM analyses showed smooth film surface, structural integrity, and uniform distribution of drug in film matrixes.

Conclusions:

The biodegradable drug loaded polymeric and polymeric/phospholipidic films were prepared by simple approach and prolonged the duration of drug release for sustained local drug delivery to prevent postoperative adhesion.

Keywords: anti-adhesion film, polycaprolactone, phospholipid, indomethacin, release

Preparation and characterization of Bosentan nanoparticles by using Microfluidic approach

Saeed Siavashy, Newsha Fallah, Madjid Soltani, Fatemeh Ghorbani Bidkorbeh*

P47

Authors' Affiliations:

Faculty of Mechanical Engineering, K. N. Toosi University of Technology, Tehran, Iran.

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

Centre for Biotechnology and Bioengineering (CBB), University of Waterloo, Waterloo, Ontario, Canada

Abstract Presenter:
Saeed Siavashy

***Correspondance:**
Fatemeh Ghorbani Bidkorbeh

Coauthors:
Newsha Fallah
Madjid Soltani

Abstract:

Bosentan as a drug currently has application in the pulmonary artery hypertension (PAH) treatment contains a dual endothelin receptor antagonist. Bosentan illustrates irregular and low bioavailability in aqueous solution due to low solubility and slow rate of dissolution in water. However, recently many efforts have been made to improve its solubility and dissolution rate. One of the most effective approaches is reducing Bosentan particles size resulting in a higher dissolution rate because of the larger effective surface area. The purpose of this project is the synthesis and optimization of Bosentan nanoparticles to enhance solubility and dissolution rate; Thus, to attain this aim precipitation method is used by a controllable reaction in a novel microreactor chip fabricated on a PMMA (polymethyl methacrylate) substrate. The chip has two inlets to inject solvent and antisolvent separately

and then they are exposed to each other parallel in a laminar flow. As a result, by controlling diffusion rate the nanoparticles form in the border of two layers of reactants. The achieved Nano drug demonstrate improved dissolution rate and solubility compared to the raw drug. Considering the flow rates of solvent and antisolvent, the size of nanoparticles was varied in the range of 200-2000 nm. The comparison between optimized nanoparticles and coarse Bosentan shows that the dissolution rate increased dramatically. The optimized drug

dissolved completely less than 30 minutes while the maximum amount of dissolved coarse Bosentan was %10 in equal time.

Design and preparation of herbal medicinal gel containing honey and cinnamon extract for acne treating

Akram Yarmohammadi*, Mostafa Yarmohammadi, Mahsa cheraghi, Saeed mohammadi

P48

Authors' Affiliations:
Faculty of Pharmacy, Kermanshah University of Medical Science, Iran.

Abstract Presenter:
Akram Yarmohammadi

****Correspondance:***
Akram Yarmohammadi

Coauthors:
Mostafa Yarmohammadi
Mahsa cheraghi
Saeed mohammadi

Introduction:

Acne is a chronic inflammatory disease of the skin, when bacteria abnormally grow in hair follicles. The most common treatment is antibiotics but because of the antibiotic resistance treatment with them are limited. In this study, anti-acne face washing gel was prepared along with the cinnamon extract.

Materials and method:

The gel formulation was prepared with Gel HPMC 200, cinnamon extract, and citric acid. The formulation was tested for the anti-acne activity by turbidimetric method and clinical trial.

100 patients participate aged between 16 to 40 years old with diagnosis of acne.

Results:

Results showed that the gel was not irritant. It was stable and had viscoelastic and hydration properties and possessed anti acne activity.

Keywords: Acne, Face washing gel, Anti acne, Cinnamon, Honey

Formulation and physicochemical evaluation of Meloxicam alginate beads

Mitra Mahmoudi Meymand, Nazanin Foroutan, Payam Khazaeli*

P49

Authors' Affiliations:
Pharmaceutics Research Center, Neuropharmacology Institute, Kerman University of Medical Sciences, Iran.

Abstract Presenter:
Mitra Mahmoudi Meymand

***Correspondance:**
Payam Khazaeli

Coauthors:
Nazanin Foroutan

Abstract:

One of the most widely used group of drugs is NSAIDs that meloxicam is one of new drugs of this group. In this investigation, it has been tried to use the capability of natural polymer and sodium alginate in order to form alginate beads of meloxicam with divalent cations such as Calcium (ca+2), Barium (Ba+2), Iron (Fe+3), Tin (Sn+2), and Lead (Pb+2) to produce the control release formulation of drug.

In study procedure, Calcium was selected as the best cation for preparing beads in gelation iontropic way, sodium alginate solution 1,2,3 % w/v was dripped to Calcium alginate solution 1,2,3, % w/v.

Prepared beads remained in Calcium chloride solution for 15 to 30 minutes, then they were separated using filter paper, washed with distilled water, and as the last procedure they were dried in 37°C using oven.

Best formulation amongs prepared ones was chosen. Due to survey amounts of drug that were loaded in beads, walls of beads were destroyed, and drug concentration was determined by UV spectrophotometry (362nm). Swelling of these beads in distilled water was examined as well. Resistancy of bead wall was checked and sizes of 100 beads were determined via optical microscope.

In addition, study of meloxicam release from beads in two condition, buffer phosphate PH:7.4 and hydrochloric acid PH:1.2 by using USP1 dissolution apparatus (basket) at 37°C was carried out.

According to the results, acidic and alkaline solutions with respect to dissolution rate differences between prepared beads and tablet on the market, it seems that this formulation is able to not only greatly reduce the risk of gastric ulcers but also supply slow and steady rate of drug release.

Keywords: meloxicam, alginate

Preparation and evaluation of o/w emulsion containing Dimethicone

Farnia Ghanbarveisi*, Leila Behbood,

P50

Authors' Affiliations:
Students Research Committee, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Farnia Ghanbarveisi

Correspondance:
Farnia Ghanbarveisi

Coauthors:
Leila Behbood

Introduction:

The human skin, the largest organ acts as a barrier to protect the underlying tissues from dryness and external mechanical, chemical, and microbial exposures. One of the important characteristics of the skin is its moisture that plays important role in its protective function. Today, the most moisturizers in the market are o/w emulsions.

In this study we tried to prepare an o/w emulsion containing dimethicone as a silicon base polymer which is used as a dressing agent and is an anti-allergic substance.

Methods:

Oil phase: Dimethicone dissolved in chloroform. The oil phase of the emulsion was prepared by dissolving span 60 in light liquid paraffin (20%) using a magnetic stirrer at 70-80 ˚C. Solution of dimethicone in chloroform was added to paraffin solution with constant stirring at a moderate speed.

Aqueous phase: the aqueous phase was prepared by dissolving propylene glycol (PG) in purified water. Finally, the oily phase was added dropwise to the aqueous phase under stirring condition. The physical properties of prepared formulation (viscosity, pH, appearance, and etc.) was investigated.

Results:

The prepared emulsion formulation was found to be stable. Viscosity and pH of formulation was in acceptable range. No change was observed in its appearance.

Discussion and Conclusion:

This formulation can be considered as a moisturizer pharmaceutical preparation.

Keywords: Dimethicone, Moisturizers, O/W emulsions, Dressing agent, Skin care

Formulation and Physio-Chemical Evaluation of Atorvastatin buccal tablets

Shima Esfandyari, Fereshteh Bagheri, Pegah Sadeghi, Sarab Ghanbari, Reza Tahvilian*

P51

Authors' Affiliations:
Kermanshah university of medical sciences, Iran.

Abstract Presenter:
Shima Esfandyari

****Correspondance:***
Reza Tahvilian

Coauthors:
Fereshteh Bagheri
Pegah Sadeghi
Sarab Ghanbari

Introduction:

Atorvastatin calcium (ATC) is an HMG-coenzyme reductase inhibitor. low Oral bioavailability (14%) of ATC is due to instability and incomplete intestinal absorption and/or extensive gut wall extraction. ATC destabilizes by oxidative environment exposure regardless of whether it is in the form of tablets, powders, granules, or within capsules. The oxidation sensitivity of ATC and its instability brings about poor solubility which is the main cause for low bioavailability of ATC's oral administration.

The oral cavity has become a subject of interest nowadays for drug delivery because of ease of administration and inhibition of GI degradation and first-pass metabolism. Also in case of toxicity, termination of drug delivery is easily reached by removing the buccal form. Buccal delivery is the administration of the drug through the buccal mucosal membrane lining of the oral cavity. Thus, mucoadhesive dosage forms are highly suggested for oral drug delivery.

The aim of this study was the formulation and assessment of atorvastatin buccal tablets in a way that the drug is released as it is inserted in the buccal region. In this formulation, gastric irritation and hepatic metabolism are inhibited while drug bioavailability, dose consumption frequency, and patient compliance are improved.

Material and method:

Polymers such as HPMC and CMC were chosen to formulate this buccal tablet, due to their adherence to buccal site for an appropriate time, in spite of tongue movement, mucus secretion or swallowing. Atorvastatin powders with polymers were mixed for 30 minutes both manual and using sieves. As a lubricant agent, Magnesium stearate 1% was then added and mixed for 5 minutes. Different formulations according to different polymer ratios were prepared in the forms of 100 milligram buccal tablets.

Results:

The evaluation of ATC buccal tablet forms regarding acceptance criteria for a proper formulation including drug Content Uniformity, dissolution and release Studies, bio adhesion, biodegradability determination, and stability testings were acceptable.

Conclusion:

The formulations are stable, having the potential to advance the oral bioavailability of ATC, and might be suitable alternatives to improve its systemic availability.

Keywords: atorvastatin, buccal tablet, bioavailability

A Systematic Study and Antibacterial Effect of Ag2S/Chitosan Nanocomposites

Neda Hedayatifar, Mohammad hasan Moshafi, Mehdi Ranjbar*

P52

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Neda Hedayatifar

****Correspondance:***
Mehdi Ranjbar

Coauthors:
Mohammad hasan Moshafi

Introduction:

The rapid and uncontrolled growth of microorganisms can lead to serious problems. With the development of nanotechnology over the last decade, golden opportunities have been created to discover the antibacterial effects of metallic nanoparticles. Metallic nanoparticles have an antibacterial effect [1-2]. Scientists believe that nanoparticles can be used as an appropriate alternative in biochemical area [3].

Method and Results:

In this research, nanoparticles were made in different sizes. Then, microbial culture media were prepared and using the MIC method, an antibacterial effect of nanoparticles with different structures on gram-negative and gram-positive bacteria was studied. 2.1 g of the Mueller-Hinton Broth was weighed in a volume of 100 ml and 7.6 g of the Mueller-Hinton agar culture medium, weighing 200 ml. The solid medium was heated to be clear. We diluted the antimicrobials in a liquid medium and added them to a solid culture medium and placed them in the numbered plates. Then, we made microbial leachate from the tested microorganisms and compared their turbidity to that of the half McFarland. Then, with a micropipette of 2.5 microns from the lagoon, the bacteria were removed from the plates, and finally the plates were placed in the incubator for 24 hours. Antibacterial activity of the Ag2S/Chitosan nanocomposites was exerted on on 7 bacterial isolates, including Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Serratia marcescense, Staphlococcus aureus, and Bacillus subtilis.

Conclusion:

In this study, the best antibacterial properties at 600 and 750 watts was over a period of 5 minutes. The resulting nanoparticles only affected the gram-negative bacteria at 600 watts and the gram-positive at 750 watts. It is suggested that these biodegradable and environmentally friendly nanostructures can be used in the formulation of antimicrobial drugs.

Keywords: Ag2S / chitosan, Chemical method, Antimicrobial properties

Thermal adaptation analysis of Bacterial chitinases: comparison of chemical Characteristics and residues composition.

Vajiheh Eskandari

P55

Authors' Affiliations:
Department of Biology, University of Zanjan, Zanjan, 45371-38791, Iran

Abstract Presenter:
Vajiheh Eskandari

****Correspondance:***
Vajiheh Eskandari

Abstract:

Chitin and chitin-derived products have wide variety of medical and industrial applications. Chitinases are glycosyl hydrolases that catalyze the conversion of chitin biopolymers to low molecular weight chitooligomers [1-2].

Computational tools and techniques can analyze and identify the sequential and structural properties, which trigger the chitinase (enzymes) to tolerate the extreme temperature and/or PH, so these results could be used for designing and reconstructing chitinases with desired temperature and/or PH characteristics.

Therefore, in this study twenty amino acid sequences of mesophilic, thermophilic, hyperthermophilic, and psychrophilic chitinase were assessed to identify the variation in their physiochemical properties and amino acids compositions which are responsible in making them to adapt in various conditions. Physiochemical properties using ProtParam tool [3], showed positivley charged residues (Arg+Lys) are stastically significant contributing to the thermostability of chitinase.

Multiple sequence alignment of the amino acid sequences of chitinases showed DxxDxDxE motis conserved among catalytic domains of variouse chitinases. Cysteine (C) was high in the psychrophilic chitinases in comparison with their counterpart.

Keywords: Chitinase, Temperature, Cysteine

Insight into the protein thermostability based on comparison of catalytic pocket of bacterial chitinases

Vajiheh Eskandari

P56

Authors' Affiliations:
Department of Biology, University of Zanjan, Zanjan, 45371-38791, Iran.

Abstract Presenter:
Vajiheh Eskandari

****Correspondance:***
Vajiheh Eskandari

Abstract:

Chitin is the second most abundant biopolymer on the earth after cellulose. Chitinases are glycosyl hydrolases that catalyze the conversion of chitin biopolymers to low molecular weight chitooligomers which have wide variety of biotechnological and industrial applications [1-2].

In present study we compare some important physiochemical properties of catalytic domain and active site pocket of psychrophilic, mesophilic, and thermophilic chitinases. The catalytic domains were retrieved from Interpro database. The 3-D models of various types of chitinases were predicted using Modeller 9 & 15 software [3]. Then, the quality of the models were evaluated with PROCHECK and PROSA II servers. The active pocketes were predicted using CastP and Ftsite servers. The physiochemical properties of mesophilic and thermophilic chitinases were compared. Our result showed cysteine and aspartic acid are two important residues that affect the thermal resistance of enzymes.

Keywords: Chitinase, Homology modeling, Active Pocket

Homology modeling and in-silico substrate binding analysis of Enterotoxigenic Escherichia coli chaperones

Vajiheh Eskandari

P57

Authors' Affiliations:
Department of Biology, University of Zanjan, Zanjan, 45371-38791, Iran

Abstract Presenter:
Vajiheh Eskandari

****Correspondance:***
Vajiheh Eskandari

Abstract:

The Pathogenic strains of Escherichia coli are always one of the major causes of infections in developing countries. The fimbriaes on the surface of E. coli mediate microbial attachment to host cells and are important virulence factors [1-2]. Chaperones and usher proteins involved in the biogenesis of the major fimbriae [3]. Our studied showed significant similarities in physicochemical properties of chaperons and also fimbrial subunits among different strains of E. coli. The 3D-structures of 20 molecules of chaperone and fimbriae subunit were modeled using Modeller 9v20 [4]. The quality of the models were assessed using PROCHECK, Verify3D and ProSA II.

The castp and FTsite servers were used for predicting interactive sites of proteins. The information of interactive pocket was used for fimbriae subunits and chaperone docking.

The physicochemical properties and 3-D structures of interaction pockets of chaperones were compared and result detected significantes similarities among various chaperones. Now we are looking for the inhibitors to block the chaperon-fimbriae major subunit interaction sites. The resulting inhibitors could be introducing as drug candidates.

Keywords: Fimbria, Chaperon, Molecular Modeling

A novel cancer treatment method with a set of immunotoxins

Ali Hakakian*, Negin Khomarlou, Mozafar Mohammadi, Peyman Bemani

P58

Authors' Affiliations:
Faculty Member of Production and Research Complex, Pasteur Institute of Iran

Abstract Presenter:
Ali Hakakian

***Correspondance:**
Ali Hakakian

Coauthors:
Negin Khomarlou
Mozafar Mohammadi
Peyman Bemani

Introduction:

Immunotoxins are proteins that consist of an antibody fragment linked to a toxin, used as agents for targeted therapy of cancers. Although the most potent immunotoxins are made of bacterial and plant toxins, obstacles which contribute to poor responses are immunogenicity in patients and rapid development of neutralizing antibodies. In the present study we proposed a new therapeutic immunotoxin for targeted cancer therapy of ROR1 expressing cancers: an anti ROR1 single chain fragment variable antibody (scFv)-endonuclease G (anti ROR1 scFv-EndoG).

Methods:

The three-dimensional structure of anti ROR1 scFv-EndoG protein was modeled and structural validation tools were employed to confirm the accuracy and reliability of the developed model. In addition, stability and integrity of the model were assessed by molecular dynamic (MD) simulation.

Results:

All results suggested the protein model was acceptable and containing good quality.

Conclusions:

Anti-ROR1 scFv-EndoG would be expected to bind to the ROR1 extracellular domain by its scFv portion and selectively deliver non-immunogenic human endonuclease G enzyme as an end-stage apoptosis molecule into ROR1-expressing cancer cells and rapidly lead to apoptosis. We believe that anti ROR1 and other anti-tumor antigens in scFv-EndoG forms may be helpful for cancer therapy.

Keywords: Cancer therapy, ROR1, Immunoconjugate, scFV, EndoG

Optimization of DNA Aptamer attachment on gold nanoparticles to develop an aptasensor for a bacterial infection

Kamyar Keshavarz F.[a], Maryam Torshabi[b], Maryam Tabarzad[a]

P59

Authors' Affiliations:
[a] Protein Technology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[b]Department of Dental Biomaterials, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Kamyar Keshavarz F.

****Correspondance:***
Maryam Tabarzad

Coauthors:
Maryam Torshabi
Maryam Tabarzad

Introduction:

Gold nanoparticles (GNPs) are one of the extensively applied nanomaterials which have unique features, such as colorimetric, conductivity, and nonlinear optical properties. They also easily functionalized with biological affinity elements such as aptamers, hold great promise for biological and medicinal applications. Aptamers as nucleic acids (DNA/ RNA) affinity ligands, have been widely used in various fields of biomedical sciences, particularly in various biosensors. Optimum attachment of aptamers on the surface of solid supports like GNPs, are important issues in the development process of aptamer based biosensors. Different factors can affect the aptamer attachment on the GNPs. Covalent attachment of oligonucleotides to GNPs easily achieved through S-Au bond, by adding a thiol group to the end of nucleic acid. Commonly, using 5' thiolated aptamers for covalent attachment to GNPs exhibited better results in application (1, 2).

Methods and Results:

Gold nanoparticles were synthesized by reducing tetrachloroauric acid with trisodium citrate. The red solution containing GNPs were filtered and concentrated, then characterized with DLS and UV-vis spectroscopy (3, 4). The resulted GNPs were in the range of 30nm with polydispersity index of 0.2. The maximum absorbance was achieved on 521 nm. Then, 5′ thiol-modified DNA aptamer was reacted directly with the GNPs through attachment of the oligo-thiol units onto the GNPs surface. Different factors like time, aptamer concentration, GNP concentration, reducing agent, and final sodium chloride concentration were evaluated and optimized to achieve a stable and non-aggregated aptamer conjugated GNPs with maximum aptamer loading (5). Best condition was achieved at 203 ng DNA aptamer (12.5 pmol) in 1 mL GNP solution (A521 nm=0.8), overnight incubation before adding NaCl, NaCl with final concentration of 100 mM, using Tris(2-carboxyethyl) phosphine (TCEP) as reducing agent.

Conclusions:

In this study, the optimized aptamer conjugated GNPs were developed, which will be applied in the development of an aptamer based biosensor or aptasensor for an oral bacterial infection.

Keywords: Aptamer, Biosensor, Chemical attachment, DNA

A new approach for preparation of an intelligent and targeted chitosan

Daliya Rashidi, Hossein Fahimi, Sepideh Khaleghi*

P60

Authors' Affiliations:
Department of Microbial Biotechnology, Faculty of Advanced Science and Technology, Tehran Medical Science Islamic Azad University, Tehran Iran

Abstract Presenter:
Daliya Rashidi

***Correspondance:**
Sepideh Khaleghi

Coauthors:
Hossein Fahimi

Abstract:

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration. Attempts are being made to develop a controlled drug delivery system that can provide a steady state targeted drug delivery system and increasing the time of drug maintenance in intestine. Many bacteria produce surface fibers allowing them to adhere to each other and to biotic and abiotic surfaces. ETEC (Enterotoxigenic Escherichia coli) is one of these bacteria which can attached and colonized in intestine and colon by CFA/I fimbriae. The cfaE is one of the subunits of CFA/I which has main role in intestinal attachment. However, its small size cannot induce mucosal immunity reactions in human. In this research, we try to prepare recombinant cfaE in BL21 strain in order to target modified chitosan nanoparticles for intestinal drug delivery.

As regards, the complete gene of cfaE was amplified by PCR and cloned in pET32a (+) vector by BamH1 and HindIII restriction sites. The final and confirmed vector was transformed in E. coli BL21 (DE3) and induced by 1mM IPTG for protein expression. The recombinant protein was purified by Ni-NTA method and 300mM Imidazole. The SDS-PAGE and western blot confirmed the recombinant protein, after that, specific attachment of cfaE is analyzed by Cell ELISA on fixed human intestine cell line (Hs.1).

The cloned gene was confirmed by restriction enzyme digestion as well as sequencing. Moreover, the expression of recombinant protein was confirmed by SDS-PAGE and western blotting. The Cell ELISA result showed this protein can be a candidate for targeted drug delivery approach by modified chitosan nanoparticles in intestine.

All of these findings favor the notion that the cfaE conjugated chitosan nanoparticles produced in our work may offer a promise for the development of an efficient therapeutic carrier for intestine cancer and improving drug absorption in the future. However, further investigation is required to provide more evidence on diff erent aspects of the targeting activity and stability of this nanoparticle in in vivo.

Keywords: Edible drug delivery, intestine, CFA/I fimbrial subunit E, chitosan nanoparticles.

Decreasing the Immunogenicity of Pegylated Uricase Using In-Silico Structure-Based Computational Approaches

Mina Shahisavandi*, Mohammad Hossein Morowvat

P61

Authors' Affiliations:
Pharmaceutical Strategic Studies Office, Tehran, Iran.

Abstract Presenter:
Mina Shahisavandi

***Correspondance:**
Mina Shahisavandi

Coauthors:
Mohammad Hossein Morowvat

Abstarct:

Uricase is a therapeutic enzyme that has application in adjuvant chemotherapy and management of treatment-resistance hyperuricemia. Krystexxa® is a hyper-PEGylated chimeric form of uricase indicates successful results in lowering plasma uric acid in almost cases. Nevertheless, Krystexxa® has some limitations due to its undesirable immunogenic response. It occurs in 91% of treated patients because of the humeral immunity and releasing anti-PEG antibodies. Immunogenicity study through in silico epitope-mapping tools can predict promiscuous B-cell epitope(s) which leads to the protein structure modification in further studies.

In this study, Scopus, PubMed, Google Scholar, and Web of Science databases were explored. A combination of the main mentioned key words were used. The inclusion criteria for this study were defined as: a) articles written in English language; b) review or original articles regarding immunoinformatics for B cell epitopes prediction, 3D structure modeling of proteins related to humeral immunogenicity. Besides, the exclusion criteria were also defined as: a) studies which have not deal with immunoinformatics or in silico approaches for therapeutic proteins b) studies that are published in a language other than English

The amino acid sequence of pegloticase, the pig-baboon chimeric uricase, was computationally analyzed for recognizing and locating its immune-reactive regions with ten data bases. The 3D structure of the bioactive form of uricase was modeled. The B-cell epitope mapping of protein was performed using ten servers with different algorithms. Six segments, including 27-31, 50-65, 113-118, 131-178, 196-229, and 269-275 were predicted to be the consensus immunogenic regions. The modification of the epitopic hot spot residue was performed to reduce immune-reactiveness. The hot spot residue was selected considering a high B-cell epitope score, surface accessibility, flexibility, and hydrophilicity. The structure stability of native and mutant proteins was evaluated through molecular dynamics simulation. A mutein was suggested as a lower antigenic and stable enzyme derivative.

Regarding to this study the results indicate immunoinformatic studies have the ability of application in predicting the immunogenicity of pegloticase. The methods that were practiced in this project can be applied for immunogenicity determination of other therapeutic proteins. Although, computational approach is an effective method to decrease the immunogenicity of a therapeutic protein, the experimental studies are essential to validate the in-silico results.

Keywords: Pegloticase, insilico B cell epitope prediction, immunoinformatics

The use of smart and active packaging for maintaining cold chain during production process and distributing biological medicines

Mohana Abdi*, Mohammad Hossein Morowvat

P62

Authors' Affiliations:
Islamic Azad University Pharmaceutical Sciences Branch

Abstract Presenter:
Mohana Abdi

***Correspondance:**
Mohana Abdi

Coauthors:
Mohammad Hossein Morowvat

Abstract:

Active packaging is a kind of packing structure that responds to changes and adds the additive to the system with the objective of preserving product quality. Intelligent packaging systems have been developed to monitor the existence of certain aspects in the product and report information to the consumer.

The main purpose of this study is to provide a smart and active packing guideline to ensure the maintenance of the cold chain during production and distribution of biological medicines. Given that biological drugs are made from living organisms, they require complex and costly production, maintenance, and distribution processes that failure to observe these processes can cause serious damage. Data collection for appropriate guideline was carried out from reputable databases and establishments, such as Pubmed, Science direct, Elsevier, and FDA.

The findings of this study showed that smart and active packages are currently widely used in the food industry, given the introduction of this science to the pharmaceuticals industry; it can be used in the pharmaceutical industry to improve the conditions for holding and transporting biological drugs and reducing the economic loss. The freshly frozen plasma should be injected within 30 minutes after leaving the freezing mode. Due to the time limit for the injection of this product, the time-temperature indicator labeled on the package can inform about the thermal load that the packaging surface has undergone in the distribution chain and shows this, as a visible response in the form of mechanical deformation or color change that can be very effective in determining the health of these products.

Keywords: Intelligent packaging, biological medicines, Active packaging, Guideline

In vitro maturation of dendritic cells pulsed with hypochlorous acid treated colon cancer cell lysates

Mohammad Roufarshbaf, Nafiseh Esmaeil, Vajihe Akbari*

P63

Authors' Affiliations:
Islamic Azad University, Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract Presenter:
Mohammad Roufarshbaf

****Correspondance:***
Vajihe Akbari

Coauthors:
Nafiseh Esmaeil

Introduction:

Cancer therapeutic vaccines are mainly developed to prevent further growth of tumor cells in patients with end-stage or recurrent cancers. Dendritic cell (DC) vaccine is one of the immunotherapy strategies in cancer treatment which its safety has been demonstrated in many studies. Previous studies suggested that the strategy of tumor cell lysate (TCL) preparation affects its immunogenicity. Here, we investigated the improvement of Dendritic Cell (DC) in vitro maturation using TCL prepared by oxidation with hypochlorous acid (HOCl) (1).

Methods:

HT-29 colon cancer cells were cultured and harvested at the concentration of 2×106 cells/ml. Then, the cells were treated to produce TCL with HOCl. To obtain monocyte-derived DCs from peripheral blood, mononuclear cells were isolated by using Ficoll density, and the isolated monocytes were co-cultured with GM-CSF and IL-4 to differentiate into dendritic cells in 9 days. Monocyte-derived DCs were treated with TCLs and supplemented by LPS on the 7th and 8th day, respectively. Finally, the cells were stained for CD14, CD83 and were assessed using Flow cytometry.

Results:

The flow cytometry analysis confirmed high purity of isolated monocytes and in vitro maturation and activation of DCs. CD83 expression was significantly higher in HOCl treated group compared to conventional lysis (freeze-thaw) and control groups. Also, there were no statistically significant differences in the CD86 expression between groups. Morphological analysis using optical microscope also confirmed the improvement of DCs in vitro maturation.

Discussion and Conclusion:

Our findings suggest that Dendritic Cells with TCLs prepared by HOCl treatment shift monocytes into mature dendritic cells more efficiently. This result is in concordance with previous studies which were conducted on ovarian cancer cell lines (2).

Keywords: Cancer immunotherapy, Dendritic Cell Vaccine, Tumor Cell Lysate, Dendritic Cell maturation

Cisplatin-induced Drp1-dephosphorylation and apoptosis in a p53- dependent manner in Ovarian Cancer cells, In Vitro

Mohammad Reza Abedini*, Benjamin K. Tsang

P64

Authors' Affiliations:
Cellular & Molecular Research Center, Birjand University of Medical Sciences, Birjand, Iran.
Chronic Disease Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

Abstract Presenter:
Mohammad Reza Abedini

***Correspondance:**
Mohammad Reza Abedini

Coauthors:
Benjamin K. Tsang

Abstract:

Mitochondria are highly dynamic organelles, and mitochondrial fission is a crucial step of apoptosis. Although Drp1 is believed to be involve in mitochondrial fragmentation, whether and how its regulation is involved in the regulation of cisplatin (CDDP) sensitivity is not known.

Chemosensitive ovarian cancer cells (OVCA) were treated with CDDP. Apoptosis, protein contents and phosphorylation were assessed by nuclear Hoechst staining and Western blot, respectively. The requirements of p53 for CDDP-induced Drp1 processing and apoptosis were examined by siRNA or cDNA. Protein interaction is also detected by Proximity Ligand assay (PLA) and Western Co-IP.

We have shown that: a) CDDP decreased Drp1 content and induces apoptosis in a concentration-dependent manner in chemosensitive OVCA; b) Chemoresponsiveness is associated with Drp1 down-regulation, decreased p-Drp1 (ser637) and increased ser616/637 ratio in response to CDDP in OVCA cells. c) p53 is required for CDDP-induced Drp1 down-regulation, ser637 dephosphorylation and apoptosis; d) intact cellular gelsolin (I-cGSN) interacts with Drp1 and transport to mitochondria in response to CDDP; e) Chemoresponsiveness is associated with increased p-p53 (ser15)-Drp1 and decreased GSN-Drp1 interaction in response to CDDP.

These findings demonstrate that CDDP induces (a) Drp-1 dephosphorylation (ser637), (b) mitochondrial fragmentation and CDDP-induced apoptosis in OVCA cells, and (c) mitochondrial dynamics may in part be involved in CDDP sensitivity in a p53-depndent manner.

Key words: Cisplatin, p53, Drp-1, mitochondrial dynamic, ovarian cancer

Determine of PHA Granule in Escherichia coli contains of Genes Encoding Poly hydroxyalkanoate Synthase

Maryam Beheshti Isfahani*, Hamid Mir Mohamad Sadeghi

P65

Authors' Affiliations:
Department of Pharmaceutical Biotechnology, School of Pharmacy, Isfahan University of Medical Science

Abstract Presenter:
Maryam Beheshti Isfahani

****Correspondance:***
Maryam Beheshti Isfahani

Coauthors:
Hamid Mir Mohamad Sadeghi

Introduction:

Over the years, the use of plastics has complicated the problem of disposal of solidwastes. One strategy to reduce plastic waste is the use of biodegradable plastics. A group of these plastics are polyhydroxyalkanoates (PHAs).

Most Pseudomonas strains are able to accumulate mcl-PHA. In previous studies, the phaC1 andphaC2 genes were identified in Pseudomonas aeruginosa (P. aeruginosa) PTCC 1310and were cloned. After transformation of competent Escherichia coli (E. coli) BL21 (DE3) cells with recombinant plasmids, expression was induced using IPTG. The PHA synthase genes were induced with IPTG and the expressed 62 kDa protein was observed and purified. By changing expression conditions, 1 mM IPTG, 37 °C and a 2 hr incubation, the highest level of protein production in E. coli cells was provided. These results suggest that induction condition of PhaC genes can influence expression of PHA synthase enzymes.

The aim of this study was to detect expression of these genes and optimize the conditions for their expression in E. coli. The optimization of conditions for phaC genes expression can serve as an important stage for establishing PHA production in E. coli.

Methods and Results:

To confirm the expression of functional PHA synthase enzymes by E. coli BL21 (DE3) cells carrying the phaC genes, the accumulation of PHA in bacteria was detected with Nile red (11). The E. coli BL21 (DE3) cells carrying the phaC gene, E. coli BL21 (DE3) without the phaC gene (as the negative control), and P. citranolleise (as the positive control) were investigated for PHA production. E. coli BL21 (DE3) cells were streaked on an LB plate supplemented with sodium-gluconate (0.5%w/v), Nile red (0.05 µg/ml), IPTG (0.1 mM), and ampicillin (100 µg/ml).

Conclusions:

Using a Nile red plate assay, the accumulation of PHA in bacteria was detected which confirmed the expression of functional PHA synthase enzymes by E. coli BL21(DE3) cells. To increase the yield of PHA production, using mutant strains of E. coli that could block the oxidation of fatty acids and accumulate greater level of PHA is also recommended.

Keywords: Polyhydroxyalkanoate, Protein expression, PhaC1, PhaC2

Fermentation optimization for soluble expression of Anakinra

Sina Moeini, Sasan Jahanshahi, Arezu Najafikhah ,
Fatemeh Hosseinpour, Amir Maghsoudi*

P66

Authors' Affiliations:
Persis Gen Par Co

Abstract Presenter:
Sina Moeini

****Correspondance:***
Amir Maghsoudi

Coauthors:
Amir Maghsoudi
Sasan Jahanshahi
Arezu Najafikhah
Fatemeh Hosseinpour

Abstarct:

Anakinra is a recombinant, manipulated human interleukin-1 receptor antagonist (IL-1Ra) protein. Anakinra possess an additional methionine in N-terminal compare to the natural form of IL-1Ra. Anakinra imitate the role of interleukin-1 type I receptor (IL-1RI) in binding to the interleukin-1 which increased levels lead to bone and cartilage destruction in rheumatoid arthritis. Anakinra expression is optimized in soluble form. Lactose utilization in different amounts is an offering method in order to optimize the expression of Anakinra in soluble form.

Synthesized gene was cloned in pET-33b(+) expression vector and transformed in E. coli BL21 (DE3) and BL21 (DE3)pLysS hosts. Expression of recombinant protein at different lactose concentration levels at induction time were evaluated in erlen. Gene expression was investigated using SDS-PAGE and Bradford assay techniques. Furthermore, soluble expression of Anakinra at different levels of Lactose was surveyed in fed-batch culture on M9 media using 70% Glucose solution as feed.

Cloning of Anakinra was confirmed by sequencing and enzyme digestion. SDS-PAGE and Bradford assay confirmed recombinant protein expression in both strains in 5 grams per liter lactose in Erlen. The expressed protein was found almost in the soluble form in the cell lysate. Soluble expression of Anakinra was optimized in induction by 10 grams per liter lactose, after eighteen hours of fed-batch fermentation at 37°C in OD about 150.

These results indicate that lactose utilization as an inducer in the expression of anakinra increases soluble form.

Keywords: interleukin-1 receptor antagonist, Soluble expression, fermentation optimization

Optimization of charge variant content in Pembrolizumab purification

Sina Moeini, Forogh Havasi, Maryam Maleki, Reyhane Akherati ,
Fatemeh Sherafat, Morteza Jafar Aghaei*

P67

Authors' Affiliations:
Persis Gen Par Co

Abstract Presenter:
Sina Moeini

****Correspondance:***
Morteza Jafar Aghaei

Coauthors:
Forogh Havasi
Maryam Maleki
Reyhane Akherati
Fatemeh Sherafat

Abstract:

Pembrolizumab (PMB) is an IgG4 antibody monoclonal used in patients with melanoma and lung cancer. Downstream purification of PMB as a monoclonal antibody fragment, need a polishing step following capture step because of product-related impurities, mainly charge variants. In addition to main protein, acidic and basic form content being in the acceptable range in polishing step is of importance. One of the main parameters in the polishing step is the type of resin. Previously, SP-Sepharose FF cation exchange resin had been used in the screening experiment in this study, which did not provide the appropriate resolution due to the gradient applied in the elution process. Moreover, it was found that the acidic form content fell beyond the acceptable range (acidic percent less than 16% and basic less than 25%).

In order to increase recovery with improved resolution, experimental design for application of Capto SP ImpRes resin was performed. first of all, a sample having an average charge variant was prepared from Mabselect eluates of several batches of cell culture which had equal properties to screening experiment sample. Numerous experiments were conducted with the aim of acidic form reduction causing to main protein increasing. To this end, some other parameters such as pH, conductivity and salt gradient were examined. Furthermore, considering high recovery percent was important.

The result of eluate's acidic and basic content obtained from Capto SP ImpRes column was in the range of 7-14% and 15-25%, respectively. In parallel, recovery percentage achieved from 60% to 90%. The best conditions resulted from experiments on Capto SP ImpRes involves: 2 CV wash, acidic and basic charge variant 10% and 20% respectively and with 88% recovery percent.

Capto™ SP ImpRes is a strong cation exchange resin that works well in purifying proteins as intermediate and polishing steps. Based on the results, it seems that the Capto SP ImpRes resin, despite lower bed height, exhibits higher resolution and recovery.

Keywords: Pembrolizumab, Purification, Charge Variant, IEX chromatography

Formulation and Charactrization of Nano-lipopeptide biosurfactant

Alireza Asadi Korom, Gholam Reza Dehghan,
Mandana Ohadi, Mehdi Ranjbar*

P68

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Alireza Asadi-Korom

****Correspondance:***
Mehdi Ranjbar

Coauthors:
Gholam Reza Dehghan
Mandana Ohadi

Abstract:

Biosurfactants are surface active molecules with hydrophilic and hydrophobic moieties produced by different microorganisms such as bacteria, fungi, and yeasts. In the present study, lipopeptide biosurfactant was isolated from A. junii B6 (GenBank accession KT946907) soil contaminated oil from the southwest part of Iran. It was partially purified by solvent extraction method and showed the lipopeptide characteristics according to its spectra analysis. Biosurfactants are amphiphilic compounds produced in living surfaces, mostly on microbial cell surfaces or excreted extracellular hydrophobic and hydrophilic moieties that confer the ability to accumulate between fluid phases, thus reducing surface and interfacial tension at the surface and interface respectively [1]. They possess the characteristic property of reducing the surface and interfacial tension using the same mechanisms as chemicals surfactants [2]. Surfactants are the active ingredients found in soaps and detergents with the ability to concentrate at the air- water interface. They are commonly used to separate oily materials from a particular media due to the fact that they are able to increase aqueous solubility of Non- Aqueous Phase Liquids (NAPLS) by reducing their surface/ interfacial tension at air–water and water–oil interfaces [3]. Methods and Results: 5 mg/ml bisurfactant was prepared and was isolated from A. junii B6 (GenBank accession KT946907) soil contaminated oil from the southwest part of Iran. These samples were put into microwave method in different times and irradiation such as 9minutes and 15 minutes in 300, 600 and 900 watts. PH was optimized in the range of 5.5-6.9. Many properties of nanobisurfactant were used in vesicular formulations. In vitro characterization of nanobisurfactant including microscopic observation, size analysis, and playability were studied. nanobisurfactant concentration was measured by second derivative UV spectroscopy at 245 nm. Conclusions: All used nanobisurfactants formed round MLVs (multilamellar vesicles) except inthe Span/Tween 80. Log-normal size distribution was observed for all prepared niosomes. Vesicles were stabled with minimum size change during 2 months storage at 4-8 oC. Maximum particle size efficiency of nanobisurfactant was 210 nm. Biphasic release profiles of compounds is under consideration obtained and the release data was best fitted with Baker-Lonsdale release kinetic model.

Keywords: Antioxidant, Optical properties, Nanobisurfactant, Drug delivery.

Isolation and identification of chitinase producing bacterial strain and evaluation of factors affecting on enzyme production

Hadis Fathaliopour, Mojtaba Shakibaie, Fateme Ghasemzadeh, Atefeh Ameri, Alieh Ameri, Hamid Forootanfar*

P69

Authors' Affiliations:
The Student Research Committee, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Hadis Fathaliopour

****Correspondance:***
Hamid Forootanfar

Coauthors:
Mojtaba Shakibaie
Fateme Ghasemzadeh
Atefeh Ameri
Alieh Ameri

Introduction:

Chitinases is hydrolytic enzyme that is produced in wide range of organisms includint g bacteria, fungi, insects and plants. It is important in terms of medical, biotechnology and agriculture to control fungi and pests. This study aimed to screen soil samples for isolation of chitinase-producing bacterial strains and identification of morphological, biochemical and molecular (16S rDNA) specifications of the selected strain and evaluation of factors affecting on maximum enzyme production.

Methods:

Twenty soil samples were collected from the Sarcheshme mine, and dried in aseptic conditions. Sample was mixed with a sterile normal saline and was then added to nutrient agar medium containing colloidal chitin and incubated at 30°C until the halo zone of chitinase activity was formed. The superior strains with large size of the halo were selected. The morphologic studies, biochemical tests, and molecular identification using 16S rDNA method were used to identify the strain. Then selected strain was cultivated into broth medium, and the production of enzymes in different times of sampling was analyzed in the following condition; presences of different carbon and nitrogen sources, various minerals, and also different pH medium.

Results:

One bacterial strains with the greatest halo as the best strain was selected. Comparison of 16S rDNA gene sequence with gene sequences available in the GenBank of NCBI revealed 99% similarity to Pseudomonas pseudoalcaligenesand. The amplified gene sequences were recorded to GenBank under accession number of KF055346. Evaluation of chitinase production in broth culture showed that after a day's ability the strain was able to produce 5800 units per liter of chitinase. Maximum amount of enzyme production were achieved in the presence of glucose (14248.65 UI/L), Ammonium nitrate (13924.32 UI/L), calcium (7735.13 UI/L), and pH: 5 (8497.295 UI/L).

Conclusion:

Isolated Pseudomonas pseudoalcaligenes is capable of producing the enzyme and can be a suitable source of chitinase. Therefore, it can be used as a medical, biotechnological and agricultural compound to control fungi and pests.

Keywords: Chitinase, Screening, Molecular identification, Ribosomal RNA.

Investigating the transfer of a three oligonucleotide by cyclic peptide nanotubetle

Mina Bolorizadeh, Farzane Abasi Juzdani, Majid Taghdir*

P70

Authors' Affiliations:
Department of biophysics, Faculty of biological science, University of Tarbiat Modares, Iran.

Abstract Presenter:
Mina bolorizadeh

Correspondance:
Majid Taghdir

Coauthors:
Farzane Abasi Juzdani

Abstract:

Gene therapy has attracted significant attention over the past two decades as a potential method for treating genetic disorders. Meanwhile the lack of safe and efficient gene-delivery methods is a limiting obstacle to human gene therapy. Commonly used viral vector gene delivery systems have fundamental problems including toxicity and immunogenicity. Recently, nonviral vector systems, including cationic lipids, polymers, dendrimers and peptide structures have overcome these issues. Peptide nanotubes (PNTs), as a unique class of peptide structures, have been regarded as a good carrier for gene-delivery. Cyclic peptide nanotubes (CPNTs) are tubular structures formed from the assembly of cyclic peptides. It has been demonstrated that peptide nanotubes can also act as transmembrane channels. In this study molecular dynamic simulations have been performed to investigate the transport of a single-stranded-DNA-oligonucleotide (ssDNA) in a CPNT embedded in POPC lipid bilayer. The stability of the CPNT was verified by RMSD calculation after 20 ns of Conventional Molecular Dynamics simulation(CMD). The competition between ssDNA and water to form H-bond with carbonyl and amide groups of the CPNT backbone causes the oligonucleotide to move through the CPNT. Further, analysis of SMD simulation demonstrates electrostatic and van der Waals interactions have key role in the transport of ssDNA through the lumen of CPNT. These results can help to design experimental investigations for the transport of genes to the cells.

Keywords: Cyclic peptide nanotubes, Single-stranded-DNA-oligonucleotide, Molecular Dynamics Simulation, POPC lipid bilayer

Evaluation of physicochemical properties and anti-biofilm activity of biogenic zinc nanoparticles synthesized by microwave irradiation

Mohammad Hosseini, Mojtaba Shakibaie, Fateme Alipour-Esmaeili-Anari, Atefeh Ameri , Alieh Ameri, Hamid Forootanfar*

P71

Authors' Affiliations:
Deputy of Research, Kerman University of Medical Sciences, Kerman, Ira.

Abstract Presenter:
Mohammad Hosseini

****Correspondance:***
Hamid Forootanfar

Coauthors:
Mojtaba Shakibaie
Fateme Alipour-Esmaeili-Anari
Atefeh Ameri
Alieh Ameri

Introduction:

The characteristic physicochemical properties of nanoparticles have led to extensive activities on these substances in recent years. The synthesis of nanoparticles using biological methods is gaining ground due to such advantages as cleanliness and low cost. The present study aimed to observe biosynthesis, purification, characterization, and anti-biofilm activity of biogenic zinc nanoparticles (Zn NPs).

Methods:

In this in-vitro study, an extract was first prepared from L. vera plant leaves. To synthesize and purify biogenic Zn NPs, the plant extract was mixed with zinc sulfate solution, and heated using microwave irradiation. The Zn NPs were examined with transmission electron microscopy (TEM), scanning electron microscopy (SEM), elemental analysis by EDX and XRD techniques, and FTIR analysis. Antimicrobial effects of Zn NPs on Pseudomonas aeruginosa, Proteus mirabilis, and Staphylococcus aureus strains were evaluated by microplate dilution method. Anti-biofilm effects of Zn biogenic NPs were also assessed through microplate and crystal violet staining. Finally, the results were compared using one-way analysis of variance (ANOVA).

Results:

The produced Zn NPs were spherical in the range of 30-80 nm (mostly 60-50 nm) according to the particle size patterns of SEM images. Increasing Zn NPs and zinc sulfate up to 640 µg/disc resulted in reduced biofilm formation by S. aureus (68.3 ± 2.1%), P. aeruginosa (93 ± 2.8%), and P. mirabilisa (82 ± 2.6%) compared to the control group.

Conclusion:

The results of this study showed that Zn NPs alone have little ability to inhibit biofilm growth. However, combined use of Zn NPs with antibiotics or other micro and/or nano structures can be an approach to overcome antibiotic resistance.

Keywords: Zinc nanoparticles, Bacterial biofilm, Microwave irradiation, L. vera

Comparative study of different methanolic extracts for partial purifying of Mycosporine-like Amino Acids in a microalgae species

Rouzbeh Gharib[a], Sepideh Teymoori[a], Maryam Tabarzad[b], Tahereh Hosseinabadi[a]

P72

Authors' Affiliations:
Department of Pharmacognosy and Biotechnology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Protein Technology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Rouzbeh Gharib

****Correspondance:***
Tahereh Hosseinabadi

Coauthors:
Sepideh Teymoori Soltani
Maryam Tabarzad
Tahereh Hosseinabadi

Introduction:

Cyanobacteria are Gram-negative, photosynthetic aerobic prokaryotes that are distributed in various habitats. They synthesize the ultraviolet (UV)-screening pigments, Scytonemin and mycosporine-like amino acids (MAA). Mycosporines and mycosporine-like amino acids (MAAs) are low-molecular-weight water-soluble molecules absorbing UV radiation, commonly in the wavelength range of 310-365 nm. MAAs are produced by a wide range of prokaryotic and eukaryotic microorganisms, including cyanobacteria, and a variety of marine macroalgae, corals, and other marine life forms. As UV absorbing molecules, MAAs can be applied potentially as a sunscreen ingredient in pharmaceuticals. In this research, we investigated the presence of MAAs in a species of cyanobacteria (1, 2).

Methods and Results:

The microalgae cells were cultivated in 250 mL Erlenmeyer flasks using BG11 liquid culture medium. The flasks were incubated at 24°C and 50% humidity. After 22 days the cultures were centrifuged and washed, twice. Then, the biomass was freeze-dried to achieve a dry powdery biomass. 0.1 g of cell mass was extracted with 10mL of 100% methanol, 80% methanol and 25% methanol (HPLC grade). Each mixture was sonicated at 35°C for 20 minutes and well vortexed. Then, it was incubated overnight at 4°C. The methanolic extracts were centrifuged and the supernatants were used for further purification. The solvent was dried up using rotary evaporator at 38 ºC. Afterwards the residues were dissolved in 1mL deionized water, centrifuged (12000 rpm, 5 min) to remove insoluble impurities. Two steps of liquid/liquid extraction with 250 µL chloroform were performed. The uppermost aqueous phase was transferred into a new Eppendorf tube and then, filtered (13mm, PVDF, 0.22µm). HPLC and UV/Vis Spectrophotometry were performed (3, 4). There was no significant difference in the electropherogram pattern between different extraction mixtures. Extraction products exhibited a sharp peak with the retention time of about 2 min with UV absorbance peak in 260-275nm.

Conclusions:

This species might produce a type of precursor of MAAs, and MAAs' production should be induced in further studies, by applying effective factors like UV irradiation, and optimization of nutrient especially phosphate and nitrate.

Keywords: Mycosporine like aminoacids, Cyanobacteria, Sunscreen, Methanolic extraction

Molecular cloning of Urate oxidase gene from Aspergillus flavus in Escherichia coli

Abouzar Shafaghi, Maryam Ebrahimi-Meymand,
Mojtaba Shakibaie, Hamid Forootanfar*

P73

Authors' Affiliations:
Kerman Medical Science University, Kerman, Iran.

Abstract Presenter:
Abouzar Shafaghi

****Correspondance:***
Hamid Forootanfar

Coauthors:
Maryam Ebrahimi-Meymand
Mojtaba Shakibaie

Introduction:

Uricase (urate oxidase, UO) is a key enzyme in nitrogen metabolism which converts uric acid to allantoin. This enzyme can be used in the treatment of hyperuricemia, gout, and tumor lysis syndrome. The recombinant form of this enzyme is prepared by expression of uricase gene from Aspergillus flavus in Saccharomyces cerevisiae. In this research, as the first step for the production of recombinant uricase, we're going to try to clone A. flavus urate oxidase gene in E. coli.

Methods:

The related cDNA of UO of A. flavus was prepared and amplified by RT-PCR method. Then, the amplified gene and pUC19 vector were cut by BamHI and EcoRI restriction endonuclease enzymes and ligation was done by T4 DNA ligase. The ligation product was transformed to E. coli XL1-Blue competent cells. In the next step, the prepared cells were spread on the LB agar medium containing ampicillin, IPTG and X-gal and the recombinant colonies were screened. After extracting the prepared plasmid from positive colonies, the presence of target gene was confirmed by colony PCR method. Finally, the inserted fragment was sequenced to ensure the presence of uricase gene in vector.

Discussions:

In this study, A. flavus urate oxidase gene was successfully cloned in E. coli by different techniques such as enzymatic digestion, RT-PCR, chemical transformation and colony PCR.

Keywords: Uricase, Molecular cloning, Aspergillus flavus, E. coli

In vitro Study of Eosin B-Based Combination Treatment of Plasmodium Falciparum Gametocytes

Sadegh Tafreshi*, Marjan Sabbaghian

P74

Authors' Affiliations:
Islamic Azad University of Medical Science, Tehran. Iran.

Abstract Presenter:
Sadegh Tafreshi

Correspondance:
Sadegh Tafreshi

Coauthors:
Marjan Sabbaghian

Introduction:

Malaria is an important human parasitic infection. In the complex life cycle of malaria parasites, gametocytes are responsible for the transmission of parasites from humans to mosquitoes, while they cause no clinical manifestations [1]. Recently, the development of transmission-blocking interventions has been a major concern for the malaria elimination campaigns [2]. Eosin B - a common laboratory dye- has recently been studied successfully as an antimalarial agent. In the present study, efficacy of eosin B-based combination treatment on Plasmodium falciparum (the most virulent human malaria parasite) gametocytes was investigated in vitro.

Methods:

P. falciparum strain 3D7 was cultured in type O+ human RBCs in a complete medium. Gametocytogenesis was induced by heparin and mature stage V gametocytes were produced about 12 days after induction [3]. Eosin B: chloroquine (Eo: CQ) and eosin B: artemisinin (Eo:Art) were tested on gametocytes. Gametocytes were distributed in a 96-well plate containing 8 serial dilutions of the medicine to test and two control wells were kept free of drug. The plate was placed in a candle jar at 37°C for 48 h. Gametocytemia was microscopically determined. Drug-treated gametocytes viability percentage was determined by spectrophotometry using Malstat assay based on parasite lactate dehydrogenase detection [4]. The results were then analyzed by ANOVA test using GraphPad Prism 6.01.

Results:

Gametocytemia (1.2%) was reduced in both Eo: CQ and Eo:Art. Microscopic study and enzymatic testing showed that Eo:CQ and Eo:Art exhibited significant effect with IC50 0.06 nM CQ:2.3 nM eosin B and 0.125 nM Art:23 nM eosin B respectively on the Plasmodium falciparum 3D7 gametocytes as compare to 30 nM for CQ, 10 nM for Art, and 23 nM for eosin B.

Conclusion:

The results showed that combination therapy containing eosin B can be considered as anti-gametocyte agent. However, it is recommended to perform further tests on these compounds and their effects on the mosquito vector.

Keywords: Malaria, Gametocyte, Eosin B, Chloroquine, Sulfadoxin-Pyrimethamine

Sensitization of breast cancer cells to doxorubicin by SMAC-loaded PLGA-based nanoparticles

Mojgan Nejabat, Mohammad Ramezani, Fatemeh Soltani ,
Mona Alibolandi, Farzin Hadizadeh*

P75

Authors' Affiliations:
Department of Medicinal Chemistry, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Mojgan Nejabat

****Correspondance:***
Farzin Hadizadeh

Coauthors:
Mohammad Ramezani
Fatemeh Soltani
Mona Alibolandi

Abstract:

Inhibitors of apoptosis proteins (IAP) are its key regulators which are suppressed by the second mitochondrial activator of caspases (SMAC) via its N-terminal AVPIAQ binding motif (1). Short peptides and peptide mimetics based on the first six residues of SMAC have been demonstrated to sensitize cancer cells to chemotherapeutics (2,3).

In this study, we developed polymeric nanoparticles based on poly (D, L-lactide–co glycolide)–block–poly (ethylene glycol) (PLGA-PEG) for co-delivery of hydrophilic drug and peptide in order to obtain potent anti-tumor effects. In this regard, we synthesized SMAC peptide, AVPIAQ, via solid phase synthesis strategy. The peptide was characterized by H1NMR and Mass spectrometry analysis. Chemotherapeutic drug, doxorubicin (DOX), and SMAC peptide were separately encapsulated in PLGA-PEG nanoparticles by double emulsion-solvent evaporation (W/O/W) method. The entrapment efficiencies for peptide and DOX were (46%±8.30) and (23.4%±2.7), respectively. The nanoparticles were characterized by laser particle size analyzer and exhibited nanometer sizes (166.6±10.1 nm,) for PLGA-PEG-DOX and (132.8±8.2 nm) for PLGA-PEG-SMAC. In vitro release kinetic measurements of the drugs from the nanoparticles showed a controlled release pattern over 14 days in both PBS and citrate buffer solutions. Also, in vitro cytotoxicity assay showed that co-delivery of synthetic SMAC peptide with DOX could sensitize human breast cancer cell lines, MCF7 and 4T1, in human and mouse models and exhibited potent anti-tumor effect in contrast to both DOX-loaded nanoparticles and SMAC-loaded nanoparticles groups at the same concentration with P0.001 for 4T1 and P0.0001 for MCF7.

Keywords: Co-delivery, Apoptosis, PLGA nanoparticles, SMAC peptide, Doxorubicin

Synthesis of modern adjuvants formulation based on modified carbon-PLGA nanoparticles

Mahboubeh Ebrahimian, Maryam Hashemi , Alireza Haghparast, Mohammad Ramezani*

P76

Authors' Affiliations:
Mashhad University of Medical Sciences, Iran.

Abstract Presenter:
Mahboubeh Ebrahimian

Correspondance:
Mohammad Ramezani

Coauthors:
Maryam Hashemi
Alireza Haghparast

Abstract:

Effective and safe vaccines with reduced dose of antigen and adjuvant require a specific vector for encapsulation and controlling release. Toll-like receptors (TLRs) and their role in innate coordination and adaptive immune response have made possible the development of potent immunomodulatory TLR ligand adjuvants. A powerful way to double TLR stimulation is incorporating both TLRs in one formulation. Polymeric nanoparticles have gained the ability to deliver antigens and adjuvants in order to improve vaccine immunogenicity which can trigger long lasting protective immunity.

In this study, modified carbon-PLGA nanoparticles were prepared by double emulsion evaporation technique (w/o/w) loaded with TLR7/8 agonist physically attached to polyethylene imine (PEI) followed by addition of TLR9 agonist in order to produce a double TLR stimulation nanoparticulate adjuvants for vaccine delivery. The resulting complex was characterized regarding their size, surface charge, adjuvant payload, and the structure was confirmed by TEM electron microscopy. Cytotoxicity of complexs was evaluated in murine macrophage cells (J774) using MTT assay. Studying of cellular uptake using FITC-labeled nanoparticles was also investigated using fluorescent cell analyzer and further confirmed by Flow cytometry.

Particle size of nanoparticles was found to be less than 158 nm with positive zeta potential. Adjuvant payload in all formulation was more than 50%. The cellular uptake of modified-carbon PLGA nanoparticles was higher than controlled groups. No more cytotoxicity in J774 cell line showed after incubation for 24h. Evaluation of in vivo immune responses by modified carbon-PLGA nanoparticles showed more induction of IgG1 and IgG2a antibodies and more IL-4 and IFN-γ cytokines secretion compare to unmodified formulations.

It was observed that modified carbon-PLGA nanoparticles could potentially be used as an ideal and nonviral nano-vectors for efficient vaccine delivery into the desired cells.

Keywords: Carbon-PLGA nanoparticles, Nonviral vaccine delivery, TLR agonists

Improvement of refolding and recovery of hGM-CSF from inclusion bodies using response surface methodology

Vajihe Akbari*, Mina Ahmadian, Ali Jahanian-Najafabadi

P77

Authors' Affiliations:
Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract Presenter:
Vajihe Akbari

****Correspondance:***
Vajihe Akbari

Coauthors:
Mina Ahmadian
Ali Jahanian-Najafabadi

Introduction:

Recombinant granulocyte-macrophage colony-stimulating factor (rGM-CSF) is clinically used for treatment of patients with non-Hodgkin's lymphoma, acute lymphoblastic leukemia and Hodgkin's disease following bone marrow transplantation. rGM-CSF was expressed in different host cells including mammalian, yeast and bacteria. High level expression of rGM-CSF in Escherichia coli led to formation of insoluble and inactive proteins and inclusion bodies. The aim of this study is to optimize solubilizing, refolding and purification of rGM-CSF protein in a full biologically active form.

Methods:

After protein expression in E. coli BL21 (DE3), inclusion bodies were extracted with lysis buffers and multiple stages of high speed centrifugation. To solubilize the inclusion bodies, different concentration of denaturing agents and chaotropes such as urea, guanidine hydrochloride and combination of them was used. The effect of pH and presence β-mercaptoethanol, dithiothreitol and n-propanol on inclusion bodies' solubilizing yield was also checked. After selecting the best solubilizing buffer, refolding of rGM-CSF was optimized using 42 different buffers in a micro titer plate format. Refolded proteins was purified using a chromatography approach such as affinity chromatography or size exclusion chromatography. To assess the biological activity of rGM-CSF, ability of produced rGM-CSF in enhancing the growth of HL-60 cells wasevaluated using MTT assay. To analyze and compare the amount of protein, the method of Bradford Protein assay and SDS-PAGE was used.

Results:

The best condition for solubilizing of inclusion bodies was using a buffer containing 4 M urea (pH 9) and 4mM β-mercaptoethanol. Sorbitol (0.235 M), imidazole (97 mM) and SDS (0.09 %) was the optimum buffer additives for refolding of GM-CSF. Circular dichroism indicated the refolded GM-CSF had correct secondary structure. In vitro, the refolded GM-CSF exhibited a comparable biological activity with the native protein**.**

Conclusions:

This study showed that the type and concentration of denaturing agents and also pH and the presence of oxidative agents and additives are effective on the efficiency of the process of inclusion body solubilizing and refolding of GM-CSF. The approach developed in this work can be important to improve the refolding of other proteins with similar structural features.

Keywords: Escherichia coli, GM-CSF, inclusion body, refolding additives, optimization

Cloning, expression and purification of a truncated form of soluble IL-6R as a drug candidate for the treatment of autoimmune diseases

Saba Faghihi Najaf Abadi*, Fatemeh Shafiee

P78

Authors' Affiliations:
Student Research Committee, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract Presenter:
Saba Faghihi Najaf Abadi

Correspondance:
Saba Faghihi Najaf Abadi

Coauthors:
Fatemeh Shafiee

Introduction:

Inflammation is considered the driving force of many autoimmune diseases especially multiple sclerosis (1). Due to the growth of autoimmune diseases in our life style we need to find a way to reduce it. Interleukin-6 (IL-6) has important roles in inflammation response (2). A new potential approach for the decreasing the inflammatory effects of this cytokine, is the use of soluble receptors for modulating its physiological effects by reducing the binding of IL-6 to specific receptor on the cell surface. This approach got stronger from here that Etanercept (Enbrel®) is a modulator of TNFα, a soluble inflammatory cytokine, via the attachment to the cytokine and inhibition the binding to membrane receptor on the cell surface (3). The aim of this study was to produce the soluble form of IL-6 receptor (IL-6R) with ability to attach to IL-6 without signal transduction.

Methods:

the coding sequence of extra cellular part of IL-6R was optimized for its expression in E. coli BL21 (DE3) as its linkage to the intein 1 of pTWIN-1 plasmid. Induction the soluble expression of IL6-R was performed using 0.4 mM IPTG in 15 0C for 16 hrs of incubation. Finally, purification was performed according to the IMPACT system manual at room temperature for 24 hrs.

Result:

Digestion of recombinant ptwin-1 containing IL-6R gene by EcoRI and BamHI revealed a band approximately in 600 bps which is confirmed by DNA sequencing. The expression results also showed a band about 66 kDa equal to the molecular weight of intein1-IL6R fusion protein in 12% SDS-PAGE. Finally, the purification was confirmed using 12% SDS-PAGE revealed a band in 35 kDa as the size of IL6-R.

Conclusions:

In this project, the expression and purification of a truncated form of IL-6R was successfully performed as the first stage for the creation of a new drug candidate for suppressing the inflammatory effects of IL-6. However, evaluation the affinity of this form of soluble IL-6R to IL-6 must be performed to decide about the initiation in vivo studies.

Keywords: IL-6R

A novel approach to anticancer and antimicrobial drug design and discovery

Negar Shafaei, Hooman Pourbala, Mohammad Hassan Houshdar Tehrani*

P79

Authors' Affiliations:
student research committee, school of pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran.

Abstract Presenter:
Negar Shafaei

***Correspondance:**
Mohammad Hassan Houshdar Tehrani

Coauthors:
Hooman Pourbala

Abstract:

Cancer, one of the main causes of death, is caused by mutation in somatic genes and it leads to increase cells' proliferation and alterations of proteins. Recurrence of tumors and therapy resistance have necessitated the ongoing research for discovery and development of new therapeutic agents.

Antimicrobial peptides are potential alternatives for new therapeutic agents. They have tumor selectivity and low toxicity for normal cells but they have significant drawbacks such as their stability in-vivo environment.

In this study, the structure-activity relationships of anticancer and antimicrobial peptides were compared in order to enhance efficiency and novelty of anticancer drug design using antimicrobial structure-activity relationships and vice versa.

Considering the fact, peptides show diversity in their structure and also targeting. Peptides use different mechanisms against cells such as cell membrane disruption which results in cell apoptosis. Their short time interaction with cells leads to decrease resistance.

As we conducted, the peptides are functional due to their tumor selectivity and low toxicity for normal cells and they have different mechanisms of action. Also, we found positive correlation between antimicrobial and anticancer peptides. Anticancer peptides target different cells and induce apoptosis so there are some peptides for different microbial diseases that we could select for diagnosis, treatment, and prevention of different types of cancers.

Since resistance to present therapeutic agents has risen, effort should be invested in designing peptides for optimizing drug efficiency and drug development. As a result, peptides designed using common SARs are promising alternative therapeutics against cancer and infectious diseases.

Keywords: anticancer, antimicrobial, SAR, cytotoxic, drug design

Dicistronic systems for rapid screening of high expressing colonies

Fatemeh Sadat Shariati, Malihe Keramati, Dariush Norouzian, Vahideh Valizadeh, Shadi Afrasiabi, Fatemeh Sadat Amjad, Reza Ahngari Cohan*

P80

Authors' Affiliations:
Pasteure Institute of Iran, Tehran, Iran.

Abstract Presenter:
Fatemeh Sadat Shariati

***Correspondance:**
Reza Ahngari Cohan

Coauthors:
Malihe Keramati
Dariush Norouzian
Vahideh Valizadeh
Shadi Afrasiabi
Fatemeh Sadat Amjad

Abstract

Identifying stable and high expressing colonies is the main bottle neck in upstream process of production of recombinant protein. Therefore, design and development of rapid screening method would lead to savingtime and decreasing costs. In current study, a dicistronic expression system including enhanced green fluorescent protein (eGFP) as a reporter protein and a bacterial enzyme as a protein model to facilitate screening was developed. The genes encoding eGFP (1152 bp) and enzyme (489 bp) were sequentially cloned in to pET28a within XbaI and NdeI restriction sites. The expression of eGFP has been induced by IPTG 1mM. Expression levels of different colonies in microplate was assessed in 485nm (excitation) and 528nm (emission) of eGFP 4h after induction. The colonies with high level of fluorescent signals (RFU) were analyzed by SDS-PAGE. The results showed that there is a direct correlation between the RFU and expression levels of enzyme. Thus, high enzyme expressing colonies among a large transformed library in rapid screening program could be just identified within 4h by fluorescent spectroscopy without further analysis. The developed system can be expanded for any target protein that express in E. coli hosts.

Keywords: Rapid screening, Dicistronic systems, eGFP.

Construction of Mtb72F Plasmid as a DNA Vaccine Candidate for Mycobacterium tuberculosis

Zahra Shafiee Ardestani, Maryam Sadat Nabavinia,
Mohammad Ramezani, Zahra Meshkat*

P81

Authors' Affiliations:
Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract Presenter:
Zahra Shafiee Ardestani

****Correspondance:***
Zahra Meshkat

Coauthors:
Maryam Sadat Nabavinia
Mohammad Ramezani

Introduction:

Tuberculosis (TB) is one of the most common infectious diseases. According to the World Health Organization, one-third of the world's population is infected to latent form of TB. Despite using BCG vaccine the efficacy of this vaccine for controlling the disease especially in adults is poor. BCG vaccine is not suitable for immune deficienct patients. Producing new and effective vaccine is a hopeful procedure to reduce incidence of TB. The aim of this study was to produce a candidate DNA vaccine against TB called Mtb72F.

Methods and Results:

pcDNA3.1 plasmid was used as a shuttle vector for cloning of mtb32C, mtb39, and mtb32N genes of Mycobacterium tuberculosis. Transformed bacteria detection was done by Colony-PCR and restriction enzyme methods. Recombinant plasmid was transferred to Chinese hamster ovary cell line by Superfect®. Gene expression.was confirmed by RT-PCR. Results: Gel electrophoresis showed the amplified gene fragments size. 429, 614, and 1200 base pairs for mtb32C, mtb32N, and mtb39, respectively. DNA sequencing confirmed desired gene position and orientation in the recombinant plasmid. New recombinant protein expressed in Cho cell line successfully.

Conclusions:

Our research has shown Mtb72F DNA vaccine was successfully constructed and expressed in eukaryotic cell line. This vaccine could be used in animal TB infected model.

Keywords: Cloning, DNA vaccine, mtb32C, mtb32N, Mycobacterium tuberculosis

Essential oil composition and bioassay-directed of Chenopodium album striatum

Negin Khomarlou, Parviz Aberoomand-Azar, Ardalan Pasdaran Lashgari, Reza Ranjbar, Ali Hakakian*

P85

Authors' Affiliations:
Department of Chemistry, Science and Research Branch, Islamic Azad University

Abstract Presenter:
Negin Khomarlou

****Correspondance:***
Ali Hakakian

Coauthors:
Parviz Aberoomand-Azar
Ardalan Pasdaran Lashgari
Reza Ranjbar

Abstract:

The objective of this study was to identify the bioactive compounds of essential oil and evaluate the antibacterial activity of that extracted from Chenopodium album subspecies. striatum against multidrug-resistant bacterial strains (MDR) which were isolated from clinical specimens by conventional methods. Furthermore, eight different Gram-negative and Gram-positive multidrug-resistant bacterial strains were used to investigate the antibacterial potential of the essential oil. The antibacterial activity was tested using MIC and MBC microdilution method, well and disc diffusion in different concentration. The hydro-distillation of aerial parts powder yield was 0.466% (v/w). Essential oil showed bactericidal activity against both MDR Gram-negative and Gram-positive bacterial strains. MIC and MBC results were ranged from 0.31 to 2.5 and 0.62 to 5.0 mg/mL. The inhibition zones in well diffusion method were ranged from 7 ± 0.6 mm to 15 ± 1.0 mm. Disc diffusion method was ranged from 7 ± 0.0 mm to 16 ± 0.6 mm depending on the type of bacterial strain and essential oil concentration. Essential oil of Ch. album had the greatest potential to be considered as an antibacterial agent against MDR bacterial strain. This potential was due to different biological and bioactive compounds like phytol, linalool, α-terpineol, and linolenic acid in the plants.

Keywords: GC analysis, multidrug-resistant bacterial strains, Chenopodium album subsp. striatum

Antibacterial, analgesic and anti-inflammatory activities of Chenopodium album (subsp striatum)

Negin Khomarlou, Parviz Aberoomand-Azar, Ardalan Pasdaran Lashgari, Reza Ranjbar, Ali Hakakian

P86

Authors' Affiliations:
Department of Chemistry, Science and Research Branch, Islamic Azad University, Iran.

Abstract Presenter:
Negin Khomarlou

****Correspondance:***
Ali Hakakian

Coauthors:
Parviz Aberoomand-Azar
Ardalan Pasdaran Lashgari
Reza Ranjbar

Abstract:

Chenopodium album (subsp striatum) is a folk and nutritious medicinal plant (Chenopodiaceae family) and mainly used as a therapeutic agent. The objective of this study was to investigate antibacterial, analgesic, and anti-inflammatory properties of the aqueous and methanolic extracts of Chenopodium album striatum. Antibacterial activity was assessed against eight Gram-negative and Gram-positive multidrug-resistant bacterial strains (MDR) which were isolated from clinical specimens by conventional methods using disc diffusion in different concentrations. Analgesic activity was evaluated by formalin test and for anti-inflammatory activity, paw volume was measured. Tissue culture of C. album striatum was used in this work. The aqueous and methanolic plant extracts (1, 3, 6, 8, and 10 mg/kg) were used to assess antibacterial, analgesic, and anti-inflammatory properties. The findings of this study corroborated and justified the antibacterial, analgesic, and anti-inflammatory properties of C. album striatum as a medicinal plant for the treatment of rheumatic and pain-related diseases. Also, it can be considered as an antibacterial agent but further studies are needed to elucidate the mechanism(s) of action and phytochemical constituent(s) of the plant.

Keywords: Antibacterial, Analgesic, Anti-inflammatory, Chenopodium album (subsp striatum)

Preparation of a nano-sized formulation from Pistacia atlantica for drug delivery purposes and optimization using Response Surface Method (RSM)

Sama Naderitabar*, Mohammad hosein Farzaei, Haniye Delfani

P87

Authors' Affiliations:
Students Research Committee, Faculty of pharmacy, Kermanshah University of Medical, Sciences, Kermanshah, Iran.

Abstract Presenter:
Sama Naderitabar

****Correspondance:***
Sama Naderitabar

Coauthors:
Mohammad hosein Farzaei
Haniye Delfani

Introduction:

Pistacia atlantica Subsp Kurdica is a flavonoids-rich plant with variety of therapeutic activities such as hypoglycemic, antioxidant, anti-inflammatory, and lots of others. Based on the variety of therapeutic applications of P. atlantica, this study for the first time introduced a nano-scale formulation from P.atlantica oleo-resin, which can be used either as a therapeutic candidate or as a nano-carrier for other therapeutic compounds.

Methods:

For this purpose, a set of experiments was designed using Response Surface Method (RSM). Two solvents (ethanol and acetone) were performed to obtain different concentrations of oleoresin (2-5 w%) and the resultant solutions were added drop-wise to distilled water under stirring condition. The volume ratio of distilled water (aqueous phase) to oleoresin solution (organic phase) was another variable range from 5:1 to 15:1. After conducting all the designed experiments, the size and polydispersity index (PDI) of nanoparticles were correlated to the variables by fitting data to different quadratic regressions.

Results:

The size and PDI of nanoparticles were optimized by RSM. P. atlantica nanoparticles obtained in the size range from 155.1-288.4 and PDI from 0.064 - 0.315. According to the data, it is obvious that by using ethanol as solvent, smaller nanoparticles can be achieved while they are more uniform in the size. Increasing the volume ratio of aqueous to organic phase also caused a reducion in the size and PDI. The optimum size and PDI were 177.032 nm and 0.073, which were obtained using ethanol as solvent at the concentration of 3 w% and volume ratio of 15:1. The SEM photograph of the optimized nanoparticles demonstrated the proper surface features of the nanoparticles obtained in this study. The stability analysis also demonstrated that in absence of any surfactant, nanoparticles were stable enough even for a 10-day timeline.

Discussion and Conclusion:

According to the results, it could be concluded that the prepared nanoparticles from P. atlantica oleoresin are promising candidates for novel drug delivery systems to be used either as a carrier for other drugs or as a nano-sized therapeutic agent with higher efficacy, in comparison with the bulk formulations. This type of drug delivery system can be used for different diseases.

Keywords: pistacia atlantica, Nanoparticels, response surface method, Traditional medicine, oleo-resin

Bioassay-oriented isolation and Molecular Modeling of Coumarin Compounds in Ferula pseudalliacea as Acetylcholinesterase Inhibitors

Samaneh Validi, Ahmad Ebadi, Dara Dastan*

P88

Authors' Affiliations:
Hamadan University of Medical Sciences, Iran.

Abstract Presenter:
Samaneh Validi

****Correspondance:***
Dara Dastan

Coauthors:
Ahmad Ebadi

Introduction:

Alzheimer's disease is a neurodegenerative disorder that resulting in memory malfunction and cognitive impairments. The activity of cholinergic system dwindles in Alzheimer's disease. Therefore, the appropriate curing is to increase the level of acetylcholine and the most developed drugs are AChE inhibitors. Ferula pseudalliacea from the genus Ferula can inhibit AChE activity. In the present study, a rational biologically orientated method was applied to discover active component of Ferula pseudalliacea as AChE inhibitor. Molecular modeling study was done to confirm the possible mechanism of inhibition.

Methods:

The dried roots of F. pseudalliacea were powdered and extracted with methanol. The obtained gum was fractionated on a silica gel column that was eluted with n-hexane/CHCl3/EtOAc mixtures in order to increase polarity to prepare fractions. AChE activity was measured by the assay described by Ellman. Molecular docking studies were done by AutoDock 4.2 programs. MD simulations of predicted complex were done by the GROMACS 4.5.6 package with standard GROMOS53A6 force field.

Results:

In this present study, we test AChEI activity of the last fractions of extraction group (1-4) in 125 µg/ml concentration by Ellman test. Table shows that E4 fraction had the maximum inhibitory effect. Focusing on E4 fraction lead to identify a coumarin compound that showed potent inhibitory effect on AChE. Extracted coumarin based compound interacted with Ser208 and Trp86 in AChE active site.

Discussion and Conclusion:

Our findings confirmed that extract of F. pseudalliacea can inhibit AChE and be useful as a lead compound in anti-Alzheimer drug development. Obtained coumarin has essential pharmacophoric groups of AChE inhibitors. Our result highlights the important role of nutrition in Alzheimer patients.

Keywords: Alzheimer, AChE, Ellman, Docking, MD simulation

Protective effects of Achillea wilhelmsii C. Koch aerial part extract on acetic acid-induced ulcerative colitis in rats

Amin Iranpanah, Mohammad Heidarian, Gholamreza Bahrami, Mohammad Hosein Farzaei*

P89

Authors' Affiliations:
Students Research Committee, Faculty of pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Amin Iranpanah

****Correspondance:***
Mohammad Hosein Farzaei

Coauthtors:
Mohammad Heidarian
Gholamreza Bahrami

Introduction:

Achillea wilhelmsii C. Koch is one of the widespread species of Achillea in Iran and a promising candidate to be used as anti-flatulence, spasmolytic, anti-niciceptive, and diuretic agent. Inflammatory bowel disease (IBD), which affects millions of people all over the world, is a chronic, recurrent-remitting inflammation of the small intestine and colon that comprises ulcerative colitis (UC) and Crohn's disease (CD). Although, the etiology of IBD has not been completely understood, recent studies have shown that it is likely influenced by the interaction of environmental, genetic, and immunological factors. The aim of the current study is to evaluate the therapeutic effects of A. wilhelmsii C. Koch aerial part extract on acetic-induced UC in Wistar rats.

Methods and Results:

The aerial parts of A. wilhelmsii were used to prepare the hydroethanolic extract. To examine the therapeutic effects of A. wilhelmsii on UC, Wistar rats were divided into seven groups (n=7) and UC was induced using 4% acetic acid solution. They received different daily doses of hydro-alcoholic extract (6.25, 12.5, 25, 50, and 100mg/kg/day) for 10 days. On the 10th day, the colon tissues were removed and examined using histopathology of lesions and compared to the Sulfasalazine treated and negative control groups. Histopathological studies revealed a decrease in signs of ulceration, necrosis, and cellular infiltration in A. wilhelmsii treated animals. Also, assessment of macroscopic score of ulcer showed that the score was significantly reduced compared to the control animals (P 0.05). The most effective dose for the treatment of UC was 12.5 mg/kg.

Conclusions:

The administration of plant extract significantly attenuated the colonic damage induced by acetic acid, thus A. wilhelmsii can be a promising candidate for treatment of UC. Conducting well-designed clinical studies is necessary to evaluate the safety and efficacy of this natural remedy in patients with IBD.

Keywords: IBD, Achillea wilhelmsii, Ulcerative colitis, Natural product, Plant

Characterization and HPLC analysis of Manna from some Cotoneaster species

Fateme Shariatnaseri, Moloud Fakhri, Mohammad Parviz,
Mohammad Azadbakht, Ali Davoodi*

P90

Authors' Affiliations:
Mazandaran University of Medical Sciences

Abstract Presenter:
Fateme Shariatnaseri

****Correspondance:***
Ali Davoodi

Coauthors:
Moloud Fakhri
Mohammad Parviz
Mohammad Azadbakht

Introduction:

One of the Rosaceae genus with high pharmaceutically and therapeutically potencies is Cotoneaster. Cotoneaster species (Shir-e-Khesht) produce a sugary secretion Manna which consists of different types of carbohydrates. The sugar composition of Cotoneaster species has been determined. In Iranian traditional medicine, the Shir-e-Khesht commonly has been used in the treatment of, particularly constipation and neonatal jaundice.

Methods:

The total amount of reducing sugar was assayed using the cupric/sodium carbonate spectrophotometric method. Free sugar compositions were separately determined using HPLC–RI. The amount of essential microelements in four Cotoneaster species were separately determined using flame Atomic Absorption Spectrometry. Finally, the total flavonoid content in manna of each Cotoneaster species was determined.

Results:

Mannas of C. nummularioides and C. discolor had higher and lower amounts of reducing sugar. HPLC was the most useful method for the analyses of manna exudates. Sugars normally have no absorbance in ultraviolet light; so, they should be detected using RI detectors. According to the HPLC data, C. nummularioides manna has a high percentage of mannitol and low amount of sucrose, which can

increase human interest, particularly in regards to patients with diabetes for its consumption.

Discussion and conclusion:

Manna is sugary exudates, obtained from some plants, such as Cotoneaster species. These secondary metabolites have several compounds, especially monosaccharides and disaccharides. In addition, manna has several types of pharmacological effects, such as antihyperbilirubinemia and laxative effects.

Keywords: Cotoneaster, Rosaceae, Mannitol, Essential microelements.

Bioassay guided isolation of phenolic anticancer agents from Berberis vulgaris fruits by apoptosis induction

Seyed Arash Mirzaei*, Ehsan Ghafourian, Sobhan Ghafourian, Fereshteh Jalilian , Yalda Shokoohinia

P91

Authors' Affiliations:
Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Seyed Arash Mirzaei

****Correspondance:***
Seyed Arash Mirzaei

Coauthors:
Ehsan Ghafourian
Sobhan Ghafourian
Fereshteh Jalilian
Yalda Shokoohinia

Introduction:

In spite of all the significant progress in cancer treatment, cancers are the second leading cause of death in the world (1,2). Cancer development is a multi-stage process that is related to numerous physiological and pathological events such as apoptosis (3). New apoptosis-inducing agents are still needed that intensify natural products research more prominent than ever as a source of lead compounds. Phenolic compounds are a group of natural products, which is extensively distributed over plants and barberry fruits are a rich source of phenolics with several biological activities that can be evaluated for apoptotic effects, too (4,5).

Methods:

In this study an ethanolic extract of Berberis vulgaris fruits was prepared by maceration method and was divided to fractions using chromatographic techniques to render a pure active compound whose structure was identified by 1- and 2-D NMR (Nuclear Magnetic Resonance) as 3-caffeoylquinic acid (chlorogenic acid). Subsequently, cytotoxic activity of chlorogenic acid against 3T3 and MCF-7 cell lines and the level of apoptosis regulating proteins including p53, BAX and Bcl-2 was measured.

Results:

The results exhibited that the prepared extract and all the fractions were potent to kill more than 50% of cancerous cells and successfully reached IC50 against MCF-7 cells; however, these samples were, on the other hand, toxic for normal 3T3 cells. The fraction B possessed the lowest IC50 concentration, 9 µg/mL, and was found to be safe for normal cells at this concentration. According to the results, the P53 expression of cancer cells increased after treatment with 9µg/mL of the selected fraction. The results obviously indicate that the selected fraction successfully up-regulates the pro-apoptotic Bax genes and down-regulated the anti-apoptotic Bcl-2 gene expression in MCF-7 cancer cells. Likewise, the similar trend could be observed in the cells treated with DOX. Considering the data and analysis of the 1H-NMR and 13C-NMR spectra was shown the presence of 3-caffeoylquinic acid (chlorogenic acid) in the ethanolic extract of Berberis vulgaris fruits.

Discussion and Conclusion:

Results supported our previously reported antineoplastic effect of Berberis vulgaris fruits and illustrated that chlorogenic acid is one of active compounds that exert its apoptotic activity by BAX level rise and Bcl-2 proteins decrease.

Keywords: Berberis vulgaris, Apoptosis, Chlorogenic Acid, Natural Product, NMR

Molecular Anti-inflammatory evaluation of rare Coumarins from Apiaceae

Negar Bakhtiari*, Shayesteh Gheibi, Amir Kiani, N. Ghiasvand, F. jafari, S.S.Mirabdali

P92

Authors' Affiliations:
Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Negar Bakhtiari

****Correspondance:***
Negar Bakhtiari

Coauthors:
Shayesteh Gheibi
Amir Kiani
N. Ghiasvand
F. jafari
S.S.Mirabdali

Introduction:

Coumarins are a group of phytochemicals with anti-inflammatory effects. Matrix metalloproteinases (MMP2, MMP9) are a group of enzymes important in inflammatory processes. Ferulago spp are used for gastric inflammations.

Methods:

The total extract of Ferulago macrocarpa was fractionated and purified using several normal and reverse phase columns [5]. Several coumarins were purified. Glioma and B lymphoma cells were used for evaluation of coumarins effect on inflammatory enzymes. In the computational processing, the structures have been docked in the active site of metalloproteinases 9, and significant interactions were detennined. Subsequently, ligand-protein complexes were subjected to molecular dynamics simulation in water, and thermodynamic properties were calculated.

Results:

Regarding cytotoxicity results IC50 of 1-methyl-1-(7-oxo-2,3-dihydro-7H-furo[3,2-g] chromen-2-yl) ethyl 3-methylbut-2-enoate and Grandivitin in B cell lymphoma line were 521.63, 232. 66, and in glioma cell line were 575.58, 322.0 lpg/ml, respectively.

Conclusion:

Two coumarins with the potential inhibitory effects on the activity of MMP 2,9 and anti-angiogenesis were purified from F. macrocarpa fruits. The application can be expected to have therapeutic efficacy in cancer cell lines U87MG and Wehi

Keywords: F. macrocarpa, Matrix Metalloproteinase, Prantschimgin, Grandivitin, Ovarian cancer

Isolation and identification of one new steroidal saponin from the flowers of Allium giganteum L.

Armaghan Baratpour Moghadam*, Masoud Sadeghi Dinani

P93

Authors' Affiliations:
Pharmacy Student, Pharmacy Student's Research Committee, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract Presenter:
Armaghan Baratpour Moghadam

***Correspondance:**
Armaghan Baratpour Moghadam

Coauthors:
Masoud Sadeghi Dinani

Introduction:

Allium species recently attracted attentions due to their polar compounds, flavonoids and steroidal sapogenins and saponins that are more stable than their famous odorant compounds, thiosulfinates (1and 2). As a member of this genus, Allium giganteum is a perennial and bulbous plant, which is used as an ornamental and edible plant worldwide (3). Since the constituents of this plant have been poorly explored, phytochemical investigation of the flowers has been subjected in this study.

Methods:

the air-dried flowers of the plant were extracted in a four step extraction method with hexane, chloroform, choloroform-methanol (9:1) and methanol. The methanolic extract was partitioned between buthanol and water and after concentration, was fractionated by MPLC, using a linear gradient of H2O to MeOH. Saponin-riched fractions were then subjected to final purification by HPLC. Chemical structure of compounds was elucidated by comprehensive spectroscopic analyses including 1D and 2D-NMR spectroscopy.

Results:

Final purification of selected fractions resulted in the isolation of new furostanol type steroidal saponin based on Gitogenin. Exact Structure elucidation was preformed using HNMR, CNMR, HSQC and TOCSY spectra, confirmed the aglycon part as gitogenin with respectively 5 sugar moieties in compound.

Conclusions:

A. giganteum is used in khorassan province as an edible plant. Phytochemical investigation of the plant was performed in this study that resulted the isolation and identification of a new steroidal saponin from the plant for the first time.

Keywords: Allium giganteum, Phytochemistry, Steroidal Saponins, Structure elicidation

Formulation and clinical evaluation of sachet from almond fruit (Prunus dulcis) with prebiotic effect in patients with irritable bowel syndrome (IBS)

Farzad Nasrpour Tahouneh, Maria Esmaeilzadeh, Mahdi Ansari, Fariba Sharififar*

P94

Authors' Affiliations:
Kerman medical university

Abstract Presenter:
Farzad Nasrpour Tahouneh

***Correspondance:**
Fariba Sharififar

Coauthors:
Maria Esmaeilzadeh
Mahdi Ansari

Introduction:

Irritable bowel syndrome (IBS) is a chronic and recurrent functional disorder of digestive system and is the most common diagnosis in gastroenterology clinic. The most signs of IBS are abdominal cramps, bloating, diarrhea, and constipation. Prebiotics are compounds in food that induce the growth or activity of beneficial microorganisms, such as bacteria and fungi. Fruits of almond (Prunus dulcis), are considered a prebiotic. In this work the sachet of almond has been formulated and evaluated clinically in IBS patients.

Methods:

Almond was gathered from Kerman province, identified in Department of Pharmacognosy, Kerman University of Medical Sciences, milled and after passing through the sieve formulated as sachet packaging in the Pharmaceutics Department. Physicochemical characteristics of the almond powder (dimension and weight, moisture and volatile matter, the amount of total ash and insoluble ash in acid, and the amount of almond protein) and sachet formulation (particle size distribution, powder flow, angle of repose, surface morphology, wettability, rheology, bulk density, and powder porosity) were evaluated. 50 patients were categorized into two groups using randomized block allocation method and received 40 g almond (intervention) or wheat flour (placebo) for 20 days and severity of abdominal pain, diarrhea, and bloating were compared as primary outcomes.

Results and Conclusions:

water content and volatile matter were about 3.2% and protein percentage and total ash were estimated 0.3% and 3.04%, respectively. Particles size of particles of powder was more than 1680 microns. The final angle of formulation was reached to 42 degrees with acceptable amount of permeability. Demographic data indicated no significant difference with respect to age, sex, occupation, and educational level between two groups of patients. The results revealed that the clinical symptoms of disease decreased in almond receiving patients, however, the differences were not significant in comparison with placebo (p0.001). Quality of life was significantly improved in almond receiving patients.

Keywords: Almond sachet, Formulation, IBS

Research in natural products: Promising scolicidal effect of Ferula gummosa essential oil and its main component on Echinococcus granulosus protoscolices

Mojtaba Hamidi, Mohadeseh Abouhosseini Tabari, Mohammad Reza Youssefi*

P95

Authors' Affiliations:
Faculty of Veterinary Medicine, Babol-Branch, Islamic Azad University, Babol, Iran

Abstract Presenter:
Mojtaba Hamidi

****Correspondance:***
Mohammad Reza Youssefi

Coauthors:
Mohadeseh Abouhosseini Tabari

Abstract:

Echinococcusgranulosus is of great public health importance. Surgery is the most efficient treatment for this infection. In order to minimize the risk of intraoperative leakage, using scolicidals is crucial. However, several side effects from conventional scolicidals have been reported. In the present study, scolicidal activity of Ferullagummosa essential oil against protoscolices of E. granulosus was evaluated. Furthermore, chemical composition of mentioned essential oil was analyzed by gas chromatographic-mass spectrometry (GC-MS) analysis, and the main constituent was also evaluated for its scolicidal activity. Four different concentrations (10, 20, 50, and 100 µg/mL) of F. gummosa and its main constituent (1, 2.5, 5 and 10 µg/mL) were tested for scolicidal activity at four different time points (10, 30, 60, and 120 min). Mortality rate was measured by eosin staining. Results of GC-MS revealed β-pinene as one of the main constituents of F. gummosa. After 60 min of exposure to 50 and 100 µg/mL of F. gummosa, mean mortality rate of protoscolices was 100%. However, β-pinene with 5 and 10 µg/mL concentrations resulted in approximately 100% mortality. F. gummosa showed a significant toxicity against E. granulosus with 50% lethal concentration (LC50) values of 15.97 µg/ml. The overall toxicity of β-pinene was significantly higher than the whole essential oil of F. gummosa. Based on these results, β-pinene can be considered as candidate ingredient for the development of novel scolicidals after toxicological studies.

Keywords: Albendazole, Cystic Echinococcosis, Hydatidosis, Drug Development, Natural Product Research.

Preparation of anti-acne gel containing Lawsonia inermis and Matricaria chamomilla extracts, and evaluation of its antimicrobial effects

Mohammad Farzandway*, Mahsa Bagheri, Yalda Shokoohinia, Leila Behbood , Shahla Mirzaie, Zahra Pourmanouchehri

P96

Authors' Affiliations:
Students research Committee, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran.

Abstract Presenter:
Mohamad Farzandway

***Correspondance:**
Mohamad Farzandway

Coauthors:
Mahsa Bagheri
Yalda Shokoohinia
Leila Behbood
Shahla Mirzaie
Zahra Pourmanouchehri

Abstract:

Regarding acne and inflammation caused by it, the use of chemical drugs to eliminate acne symptoms is not cost-effective, and because of their side effects, they are not accepted by the public. Consequently, in this project, we will improve the symptoms of acne by using a topical gel containing Chamomile and Henna herbs. The results show that it is possible to make two extracts of henna and chamomile in the form of a topical gel in combination, with proper release, and present it to the drug market.
In order to prepare the gel formulation from the CMC material as a gelling agent, PG was used as a diffusion agent. Phosphorous with pH close to the skin as the solvent, and the active ingredients of Lyophilized Henna and chamomile extracts were used as well as preservative against microbial contamination. To extract the henna leaves and chamomile flowers, the solvents Ethanol 70% and water were used. Using Folin-Ciocalteu, total phenolic compounds were determined in extracts and the gel formulation by UV Spectrophotometry. The antibacterial activity was tested by Disc diffusion method Minimum Inhibitory Concentration (MIC) for optimal formulation
The total phenol content of aqueous extract of inermis leaves, hydroalcoholic extract of chamomile flowers and optimum formulation were calculated 57.8 mg/100 g DW, 181.08 mg/g, and 202.75 mg/g, respectively. Nearly 80 % of Phenolic compounds in the optimal formulation were released during the first 4 hours. The MIC values for S. aureus and P. aeruginosa were calculated. 50 g/ml (chamomile extract), 5 µg/ml (inermis extract) and 1 µg/ml (optimum formulation). According to the results of microbial and physicochemical tests, the prepared formulation has a constant and unobtrusive appearance and is usable as a topical anti-acne pharmaceutical dosage form.

Keywords: Acne, Henna, Chamomile, Gel formulation, Cell diffusion.

Which method is more applicable for analysis of isoquinoline alkaloids? High Performance Liquid Chromatography or Ion Mobility Spectrometry?

Farahnaz Khalighi Sigaroodi, Fateme Tajabadi*

P97

Authors' Affiliations:
Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR

Abstract Presenter:
Farahnaz Khalighi-Sigaroodi

Correspondance:
Fateme Tajabadi

Abstract:

Ion mobility spectrometry (IMS) is a straightforward, low-cost method for fast and sensitive determination of organic compounds. Nowadays, IMS has received increasing attention in environmental and biological analysis, and in food quality determination [1]. Papaveraceae family contains isoquinoline alkaloids such as morphine, codeine and thebaine. This family is relatively large, comprising 26 genera and about 250 species [2]. Morphine and codeine are the most important analgesics for the management of moderate to severe pain. Thebaine is the starting point for the synthesis of many ingredients, including codeine [3]. Liquid chromatography is the standard method for qualitative and quantitative analyzing of isoquinoline alkaloids in British Pharmacopoeia. The aim of this study was the comparison between two methods of analyzing, high performance liquid chromatography (HPLC) and ion mobility spectrometry (IMS). Several parameters of IMS that affected analysis method were optimized through chemometric methods. Validation of the method was done under optimal conditions. Linearity, specificity, precision, accuracy, limit of detection and quantification of the proposed method were investigated. Different parts of some Papaver species were assayed for three isoquinoline alkaloids with both IMS and HPLC methods and the results were compared with each other. Under the optimal conditions, the linearity of the IMS method was determined to be in the range of 0.5-50 µg mL−1. The limits of detection for the target alkaloids for IMS and HPLC system were in the range of 0.1-0.5 µg mL−1 and 0.5-1 µg mL−1, respectively. Regarding to the results, IMS created better sensitivity through fast quantification than HPLC method.

Keywords: Isoquinoline alkaloids, Papaveraceae, IMS, HPLC.

The Leader of addiction treatment in Traditional Iranian Medicine

Niki Vakili Zahir, Shabnam Khatami, Mohsen Naseri*

P98

Authors' Affiliations:
Sanabel Darou, Knowledge-based Company, Tehran, Iran.

Traditional Medicine Clinical Trial Research Center, Shahed University, Tehran, Iran.

Abstract Presenter:
Nik Vakili Zahir

Correspondance:
Mohsen Naseri

Coauthors:
Shabnam Khatami

Introduction:

Regarding to historical evidence, the opium abuse has been reported all over the globe especially since the sixteenth century. Traditional Iranian Medicine has a great potential for solving some of the present problems such as drug abuse. Hakim EmaddodinMahmood-Ben-MasoodShirazi has been a well-known physician of TIM in the sixteenth century. He was confronted with the social new problem of opium addiction in Iran.

Materials and methods:

Present study is to introduce an Iranian sage, Emaddodin and his valuable treatise, Afyunieh, discussing about opium and treatment of opium addiction. Data was collected from historical sources and the book of "Afyunieh". Results: According to Imad al-Din Mahmud, there were three methods for the treatment of opium addiction. The first was increasing the time between opium consumption. The second was the regular reduction of the opium dose. The third—and, according to the author, the best—method was replacing opium with drugs similar or dissimilar to opium and then tapering off these drugs. Several herbs that could be viable alternatives to opium were mentioned in detail in "Afyunieh". Imad al-Din Mahmood also discussed withdrawal symptoms and their remedies. Imad al-Din Mahmood has recommended opium conversion to the use of other materials like Hyoscyamusniger L. as a good substitute for opium.

Conclusion:

He has completely explained the opium in the view of phytology, pharmacological effects, clinical signs and symptoms of addiction, different method and drugs of detoxification, and many other aspects of this matter. Furthermore, Persians were the first to discuss various ways of opium addiction treatments.

Keywords: Traditional Iranian Medicine, Addiction treatment, Hakim Emaddodin Mahmood.

Clinical evaluation of bucoadhesive paste containing Trigonella foenum graecum L. liquid extract

Mohammad Hosseini, Mehdi Ansari*

P99

Authors' Affiliations:
Deputy of Research, Kerman University of Medical Sciences, Kerman, Iran

Abstract Presenter:
Mohammad Hosseini

***Correspondence:**
Mehdi Ansari

Introduction:

Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosal diseases characterized by recurrent and painful ulcerations on the movable or nonkeratinized oral mucosae [1]. One of the most important factors in treating aphthous lesion is continuous contact of drug with lesions. For this purpose, mucoadhesive drug delivery system was selected which has adhesive properties and will decrease the time of burning sensation. Fenugreek seeds extract have shown to be an anti-inflammatory and antinociceptive agent and has shown to be useful for RAS [2]. In this work, fenugreek bucoadhesive paste (FBP) has been formulated and clinically evaluated for RAS treatment.

Methods:

FBP paste and dexamethasone (DM) mouthwash as control and test preparations, respectively, were formulated and packed in coded containers. Patients (60) referring to oral disease department of dentistry at faculty of dentistry were randomly divided into two groups of 30 participants each (control and test). The FBP was used on the aphthous ulcers every 6 hours and DM was gargled three times a day and spit out. Patients checked up at zero, first, sixth and tenth day of the trial and the proper drug usage was reviewed. The diameter of ulcer was measured by a periodontal probe and the score of pain was evaluated using visual analogue scale (VAS) through the experiment. The erythema intensity and exudates were also recorded. All data were analyzed by SPSS18.

Results:

60 patients (29 males, 31 females) with average age of 27.7 yrs. in control and 28.0 yrs. in test group were participated. The results showed that FBP decreased the pain score, ulcer size, erythema and exudation compared to DM group.

Conclusion:

Results indicated that bucoadhesive paste of fenugreek was more effective than dexamethasone mouthwash while it hadfewer side effects as was expected from medicinal plants. Fenugreek extract preparation would be a good candidate for further studies.

Keywords: Recurrent aphthous stomatitis, Bucoadhesive past, Fenugreek

The potential anti-influenza activity of glabrone: blocking cell attachment and virus entry

Nikdokht Ebrahimi*, Shahla Shahsavandi, Mahdi Vazirian

P100

Authors' Affiliations:
Faculty of Pharmacy, Tehran University of Medical Science, Tehran, Iran.
Razi Vaccine and Serum Research Institute, Tehran, Iran.
Agricultural Research Education and Extension Organization, Karaj, Iran.

Abstract Presenter:
Nikdokht Ebrahimi

***Correspondance:**
Nikdokht Ebrahimi

Coauthors:
Shahla Shahsavandi
Mahdi Vazirian

Abstract:

From the first record of influenza in 1580, the disease remains a serious threat to global health. Chemoprophylaxis with antiviral drugs is a major tool to treat influenza infection. The occurrence of frequent antigenic drifts and sometimes antigenic shift in virus genome can lead to the emergence of drug-resistant strains. The selective pressure highlights the need to developnew influenza therapies. Several herbs with alternative modes of action have been introduced as potential sources of anti-influenza drugs. In this study, we investigated the mechanism by which glabrone, a component of Glycyrrhizaglabra root, affects influenza virus replication in human alveoular epithelium (A549) cells.
Monolayers of A549 cells at a concentration of 1×106 cells/ml and influenza virus at MOI of 0.1 PFU/cell were prepared. The cells were treated with glabrone before attaching the virus and after virus adsorption to cells. Cell culture without glabrone treatment was considered as virus replication control. After incubation for 72 days at 37C, the relative viable cell number was quantified by MTT to yield 50% of cytotoxic concentration (CC50) and 50% of effective concentration (EC50). Anti-influenza activity of glabrone was evaluated by selectivity index (SI= CC50/ EC50) and virus titration using median tissue culture infection dose (TCID50). From our data, cytopathic effects were produced and the cell viability was dropped in control cell culture in contrast to the treated cells. The SI>39.83 for both treatments showed the high anti-influenza activity of glabrone. The reduction in viral TCID50 titer by 90% in pre-treatment and treatment during virus adsorption suggested that the antiviral effect of glabrone was limited to an early step in the virus replication cycle. In conclusion, the potential antiviral activity of glabrone is mediated by an interaction with the cell attachment which precedes via the sialic acid-binding of viral haemagglutinin results in reduced virus uptake.

Keywords: Glycyrrhiza glabra root, Glabrone, Influenza virus, Antiviral activity

Study of antioxidant and polyphenolic effects of Lens culinaris on red and green varieties

Marzie Ataii, Anahita Amid Rad, Amir Siahpoosh*

P101

Authors' Affiliations:
Jundishapur University of Medical Science, Ahvaz, Iran

Abstract Presenter:
Marzie Ataii

****Correspondance:***
Amir Siahpoosh

Coauthors:
Anahita Amid Rad

Introduction:

Plants contain compounds such as polyphenols, Nitrogen compounds, vitamins and etc, therefore, they possesshigh antioxidant properties and play a tremendous role in the treatment of diseases. In this study, the antioxidant effect and polyphenolic compounds of Lens culinaris of red and green varieties were studied.

Method:

Green and red lentil fruits were collected from the natural habitat around Hamedan. After drying, they were stored in a refrigerator until they were tested. Then, the powder was extracted using methanol. For antioxidant activity, DPPH, ABTS, FRAP and iron scaling methods were used. Also, phenol compounds were measured using FolenSioukalto test. The level of inhibition of lipid peroxidation of these extracts on the brain, liver and kidney of rats was investigated in laboratory. Results: The amount of phenolic compounds of green lentils was 57168/17 mg / g and red lentils were 76966/15 mg / g. The antioxidant capacity of the extracts was evaluated using DPPH and ABTS methods, In both methods, concentration dependence of antioxidant activity of green lentils was more than red lentils in both methods. Oxidant activity on both virions was observed. With two methods of FRAP and iron scaling test, green lentils with less EC1 than the red lentil extract had more potent effects on trapping iron in the TPTZ complex and reducing it in the environment. In conclusion, it has a stronger antioxidant effect. The iron shake rate is the same for both red and green lentils, meaning the iron shale strength in both lentils is the same.

Conclusion:

In all tests, green lentils have stronger antioxidant activity than lentils. Finally, green lentils proved to be a good source of antioxidant compounds and can be used to make herbal medicines as a potent antioxidant source.

Keywords: Green lentils, Red lentils, Phenolic compounds, antioxidant property

Evaluation and comprarison of antioxidant and anti-lipid peroxidation activity methanolic and hydrolyzed extract of cuttle fish (Sepia pharaonix) of Persian Gulf

Marzieh Ataii, Kosar Alikhani, Behzad Norouzi, Amir Siahpoosh*

P102

Authors' Affiliations:
Jundishapur University of Medical Science, Ahvaz, Iran

Abstract Presenter:
Marzieh Ataii

****Correspondance:***
Amir Siahpoosh

Coauthors:
Kosar Alikhani
Behzad Norouzi

Introduction:
Cuttlefish belongs to cephalopodaclassand their muscle tissue, skin and ink shows various therapeutic effects such as significant antioxidativeones,consideringthat free radicals are the cause of several degenerative diseases such as cardiovascular diseases, cancer, Alzheimer's,etc. This study was designed and conducted to evaluate and compare antioxidant activity of aqueous, methanolic extract of cuttlefish.

Materials and methods:

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

Results:

in DPPH, FRAP and ABTS tests, the antioxidant activity of aqueous extract was more than other extracts. Also aqueous extract had a greater impact on inhabiting lipid peroxidation in the brain, liver and lungs.By comparing hydroxyl radical scavenging with and without the presence of EDTA, it was observed that this extract could directly inhibit the hydroxyl radical.bleomycin assay results showed that pro-oxidant effect increases with increase in concentration.

Conclusion:

The result showed that all extracts have an acceptable antioxidant power. Higher effects of aqueous extract could be due to proteins copounds and water-slouble vitamins in it.

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

A Histological, Histochemical and Ultrastructural Study on the Fundic Region of the Stomach of Capoeta damascina

Mahta Larki*, Nikoo Jafari, Mohammad Shadkhast, Behnam Bakhtiari, Navid Farhadi, Milad Nourozy

P103

Authors' Affiliations:
Shahrekord University of Medical Science, Shahrekord, Iran.

Abstract Presenter:
Mahta Larki

Correspondance:
Mahta Larki

Coauthors:
Nikoo Jafari
Mohammad Shadkhast
Behnam Bakhtiari
Navid Farhadi
Milad Nourozy

Abstract:

The present work was carried out on 20 specimens of both sexes of Capoeta damascina in order to observe the morphological and histological as well as the fine structure of fundic gland region of the stomach. The present study demonstrated the presence of folded mucosa in the fundic region of the stomach and its surface epithelium was lined by simple columnar mucosecretory cells. The lamina propria contained simple tubular branched glands. The fundic glands were made up of oxyntico-peptic cells. The glandular cells were positive to PAS and negative to Alcian blue and showed strong positive activity for acid phosphatase. The electron microscopic examination revealed that the oxyntico-peptic cells contained a dense tubulovesicular system that may participate in hydrochloric acid production, in addition to the extensive presence of mitochondria and rough endoplasmic reticulum. The Golgi complex is involved in the formation of secretory or zymogen granules. Oval to round- shaped enteroendocrine cells were scattered among the glandular and superficial columnar cells, which stained positive to Grimelius stain. The glands were surrounded by collagenous fibers and smooth muscle fibers.

Keywords: Fundic stomach, Histology, Ultrastructure, Capoeta damascina, Gastric glands

The study on synergistic effect of boiling Cumin (Cumin cyminum L) with three- and four-drug treatment protocols based H pylori eradication

Mohammad Bagher Majnooni*, Mari Ataei, Turaj Ahmadi-Jouiybari, Yalda Shokoohinia

P104

Authors' Affiliations:
Department of Pharmacognosy and Biotechnology, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Mohammad Bagher Majnooni

***Correspondance:**
Mohammad Bagher Majnooni

***Coauthors**:*
Mari Ataei
Turaj Ahmadi-Jouiybari
Yalda Shokoohinia

Abstract:

Helicobacter pylori as a human pathogen, a Gram-negative bacteria and a major cause of peptic ulcer disease. This study aimed at determining the synergistic effects of boiling cumin (cumin cyminum L) with three- and four-drug treatment protocols against H. pylori in patients with peptic ulcers. This study included peptic ulcers patients with confirmed Helicobacter pylori that were randomly selected. Then the patients were divided to five groups and treated with boiling cumin with and without three and four drugs treatment protocols. To measure the eradication of Helicobacter pylori the 14C urea measurement method was used. This test was performed before and four weeks after completion of treatment. This study included 75 patients (48 males and 27 female) who were diagnosed with peptic ulcers disease. Based on the results, in all five groups eradication of H pylori was observed. H pylori eradication in third groups (cumin with quadruple therapy) and group IV (triple therapy) were about 3.5 times higher than fifth groups (quadruple therapy), respectively. Based on the results of this study, the boiling cumin can be used as a complementary therapy and synergistic medicine alongside conventional medicine protocols.

Keywords: Cumin cyminum L, eradication, Helicobacter pylori, peptic ulcers, synergistic effect

The analysis of fixed oil from Spinacia oleracea and Lactuca sativa

Zahra Moayyedi Banan*, Niloofar Mohammadi

P105

Authors' Affiliations:
Shahid Beheshti University of Medical Sciences - School of Pharmacy, Tehran, Iran.

Abstract Presenter:
Zahra Moayyedi Banan

****Correspondance:***
Zahra Moayyedi Banan

Coauthors:
Niloofar Mohammadi

Abstract:

In Iranian traditional medicine spinach seed used as a laxative, and cooling applications and lettuce seed used as hypnotic and narcotic agent; also it is beneficial for urinary tract. The fixed oil from seeds of Spinacia oleracea from Chenopodiaceae and Lactuca sativa from Compositae were extracted and analyzed by GC/MS.

The seeds were obtained from the herbal market of Tehran in the summer of 2009. The seeds were powdered with an electrical mill and their oils were extracted by n-hexane. The oils were reacted with BF3 in methanol resulting in the release of volatile methyl-ester.

Next, solution containing methyl esters were analyzed by GC/MS and mass spectra were obtained. The components were identified by comparison based on mass spectra with standard and the library system.

Based on the findings, in spinach seed, 8 fatty acids identified. Methyl stearate (% 6.7) and methyl palmitate (% 8.1) were the major components. In the oil of lettuce seed 15 acids were identified. Methyl linoleate (22.2 %) and methyl eicosanoate (6.2%) were the major components.

Keywords: Spinach seed, Lettuce seed, Fatty acids, Methyl stearate, Methyl palmitate

Screening of Total Phenolic, Flavonoid and Flavonol content of Capparis Spinosa

Mohsen Azad

P106

Authors' Affiliations:
Department of Pharmacology & Toxicology, Faculty of pharmacy, Ardabil University of Medical Science, Ardabil, Iran.

Abstract Presenter:
Mohsen Azad

****Correspondance:***
Mohsen Azad

Introduction:

Capparis spinose L. belongs to the Capparidaceae family. Caper has been reported to have many pharmacological activities such as cytotoxic, anti-diabetic, anti-inflammatory, antimutagenic and antioxidant effects. It has very active chemical groups such as alkaloids, phenolic, flavonoids, tannins and many other minerals. Phenol compounds in plants have antioxidant activity and ability to scavenge free radicals and have beneficial effects on human health. This experiment was conducted in order to compare the phenolic, flavonoid and flavonol content of different parts (leaf, bud and root) of Capparis spinosa.

Methods:

Different parts of plant (leaf, bud and root) were collected from the lands in the moghan region of the Ardabil province, Iran, during the June of 2018. The collected plants were cleaned, dried under shade at room temperature and powdered and soaked in ethanol/ methanol solution in a large container for 3 days. The extract was filtered and the filtrate was dried by using a rotary evaporator.

The amount of total phenolic content in the extracts was determined with the Folin- Ciocalteu reagent and Gallic acid was used as a standard. The amount of flavonoid in the extracts was determined by a State Pharmacopeia of USSR method and rutin was used as a reference compound. Yermakov, Arasimov, & Yarosh method was used for determination of flavonol contents and rutin was used as a standard.

Results:

Comparing different components (phenols, flavonoids and flavonols) in the plant extract, phenolic content was more than the other component and the leaf extract had the most phenolic (534.55 mg/g GAE) content. The amount of all components in the root was very low and can be ignored.

Conclusions:

The present study indicated that leaf extract of Capparis spinosa has the greatest antioxidant activity and can be used to explore new medicines in treatment of diseases manifested by oxidative stress and inflammation.

Keywords: Capparis Spinosa L, Extract, phenols

Study the invitro cytotoxicity of some plants in Asteraceae family on breast cancer cells

Faezeh Fakhar*, Shirin Moradkhani, Meysam Soleimani Badia

P107

Authors' Affiliations:
Hamedan University of Medical Sciences, Hamedan, Iran.

Abstract Presenter:
Faezeh Fakhar

****Correspondance:***
Faezeh Fakhar

Coauthors:
Shirin Moradkhani
Meysam Soleimani Badia

Introduction:

Cancer is the most common cause of death in the world. The majority of deaths from cancer occur in women with breast cancer. Therefore, further research is needed for the development of safe products for the prevention and treatment of all human cancers. Natural products are lead molecules for many of the drugs that are currently in use. About 50% of prescribed drugs in the world originate from plants. According to the previous research acetone extract of Calendula officinalis have anticancer activity and sesquiterpenoids from the aerial parts of Inula lineariifolia have inhibitory effects on breast cancer cells. The aim of present study was to investigate the in-vitro cytotoxicity of hydro-alcoholic extracts of Calendula officinalis and Inula helenium.

Methods and Results:

The rhizome of Inula helenium and the flower of Calendula officinalis were collected from cultivated populations in Hamadan province. Each dried plant material was macerated in hydro-alcohol (80%), for three times, each time three days. The resulting macerate was filtered and concentrated by means of rotary evaporation. MCF-7 (5×10^3) cell line was incubated at 37° c in a CO_2 incubator. Cells were exposed with different concentration of each extract ranging from 10-400 µg/mL. after treatment, 20 µl of MTT solution added into each of the well, and the plate was further incubated for 3h. The medium was removed and 200 µl of DMSO added into each well for solubilizing the formazan. The absorption was measured using an ELISA reader at 570 nm. Cell viability expressed as a percentage of absorbance values in treated cells to that in control cells.

Conclusions:

The cytotoxicity results for Inula helenium and Calendula officinalis against MCF-7 human tumor cell lines were significant, with IC50 values of 468µg/ml and 289µg/ml. The above tested species also have cytotoxicity for MCF-7 human tumor cell lines.

Keywords: Inula helenium, Calendula officinalis, MCF-7, Asteraceae

Chemical Composition and Anti-Helicobacter pylori Activity of the Essential Oil Isolated from Ferulago carduchorum Aerial Parts

Saeed Rezaee, Shirin Moradkhani, Meysam Soleimani Badia, Fereshteh Golfakhrabadi*

P108

Authors' Affiliations:
Ahwaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract Presenter:
Saeed Rezaee

****Correspondance:***
Fereshteh Golfakhrabadi

Coauthors:
Shirin Moradkhani
Meysam Soleimani Badia

Introduction:

Ferulago carduchorum (Apiaceae family) which grows in west part of Iran, is added it to dairy and oil ghee by local people to delay expiration date and give them a pleasant taste. Helicobacter pylori (H. pylori) colonizes in the stomachs of about 50% of the world's population. This organism is the main risk factor for peptic ulceration as well as gastric mucosal-associated lymphoid tissue (MALT) lymphoma and gastric adenocarcinoma [1]. The aim of this study was to investigate the composition of essential oil of F. carduchorum and to evaluate the activity of F. carduchorum against clinical isolates of H. pylori.

Methods and Results:

The essential oil was obtained by hydro distillation using a Clevenger type apparatus. Micro-well dilution assay was conducted for the assessment of plant's minimal inhibition concentration (MIC) using the CLSI (The Clinical & Laboratory Standards Institute) method [2].

The results of essential oil analysis of F. carduchorum were led to identification of 43 compounds, represented 92.3% of the total oil. Major components of essential oil were identified as (Z)-β-ocimene (43.3%), α-pinene (18.23%), bornyl acetate (3.98%) and myrcene (3.15%). Minimum inhibitory concentrations (MIC) measured for essential oil of Ferulago carduchorum against 6 clinical isolates of H. pylori were 18.97, 9.48, 18.97, 9.48, 18.97, 18.97 mg.ml-1, respectively. The MIC of Clarithromycin as positive control against 6 clinical isolates of H. pylori was 0.002 mg.ml-1.

Conclusions:

Results showed that among 43 identified components, monoterpenes were the most identified compounds (84.63%) that only 5.99% of them were oxygenated whereas, sesquiterpenes were totally detected about 6.65% with 0.71% oxygenated sesquiterpenes. (Z)-β-ocimene and myrcene as acyclic monoterpene hydrocarbons and α-pinene as a cyclic monoterpene hydrocarbon were identified as main compounds. The essential oil of F. carduchorum showed antibacterial activity against 6 clinical isolates of H. pylori. The Minimum inhibitory concentrations of essential oil against clinical strain 2 and 4 were lower than other strains.

In comparison with other herbal essential oil, F. carduchorum showed potent anti H. pylori activity. The determination of antibacterial activity of the essential oil have great importance in pharmaceutical industry for finding new drugs from natural sources.

Keywords: Ferulago carduchorum, Essential oil, Antimicrobial, Helicobacter pylori

Effect of aqueous extract and different fractions of Prosopis farcta on the atherosclerosis in human endothelial cells (HUVEC)

Haniye Delfani*, Zahra Azadi, Mohammadhosein Farzaee

P109

Authors' Affiliations:
Kermanshah University of Medical Sciences, Kermanshah, Iran.

Abstract Presenter:
Haniye Delfani

****Correspondance:***
Haniye Delfani

Coauthors:
Zahra Azadi
Mohammadhosein Farzaee

Introduction:

Atherosclerosis is a common chronic inflammation that is considered as one of the main causes of heart and brain strokes in industrial and developing countries. Prosopisfarcta root has been proposed as an efficacious natural drug for cardiovascular disorders in traditional medicine. The present study evaluates the cytotoxicity of aqueous extract and different fractions of P. farcta root toward Human umbilical vein endothelial cells (HUVECs).

Methods and Results:

By sedimentation and SPE methods three different fractions were isolated from aqueous extract of P. farcta. Cellular toxicities of LPS, aqueous extract, and polysaccharide-enriched fraction were analyzed in cells using the methyl thiazoltetrazolium bromide method (MTT). In order to measure oxidative stress induced by LPS, ROS accumulation was detected in cells using the DCF fluorescence probe.

The results showed that both the aqueous extract and its effective fraction had no cytotoxic effect on HUVEC cells and LPS doesn't induced cytotoxicity in this cell line. Adding LPS to HUVEC cells caused a significant increase in ROS levels.

Conclusions:

According to several reports on the potential of P. farcta as a candidate against atherosclerosis, further understanding about its cyto-compatibility might be of utmost importance. This study demonstrated that the aqueous extract and the active fraction of P. farctaexert no toxicity toward HUVECs. This finding confirm the cyto-compatibility of this medicinal plant and reveals that it can be used in managing cardio vascular disease particularly atherosclerosis, without causing any toxicity. The present study can serve as basis for future investigation on the treatment of atherosclerosis in human studies.

Keywords: Atherosclerosis, Prosopis farcta, cytotoxicity, LPS

Phytochemical study and antibacterial activity of Rosa damascena Mill. against Klebsiella pneumoniae and Acinetobacter baumannii, in vitro

Vahid Reisi Vanani*, Sajad Maghareh-Dehkordi, Zahra Lorigooni, Abolfazl Gholipour

P110

Authors' Affiliations:
Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran

Abstract Presenter:
Vahid Reisi Vanani

****Correspondance:***
Vahid Reisi Vanani

Coauthors:
Sajad Maghareh-Dehkordi
Zahra Lorigooni
Abolfazl Gholipour

Introduction:

Emergence of antibiotic resistant pathogens is threatening medical achievements in healing infections. In the United States, for example, 2 million people are affected by these organisms annually and among them 23000 individuals pass away. Natural bioactives are rich sources for developing antibacterial agents. The petals of Rosa damascena Mill. (PR) is one of those sources with many therapeutic properties, as a result, the aim of this study is to evaluate antibacterial effect of its extract on two multidrug-resistant (MRD) bacteria.

Methods:

In this experimental study, total phenolic content (TPC) and total flavonoids content (TFC) of hydroalcoholic extract of PR were determined by Folin-Ciocalteu and Aluminum chloride colorimetric method. Minimal inhibitory concentration (MIC) of PR extract on the standard strain of Klebsiella pneumoniae (ATCC 700603) and Acinetobacter baumannii (ATCC BAA-747) were determined by resazurin-microdilution assay, each test was repeated for three times.

Results:

TPC and TFC of this extract were measured 57.70 mg equivalent Gallic acid/g dried extract and 10.1 mg equivalent Rutin/g dried extract respectively. MIC of PR on K. pneumoniae (4096 µg/ml) and A. baumannii (128 µg/ml) were reported by detecting the last wells with the lowest concentration of agents that had no color change from blue to pink and finally Minimum bactericidal concentration (MBC) of PR on A. baumannii (512 µg /ml) and K. pneumoniae (8192 µg/ml) were determined by adding 10 µl of the wells that had no color change on agar plates, the lowest concentration that caused 99.9% reduction in the original inoculum was considered as MBC.

Conclusions:

Results indicated that PR is a good source for phenolic components and these components could be purified and used against MDR bacteria, especially A. baumannii that showed noticeable susceptibility to PR's crude extract in this study, although more studies in in-vivo conditions are needed.

Keywords: Rosa damascena Mill, Klebsiella pneumonia, Acinetobacter baumannii, Flavonoids

Determination of essential oils effect of Zingiber officinale, Cinnamomum verum, trachyspermum ammi, Cuminum cyminum and carum carvi on Bacteria inducing clonal dysbiosis in vitro

Leila Ebrahimi Ghasour*, Ahmad Yari Khosroushahi, Azita Dilmaghani

P111

Authors' Affiliations:
Faculty of Pharmacy, Tabriz University of Medical Sciences, East Azerbaijan, Iran

Abstract Presenter:
Leila Ebrahimi Ghasour

***Correspondance:**
Leila Ebrahimi Ghasour

Coauthors:
Ahmad Yari Khosroushahi
Azita Dilmaghani

Introduction:

Modern lifestyles, misuse of antibiotics, and etc, can cause the emergence of new diseases by demolishing the microbial balance of the body. In the colon dysbiosis, microbial balance of the colon disappears, and causes many problems, including IBS and IBD and etc. Medicinal plants with potentially antibiotic activity can be beneficial by modifying colon flora and preventing damage progression. In this study, the effect of essential oils of Zingiber officinale, Cinnamomum verum, trachyspermum ammi and carumcarvi on intestinal microorganisms effective in dysbiosis were investigated under laboratory conditions.

Methods:

Essential oils were purchased from Barij Essence Kashan. Purified and Lyophilized Microorganisms were purchased from Iranian Research Organization for Science and Technology (IROST). Essential oils antibacterial effects were studied by well assay method, Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC). Essential oil was diluted with ethanol and tween 80 for MIC and MBC assay. Results were interpreted using CLS1 standards.

Results:

Cinnamomum verum had the most significant inhibitory effect on all pathogens. The highest diameter of inhibition zone was observed Bacillus cereus. Trachyspermum ammi essential oil had moderate inhibitory effects on pathogens but no effects on shigella Flexneri. Cuminumcyminum and carumcarvi had similar inhibitory effects on Klebsiellapneumoniae, ShigellaFlexneri and Pseudomonas aeruginosa. Zingiber officinale had the least inhibitory effect on all pathogens. In the case of useful microorganisms, Cinnamomum verum showed the highest inhibitory effect, but no effect on the Saccharomyces cerevisiae, Pichia kudriavzevii, Kluyveromyces marxianus, Candida krusei. Extract of Cinnamomumverum at concentrations of 50 mg/mL on ShigellaFlexneri, Pseudomonas aeruginosa and Lactobacillus paracasei and carumcarvi extract at concentration of 50 mg/mL on ShigellaFlexneri showed bactericidal effect. Other extracts showed bacteriostatic activity.

Conclusions:

The inhibitoriest effect on the pathogens was found in the trachyspermum ammi essential oil, while it had the least inhibitory effect on beneficial microorganisms. Cinnamomum verum essence, with very good inhibitory effect on pathogens and inhibition of some useful microorganisms, can be promising to make effective drug.

Keywords: Medicinal plants, clone Dysbiosis, Minimum inhibitory concentration, Minimum Bactericidal Concentration, Antibiotic

New terpenoids isolated from Cleome khorassanica Bunge & Bien with cytotoxicity against DU-145 and LNCaP prostate cancer cell lines

Seyed Arash Salehi*, Seyed Mustafa Ghanadian,
Seyed Ebrahim Sajjadi, Mahmud Aghayi

P112

Authors' Affiliations:
Department of Pharmacognosy, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract Presenter:
Seyed Arash Salehi

***Correspondance:**
Seyed Arash Salehi

Coauthors:
Seyed Mustafa Ghanadian
Seyed Ebrahim Sajjadi
Mahmud Aghayi

Introduction:

In recent pharmacological investigations on different cleome species showed interesting biological activities including antitumor, antihyperlipidemic, antihyperglycemic, anthelmintic, antibacterial and antiinflammation properties [1,2]. In many cases, terpenoidal compounds were responsible for observed biological activities. For example, dammarane-type triterpenes and cembranoid-type have significant cytotoxic activity against P388 leukaemiacells [3]. The present analytical study was designed to identification of terpenoidal content of Cleome khorassanica and evaluation of their cytotoxicity.

Method and Materials:

In this phytochemical study, aerial parts of C. khorassanica were collected from torbateheydarieh, deposited with herbarium code of 3989, dried and grinded. Acetone/Methanol (1:1) extract was prepared using perculation method. The extract was subjected to column chromatography on silica gel to separate the components of total extract. Based on TLC spots, fractions were subjected to size exclusion chromatography on sephadex LH- 20 to achieve more purification. Finally, subfractions were purified using HPLC on YMC silica column. Isolated compound was identified by NMR (HNMR, CNMR, HMBC, HSQC, COSY, NOESY) and high resolution mass and were screened for in vitro anticancer activity against breast (MCF-7) and prostate (DU-145 and LNCaP) cancer cell lines, by MTT assay.

Result:

Three compounds were isolated, purified and elucidated as a new dammaranetriterpene named: 1,11diacetoxy-3- oxo-4-oxa-A-homo-25,26,27-trinordammarano -24,25lactone (2), and another new dammaranetriterpene in natural sources as 24-acetyl-3,25-dihydroxy- 17,24-epoxydammarane (3), together with a known flavonoid: 5-hydroxy-3,6,7,8,3',4',5'- heptamethoxyflavone (1). Data from the MTT test showed decrease in all three cell lines viability, especially in compound 3. For MCF-7 cells reported IC_{50} were 94.7µg/ml, 197µg/ml, 31.6µg/ml. Also the numbers, 134.6µg/ml, 178µg/ml, 21.6µg/ml were found as IC50 for DU-145 cells. Finally, for LNCaP cells IC50 defined as 154µg/ml, 180µg/ml, 34.9µg/ml (respectively for compounds 1, 2 and 3).

Discussion:

This phytochemical study on C. khorassanica resulted in isolation and structure elucidation of two new dammarane-type triterpenes (1-2) for the first time from the natural sources, and a flavonoid compound (1). According to the data from the MTT test, compound 3 has significant cytotoxicty against breast and prostate cancer cell lines. The most cytotoxicy of compound 3 obtained against DU-145 cell line. Expected cytotoxity for compounds (1,2) was not observed.

Keywords: Cleome khorassanica, Terpenoid, DU-145, LNCaP

Molecular anti-inflammatory evaluation of meroterpenoids from asafetida

Sara Kazemi*, Yalda Shokoohinia, Khadije Almasi, Nastaran Ghiasvand, Fatane Jafari, Fereshteh Jalilian, Amir Kiani, Mohsen Shahlaei

P113

Authors' Affiliations:
Student Research Committee, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Sara Kazemi

****Correspondance:***
Sara Kazemi

Coauthors:
Yalda Shokoohinia
Khadije Almasi
Nastaran Ghiasvand
Fatane Jafari
Fereshteh Jalilian
Amir Kiani
Mohsen Shahlaei

Introduction:

Ferula assafoetida of Apiaceae bears sesquiterpenecoumarine from phenolic class. Coumarins are a group of phytochemical that have anti-inflammatory effect and inhibit matrix metalloproteinase 2, 9 (MMP2, 9) that contribute in inflammatory process. Reported studies on medicinal plants for their inhibitory effect on MMP are very limited. Due to high levels and diversity of coumarin in this plant, the ability of compounds to inhibit the enzymes mentioned above seems to be useful.

Methods:

Sesquiterpenecoumarins are purified using HPLC column and applied on cell line U87MG and Wehi for studding VEGF, MMP2,9 activities in the computational part, the structure has been docked in active site of metalloproteinase 9, and significant interactions were determined. Subsequently ligand-protein complexes were subjected to molecular dynamics simulation in water and thermodynamic properties were calculated.

Results:

In the computational part, the structure has been docked in active site of metalloproteinase 9, and significant interactions were determined. Subsequently ligand-protein complexes were subjected to molecular dynamics simulation in water and thermodynamic properties were calculated.

Conclusions:

Four coumarins, galbanic acid, mogoltadone, kellerin, polyanthin and polyanthinin with the potential inhibitory effects on the activity of MMP 2,9 and anti-angiogenesis were purified from F. assafoetida. Therefore, they can be potentially effective in the treatment of cancers.

Keywords: Galbanic acid, Mogoltadone, Kellerin, Polyanthin, Polyanthinin, Matrix Metalloproteinase.

Effect of Artaderm herbal Ointment containing alcoholic extracts and Alpha ointment on the healing process of Rat's second degree burn

Saeed Naseri*, Seyedeh Simin Dakhilpour, Mahsa Hadipour Jahromi, Mohammad Shourmij, Masoud Fardin

P114

Authors' Affiliations:
Herbal Pharmacology Research center, Tehran Medical Sciences, Islamic azad University, Tehran, Iran.

Abstract Presenter:
Saeed Naseri

***Correspondance:**
Saeed Naseri

Coauthors:
Seyedeh Simin Dakhilpour
Mahsa Hadipour Jahromi
Mohammad Shourmij
Masoud Fardin

Introduction:

Burn and damage to tissues caused by heat, one of the most severe type of cell damage is localized and systemic forms on the body. After car accidents, burn injuries are the second leading cause of death from accidents. Burns strongly associated with the depth and size of apartments available in second degree burns of moderate intensity, only the epidermis and dermis damaged part of the underlying tissues do not harm, but because of the severity of the injury and abundance, this type of burn is inevitable. Given the existence of these types of problems and accidents in our country and other countries, synthesis new drugs with faster wound healing, control all aspects of health and mortality, one of the main factors management and research priorities in this field.

Methods:

In this study, after survey and selection of effective herbs organs, matching identification and verification to ensure the selection of unit Herbarium, extraction is done. And the healing effects Artaderm and clinical, biological tests was performed. on 30 female rats, wistar, weighting 200-220 g. for better study and availability of reliable empirical evidence of these tests, were studied to compare to fundermol (Alpha). After causing damage to the wound, the rats were randomly divided into four groups. The control group received no treatment, group therapy once a day with Artaderm at a certain time, a group of daily time with fundermol (alpha) at a certain time, a day at a certain time of the dressing were eucerin. Evaluation of healing, the wound, with the wound area, on days 0 -7 - 14 to 21, from all groups of mice, were studied with photography and AutoCAD software.

Results:

Statistical comparison of the burn area of study groups on days 7-14 and 21 post-burn, showed that between the control group and other groups, there was significant difference (P 0.05). While the best results for the treatment group Artaderm with eucerin. According to studies, pathology, quickly restored with remarkable Artaderm was a significant difference between the effects of the other drugs.

Conclusions:

In the end, according to the results, medication Artaderm in terms of healing the wounds and the healing has successfully demonstrated its therapeutic effect, can be found in the fundermol (alpha) is an appropriate medication Wound treat in Iran and abroad offered.

Keywords: herbal ointment, artaderm, second degree burn, rat, wound

Variations in Fatty Acid Contents of Sesame Oil Due to Roasting Duration and Temperature

Fariba Hajifathaliha*, Nafiseh Sadeghi

P115

Authors' Affiliations:
Department of drug and food control, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Fariba Hajifathaliha

****Correspondance:***
Fariba Hajifathaliha

Coauthors:
Nafiseh Sadeghi

Abstract:
Sesame oil contains Palmitic, Stearic, Oleic and Linoleic acids as its four main fatty acids. Several pretreatments such as roasting, steaming, microwaving and etc., are applied to sesame seeds. This study was conducted to evaluate the changes in amount of fatty acids in sesame oil due to roasting temperature and duration. The samples were treated as in the AOAC (Association of Agricultural Chemists) method for preparation of fatty acid solution and the method adopted for this analysis was GC, without using derivation. Two Iranian cultivars; Moghan and non-branching Naz, were chosen and roasted at 180°C, 200°C and 220°C in electric oven, with durations of 10, 15 and 20 minutes at each temperature. One unroasted group was kept for the purpose of comparison. The results showed that in Moghan cultivar, the maximum amount of all four fatty acids occurs when the seeds are roasted at 220°C. At this temperature, Palmitic and Linoleic acids reach their highest amount (12.2± 0.79(P0.05) and 46.53±0.22 respectively) after 20 minutes, while Stearic and Oleic acids become maximal (6.46±0.2 and 48.33±0.62 respectively) after 15 minutes (P0.05). According to this study, roasting does not significantly affect fatty acid contents in non-branching Naz, except for Palmitic acid, which reaches (8.69±0.33) after roasting at 220°C for 10 minutes (P0.05).

Keywords: Sesame oil, Roasting, Gas chromatography

Compare Rheum khorasanicum B. Baradaran & A. Jafari roots composition with Rheum ribes roots

Saeede Vasei*, Mitra Mehrabani, Mehrnaz Mehrabani, Mehrzad Mehrabani

P116

Authors' Affiliations:
Kerman University of Medical Science, Kerman, Iran.

Abstract Presenter:
Saeede Vasei

Correspondance:
Saeede Vasei

Coauthors:
Mitra Mehrabani
Mehrnaz Mehrabani
Mehrzad Mehrabani

Introduction:

Rheum khorasanicum B. Baradaran & A. Jafari is described and illustrated as a new species from NE Iran.

No studies have ever been done on chemical compounds of this genes.

The purpose of this research is to determine the amount of the main substance Rheum khorasanicum B. Baradaran & A. Jafari roots in available methods and compared with Rheum ribes roots.

Methods:

After collecting the plant from the Neyshabur area in december, february and april, the root skin was removed and dried in shade, and then extracted by ethanol 80 ° after grinding.

The aluminum chloride colorimetric technique was applied to estimate the total flavonoid content and The amount of routine and quersetin was measured according to the Folin–Ciocalteu method. Thin-layer chromatography was performed.

Results:

The results showed that the root of this plant has flavonoids, tannins and alkaloids The amount of routine and quercetin was measured based on the Gallic acid standard and it was determined that the amount of routin and quercetinin the Rheum khorasanicum B. Baradaran & A. Jafar is higher than the Rheum ribe.

Keywords: khorasanicum B. Baradaran & A. Jafari, flavonoid, neyshabur

A study on Anti-inflammatory effect of alcoholic extract of the seeds from the plant Albizia lebbeck on formalin-induced inflammation of the rat paw and identification of specific inflammatory pathway

Saeed Rezaee, Neda Sistani, M.Vazirian, Samira Hosseindoust, Kiana Naderinia*

P117

Authors' Affiliations:
Ahwaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract Presenter:
Saeed Rezaee

****Correspondance:***
Kiana Naderinia

Coauthors:
Neda Sistani
M.Vazirian
Samira Hosseindoust
Kiana Naderinia

Introduction:

Gastrointestinal side effects of nonsteroidal anti-inflammatory medications are increasing the interest of researchers on studies of medicinal plants with anti-inflammatory effects. A. lebbeck is a tropical plant that grows in Iran. Its different parts are having numerous health benefits including anti-inflammatory, analgesic, and anti-tumor.

The aim of this study is to demonstrate anti-inflammatory effects of hydro alcoholic extract of seeds and to identify the exact inflammatory blocked pathway.

Methods:

Hydro alcoholic extract was prepared by maceration in 70% alcohol and injected to the paw of Wistar rats classified to 6 groups each including 6 rats at doses of 200-300-400-500 $_{mg/kg}$.

The Positive control group received 300 mg / kg aspirin and the negative control one recived 5 ml / kg normal saline intraperitoneally. Half an hour later, 100 ml of Formalin was injected subcutaneously. The rat paw volume changes are measured at the first hour every 15 minutes and every 1 hour to 5 hours with Lactometer.

We investigated the anti-inflammatory mechanisms of the fraction using in vitro and in vivo inflammatory models.

Results:

The doses of 200 and 300 $_{mg/kg}$ of extract compared to aspirin were significantly weaker ($P < 0.5$) and doses of 400 and 500 $_{mg/kg}$ had stronger anti-inflammatory effects. Finally, the dose of 400 $_{mg/kg}$ as the best dose was chosen.

Conclusions:

A. lebbeck plant extract at a dose of 400 $_{mg/kg}$ could have more powerful effect than aspirin. The inhibition of histamine H1 receptor, histidine decarboxylase gene transcriptions, and Nitric oxide pathway blockade were observed.

Keywords: A lebbeck, Anti-inflammation, Formaline, H1 receptor, Nitric oxide pathway

Microalgae Applications in the Treatment of Alzheimer's disease

Niloufar Asadbeygi, Leila Beykmohammadi, Tahereh Hosseinabadi*

P118

Authors' Affiliations:
Department of Pharmacognosy and Pharmaceutical Biotechnology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Niloufar Asadbeygi

****Correspondance:***
Tahereh Hosseinabadi

Coauthors:
Leila Beykmohammadi

Introduction:

Alzheimer's disease (AD) is a neurological disorder caused by various mechanisms which results in memory loss, neuronal death, loss of synapses and cholinergic neurons, brain damage, and ultimately cell death. There is no certain cure for AD available today. Current pharmacological strategies towards the treatment and management of AD involve the use of cholinesterase and β-secretase inhibitors.

Recent studies seek to discover new compounds with robust neuroprotective potential with less or no adverse effects. Microalgae have recently attracted much attention because of their numerous secondary metabolites such as carotenoids, polyphenols, sterols, fatty acids, and polysaccharides that exhibit different biological activities and own neuroprotective potential. Hence, in this review we focused on the potentials of microalgae and their active compounds in AD treatment.

Methods and Results:

Searching keywords of microalgae, Alzheimer`s disease and acetylcholinesterase in different search engines like Google scholar, Scopus, PubMed, and etc. resulted in numerous published articles.

Some microalgae like Spirulina, Chlorella, Nostoc, and Synechococcus species exhibited neuroprotective role via inhibition of radical-induced neuronal damage and nerve cell injury prevention due to their antioxidant compounds include carotenoids like astaxanthin and also phenolic compounds. In a study, Dunaliella salina has the highest content of 9-cis β-carotene protecting the brain cells from oxidative stress in AD.

Also, red, brown, and green microalgae have potential to be used as functional neuroprotective agents due to their effectiveness in inhibiting cholinesterase. Some compounds obtained from microalgae provide 2 types of ChE (AChE and BChE). For example, dieckol and phlorofucofluoroeckol derived from Ecklonia estilonifera showed memory enhancing and AChE inhibitory activity. Two sterols and eight phlorotannins were isolated from E. stolonifera demonstrated inhibitory activities AChE.

Furthermore, there are some studies on defensive effects of microalgal extracts against β-secretase inhibition and Aβ-aggregation. Fucoidan is a sulfated polysaccharide isolated from brown algae, Focus vesiculosus was able to protect rat cholinergic neuronal death and can block Aβ (beta-amyloid) neurotoxicity. Nannochloropsis ocaenia's extract showed protection on neuronal cells against Aβ-induced toxicity.

Conclusions:

According to the clinical and commercial importance of the algae-derived bioactive components for curing AD, review of the related studies of these natural sources guides us for discovering of new compounds using in treatment of AD.

Keywords: microalgae, Alzheimer`s disease

The effect of scrophularia Spp for scar treatment

Negar Tahmasebi, Maryam Ghaderi , Fereshteh Bagheri, Ali Ebrahimi, Soheila Shahryari, Reza Tahvilian*

P119

Authors' Affiliations:
Kermanshah University of Medical Science, Kermanshah, Iran.

Abstract Presenter:
Negar Tahmasebi

****Correspondance:***
Reza Tahvilian

Coauthors:
Maryam Ghaderi
Fereshteh Bagheri
Ali Ebrahimi
Soheila Shahryari

Introduction:

Scrophularia striata (S.striata) is a plant growing in west part of Iran and has been used practically in traditional folk medicine in different disorders like wounds, burns and etc. this plant contains components with inflammatory effects like NO2 . In this study we prepared a cream containing 10% hydro-alcoholic extract of S.striata based on gallic acid and measured them by spectrophotometric method.

Aim of the study: to investigated the effect of 10% S.striata cream on wound healing in rats and human.

Methods:

21 male Wistar rats were divided into three groups (7 rats were used in each group). We punched a thickness wound in right side skin of each Wistar rat. Then damaged area of groups one and two are separately covered with topical cream phenytoin and 10% extract cream of S. striala two times a day for 28 days, while the control group has no received any treatment with cream. All animals of each group were sacrificed on the 14 and 28 days for histological analysis.

In clinical trials, 13Volunteers with skin injuries such as burn, excision, incision and etc. were selected. All subjects were treated two times a day for 28 days with S. striata cream. Wound healing in rats and subjects was assessed by digital photography and statistical analysis according to visual scoring performed by Spss software.

Results:

Experiments showed significantly faster wound healing findings for S.striata cream vs control group and with significant difference and slightly faster results vs reference cream. Observable re-epithelialization was recorded from day 7 on. Wounds covered with S.striata 10% at day 14 and reference ointment at 28 day were entirely or almost fastened?healed. A significant difference between groups was seen for S. striata and reference cream.

Keywords: S.striata extract, cream, wound healing, Human, rat

Bioactive Compounds from "Marine Organisms" and Their Anticancer Activity

Ebrahim Salimi Sabour*, Tahereh Hossein Abadi, Faraz Mojab, Samira Gheisari

P120

Authors' Affiliations:
Department of Pharmacognosy, School of Pharmacy, Shahid Beheshti Medical Sciences, Tehran, Iran

Abstract Presenter:
Ebrahim Salimi Sabour

****Correspondance:***
Ebrahim Salimi Sabour

Coauthors:
Tahereh Hossein Abadi
Faraz Mojab
Samira Gheisari

Abstract:

The oceans are considered as "mother of life", they cover more than 70% of the earth's surface and they contain highly ecological, chemical and biological diversity with different ranges of aquatic plants and animals from microorganisms to vertebrates.

The scientists estimate that marine environments (ME) contain over 80% of world's plants and animal species; additionally, it has an especial store house of novel bioactive natural compounds with great structural and chemical diversity and complex features, so it can provide the potential to produce valuable therapeutic entities.

In the last decade, more than 3000 new molecular structures had been isolated from ME, this is important that ME may offer a variety of novel therapeutic lead compounds and the bioactive natural products from marine were demonstrated different structural or chemical characteristics from those are found on land.

arine organisms like: sponges, sea slugs, octopuses, algae and … are a rich sources of bioactive compounds and many researches focused on evaluation of their biological activities such as: anticancer (AC) activity, antibacterial, anti-inflammatory and ….

Despite advances in biomedical research and novel technologies, cancer is a growing public health problem and according to the World Health Organization (WHO) the incidence of this illness is about 6 million cases per year.

Owing to unwanted side effects, high toxicity, drug resistant, new kinds of cancers and ... observed with current AC agents and especially synthetic drugs, many researches have oriented toward natural components and especially from marine organism because of diverse unique structures. Now, there are several drugs in clinical trial that they are isolated from marine organisms.

In this lecture, we will explain about importance of marine organisms' potential in new drug discovery and highlight the human? drugs that are currently in clinical trials.

Keywords: Marine organisms, Bioactive compounds, Anticancer activity, Clinical trials

Evaluation of acute and subchronic toxicity of ethanolic extract of Thymus kotschyanus in Wistar rats

Niloufar Sharifpour Langeroudi, Seyyed Naser Ostad,
Mohamadreza Shams Ardekani, Mahdi Vazirian*

P121

Authors' Affiliations:
Tehran University of Medical Sciences, Iran.

Abstract Presenter:
Niloufar Sharifpour Langeroudi

***Correspondance:**
Mahdi Vazirian

Coauthors:
Seyyed Naser Ostad
Mohamadreza Shams Ardekani

Abstract:

The acute and subchronic toxicity of the ethanol extract of Thymus kotschyanus was evaluated in Wistar rats. For acute toxicity, five rats received different doses of the plant's extract and were kept under observation for 14 days. In subchronic toxicity study, 20 rats, divided in to two groups, were administrated 1000 mg/kg of the extract daily, for 45 days. Animals' food and water consumption, body weight changes, hematological, biochemical, and histopathological parameters were determined periodically. According to the results, there was no mortality in the maximum administrated dose (6000 mg/kg). The extract caused no significant (p0.05) changes in all of the biological test parameters. In microscopic examination, there were not any differences between the two groups of control and test. Based on the results of acute and subchronic toxicity study, it can be concluded that the extract is relatively non-toxic after oral consumption.

Keywords: Toxicity, T. kotschyanus, rat, Ethanolic extraction, LD50

Study of the effect of intraperitonal injection of methanolic extract of Zataria multiflora Boiss. on learning and spatial memory of male rat

Nima Vaziri, Elham Vazifehkhahan, Vahid Sheibani, Fariba Sharififar*

P122

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Science, Kerman, Iran.

Abstract Presenter:
Nima Vaziri

****Correspondance:***
Fariba Sharififar

Coauthors:
Elham Vazifehkhahan
Vahid Sheibani

Introduction:

Zataria multiflora (Zm), has been proposed for memory enhancing in Persian traditional medicine, but has not been studied yet. In this research, we aimed to study the plant effect on spatial memory in scopolamine-induced amnesia animasl as well as in vivo anticholinesterase effect.

Methods and Results:

Aerial parts of the plant were extracted with methanol and standardized on the basis of rutin content. Male rats received three doses of Zm extract (100, 200 and 400mg/kg, i.p for 7 days) and 30 min after the last dose, scopolamine (1mg/kg) was administered in animals. Learning capacity and spatial memory were studied using morris' water maze (MWM) and passive avoidance test (PAT) methods. Anticholinesterase activity was studied using Ellman's method. Physostigmine (0.3mg/kg) and piracetam (200mg/kg) were used as positive control.

All doses of Zm extract significantly decreased the distance and time spent to find platform in MWM and increased the time latency in PAT test. The highest effect of Zm was observed at 200mg/kg which showed the greatest AChE inhibition too.

Conclusions:

Considering the reported antioxidant and anti- inflammatory effects of the plant, these results might have collective beneficial effects on memory and can lead to positive outcomes in AD management.

Keywords: Cognition disorder, Zataria multiflora, Morris water maze, Passive avoidance test, Anticholinesterase

Cytotoxic Effect of curcumin on B16 and L929 cell line

Zahra Yazdani*, Alireza Rafiei, Pooyan Mehraban , Pouria Biparva

P124

Authors' Affiliations:
Department of basic Sciences, school of animal science and fisheries, University of Sari agricultural sciences and natural resources, Sari, Iran

Abstract Presenter:
Zahra Yazdani

Correspondance:
Zahra Yazdani

Coauthors:
Alireza Rafiei
Pooyan Mehraban
Pouria Biparva

Introduction:

Melanoma is one of the most malignant skin cancers that has been developing rapidly over the last few years. Using of herbal compounds is very important in the cure of cancer. In this study, for the first time, the effect of cytotoxicity of curcumin has been investigated on B16 (melanoma cancer cell line) and L929 (fibroblast cell line)

Materials and methods:

Cytotoxicity of curcumin was evaluated at concentrations of 100, 50, 25 and 12 (µM) in B16 (melanoma) and L929 (Normal fibroblast) cell lines by MTT method. Statistical analysis was performed using SPSS 23 and T-Test method. The value of P 0.05 was considered for determining the significance level.

Results:

According to the findings of this study, the cytotoxicity of curcumin is significantly dependent on the concentration and increases with increasing concentrations on two cell lines and this compound has higher cytotoxicity on cancer cell line than normal cell line.

Conclusion:

Curcumin is a pure herbal compound and thus can produce a potent cytotoxic effect on melanoma cancer cells than normal cells, therefore it can be used as a drug for melanoma cancer

Keywords: Curcumin, cytotoxicity, melanoma cancer, MTT assay

Cytotoxic Effects of acetate Extract of Galanthus transcaucasicus bulb On B16 and L929 cell lines

Zahra Yazdani*, Alireza Rafiei, Pooyan Mehraban , Pouria Biparva

P125

Authors' Affiliations:
Department of basic Sciences, School of Animal Science and Fisheries, University of Sari Agricultural Sciences and Natural Resources, Sari, Iran

Abstract Presenter:
Zahra Yazdani

****Correspondance:***
Zahra Yazdani

Coauthors:
Alireza Rafiei
Pooyan Mehraban
Pouria Biparva

Introduction:

Cancer is one of the biggest problems in the world and According to 2012 global statistics, 8.2 million deaths per year have occurred in world because of cancer. The use of medicinal plants in the cure of this disease is very important due to the lack of side effects? Galanthus transcaucasicus from Galanthus genuse and Amaryllidacea family has High amounts of phenols and flavonoids and antioxidant compounds. In this study, for the first time, the cytotoxic effects of bulbs of this plant on melanoma tumor and normal cell lines are examined.

Materials and methods:

The acetate extract of the Galanthus transcaucasicus was extracted. Cytotoxicity of Galanthus transcaucasicus extract at concentrations of 25, 50, 100 and 200µg / ml was evaluated on B16 (melanoma) and L929 (Normal fibroblast) by MTT method. Statistical analysis was performed using SPSS 23 and ANOVA. The value of P 0.05 was considered for determining the significance level.

Results:

According to the findings of this study, the cytotoxicity of the Galanthus transcaucasicus extract is significantly dependent on the concentration and increases with increasing? concentrations, also cytotoxicity of this extract on B16 (melanoma cancer cell line) is higher than cytotoxicity of it on L929 (normal cell line).

Conclusion:

The results showed that the extract of this plant can be used in treatment of cancers such as melanoma because it has mixture antioxidant and pro-oxidant compounds with different cytotoxic effect, also it has higher cytotoxicity on cancer cell line than normal cell line.

Keywords: Galanthus transcaucasicus, cytotoxicity, melanoma cancer, MTT assay

Effect of Aqueous Extract of Hyphaen thebaica (L) Seed on Some Haematological, Biochemical and Histological Features of Surri Mice

Nikoo Jafari*, Mahta larki, Mohammad Shadkhast, Behnam Bakhtiari Moghadam, Navid Farhadi, Kazem Noruzi

P126

Authors' Affiliations:
Department of Veterinary Histology, School of Veteriniry Medicine, Shahrekord University_Shahrekord, Iran

Abstract Presenter:
Nikoo Jafari

***Correspondance:**
Nikoo Jafari

Coauthors:
Mahta larki
Mohammad Shadkhast
Behnam Bakhtiari Moghadam
Navid Farhadi
Kazem Noruzi

Abstract:

It is well known that many diseases throughout the world are well treated with medicinal plants which have great protective and therapeutic effects. The effect of crude ethanolic extract of Hyphaenethebaica (L) Mart (HT) on some hematologicalindices and some biochemical parameters in normal albino miuse in addition to the histological studies on liver and kidney tissues of these mice were investigated. Thirty-two normal white male surri mice were divided into four groups of eight mice/each group. Group one served as the control group, group 2, 3 and 4 served as the test groups for the crude aqueous extract of HT seeds to which oral intubation of 100 mg/Kg, 200 mg/Kg and 400 mg/Kg dosages of the extracts were administered, respectively. All the mice were fed with normal diet and water ad-libitum for 21 days then after then, all groups were sacrificed, two blood samples were collected for haematological and biochemical parameters. Specimens from liver and kidney were collected for histopathological examination. Group (3; 200 mg/Kg) and group (4; 400 mg/Kg) revealed a significant increase ($P \leq 0.05$) increase in total WBCs, total RBCs, and haemoglobin concentration compared with the control. However, significant decrease ($P \leq 0.05$) was observed in the level of cholesterol and triglycerides after treating with 400 mg/Kg dose only when compared with the control. There was no significant change in platelets count, liver functions (alanine transaminase (ALT), asparatate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyltranspeptidase (GGT), Albumin and total protein) and kidney functions (urea and creatinine).Histopathological results of taken liver and kidney tissues revealed no significant changes when compared with the control group.

Keywords: Seeds; Hyphaenethebaica; Surri mice; Haematological studies; Biochemical studies; liver histopathology

The improving effects of hydroalcoholic extract of Pinus eldarica bark extract on dexamethasone-induced dyslipidemia, hyperglycemia and oxidative stress in rats

Najmeh Assarzadeh, Behzad Zolfaghari, Leila Safaeian*

P127

Authors' Affiliations:
Isfahan University of Medical Sciences, School of Pharmacy and Pharmaceutical sciences, Isfahan, Iran.

Abstract Presenter:
Najmeh Assarzadeh

****Correspondance:***
Leila Safaeian

Coauthors:
Behzad Zolfaghari

Abstract:

Pinus eldarica is a widely growing pine in Iran, which consists of biologically active constituents with antioxidant properties. The present study is an attempt to investigate the beneficial effects of hydroalcoholic extract of P. eldarica bark on dexamethasone-induced dyslipidemia in rats. Total phenolic content of P. eldarica bark hydroalcoholic extract was determined using Folin-Ciocalteu method. Thirty-six male Wistar albino rats divided in 6 groups of 6 were studied. Group 1 (dyslipidemic control) received dexamethasone (10 mg/kg/day, s.c.) for 7 days, groups 2-4 (treated) received dexamethasone and was simultaneously treated orally with 100, 200 or 400 mg/kg of P. eldarica extract, group 5 (normal control) received daily injection of saline (1 ml/kg, s.c.) and oral administration of the vehicle and group 6 (reference) received dexamethasone and atorvastatin (40 mg/kg, orally). At the end of experiment, blood glucose, lipid profile and malondialdehyde (MDA) levels were assessed in serum samples. Livers were processed for histopathological examination. Total phenolic content of A. elburzense extract was estimated as 37.04 + 1.8 % (mg/100 mg) gallic acid equivalent. The plant extract significantly reduced serum blood glucose, triglyceride, total cholesterol, and MDA levels and also improved liver steatosis compared to the dyslipidemic control group. These results suggest the hydroalcoholic extract of P. eldarica bark has anti-dyslipidemic, anti-hyperglycemic and antioxidant effects on rats receiving high doses of dexamethasone.

Keywords: Pinus eldarica, Hyperlipidemias, Lipid peroxidation.

Evaluation of analgesic and anti-inflammatory actsactivity of compounds

Ali Hakakian*, Negin Khomarlou, Tayebeh RadjabianMehdi Zarrei, Amin Davari , Majid Hassanpour-Ezatti

P128

Authors' Affiliations:
Faculty Member of Production and Research Complex, Pasteur Institute of Iran

Abstract Presenter:
Ali Hakakian

****Correspondance:***
Ali Hakakian

Coauthors:
Negin Khomarlou
Tayebeh RadjabianMehdi Zarrei
Amin Davari
Majid Hassanpour-Ezatti

Abstract:

The aim of the present study is to investigate and evaluate analgesic and anti-inflammatory potential of aqueous and methanolic extracts of Drosera spatulata using different models in rats. The aqueous and methanolic extracts of D. spatulata (at the doses of 3, 4, 5, 8, and 10 mg/Kg body weight) was investigated for anti-inflammatory and analgesic activities using various experimental models. Analgesic activity was evaluated using formalin induced paw licking models in rats. Anti-inflammatory activity was evaluated using measurement of paw edema volume model in rats. Our results showed that both extracts caused a significant ($P < 0.05$) dose-dependent reduction of inflammation and pains induced by agent used. These results provide support for the use of aqueous and methanolic extracts of Drosera spatulata in relieving inflammatory and pain. It also give an insight into the development of new agents for treating inflammatory and pain diseases but further studies are needed to elucidate the mechanism(s) of action and phytochemical constituent(s) of the plant.

Keywords: D. spatulata, Analgesic, Anti-inflammatory, extracts, Formalin Test

Effects of Vildagliptin on TLR2 and TLR4 in insulin resistance Rat's liver

Kolsoom Alizadeh, Siamak Sandoghchian*

P129

Authors' Affiliations:
Immunology Research Center, Tabriz University of Medical Sciences

Abstract Presenter:
Kolsoom Alizadeh

Correspondance:
Siamak Sandoghchian

Introduction:

Diabetes is known as a chronic hyperglycemia mainly due to two major defects, insulin resistance, and inefficiency of beta cells. In other words, type 2 diabetes is an imbalance in glucose homeostasis and its normal metabolism. Obesity is one of the most important risk factors for diabetes and it can be induced by insulin resistance by various mechanisms such as nervous, endocrine, and inflammatory mechanisms. Given that inflammation in the adipose tissue is associated with insulin resistance. Therefore, the aim of this study was to investigate the effect of vildagliptin on TLR-2 and TLR-4 in the liver of insulin resistance rats.

Materials and Methods:

In this study, 30 rats were randomly divided into 3 groups. 1- Non-diabetic healthy group. 2- Diabetic group (induction of diabetes through a saturated fat diet for 10 weeks). 3- Diabetic group treated with vildaglitin (? mg / kg / for 3 days) via gavage.

The tissue samples extracted from the rat liver were evaluated for determination of TLR-4 and TLR-2 using Real Time PCR.

Results:

The results showed that insulin resistance significantly increased (P 0.001) the expression of TLR-2 and TLR-4 in both liver and macrophage, wheras treatment with vildagliptin significantly decreased TLR-4 and TLR-2 expression (P 0.001). A marked difference was shown in reduction of TLR4 and TLR2 expression comparing control and untreated diabetic rats against each other.

Discussion and Conclusion:

According to the results, it can be concluded that vildagliptin caused a reducing expression of TLR-2 and TLR-4 in kupffer and macrophage and also inhibited the inflammatory pathways. Further investigations are required to determine exact mechanisms underlying interactions between vildagliptin and other inflammation parameters.

Keywords: Vildagliptin, Insulin resistsnce, TLR4, TLR2, Rat

Serum Levels of Interleukin-33 and sST2 in Opioid Users

Kimia Javdani, Ali Dehshahi, Negar Firouzabadi*

P130

Authors' Affiliations:
Shiraz University of Medical Sciences, Iran.

Abstract Presenter:
Kimia Javdani

****Correspondance:***
Negar Firouzabadi

Coauthors:
Ali Dehshahi

Introduction:

There are evidences that show addiction have a suppressive impact on immune function. This may result in serious infectious and inflammatory diseases. Many experiments indicate that opiate abusers are more susceptible for different kinds of infection due to the impaired innate immunity. Today, there are many studies that show opioids may have different effects on the immune system including suppressive effect, modulatory effect or binary effect. Interleukin-33 (IL-33) is a novel member of interleukin-1 family which shows to have a crucial role in innate and adaptive immune system. ST2 is known as a receptor for IL-33. Soluble IL-33 binds to soluble ST2 (sST2) in the blood. This study evaluated the effect of opium abuse on the expression of IL-33 and sST2 receptor genes.

Methods:

The concentration of IL-33 and sST2 in blood samples of opioid abusers (n=22) and healthy volunteers (n=22) were measured by ELISA method.

Results:

IL-33 level in blood samples was significantly higher in opioid abusers compared with control group (p0.001) while sST2 concentration in blood samples was significantly lower in opioid abusers (p0.001).

Conclusion:

Few studies show that IL-33/ST2 signaling pathway has an important role in anti-tumor immune function, metastasis, and tumor growth. Therefore, lower level of sST2 may be significant for the risk of cancer. In addition, sST2 have a regulatory effect for inflammatory and Th2 cytokines. Thus, inflammatory responses can be suppressed in the result of a decreased sST2 level. High level of IL-33 is in correlated with inflammatory diseases, lung inflammation, asthma, and various rheumatological diseases like rheumatoid arthritis (RA). Thereby, high IL-33 serum level in the blood sample of addicts to opium may indicate that addiction to opium result in an inflammation in the body. Besides, sST2 acts as a decoy receptor which binds to free IL-33 in blood in order to restrict the potential deterious effect of elevated IL-33. To conclude, however IL-33 seems to be elevated due to an inflammation in addicted people, lower level of sST2 can restrict the inflammatory responses and may be a risk factor for some cancers.

Keywords: opioids, interleukin 33, sST2

Pramlintide, an amylin analogue promotes angiogenesis in vitro

Mahdi Dehghani Firooz Abadi, Golnaz Vaseghi, Mina Mirian, Leila Safaeian*

P131

Authors' Affiliations:
Isfahan university of medical sciences, Iran

Abstract Presenter:
Mahdi Dehghani Firooz Abadi

****Correspondance:***
Leila Safaeian

Coauthors:
Golnaz Vaseghi
Mina Mirian

Abstract:

Abnormalities of angiogenesis may contribute in the pathogenesis of diabetes complications. Pramlintide is an injectable amylin analogue drug for treatment of type 1 and type 2 diabetes. This study aimed to investigate the effect of pramlintide on angiogenesis in human umbilical vein endothelial cells (HUVECs). Cell proliferation and migration were evaluated using 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and Transwell methods. In vitro angiogenesis was assessed by tube formation assay. VEGF secretion by HUVECs was also determined using an enzyme-linked immunosorbent assay (ELISA) kit. Pramlintide significantly increased cell migration at the concentrations of 1 and 10 µg/ml. It also enhanced average tubules' length and size and mean number of junctions. However, there was not any change in HUVECs viability and VEGF release. Findings of this investigation provided in vitro evidence for pro-angiogenic activity of pramlintide through promoting migration and tubulogenesis in HUVECs.

Keywords: Angiogenesis, Cell migration, HUVEC, Pramlintide, VEGF

Evaluation of 5HT3 receptor expression and microinjection of ondansetron in medial prefrontal cortex on fear extinction in rats with PTSD

Sara Raziee*, Ahmad Mohammadi Farani

P132

Authors' Affiliations:
Students Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran.

Abstract Presenter:
Sara Raziee

Correspondance:
Sara Raziee

Coauthors:
Ahmad Mohammadi Farani

Introduction:

Post-traumatic stress disorder (PTSD) is a mental disorder that can develop after exposure to a traumatic event. Drugs that facilitate fear extinction in animals are promising agents in treating this condition. Studies show that 5HT3 receptors have key role in fear extinction process. The aim of the present study is first to find if 5HT3 receptor expression is changed in medial prefrontal cortex (m-PFC) of PTSD rats, and second to find the effects of microinjection of ondansetron on receptor expression in this region and its effects on fear extinction in rats.

Methods:

Different groups of rats were cannulated in the m-PFC through the stereotaxic method of surgery. Single prolonged stress was used as an animal model of PTSD. Different doses of ondansetron were microinjected to the animals and fear extinction was measured by evaluation of freezing time in contextual fear conditioning paradigm for rats. Other animal tests such as Elevated plus maze (EPM) and locomotor activity was also conducted for more behavioral evaluations. 5HT3 m-RNA expression of dissected m-PFC was measured by real time RT-PCR method.

Results:

5HT3 expression was increased in PTSD rats compared to control (P0.05) which was inversed by ondansetron. Microinjection of ondansetron significantly decreased the freezing time in PTSD rats (p0.05) compared to control.

Discussion and conclusion:

Our results suggest that PTSD may increase fear extinction by inducing 5HT3 receptor expression and 5HT3 antagonists are good candidates to alleviate the symptoms of this disorder.

Keywords: PTSD, Fear extinction, Stereotaxic surgery, Ondansetron, Mpfc

Evaluation of the protective and healing effect of Heracleum lasiopetalum Boiss in acetic acid-induced ulcerative colitis in rats

Hossein Malekshahi, Shahram Miraghaee, Gholamreza Bahrami, Mohammad Hossein Farzaei, Atefeh Babaie*

P133

Authors' Affiliations:
Students Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Hossein Malekshahi

****Correspondance:***
Atefeh Babaie

Coauthors:
Shahram Miraghaee
Gholamreza Bahrami
Mohammad Hossein Farzaei

Introduction:

Ulcerative colitis is a chronic inflammatory disease with unknown etiology. So far no definitive treatment for this disease has been identified. Therefore, research to produce new drugs seems necessary. Heracleum lasiopetalum has been traditionally used to treat disease of the GI. This study aims to evaluate the protective and healing effects of Heracleum lasiopetalum Boiss in acetic acid-induced ulcerative colitis in rats.

Methods:

Female wistar rats were randomly divided into different protective and treatment groups. 1 ml of 4% acetic acid was administered intracolonically and the duration of contact of acetic acid with the colon was 10 minutes. In the different treatment groups 5, 10 and 40% of aqueous plant extract, positive control and negative control rats were gavaged 3 days after administering acid (for 6 days). In the different protective groups rats were gavaged 7 days before to 3 days after administering acid. The extent of the mucosal ulcers, hyperemia, inflamation, mucosal bleeding was studied and scored according to Gerald Classification System Score (Macroscopic). Slides were prepared in order to do a pathologic evaluation by using modified Wallace method (Microscopic). The body and colon weight changes and food and water intake were also assessed.

Results:

There was a significant change in the intake of food in the extracts and positive control treatment groups compared to the negative control group p0.05. Body weight changes in control positive treatment group significantly increased in comparison to the negative control group p0.05. There was no significant difference between the different protective groups regarding water and food intake and weight changes p>0.05. According to microscopic and macroscopic studies, the improvement of colon in the final day was significant in extract and control positive treatment groups compared to the negative control group p0.05.

Discussion and Conclusion:

It was found that the extract of Heracleum lasiopetalum reduces the severity of the histopathologic symptoms of ulcerative colitis.

Keywords: Ulserative colitis, Heracleum lasiopetalum Boiss, Inflammation, Acetic acid

Measurement of serum IL-33 level and sST2 in patients with heart failure receiving Carvedilol

Maryam Dashti, Negar Firouzabadi*

P134

Authors' Affiliations:

School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

Department of Pharmacology & Toxicology, school of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran.

Abstract Presenter:
Maryam Dashti

Correspondance:
Negar Firouzabadi

Introduction:

Heart failure is a complex clinical syndrome due to the inability of heart to pump enough blood to meet the metabolic needs of body. Interleukin-33 is an intranuclear factor. Its receptor is ST2 with three isoforms: sST2, ST2L, and ST2V.IL-33 increases Th2-dependent immune responses by binding to dimeric receptor; complex of ST2L and receptor accessory protein. sST2 prevents this interaction and limits the IL-33 activity. IL-33 has a dual role in different diseases; reduces cardiac remodeling and develops diseases such as asthma.

Increase in sST2 level is associated with weak cardiac output and can be a predictor of mortality in HF. This hypothesis arose from findings that one of the mechanisms of carvedilol in HF may be due to its effect on IL-33/sST2 pathway. This pathway plays a fundamental role in cardiovascular system and can be a new therapeutic strategy.

Method:

We have used Human sST2 ELISA Kit and ab119547– IL-33 Human ELISA Kit to measure these parameters in serum of 66people; 22 were healthy and 44 suffered from HF; 25patients received carvedilol. 19patients did not receive carvedilol.

Result:

Regarding IL-33 and sST2, no significant difference was observed between HF patients and healthy controls, and also between HF patients who did not receive drug and patients receiving carvedilol.

Discussion:

Although our patients suffered from HF, but probably due to the fact that they did not have a sudden cardiac event, they did not show high level of sST2. Serial measurements, checking changes in levels, and their increase compared to the previous periods will further help to predict the status of these patients. Signals related to IL-33 can have both pro-inflammatory and cardioprotective properties. Many studies tried to measure serum IL-33 in HF but because of the low sensitivity and its low level, they have not been successful in measurement. Probability of the effect of beta-blocker-therapy on the IL-33/sST2 complex has, still not been fully understood and requires more research but many studies have mentioned that there may be a link between them. To investigate this hypothesis, prospective-randomized studies are required.

Keywords: Interleukin-33, sST2, Heart failure, Carvedilol

Quercetin can down regulation of Toll like Receptor4 via HMGB1 blocking on Kupffer cells from hepatocellular carcinoma patients

Shirin Sheykh Najafi

P135

Authors' Affiliations:
Tabriz University of Medical sciences, Tabriz, Iran.

Abstract Presenter:
Shirin Sheykh Najafi

****Correspondance:***
Shirin Sheykh Najafi

Introduction:

Quercetin, a pharmacological flavonoid which can inhibit HMGB1 (high-mobility group box 1) a non-histone nuclear protein, has been implicated in cancer. Th17 cells are important cells in the pathogenesis of cancer.

Material and method:

In the present study, we attempted to compare blocking of HMGB1 function and stimulation of HMGB1 function with Quercetin and investigate the effects of the blockade on Th17 cells and the MAPK-TLR4 signaling pathway. We also isolated Kupffer cells using new methods.

Results:

Our results indicated that the levels of IL-17, IL-33 and IL-6 in supernatants from cultured Kupffer cells from patients increased after stimulation with HMGB-1, but after Quercetin was used to prevent inflammation, the levels of these cytokines decreased. Also, western blot data showed that Quercetin can decrease the MAPK signaling pathway via inhibition of HMGB1 on Kupffer cells.

Conclusion:

This implies that the reduction of the TLR4 pathway and Th17 cell polarization may be due to HMGB1 blocking with Quercetin in hepatocellular carcinoma.

Keywords: HMGB1, Quercetin, TLR4, HCC, Th17

Sequential Microwave -Assisted Extraction for Isolation of Quercetin from Red Kidney Bean

Soheila Aghajanian, Sohrab Kazemi , Sorayya Esmaeili, Ali Akbar Moghadamnia*

P136

Authors' Affiliations:
Azad university of Amol, Amol, Iran.

Abstract Presenter:
Soheila Aghajanian

****Correspondance:***
Ali Akbar Moghadamnia

Coauthors:
Sohrab Kazemi
Sorayya Esmaeili

Introduction:

Quercetin is a biological flavonoid, which can be found in red kidney bean with higher concentration. Several potential beneficial properties for Quercetin are reported in the literature, namely, neuroprotective, anticancer effects, antiviral, anti-inflammatory effects and inhibits platelet aggregation.

Methods:

In this study, a comparison was conducted between traditional and modern methods of extraction. Sequential microwave-assisted extraction was used for isolation of quercetin from red kidney bean. The effect of several factors such as particle size of grinned kidney bean, extraction solvent, microwave power and time on the extraction yield of quercetin was considered. To assay of quercetin, the HPLC method were used which consist of the following specifications: C18 column, mobile phase acetonitrile & water, UV detector wavelength of 260nm and flow rate 1 mL/min.

Results:

The highest extraction efficiency was obtained (35.8 mg quercetin /g kidney bean) when 60 w/w% acetone used as the solvent; in addition, the solvent to solid ratio was 10:1 and the radiation power of 800w was applied during 1 minute. The acquired extraction yield according to the current method was higher than extracted quercetin from Soxhlet (24.6 mg quercetin /g kidney bean) and maceration (32.75 mg quercetin /g kidney bean). By HPLC method, the purity of the extracted quercetin was determined (75.3%).

Conclusion:

In the present study, quercetin was successfully extracted from kidney bean by microwave-assisted extraction. The quercetin structure remains intact, which can be used to produce effective and helpful therapeutic compounds.

Keywords: kidney bean, quercetin, microwave-assisted extraction, purification

Evolution and compare effects of fludrocortisone and betamethasone on blood glucose level and lipid profile in rat

Faeze Taheri*, Mohammad Naeim Malmir, Hamid Reza Jamshidi

P137

Authors' Affiliations:
Pharmacy School, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

Abstract Presenter:
Faeze Taheri

****Correspondance:***
Faeze Taheri

Coauthors:
Mohammad Naeim Malmir
Hamid Reza Jamshidi

Introduction:

Diabetes mellitus is the one of the most common metabolic disorders and one of the most common non-communicable diseases worldwide. Hyperglycemia is associated with insufficient insulin secretion, impaired insulin function, or both, and is associated with complications such as hypertension, various heart failure, retinopathy, neuropathy and nephropathy. Research suggests that proper control of blood glucose and lipid disorders, which significant proportion of diabetic patients suffer from, can delay the onset and progression of complications from the disease.

Materials and Methods:

This was an experimental study. The aim of this study was to compare the effects of two drugs, Fludrocortisone and Betamethasone, on the improvement of the quality of corticosteroid use on 40 male Wistar rats from Yazd Animal infertility center. Initially, the rats were randomly divided into 2 groups and then each group was divided into 4 groups. Subsequently Fludrocortisone doses of 12 mg / kg, 24 mg / kg and 36 mg / kg were administered, and dosages of 6kg mg / kg, 12 mg / kg, and 18 mg / kg of betamethasone administered on rats on a daily basis at 1 o'clock for 21 days by intraperitoneal injection.

Results:

Betamethasone and Fludrocortisone have increased blood glucose, AST, ALT, TG, LDL and VLDL, and have decreased HDL, causing red pigmentation in the skin, and obesity and puffiness in the rats. In all of the measured factors, Fludrocortisone changes were more than betamethasone. Fludrocortisone and betamethasone also had significant effects on weight, which was more pronounced with Fludrocortisone.

Discussion and Conclusion:

As the dose increased, the levels of AST, ALT, cholesterol, TG, LDL, VLDL and LDL in the blood increased significantly and HDL levels decreased in the blood, but fludrocortisone showed a stronger effect than betamethasone. Therefore, it can be expected that the use of betamethasone would be logical due to fewer side effects than flood control.

Keywords: Fludrocortisone, Betamethasone, Fat Profile, Glucose, Type 2 Diabetes

Heavy metals induced toxicity on Solen dactylus scallop used for the filteration of the industrial waste water

Farahnaz Tanbakousazan, Jalal Pourahmad*

P138

Authors' Affiliations:
Department of Pharmacology and Toxicology, Faculty of Pharmacy, ShahidBeheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Farahnaz Tanbakousazan

***Correspondance:**
Jalal Pourahmad

Introduction:

Heavy metals are known as harmful pollutants, are freely dispersed in the environment. Recent research has suggested that these heavy metals can cause various toxicity via mitochondria-involved mechanisms.

Now a day the heavy metals well known biosensors such as *Solen dactylus* scallop are widely used to filtrate the industrial waste water usually obtained in cement industry. Therefore, we decided to investigate the toxicity of silver and titanium oxide which are the main components of cement industry waste water on muscle mitochondria isolated from *Solen dactylus* scallop.

The importance of mitochondrial study in the cytotoxicity is very high. Mitochondria is one of the most important intracellular organelles that is the main source of production of active oxygen species in the cell. The mitochondria are actually a cellular respiratory organelle that, during the oxidative phosphorylation process, generates most of the ATP required by the cell, and on the other hand, active oxygen species are produced as a byproduct during this process.

Methods:

Muscle mitochondria of Solen *dactylus* scallop were obtained by high speed centrifugation and incubated with different concentrations of silver and titanium oxide. The toxicity of silver and titanium oxide on mitochondrial related parameters including succinate dehydrogenase activity, generation of reactive oxygen species (ROS) formation, mitochondrial membrane potential (MMP) collapse, Lipid peroxidation and GSH oxidation were determined.

Results: Our results showed that both heavy metals induced mitochondrial dysfunction via an increase in mitochondrial ROS production, Lipid peroxidation, GSH oxidation and membrane potential collapse on muscle mitochondria isolated from *Solen dactylus* scallop.

Conclusions:

Our results show that scallops used as biofilter of industrial wastewaters are in serious jeopardy to poisonings.

Keywords: *Solen dactylus* scallop, Waste water, Isolated mitochondria, reactive oxygen species (ROS), Silver oxide, Titanium oxide.

Betanin exert selective toxicity on cancerous neural mitochondria and lysosomes isolated from the mouse model of glioblastoma

Tannaz Bahiraei, Parvaneh Naserzade, Jalal Pourahmad*

P139

Authors' Affiliations:
School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran.

Abstract Presenter:
Tannaz Bahiraei

****Correspondance:***
Jalal Pourahmad

Coauthors:
Parvaneh Naserzade

Abstract:

Glioblastomas are the most common high grade (cancerous) primary brain tumor in adults. They can also occur, rarely, in children. Glioblastomas belong to a group of brain tumors known as gliomas, as they grow from a type of brain cell called a glial cell. Glioblastoma is the more common name for a type of brain tumor called a grade 4 astrocytoma. In this research the anti-cancer activity of betanin a main component of red beetroot extract which has well known inhibitory effect on the microglia cells will be investigated against cancerous brain neurons and mitochondria obtained from mouse model of glioblastoma.

Our results revealed that Betanin significantly has induced ROS generation and lipid peroxidation in neural mitochondria isolated from the mouse model of Glioblastoma, moreover, Betanin significantly declined complex II activity, GSH level, and mitochondrial membrane potential, in neuron mitochondria compared to those of non-cancerous group. Furthermore, we found that Betanin significantly reduced ATP content in brainmitochondria isolated from the mouse model of glioblasoma. On the other hand our results revealed that Betanin treatment to the cells also induced the release of cytochrome c into the cytosol, the current study showed that Betanin could significantly induce selective cytotoxicity on glioblastoma neurons and mitochondria. Therefore, this compound may be considered as a promising candidate for the further in vivo and clinical studies to reach to a new anti-glioblastoma drug.

Keywords: Glioblastoma, Neural Mitochondria, Betanin, Cytotoxicity

Refractory arrhythmias in young patients can be suggestive of cardiotoxic drug poisoning

Mahshid Ataei, Omid Mehrpour*

P140

Authors' Affiliations:
Medical Toxicology and Drug Abuse Research Center (MTDRC), Birjand University of Medical Sciences, Birjand, Iran.
Rocky Mountain Poison and Drug Center, Denver, CO, USA.
Cardiovascular Diseases Research Center, Department of Cardiology, School of Medicine, Birjand University of Medical Science, Birjand, Iran

Abstract Presenter:
Mahshid Ataei

***Correspondance:**
Omid Mehrpour

Abstract:

Tricyclic antidepressants are used to treat a variety of mental disorders, including depression, anxiety and chronic pain. Since these drugs are easily available and have toxic effects like cardiac toxicity they are considered a common cause of fatal drug poisoning.

This study reports a 19-year-old woman with no history of cardiac diseases who presented to the emergency department with heart palpitation, weakness, and lethargy. After a short period of time, she became unconscious and experienced hypotension and refractory arrhythmia. She immediately underwent cardiopulmonary monitoring, and an electrocardiogram (ECG) was performed which showed regular wide complex tachycardia. Her blood pressure was 100/80. Eventually, the patient was diagnosed with PSVT but did not recover with medications. Accordingly, a drug screening urine test was performed.

Based on the results of this test along with a more accurate history of the patient taken from her family, it was revealed that she had had access to her mother's imipramine pills and might had ingested imipramine as a non-supervised action.

Accurate history taking and the possible causes of these complications including cardio-toxic drug poisoning should be considered in such patients.

Keywords: tricyclic antidepressant

Methadone-associated hearing loss and nephrotoxicity: a case report

Mahshid Ataei, Omid Mehrpour*

P141

Authors' Affiliations:
Medical Toxicology and Drug Abuse Research Center (MTDRC), Birjand University of Medical Sciences, Birjand, Iran.
Rocky Mountain Poison and Drug Center, Denver, CO, USA.
Cardiovascular Diseases Research Center, Department of Cardiology, School of Medicine, Birjand University of Medical Science, Birjand, Iran

Abstract Presenter:
Mahshid Ataei

Correspondance:
Omid Mehrpour

Abstract:

Methadone is a long-acting opioid receptor agonist. Reported side effects of methadone include constipation, respiratory depression, dizziness, nausea, vomiting, itching, sweating, rhabdomyolysis, QT prolongation, and orthostatic hypotension. Hearing loss has been rarely reported following methadone use. Herein we report a case of methadone poisoning with acute kidney injury and hearing loss.

Case Report:

The patient was a 34 years old male and who presented after an ingestion of 40 mg of methadone after some familial challenge with suicidal purpose, with a reduced level of consciousness and hearing loss. He had no prior history of methadone abuse or addiction.

Initial laboratory testing was significant for a serum creatinine concentration of 4.1 mg/dl and abnormal hepatic transaminases and coagulation tests (partial thromboplastin time (PTT), prothrombin time (PT). The patient had metabolic acidosis acute oliguric renal failure and rhabdomyolysis. Audiometry showed a bilateral sensorineural hearing loss.

The patient required hemodialysis for 11 days while his metabolic abnormalities gradually resolved. However, his hearing loss was persistent after two years of follow up.

Conclusion:

This report described a case of permanent opioid-associated hearing loss (OAHL) in a previously healthy and not addicted man after methadone overdose. Patient presenting with hearing loss.

Keywords: methadone

Protective effects of galangin nanoparticlesagainst acetaminophen-induced Hepatotoxicity in Mice

Arezoo Mohammadi*, Sohrab Kazemi, Ali Akbar Moghaddamnia

P142

Authors' Affiliations:
Babol University of Medical Sciences, Babol, Iran

Abstract Presenter:
Arezoo Mohammadi

****Correspondance:***
Arezoo Mohammadi

Coauthors:
Sohrab Kazemi
Ali Akbar Moghaddamnia

Introduction:

Acetaminophen overdose is one of the main causes of acute liver failure. Excessive consumption of acetaminophen leads to the production of NAPQI through the activity of enzyme cytochrome c oxidase by saturating other pathways (sulfation and glucuronidation). For this purpose, the effect of galangin with antioxidant activities will be evaluated for the treatment of acetaminophen-induced hepatotoxicity.

Materials and Methods:

In this study, after the synthesis of galanginnanoparticle and particle sizedetermination, small white laboratory mice were divided into 5 groups of 6: saline, galangin nanoparticle (10 mg/kg), galangin nanoparticle (20 mg/kg), silymarin (20 mg/kg) and control. Before treatment,a single dose of acetaminophen was administered in all groupsby gavage(350 mg/kg). The activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) in serum, and thetotal antioxidant activity was evaluated by FRAP method and histopathologic study.

Results:

The nanoparticle produced by this method was uniform and the average particle size was obtained in the range of 50 nm. Serum levels of liver enzymes (AST, ALT) in the nanoparticle group decreased significantly compared to the control group (P0.05). In the APAP group, the activity of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) enzymes increased significantly compared with the control group. In addition, galangin nanoparticle (20 mg/kg) improved hepatocyte injury and ultimately protected liver tissue structure.

Conclusion:

Galangin nanoparticles reduces the APAP-induced hepatotoxicity by reducing the amount of liver function indices (AST and ALT). In histopathologic findings, hepatocytes showed severe inflammation in untreated groups, while the lowest levels of inflammation were seen in the groups treated with nanoparticles. The liver-protective effects of the nanoparticle may be due to its antioxidant properties and trapping of free radicals by this compound.

Keywords: Acetaminophen, Galangin nanoparticle, Silymarin, Aspartate aminotransferase, Antioxidant.

Hepatoprotective effects of the hydroalcoholic extract of Capparis spinose L. against Mercuric Chloride-induced acute liver damage in rats

Mohammad Amin Mombeini, Heibatullah Kalantari, Mehdi Goudarzi, Mojtaba Kalantar, Hossein Forouzandeh*

P143

Authors' Affiliations:
Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract Presenter:
Mohammad Amin Mombeini

****Correspondance:***
Hossein Forouzandeh

Coauthors:
Heibatullah Kalantari
Mehdi Goudarzi
Mojtaba Kalantar

Introduction:

Mercury (Hg), as a naturally-occurring heavy metal, is used in a wide variety of industrial applications and it is also known for its hepatotoxic, neurotoxic, genotoxic and hematotoxic effects. Capparisspinose L. is a plant from the dry regions in west or central Asia. This plant is used in traditional medicine for its antioxidants, diuretic, antihypertensive effects and by many pharmaceutical industries for cosmetic and nutritional purposes. This study attempted to evaluate the hepatoprotective effects of C. Spinosa extract (CSE) in Mercuric Chloride (HgCl2) induced acute liver damage.

Material and methods:

Adult Wistar male rats were divided into six groups (n:8) Group 1 as negative control group, received normal saline for 5 days; while group 2 received only CSE (400 mg/Kg/po) for five days and group 3 received HgCl2 (0.4 mg/kg/day, p.o.) as positive control only on the 5th day; groups 4-6 received CSE orally by gavage in doses of 100, 200 and 400 mg/kg respectively, during 5 days and HgCl2 (0.4 mg/kg/day, p.o.) on the 5th day. The animals were sacrificed on the sixth day. Blood samples were collected to determine the serum aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) levels. The malondialdehyde (MDA) and glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD) were assayed in liver tissue. Furthermore, the changes of tissue were assessed by histopathologic examination.

Results:

Pre-treatment of CSE in dose of 400mg/kg showed liver protection against HgCl2 induced hepatic injury, as it was evident from a significant decrease in serum enzymes marker and MDA and an increase in the GSH, SOD, and CAT activities. Histological results also showed that HgCl2 led to liver damage and CSE could improve histological changes.

Conclusion:

This study suggests that possible mechanism of this protection may be associated with its property of scavenging free radicals which may be due to the presence of phenolic compounds in extract.

Keywords: Capparis Spinosa L, $HgCl_2$, Hepatoprotective.

Efficient amelioration of Copper induced hepatotoxicity in mice by Trametes versicolor extract via suppression of oxidative stress and inflammation

Pegah Bathaeian, Emran Habibi, Maryam Ghasemi, Fatemeh Shaki*

P144

Authors' Affiliations:
Mazandaran University of Medical Sciences, Iran.

Abstract Presenter:
Pegah Bathaeian

****Correspondance:***
Fatemeh Shaki

Coauthors:
Emran Habibi
Maryam Ghasemi

Introduction:

Copper (Cu) has a key role in various enzymes function and biological process, but high concentration of this element showed toxicity effects on human
(1). The purpose of this study was to evaluate the protective effects of water and methanol extracts of Trametesversicolor against Cu-induced hepatotoxicity in mice.

Method:

Male albino mice, were divided into eleven groups of 6 mice each, including control, Cu, Cu plus different doses of water and methanol extracts (100, 200,400 mg/kg) respectively, and Cu with vitamin C (500 mg/kg). After 24 hours, mice were anesthetized and their livers were collected and oxidative stress markers including reactive oxygen species (ROS), glutathione, lipid peroxidation (2), protein carbonyl contents, superoxide dismutase and glutathione peroxidase activity and in the liver tissue and also histopathological parameters were evaluated. Inflammatory parameters including nitric oxide and TNF-α(3) as well as liver enzyme including ALT and AST were assayed in serum samples.

Results:

Single dose of intraperitoneal administration of Cu caused changes in liver pathological and biochemical parameters. In addition, increase in oxidative stress and inflammatory parameters were observed in the group which received Cu. Treatment with both methanol and water extract of T. versicolor reduced oxidative stress and as well as inflammatory markers and attenuated pathological changes in liver tissue due to Cu injection.

Conclusion:

Our study indicated the role of inflammation and oxidative stress in Cu-induced liver toxicity, which prevented by treatment with extracts of T. versicolor.

Keywords: Copper, Trametes versicolor, Liver toxicity, Inflammation, Oxidative stress

Screening of cytotoxic effects of diethyl ether, methanol and n-hexane extracts of three species of Persian Gulf native sponge, sea cucumber and tunicate on skin cells and mitocondria isolated from melanoma induced mouse

Yalda Arast, Nina Seyed Razi, Melika Nazemi, Jalal Pourahmad*

P145

Authors' Affiliations:
Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Yalda Arast

****Correspondance:***
Jalal Pourahmad

Coauthors:
Nina Seyed Razi
Melika Nazemi

Abstract:

Skin cancer is one of the most prevalent cancers and one of the major causes of mortality worldwide. Marin animals have attracted much attention in recent years as useful substancesin medicine. It was shown that Phallusianigra (P. nigra), HolothuriaParva (H. parva) and Irciniamutans (I. mutans) known as Persian Gulf species could play an important role in cancer therapy. Methods: This study was designed to figure out the possible selective toxicity of n-hexane, diethyl ether, methanolic and aqueous extracts of P. nigra, H. parva and I. mutans on cancerous mitochondria isolated from the skin of melanoma-induced mice. In this study, mitochondria were isolated from the skin tissue of both melanomas-induced and normal healthy mice. Different concentrations of four different extracts of P. nigra, H. parva and I. mutans (250, 500 and 1000 µg/ml) were added to mitochondrial samples obtained from normal and melanoma groups, separately. Results: Our results showed that n-hexane, diethyl ether and methanolic extracts (but not aqueous extract) of P. nigra, H. parva and I. mutans in all concentrations applied (250, 500 and 1000 µg/ml) significantly induced toxic alterations only in the cancerous but not normal healthy skin mitochondria including; increased reactive oxygen species (ROS) formation, mitochondrial swelling, decreased mitochondrial membrane potential (MMP) and cytochrome c release. Flow-cytometry analysis demonstrated that n-hexane, diethyl ether and methanolic extracts of P. nigra, H. parva and I. mutans progressively induced apoptosis and necrosis only on melanoma cells but not healthy skin cells. Conclusions: Our results suggest that non-polar bioactive compounds in P. nigra, H. parva and I. mutans may be hopeful candidates for further studies including molecular identification, confirmatory in vivo experiments and finally clinical trials designed for new drug treatment of melanoma skin cancer.

Keywords: Phullusia nigra, Holothuria parva, Ircinia mutans, Melanoma, Mitochondria.

Introduction of potent 2-aryl-1H-phenanthro [9,10-d] imidazole derivatives as cytotoxic agents vs AGS, Hep-G2 and MCF-7 cell Lines

Amir Mohammad Ghorbanpour, M.K. Mohammadi, S. Bohlooli, A. Javid, D. Doostkamel, N. Etefaghi, H. Tavakkoli, N. Zahedi, Nima Razzaghi Asl*

P146

Authors' Affiliations:
Student Research Committee, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran, PO code: 5618953141

Abstract Presenter:
Amir mohammad Ghorbanpour

***Correspondance:**
Nima Razzaghi Asl

Coauthors:
M.K. Mohammadi
S. Bohlooli
A. Javid
D. Doostkamel
N. Etefaghi
H. Tavakkoli
N. Zahedi
Nima Razzaghi Asl

Abstarct:

Some 2-aryl-1H-phenanthro [9,10-d] imidazoles (3a-I) were synthesized for evaluating their cytotoxicity against MCF-7, HepG2, and AGS cell lines using MTT assay. Cell cytotoxic tests showed phenanthramidazoles are very potent cytotoxic agents (IC50 sub-nanomolar). The maximum effect was recorded for 3i against AGS (IC50 0.07 nM). It has also been shown that the phenanthomidazoles were less toxic to HepG2 cells in comparison with MCF-7 and AGS cells. The minimum cell cytotoxicity was reported for 3c in HepG2 cancer cells (IC50 7608.07 nm). Structural studies showed that the synthesized nitrogen/oxygen containing polar groups such as N-acetyl or nitro in para/meta position of the phenyl ring significantly increased the toxicity against AGS cells (3h). A similar trend was observed in the meta nitro derivatives versus MCF-7 (3b, IC50 0.17 nM). It was found that even the weakest cytotoxic compounds exhibited IC50s in low micromolar range whereas most IC50s were lower than the concentration of cis-platin against each cell line. The results of this study showed 2-aryl-1 H-phenanthro [9, 10-d] imidazoles are potential enough structures for more in vivo studies.

Keywords: Phenanthro [9, 10-d] imidazoles, Synthesis, MTT assay, Anticancer activity

Using marine scallop Solen dactylus to clean up industrial waste water containing Ag/Tio2

Farahnaz Tanbakousazan, Jalal Pourahmad*

P147

Authors' Affiliations:
Department of Pharmacology and Toxicology, Faculty of Pharmacy, ShahidBeheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Farahnaz Tanbakousazan

***Correspondance:**
Jalal Pourahmad

Introduction:

Pollution of water after air pollution is one of the most important problems of the world and Iran. One of the main causes of diseases and deaths in the world is pollution of water. Surface and underground water are both subject to various contaminants.

Water contamination is one of the main reasons of disturbance in nature balance. The sources of water and its purification are crucial for maintaining quality and safety of human society. Industrial waste water is of global concern due to its severe effects on the environment. Marine organisms, such as fish, are exposed to a variety of metal contaminants These pollutants can affect the health of these marine organisms, causing a lot of damage to them. There are various methods for treating industrial wastewater, such as the use of ozone gas, chlorination, there are various methods for water treatment, each of which will cost a lot to clean contaminated water.The scallops of the Shell is belong to the Solenidae family (Solen dactylus)
These scallops purify water from industrial waste released from factories, and cleanse the water from all nano-particles, especially titanium oxide and silver oxide.In this study, we will use a biosensor (scallops) to treat the contaminated water from industrial plants at a lower cost.

Methods and Results:

The amount of water abstinence before and after exposure to scallops in reducing the burden of pollution was examined. specially the amount of nanoparticles of titanium oxide and silver oxide in industrial wastewater were reduced after one-month exposure to solen dactylus scallops.

Conclusions:

The importance of this study comes from the fact that, in order to save on the many costs involved in the treatment of industrial waste water, we can use the organisms that live in their constant ecosystem to clean up their own environment and industrial wastewater.

Keywords: scallop, industrial wastewater, titanium oxide, silver oxide.

Effects of hydrocortisone as stress alternative hormone on beta-cells signaling of mice exposed to diabetes induced by streptozotocin

Mohammad Basiri, Ali Ashrafian, Tohid Vahdatpour*

P148

Authors' Affiliations:
Department of Physiology, Faculty of Animal and Veterinary Sciences, Shabestar Branch, Islamic Azad University, Shabestar, IRAN

Abstract Presenter:
Mohammad Basiri

****Correspondance:***
Tohid Vahdatpour

Coauthors:
Ali Ashrafian

Introduction:

Cortisol plays essential roles in glucose metabolism and energy homeostasis by lipolysis, proteolysis. Gluconeogenesis and hepatic glucose production stimulate glucagon secretion and reduce glucose consumption by cells. All of these effects lead to elevation of the blood glucose level and may play an important role in the development of stress-induced hyperglycemia. Hydrocortisone (HC) as medication of cortisol has strong anti-inflammatory, anti-allergic, and immunosuppressive properties. Despite their excellent efficacy, supra physiological doses of HC induce adverse effects related to glucose homeostasis, such as glucose intolerance, insulin resistance, β-cell dysfunction, and overt diabetes.

Methods:

Diabetes induced by Incremental Multiple Low-Doses of Streptozotocin (IMLDS) protocol in 4 consecutive days by injections of 20, 40, 80, and 160 mg/kg BW/day of streptozotocin and at the same time, to surveyed the effects of HC on diabetes induction and pancreatic beta cells signaling by injections of 5, 10, and 20 mg/kg BW/day of HC in mice. At the end of experimental period, the glucose, insulin, glucagon-like peptide-1, RAC-beta serine/threonine-protein kinase, and dipeptidyl peptidase-4 of blood were assessed by ELISA.

Results:

Daily injections of HC raised blood glucose, glucagon-like peptide-1, and RAC-beta serine/threonine-protein kinase but reduced serum insulin and dipeptidyl peptidase-4 activity (p0.05). By executing diabetes inducing protocol the serum insulin increased, whereas HC injection caused reduction of the insulin (p0.05). The HC administration reduced glucagon-like peptide in the control mice, while enhanced glucagon-like peptide after IMLDS (p0.05).

Conclusion:

The stress induced by hydrocortisone depending on the doses, intensifies diabetes in this animal model which illustrates the effective role of stress in diabetes induction.

Keywords: Cortisol, DPP-4, GLP-1, Glucose, Insulin

Antidiabetic activity of methyl-2-(5-chloro-3-hydroxy-2-oxindoline-3-yl)-acrylate in streptozotocin-induced diabetic Rats

Faezeh Mataji, Leila Youseftabar-Miri*

P149

Authors' Affiliations:
Students Research Committee, Faculty of pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Faezeh Mataji

****Correspondance:***
Leila Youseftabar-Miri

Abstract:

Development of new anti-diabetic agents is one of the fundamental goals in medicinal chemistry. Substituted 3-hydroxy-oxindole as an isatin derivatives are important structural motif, found in many biological active products [1-2], and pharmaceutical lead compounds [3-4]. The present study was evaluated the antidiabetic activity of title compound in diabetic rats. The antidiabetic activity of methyl-2-(5-chloro-3-hydroxy-2-oxindoline-3-yl)-acrylate (figure 1) was evaluated against streptozotocin induced diabetes in rats.

A comparison was made between test compounds and a known antidiabetic drug glibenclamide (10 mg/kg). Diabetes in rats was induced by administration of streptozotocin (60 mg/kg) as a single does [5].

The study was conducted 14 days in 4 different groups-control, diabetic control, standard drug, and test compound containing 6 rats in each group. The diabetic rats were treated with single dose of test compound at a dose of 10 and 50 mg/kg. Blood samples were collected from the heart.

The test compound at 50 mg/kg elicited significant (P 0/01) reduction of blood glucose level after 7h, 121.7 ±6.3 mg/dl , which was comparable to glibenclamide and also made good changes in lipid profiles (Tc, TG, HDL-C) indicating the antidiabetic activity of the test compound.

Keywords: Oxindole, Anti-diabetic, Isatin

Evaluation of anti-apoptotic effect of Simvastatin in heart failure using isoproterenol

Mahsa Rahimi

P150

Authors' Affiliations:
Tehran University of Medical Science, Tehran, Iran.

Abstract Presenter:
Mahsa Rahimi

****Correspondance:***
Mahsa Rahimi

Introduction:

This study examines the anti-apoptotic effect of Simvastatin with isoproterenol. Cardiovascular problems are one of the most important causes of death. Isoproterenol is an adrenergic compound which is a cardiac stimulator and extensor bronchodilator. Isoproterenol is excreted in the urine.

Methods and Results:

At first 50 male rats were randomly divided into 5 groups of 10:

1. Healthy group, 2. patient group (heart failure), 3. Healthy mice treated with low dose Simvastatin, 4. Healthy mice treated with medium dose Simvastatin, and 5. Healthy mice treated with High dose Simvastatin .For cause the disease?? Isoproterenol 0.5 mg/kg daily was injected subcutaneously for 10 days. Group 1 and 2 received only normal saline, Group 3-5 received Simvastatin 5, 10, 15 mg/kg respectively. All sample treated with oral solution in normal saline (10mg/kg) were started daily for 3 weeks?? Before injection and continued until the end of the experiment. Twenty-four hours after the last treatment the mice were killed and from the left ventricle they were prepared with tannel dye. The apoptotic cells were stained with light microscopy.

Conclusions:

In group 2 isoproterenol increased apoptotic cells in comparison with healthy controls(p0.001) and in group 3,4and 5 Simvastatin decreased (p0.05, p0.01, p0.001) apoptotic cells in comparison with group 2, the results show that Simvastatin in adose dependent manner prevents apoptotic death in muscle cells of the heart.

Keywords: cardiovascular problems, Simvastatin, isoproterenol

Effect of L-NAME and KT5823 coadministration on spatial memory deficit induced by amyloid beta in hyppocampus of rats

Marjan Shariatpanahi*, Mohammad Sharifzadeh

P151

Authors' Affiliations:
Department of Toxicology & Pharmacology, School of Pharmacy, International Campus, Iran University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Marjan Shariatpanahi

****Correspondance:***
Marjan Shariatpanahi

Coauthors:
Mohammad Sharifzadeh

Introduction:

It has been proposed that the appearance of amyloid beta (Aβ) in hippocampus is one of the characteristic features of Alzheimer's disease (AD). The role of Nitric oxide/Protein Kinase G (NO/PKG) in neurodegenerative diseases is controversial in different contexts. This study aims to evaluate the effect of L-NAME and KT5823 coadministration on spatial memory deficit induced by amyloid beta in hyppocampus of rats.

Methods and Results:

We examined the role of NO/PKG pathway in spatial memory using Morris water maze (MWM). For this purpose, the effects of coadministrating L-NG-Nitroarginine Methyl Ester (L-NAME) as a nitric oxide synthase (NOS) inhibitor and KT5823 as a PKG inhibitor was evaluated in AD rats. The behavioral alterations were studied on 14th day after drug injections. Results: Results revealed that in Aβ pretreated rats, intra-hippocampal injection of 1 μg/side of L-NAME or KT5823 (5 μM /side) caused a significant reduction in escape latency and traveled distance comparing to AD rat group. On the other hand, intra-hippocampal injection of L-NAME (1 μg/side) + KT5823 (5 μM /side) could improve spatial memory deficiency induced by injection of Aβ, but there was not a significant difference between the combination group and each of L-NAME or KT5823 (5 μM /side) alone.

Conclusions:

The results propose that using KT5823 or L-NAME could improve spatial memory in Aβ-exposed rats at individual doses, but in combination they showed no additive effects.

Keywords: L-NAME, KT5823, Spatial memory, Amyloid beta

Study expression of RIP1, RIP3 and MLKL in Alzheimer's rat model following intravenous administration of human adipose derived stem cells (hADSCs)

Marjan Shariatpanahi*, Mina Eftekharzadeh

P152

Authors' Affiliations:
Department of Toxicology & Pharmacology, School of Pharmacy, International Campus, Iran University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Marjan Shariatpanahi

***Correspondance:**
Marjan Shariatpanahi

Coauthors:
Mina Eftekharzadeh

Introduction:

Alzheimer's disease is a neurodegenerative disease that is the result of injured neurons which are responsible for cognitive functions. Neuronal damage can cause decline in memory, cognitive behaviors, basic body tasks and language which affects daily activities of patients. It seems that there is a correlation between necroptosis and various neurodegenerative disorders. The present study was aimed to evaluate RIP-1, RIP-3 and MLKL expression as necroptotic factors after administration of human adipose derived stem cells (hADSCs) in Alzheimer's disease (AD) rat model.

Methods:

In this investigation, thirty-two male rats were randomly selected in four groups: Control, Sham, AD rat, and hADSCs treatment group. Thioflavin S was used for detecting Aβ plaques. We also utilized immunofluorescent method for assessing RIP-1, RIP-3 and MLKL expression in different groups.

Results:

Statistical analysis indicated that Thio-S positive plaques number increased significantly in AD rats while administratinghADSCs significantly decreased Thio-S positive plaques number in AD group. Consequently, there was a significant increase in RIP-1, RIP3 and MLKL expression in AD rat model comparing to the control group. We found for the first time that there was a significant reduction in expression of RIP-1, RIP-3 and MLKL in hADSCs treatment group comparing to AD rat model.

Conclusions:

According to the findings, the protective effects of hADSCs might be related to reduction of necroptotic markers in Alzheimer's rat model.

Keywords: Alzheimer's, hADSCs, RIP1, RIP3, MLKL

Effect of Caffocymen Herbal Syrup on citric acid induced asthmatic model in rat

Saeed Naseri*, Seyedeh Simin Dakhilpour, Seyedeh Zahra Mousavi, Samira Mirshafieyan, Mohammad Shormij, Masoud Fardin

P153

Authors' Affiliations:
Herbal Pharmacology Research Center, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Abstract Presenter:
Saeed Naseri

****Correspondance:***
Saeed Naseri

Coauthors:
Seyedeh Simin Dakhilpour
Seyedeh Zahra Mousavi
Samira Mirshafieyan
Mohammad Shormij
Masoud Fardin

Introduction:

Asthma is an obstructive airway disease that causes chronic inflammation of the respiratory tract. Drugs with different properties such as bronchodilator, anti-inflammatory and antileukotriene effects have not been effective in all cases, because of their low potency and side effects. As a result, looking for other alternatives is necessary. Herbal Plants are important sources of new phytochemicals that possess significant therapeutic effects. Caffocymen, herbal and medicinal syrup, contains lemon, penicillo and thymol liquid oils with therapeutic properties, such as sedative and anti-inflammatory effects. We were prompted to investigate the anti-asthmatic activities of Caffocymen syrup on experimental animals.

Methods and Results:

This study was performed on 24 Wistar rats weighing 220 ±10gr. Asthma was induced with citric acid0/1mg by being sprayed for 3minutes during 10days in rats. The animals were divided to 3groups: control group, Caffocymen syrup group and salbutamol syrup for 5 weeks. On the 35th day, all the animals were scarified and lung tissue samples were prepared. The histopathological changes were assessed and compared to those in the control group. Statistical significance was determined by one-way analyses of variance, followed by the Tukey test using SPSS software.
Results: In the treatment group, a significant difference was noted with Caffocymen's syrup. These differences included the reduction of epithelial hyperplasia, a distinctive marked decreased BALT hyperplasia with the inflammatory process of fibrolinophytes.

Conclusions:

In this study, hyperplasia of epithelium Bronchial, metaplasia of goblet cell proliferation, BALT hyperplasia fibrosis proliferation and lymphocyte infiltration were devaluated in all groups, this decrease was statistically significant in comparison with the control group. Statistical and histopathological results also confirmed that all of the above mentioned factors reduced in all cases in the group receiving Caffocymen's syrup. . (P Value.0=00).

Keywords: Herbal Syrup, Caffocymen, citric acid, Asthma, Rat

Isolation of Escherichia coli from raw milk and non-pasteurized yogurt drink

Razieh Aliyan Aliabadi*, Abdolghani Ameri , Effat Abbasi MontazeriMansour Amin

P154

Authors' Affiliations:
Student Research Committe, Ahvaz Jundishapur University of medical sciences, Ahvaz, Iran.

Abstract Presenter:
Razieh Aliyan Aliabadi

****Correspondance:***
Razieh Aliyan Aliabadi

Coauthors:
Abdolghani Ameri
Effat Abbasi
MontazeriMansour Amin

Introduction:

Milk and yogurt drink are a good environment for the growth of many microorganisms. Many microorganisms including Escherichia coli (E.coli) produce toxins in food like milk and yogurt drink that cause poisoning and diarrhea in human. Milk is often infected by E.coli stored under unsuitable conditions can affect general health. Coliform bacteria are the health index for the consumption of milk. Enterotoxigenic Escherichia coli (ETEC) strains produce heat-stable (ST) and heat-labile (LT) microbial toxins that cause food poisoning in humans.

Such food requires monitoring to control and prevent the presence of E.coli in dairy products, including milk and yogurt drink.

Methods:

A total of 163 samples including 93 (57.05%) milk and 70 (42.95%) yogurt drink were collected from dairy suppliers in Ahvaz (April to November 2018). Then transferred to the laboratory and cultured on MacConkey Agar. Samples were incubated at 37° C for 24 hours, then examined for growth and level of contamination. Confirmed by differential tests.

Results:

Among the 163 samples, 35 (37.63%) milk samples and 13(18.57%) yogurt drink samples were positive for E. coli. The results for total count are presented in the table.

Total count	Milk	Yogurt drink
Below 10000	18	66
10000-100000	24	3
More than 100,000	51	1

Conclusions:

E. coli infected milk and yogurt drink can be a threat to the general health of consumers. Therefore, investigation of the prevalence of E.coli is important in dairy products. This study showed that the level of E. coli is high in dairy products and requires more control and care in this area by the authority concerned.

Keywords: enterotoxigenic Escherichia coli, ETEC, Milk, yogurt drink

Exposure to heavy metals: Role of Mitochondrial Damage and Oxidative Stress

Mahshid Soltani*, Maral Ramazani, Jalal Pourahmad

P155

Authors' Affiliations:
Shahid Beheshti University of Medical Science, Tehran, Iran.

Abstract Presenter:
Mahshid Soltani

****Correspondance:***
Mahshid Soltani

Coauthors:
Maral Ramazani
Jalal Pourahmad

Abstract:

Cytotoxicity and mitochondrial parameters were studied in isolated lymphocytes, and their mitochondria, obtained from occupationally exposed minors through inhalation exposure to lead, were investigated and the results were compared to those of unexposed persons. The group of occupationally exposed mine workers consisted of 11 individuals, ranging in age from 25 to 65 years. The control included 11 people who were not occupationally exposed to heavy metals, such as lead and zinc and their anthropometric and biochemical characteristics were similar to those of the exposed group. All cytotoxicity and mitochondrial parameters, evaluated in the exposed group, were significantly increased (P 0.05) compared to those of the unexposed control group.

Based on our findings, using antioxidant, mitochondrial and lysosomal protective agents can be promising drug candidates for the mine workers at the risk of exposure to lead and zinc induced chronic toxicity. In order to reduce the risk of absorption of toxic agents and their subsequent hazards for workers, the proper use of safety equipments and taking daily showers is recommended.

Keywords: minors, Inhalation Exposure, Mitochondrial Damage, reactive oxygen species, lead toxicity

Investigating the Effect of thiosemicarbazones Complex Ni on Expression Changes of Nalt1 in controlling of notch signaling pathway in jurkat E.6.1

Nedaa Zahmatkesh*, Golnaz Asadi, Sina Mirzaahmadi

P156

Authors' Affiliations:
Zanjan Azad University, Zanjan, Iran.

Abstract Presenter:
Nedaa Zahmatkesh

****Correspondance:***
Nedaa Zahmatkesh

Coauthors:
Golnaz Asadi
Sina Mirzaahmadi

Introduction:

Acute lymphoblastic leukemia (ALL) is the most common cancer in children. It accounts for about a quarter of all cancers among people under the age of 15 years. Acute lymphoblastic leukemia is a type of leukemia. Searching for the cytotoxic activity of thiosemicarbazones and their metallic complex, creates a variety of different types of human tumor cells. The aim of this study was to evaluate the effect of thiosemicarbazones on the expression of Nalt1 in the Notch signal pathway in acute lymphoblastic leukemia in the Jurkat E.6.1 cell line.

Materials and Methods:

Thiosemicarbazones complex Ni was prepared. Different doses of Ni were investigated with MTT test. Then, the Thiosemicarbazones complex Ni was prepared at 1 and 2doses and then investigated at two doses using Jurkat E.6.1 cancer cells for 48 hours. RNA extraction and cDNA synthesis were performed and the expression of Nalt1 and GAPDH gene was evaluated as Real Time PCR housekeeping gene. Finally, the results were analyzed by Rest Software.

Results:

Results of the research showed that the expression of long non coding Nalt1 was significantly decreased after treatment with Thiosemicarbazones complex Ni (p-value <0.001)

Discussion and Conclusion:

Given the results, it was found that doses of 1 and 2 Ni in 48 hours are the optimal doses and time of the effect of this complex.

Keywords: Nalt1, long non codingRNA, Acute Lymphoblastic Leukemia, Thiosemicarbazones Ni

Lipid peroxidation in Pregnant Mice after Radiofrequency Radiation Exposure

Nargess Moghadasi, Iraj Alimohammadi, Ali Safari Variani, Batol Masruri, Azadeh Ashtarinezhad*

P157

Authors' Affiliations:
Iran University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Nargess Moghadasi

****Correspondance:***
Azadeh Ashtarinezhad

Coauthors:
Iraj Alimohammadi
Ali Safari Variani
Batol Masruri

Introduction:

As the rapid growth of using radiofrequency radiation (RFR) in many fields and vulnerability of pregnant women and their fetus, we aimed to investigate the possible lipid peroxidation induced-RFR in pregnant mice and protective role of vitamin C as an antioxidant.

Material and methods:

21 pregnant mice were divided into 3 groups (control, exposure, and exposure plus vitamin). The exposure groups were exposed to mobile phone (915 MHz and 0.045 µw/cm2 power density) during pregnancy (8 h/d for 10 days). The exposure plus vitamin group was received vitamin C (200 mg\Kg) by gavage. After 5 days, the mice were anesthetized and their blood samples were collected from the heart. MDA level was measured using Thiobarbituric Acid Reactive Substances (TBARS) commercial kit and monitored at the wavelength of 535 nm. The MDA concentration in plasma samples was expressed as µM. All data were analyzed by ANOVA-Tukey test using SPSS (version 22).

Results:

Significant difference in MDA level was observed in exposure group (8.28±0.590 µM) (p0.002). The MDA level in the exposure plus vitamin C group (7.134±0.273 µM) increased in comparison with the control group (6.711±0.936 µM) but it wasn't significant (p0.56).

Conclusion:

RFR caused lipid peroxidation in pregnant mice and increased MDA level. Consumption of vitamin C could diminish the changes. Studies on non-ionizing radiation during pregnancy will help define threshold limit of its exposure for pregnant women and protect them effectively.

Keywords: lipid peroxidation, Pregnant mice, Radiofrequency radiation, Oxidative stress

Effects of Quercetin on Bisphenol A-induced Mitochondrial Toxicity in Rat Liver

Mohammad Amin Dehghani, Masoud Mahdavinia, Saeid Alizadeh , Atefeh Raesi Vanani, Maryam Shirani, Masoud Mahdavinia*

P158

Authors' Affiliations:
Department of Toxicology, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract Presenter:
Mohammad Amin Dehghani

****Correspondance:***
Masoud Mahdavinia

Coathuors:
Masoud Mahdavinia
Saeid Alizadeh
Atefeh Raesi Vanani
Maryam Shirani
Masoud Mahdavinia

Introduction:

Recognized as a distinguished environmental and global toxicant, Bisphenol a (BPA) affects the liver, which is a vital body organ, by the induction of oxidative stress. The present study was designed to have protective effect of Quercetin against BPA in hepatotoxicity in Wistar rats and the commotion of mitochondrial activities of enzymes were evaluated.

Methods:

To this end, 32 male Wistar rats were divided into four groups (six rats per group), including control, BPA (250 mg/kg), BPA + Quercetin (75 mg/kg) and Quercetin (75 mg/kg).

Results:

The BPA -induced alterations were restored in concentrations of alanine aminotransferase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST) due to the Quercetin treatment (75 mg/kg) (All P0.001). While the levels of mitochondrial membrane potential (MMP) reactive oxygen species (ROS), malondialdehyde (MDA) decreased by the Quercetin treatment in the liver mitochondria (P0.001), on the other hand, Catalase (CAT) and glutathione (GSH) increased (p0.001).

Conclusions:

According to the results, the potential hepatotoxicity of BPA can be prevented by Quercetin, which protects the body against oxidative stress and BPA-induced biochemical. Moreover, the reproductive toxicity of BPA after environmental or occupational exposures can be potentially prohibited by Quercetin.

Keywords: Liver, Mitochondria, Oxidative stress, Bisphenol A, Quercetin

An in vitro study of novel 3,4-dihydropyrimidine-2(1H)-one derivatives as anticancer agents on breast cancer and normal cell lines

Hoda Sharifi, Ahmad Ebadi, Meysam Soleymani*

P159

Authors' Affiliations:
Department of Pharmacognosy and Pharmaceutical Biotechnology, School of Pharmacy, Medicinal Plants and Natural Products Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

Abstract Presenter:
Hoda Sharifi

****Correspondance:***
Meysam Soleymani

Coauthors:
Ahmad Ebadi
Meysam Soleymani

Introduction:

Breast cancer is the most common cancer in women and causes of 41400 death in 2018. In recent years, the effective role of dihydropyrimidine-2-one compounds has been shown to inhibit the polymerization of tubulin as the main source of cell division. Due to the efficacy of these compounds and less side effects than other drug categories, this study examined the efficacy of a number of new derivatives of these compounds on normal and breast cancer cells.

Methods:

In this study, the cytotoxic effects of different concentrations of these compounds were investigated using MTT assay on MCF-7 and MDA-MB-231 breast cancer cell lines and HEK-293 normal cell line. Then, cell death mechanism was evaluated by measuring the Caspase 3 activity.

Results:

The results of the MTT test showed that DHPM derivatives, as dose-dependent, were able to kill cancer cells. In the Caspase 3 activity assay, a significant increase in activity was observed in the treated cells compared to the control group.

Discussion and Conclusion:

This study showed that DHPM compounds have significant cytotoxic effects in cancer cells compared to normal cells, and the cell death mechanism is caspase-dependent apoptosis. According to the obtained results, C5 amide derivatives showed more potency than ester ones. Derivatives with N-(benzothiazol-2-yl) acetamide at C6 position had premier activity. The order of activity for C4 substitutions was 4-Acetoxyphenyl > 4-Nitrophenyl > phenyl. Further in vitro and in vivo investigations of these new anti-cancer derivatives are ongoing.

Keywords: Breast cancer, DHPM, SAR,

Genetoxic and Cytotoxic effect of Salgam

Mostafa Norizadeh Tazehkand*, Mehmet Bertan Yilmaz, Orkideh Hajipour

P160

Authors' Affiliations:
Department of Pharmaceutical Biotechnology, Faculty of Pharmacy, Bulent Ecevit University, Zonguldak, Turkey

Abstract Presenter:
Mostafa Norizadeh Tazehkand

****Correspondance:***
Mostafa Norizadeh Tazehkand

Coauthors:
Mehmet Bertan Yilmaz
Orkideh Hajipour

Abstract:

Salgam is one of the traditional fermented beverages that produces and consumes by Turkish people. Salgam is a reddish colored, sour, and soft beverage. So regarding the highly usages of salgam, the aim of this study was to determine the cytotoxic and genotoxic effect of Salgam. In this research cytotoxic effect of Salgam was studied by MTT assay using K562 (human bone marrow cells) cell line. Genetoxic effect of salgam was studied by pET22b circular DNA.

K562 cells was treated with Salgam concentrations of 0,3125% - 10% for 24 hours, after that cytotoxic effect of Salgam was studied by MTT test. Also, DNA damaging assay was analyzed with four concentrations of salgam against pET22b circular DNA.

Salgam inhibited proliferation of K526 cells at just highest concentration for 24h treatment period. The result of pET22 plasmid DNA breaking analysis revealed that salgam did not effect on pET22b breaking. Therefore, it can be concluded that salgam might not a potential risk for human's cells.

Keywords: Genotoxicity, Cytotoxicity, Salgam, pET22b

Polymeric substrates with specific physical features for selective pulmonary cell attachment

Mojdeh Mohseni, Sahar Barzegari, Abolfazl Dashti, Golrokh Farnam, Kamyar Keshavarz, Farshad H. Shirazi*

P162

Authors' Affiliations:
Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran

Abstract Presenter:
Mojdeh Mohseni

****Correspondance:***
Farshad H. Shirazi

Coauthors:
Sahar Barzegari
Abolfazl Dashti
Golrokh Farnam
Kamyar Keshavarz

Introduction:

Control of cell attachment and other dependent features are the main means to treat many diseases. Surface properties of the substrate in contact with lung cancer cells were examined and specified attachment characteristics were studied.

As lung cancer is a common disease with the high mortality rate, many research topics belong to this matter. Among different methodology for lung cancer treatment, using natural physical cues to remove cancer cells is limited. In this regard, to obtain the high level of cell death in A549 (adenocarcinoma humans alveolar basal epithelial cells), stiffness and roughness of the substrate was altered, and the interaction of the mentioned cell was analyzed.

Methods and Results:

Three compositions of the precursor and curing agent of SYLGARD 184 (silicone elastomer kit) from Dow Corning, Tokyo, Japan were mixed and samples of S1, S2, and S3 with the ratio of 1.6, 5 and 16 bases: curing agent were prepared, respectively. Mechanical stirring was chosen as the mixing method and temperature of 75 °C and 24 hours were selected for the curing process. Different roughness in samples was obtained by changing plasma SDBD (Iran) time radiation. Atomic force microscopy (AFM) and bulk elasticity were measured by the tensile test. Cell survival and morphology parameters were analyzed by MTT assay and MATLAB image processing. Variation in plasma time, diverse topography has created and the maximum of stiffness has gained in the ratio of 16 bases: curing agent. More lung cancer mortality on the harder surface was obtained, and our results illustrate that roughness can promote A549 cells to die. Maximum stiffness has induced high detached cells and high mean space of detached cells was gained, and with the increase in cell roughness cellular coverage was decreased. In this aspect the number of detached cells was the factor which is not dependent on surface roughness.

Conclusions:

Our results demonstrate that physical features particularly stiffness and surface roughness are the chief characteristics which can have some effect on cell survival and growth factors. Hence engineered PDMS surface in this research can be introduced as a novel approach for eliminating tumor cells.

Keywords: Stiffness, roughness, cell survival

Cytotoxic effect of synthesized ciprofloxacin conjugated peptide compounds on T47D cell line

Behnoosh Safaei, Kiana Esfandiari, Sara Hariri, Farshad H. Shirazi, Mohammad Hassan Houshdar Tehrani*

P163

Authors' Affiliations:
Department of Pharmaceutical chemistry, School of pharmacy. Shahid Beheshti University of Medical Science, Tehran, Iran

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

Abstract Presenter:
Behnoosh Safaei

Correspondance:
Mohammad Hassan Houshdar Tehrani

Coauthors:
Kiana Esfandiari
Sara Hariri
Farshad H. Shirazi
Mohammad Hassan Houshdar Tehrani

Abstract:

Breast cancer is the most common cancer among women accounting for nearly 1 in 3 cancers and the second leading cause of cancer-related death among women after lung cancer. Finding new approaches to treat such cancers is critically important. Anticancer peptides(ACPs) offer the possibility of efficient anticancer drugs potency, and, therefore the development of drug delivery systems using ACPs as synergism factor is an attractive strategy to address the current drawbacks of cancer therapeutics. Oral ciprofloxacin might achieve higher concentration in urine than in serum; theoretically, this drug might act as an anticancer drug against bladder cancer cells for this reason we think that ciprofloxacin can be used as a synergism agent for anticancer peptides.

This work investigated the ability of system based on ciprofloxacin conjugated peptides to induce efficient cytotoxicity against T47D breast cancerous cells.

For the synthesis of peptides, the solid phase peptide synthesis (spps) method was chosen using Fmoc strategy and Wang resin was employed as a solid support. The first fmoc protected amino acid was connected to the resin through ester bond. After Fmoc removal, the second and other fmoc- amino acids were used, one by one, to make peptide bond through their carboxyl terminal with the N-terminal of amino acid (or peptide) bound resin. After making the whole peptide, protected ciprofloxacin was used to make amide bond to the N-terminal of the peptide-bound resin. Finally, peptide carrying ciprofloxacin was detached from the resin where deportation of all the all protected groups of the peptide was done, simultaneously. Cytotoxicity of the synthesized peptide compounds and was evaluated by MTT assay. Cells (briefly 6x103 cells/well) were transferred in to 96 well tissue culture plate and incubated for 24 h. Cells were treated with pure

peptides(0.1,0.5,1,2.5,5,10,25,50,100,250,1000nM) and ciprofloxacin conjugated peptides(0.1,0.5,1,2.5,5,10,25,50,100,250,1000nM and then incubated for 24 h. After 24 hours of incubation, 100 mL MTT reagent with final concentration 0.5 mg/mL was added into each well and incubated again for 3-4 hours to form formazan crystal. The stopper reagent (10% SDS in 0.01 N HCl) was used to dissolved and incubated overnight at room temperature and in the dark (covered with aluminum foil). The next day, the absorbance from each well was measured by ELISA reader with 570 and 630 nm wavelengths.

The experimental substances have proven to be safe for the breast cancer cells and not only do they not cause significant apoptosis (compared to cisplatin positive control group), three groups have also shown proliferative properties to the extent of an average of 10% increase. These results are remarkable in the sense that the substances were made purely based on theoretical data obtained using quantitative structure activity relationships and it is worth noting that these substances may be used as an external amino acid source for cells.

Keywords: Breast cancer; T47D; drug release; conjugated peptide; Anticancer drug; Cell penetrating peptide; Cytotoxicity; Drug delivery; Tumor targeting

Cytotoxic effect of synthesized triazole conjugated peptide compounds on T47D cell line

Behnoosh Safaei, Maryam Baharloui, Golrokh Farnam, Farshad H. Shirazi, Mohammad Hassan Houshdar Tehrani*

P164

Authors' Affiliations:
Department of Pharmaceutical chemistry, School of pharmacy. Shahid Beheshti University of Medical Science, Tehran, Iran

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

Abstract Presenter:
Behnoosh Safaei

****Correspondance:***
Mohammad Hassan Houshdar Tehrani

Coauthors:
Maryam Baharloui
Golrokh Farnam
Farshad H. Shirazi
Mohammad Hassan Houshdar Tehrani

Abstract:

Breast cancer is the most common cancer among women accounting for nearly 1 in 3 cancers and the second leading cause of cancer-related death among women after lung cancer. Finding new approaches to treat such cancers is critically important. Anticancer peptides(ACPs) offer the possibility of efficient anticancer drugs potency, and, therefore the development of drug delivery systems using ACPs as synergism factor is an attractive strategy to address the current drawbacks of cancer therapeutics.

This work investigated the ability of system based on triazole conjugated peptides to induce efficient cytotoxicity against T47D breast cancerous cells.

Wang resin was used for constructing peptide sequence on solid support using the method of solid phase peptide synthesis (spps) with the fmoc strategy. Protected amino acids with general formula Fmoc-AA-OH were used to load and connect them with each other through amide bond formation on resin. For each time loading, appropriate reagents were used to ensure the N-terminal of the peptide bound on resin is free and ready for the next amino acid application. At the end of peptide synthesis on resin, a previously made triazole moiety was connected to the N-terminal of the peptide while still attached to the resin. The peptide was finally cleaved from the resin as a deprotected triazole peptide. Cytotoxicity of the synthesized peptide compounds and was evaluated by MTT assay. Cells (briefly 6x103 cells/well) were transferred in to 96 well tissue culture plate and incubated for 24 h. Cells were treated with pure peptides(0.1,0.5,1,2.5,5,10,25,50,100,250,1000 nM) and triazole conjugated peptides(0.1,0.5,1,2.5,5,10,25,50,100,250,1000nM and then incubated for 24 h. After 24 hours of incubation, 100 mL MTT reagent with final concentration 0.5 mg/mL was added into each well and incubated again for 3-4 hours to form formazan crystal. The stopper reagent (10% SDS in 0.01 N HCl) was used to dissolved and incubated overnight at room temperature and in the dark (covered with aluminum foil). The next day, the absorbance from each well was measured by ELISA reader with 570 and 630 nm wavelengths.

The experimental substances have proven to be safe for the breast cancer cells and not only do they not cause significant apoptosis (compared to cisplatin positive control group), three groups have also shown proliferative properties to the extent of an average of 10% increase. These results are remarkable in the sense that the substances were made purely based on theoretical data obtained using quantitative structure activity relationships and it is worth noting that these substances may be used as an external amino acid source for cells.

Keywords: Breast cancer; T47D; drug release; conjugated peptide; Anticancer drug; Cell penetrating peptide; Cytotoxicity; Drug delivery; Tumor targeting

Chemometric methods application for the identification and quantification of Meat and soy protein species using ATR-FTIR spectroscopy

Zahra Keshavarzi, Sahar Barzegari, Maryam Ghasemi, Farshad H Shirazi*

P165

Authors' Affiliations:
Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran
Pharmaceutical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Niayesh Highway, Valiasr Ave, Tehran, Iran, 14155-1817

Abstract Presenter:
Sanaz Keshavarzi

***Correspondance:**
Farshad H Shirazi

Coauthors:
Sahar Barzegari
Maryam Ghasemi

Abstract:

Meat is one of the essential main parts of diet with special concerns on its accurate labeling. In this study Fourier transform infrared (ATR-FTIR) spectra were employed for differentiation and classification of lamb, chicken, beef meat and texture soy protein from each other. A multivariate statistical procedure based on unsupervised principal component analysis (PCA) and supervised artificial neural networks (ANN) in spectral range 1700–1071 cm-1 were performed for classification and discrimination. Spectral preprocessing was carrying out on each spectra including: Savitzki-Golay (SG) smoothing filter, Standard Normal Vitiate (SNV) and min max normalization. As a result the classification accuracy of 100% has been achieved using these methods, provided that in both methods we classified the groups by inputting two category in each run. Also Models built with PLS-R using FTIR data sets containing texture soy protein with beef demonstrated a high correlation value and good linearity of R2>0.97. Our investigation shows that FTIR- ATR spectroscopy coupled with ANN and PCA can be used for the detection and classification of lamb, chicken, beef meat and texture soy protein from each other.

Keywords: FTIR, identification, meat

FTIR and ATR spectra for discrimination between beef and chicken meat: A comparative study using Principle Component Analysis (PCA)

Zahra Keshavarzi, Sahar Barzegari, Farshad H Shirazi*

P166

Authors' Affiliations:
Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran
Pharmaceutical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Niayesh Highway, Valiasr Ave, Tehran, Iran, 14155-1817

Abstract Presenter:
Sanaz Keshavarzi

****Correspondance:***
Farshad H Shirazi

Coauthors:
Sahar Barzegari

Abstract:

Detecting meat adulteration for quality control and accurate labeling is important and needs convenient analytical methods. This study aimed to investigate and compare the application of transmission and ATR approaches of Fourier Transformed Infrared Spectroscopy (FTIR) followed by principle component analysis (PCA) to discriminate chicken and beef meat, both with preprocessing the spectra (wavenumber region of 1700–1071 cm-1) and without it where PCA was applied on the whole spectra range. Preprocessing included Savitzki-Golay (SG) smoothing, standard normal variant (SNV), scatter correction (MSC) and Min-Max Normalization. The results suggest that applying PCA on specified preprocessed spectra could detect hidden relationships between variables in chicken and beef in both approaches. PCA successfully clustered these meats when applied on transmission mode spectra without any preprocessing treatment, while applying it on ATR mode's raw spectra failed to cluster them. This may be due to the significantly higher reproducibility, intensity of peaks and signal-to-noise (S/N) ratio in transmission mode spectra compared to ATR.

Keywords: FTIR, identification, meat

Biological monitoring of mine workers by human isolated lymphocytes: cytotoxicity assessment of Lead (Pb) exposure

Maral Ramezani, Mahshid Soltani, Jalal Pourahmad Jaktaji*

P167

Authors' Affiliations:
Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran

Abstract Presenter:
Maral Ramezani

****Correspondance:***
Jalal Pourahmad Jaktaji

Coauthors:
Mahshid Soltani

Abstract:

Lead poisoning is a public health problem that is old but permanent in developing countries. High lead concentration in environment should be considered due to its harmful effects on health and longevity. Unfortunately, exposure to lead is inevitable, because the use of this metal in everyday life of human is from work to home and accumulated in environment. The purpose of this study is to investigate cytotoxicity of lead in mine workers due to exposure to heavy metal lead (Pb) on human isolated lymphocytes.

All mine workers were selected and control group who Don't work in mine were chosen by the same criteria. Blood samples were taken and all cytotoxicity parameters (cell viability, ROS formation, MMP collapse, Lysosomal membrane damage, GSH & GSSG concentration) were measured. All cytotoxicity parameters in minerals were significantly ($p<0.001$) higher than those of control group.

Our results indicate that the lymphocytes of mine workers exposed to Lead are more susceptible to oxidative stress than controls group. Due to the impacts of Lead (Pb), the proper use of safety equipments and daily showers can reduce the risk of absorption of toxic agents and their subsequent hazards for workers.

Keywords: Lead poisoning, Mine workers, Lymphocytes, heavy metal, Lead (Pb), Cytotoxicity

Occurrence of organochlorine pesticide residue levels in Nashtarud River, Mazandaran Province, Iran

Razieh Aliyan Aliabadi*, Zahra Nazari khorasgani, Abdolazim Behfar

P168

Authors' Affiliations:
Student Research Committee, Ahvaz Jundishapur University of medical sciences, Ahvaz, Iran.

Abstract Presenter:
Razieh Aliyan Aliabadi

****Correspondance:***
Razieh Aliyan Aliabadi

Coauthors:
Zahra Nazari khorasgani
Abdolazim Behfar

Introduction:

This River is located in the Mazandaran province, and the other name of Nashtarud River is Azarud. this river originates from the southeast of Tonekabon (formerly Shahsavar), and flows toward the altitudes 40 km south of Tonekabon, and flows northward into the Chalou villages, the Pila Sara and Nashtarod, and finally goes to the Caspian Sea.

One of the pollutants that threaten the quality of water in Tajan River is pesticides. Pesticides can create serious health problems and there is increasing public concern about pesticide contamination in water, so separation and quantification of selected organochlorine pesticides residues [(OP'DDT, PP'DDT, alderin, dieldrin, heptachlor, (β, γ, δ) HCH, and metoxychlor] in water of Tajan River was investigated.

Materials and methods:

For this purpose, one composite sample was taken every month which comprised 20 grab samples. Water samples were acidified to pH 2 and extracted three times with n-hexane, concentrated using a rotary vacuum evaporator for Florisil column chromatography cleanup and fractioned by elution with 3 different solvent mixtures of petroleum and diethyl ether. Finally, elutes concentrated to dryness using rotary vacuum evaporator and then the residues was dissolved in hexane and analyzed by GC-ECD.

Results:

In general, all of 9 investigated organochlorine pesticides were detected. Regardless to the kind of organochlorine pesticide the most pollution was seen in April with 3.327 and the least contaminated water of Nashtarud River was in December with 0.722µg/L. The highest and lowest mean concentrations of 9 investigated pesticides belonged to heptachlor and metoxychlor in 0.920 and 0.025 µg/L respectively.

Conclusion:

the concentrations some of the investigated organochlorine pesticide were above permitted maximum residue limits (MRLs) by Iranian government.

Keywords: organochlorine pesticide, DDT isomers, HCH isomers, alderin, dieldrin

Mitochondrial/lysosomal toxic cross-talk plays a key role in Zolpidem neurotoxicity

Nasim Akbarizadeh, Parvaneh Naserzadeh, Jalal Pourahmad*

P169

Authors' Affiliations:
Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Nasim Akbarizadeh

****Correspondance:***
Jalal Pourahmad

Coauthors:
Parvaneh Naserzadeh

Introduction:

Zolpidem is a nonbenzodiazepine hypnotic drug that is used in the treatment of short-term insomnia. Common symptoms that occur with taking medication include forgetfulness, anxiety, confusion, depression, dizziness, drowsiness, irritability, anger, speech abnormality, fatigue, and difficulty concentrating. Neurotoxicity is one of the common side effects of zolpidem drug, its severity and prevalence are related to the dose, drug schedule, age, and history of the patient in the development of brain diseases. in this research we decided to investigate cellular mechanisms involved in zolpidem induced neurotoxicity using isolated rat brain neurons.

Methods:

In this research rat brain neurons were isolated using ultra centrifugation technique. Cytotoxicity parameters including reactive oxygen species (ROS) formation, decline of mitochondrial membrane potential, increase in caspase-3 activity and lysosomal membrane leakiness were then evaluated using ACMS techniques.

Results:

Our results showed that cytotoxic action of zolpidem on neuron cells is mediated by reactive oxygen species (ROS) formation, decline of mitochondrial membrane potential, increase in caspase-3 activity and lysosomal membrane leakiness before cell lysis ensued.

Discussion and Conclusion:

All of the above mentioned Zolpidem -induced oxidative stress cytotoxicity markers were significantly ($p < 0.05$) prevented by ROS scavengers, antioxidants, mito¬chondrial permeability transition (MPT) pore sealing agents, endocytosis inhibitors and adenosine tri¬phosphate (ATP) generators. It seems that Zolpidem neurotoxicity is associated with mutual mitochondrial/lysosomal potentiation (cross-talk) of oxidative stress in neuron cells. This cross-talk finally results in release of lysosomal digestive proteases and phospholipases and mitochondrial MPT pore opening leading to cytochrome c release and activation of caspases cascade which signal apoptosis.

Keywords: Zolpidem; neurotoxicity; neuron cells; oxidative stress; mitochondrial/lyso¬somal cross-talk

Assessment of Pharmacist Medication Consultation in Community Pharmacies located in Tehran

Fatemeh Izadpanah*, A. Akbari Sari, M.Zargaran

P170

Authors' Affiliations:
Food & Drug Administration of I.R.I, Tehran, Iran

Abstract Presenter:
Fatemeh Izadpanah

****Correspondance:***
Fatemeh Izadpanah

Coauthors:
A. Akbari Sari
M.Zargaran

Introduction:
A patient-centered approach is an important component in the evaluation of healthcare services. To evaluate the effect of medication consultation on patients, we did our study from April 2016 through September 2017.
Methods:
A total of 315 patients, who referred to pharmacy for receiving his/her their prescriptions, were enrolled. Patients could freely choose for getting or refusing medication consultation. Both groups were followed up after two weeks
Results:
Of 136 patients, 43.17% intended to take consultation. There was a significant relationship between education level and drug use (P = 0.02). The chief complaints of patients consulted were significantly more resolved than patients who were not willing to take medical advice (P = 0.02) and consulted patients, had better knowledge about taking their antibiotic in comparison with patients without consultation. Patients characteristics are shown in table 1.
Conclusion:
Pharmacist intervention was associated with significant and positive changes in patient satisfaction. While patients probably
continue to prefer a physician-led service, they value aspects of a pharmacy service. Patients generally prefer discussing medications with the family physician, but experiencing the community pharmacy-led service results in an attitudinal shift toward the pharmacist.

	Consulted group N=136	Non-consulted group N=179	p
Gender	M=41(30%) F=95 (70%)	M=104(58.1%) F=75 (41.9%)	
Mean age	34±8.5	47±9.1	0.03
Resolved chief complaints	81%	62%	0.02
Difficulty in taking antibiotics	43%	13.2%	0.01
Difficulty in drug use	10.2%	16.7%	P0.05
Herbal medicine use	17.5%	31.6%	P0.05
Drug supplements use	5.8%	7.9%	NS

Key words: pharmacist, consultation, medication, safety

Study on the Anti-aphthous effects of oral thin Film of olive leaf (Olea europea L.) extract

Sara Zahedi*, Laya Samimi Fard

P171

Authors' Affiliations:
Kerman University of Medical Science Faculty of Pharmacy, Kerman, Iran.

Abstract Presenter:
Sara Zahedi

Correspondance:
Sara Zahedi

Coauthors:
Laya Samimi Fard

Introduction:

Aphthous stomatitis is one of the most Prevalent painful, and recurrent oral wounds. This study is about OLE (olive leaf extract) and its bioactive Agent called oleuropein (OLEO). Recent Researches have shown that OLE had Antibacterial, Antioxidant, Anti-inflammatory and Antiviral Activity and can be used in Aphthous treatment.

Oral delicate films are new drug targeting systems which is been settled in palate and freed the drug. This study tries to find the most appropriate formulation for preparation of the pharmaceutical trip film of OLE.

Methods:

Using warm smearing method with 80% ethanol, olive leaf juice (OLJ) was prepared in 72 hours, then concentrated in rotary for 24 hours, and dried in 40-degree oven and standardization was performed. After mixing OLJ with dissolved polymer and plasticizer, the drug thin film sheets were prepared and its physicochemical properties were evaluated.

This study was a double-blind clinical trial in which 30 patients were randomly assigned into two 15-groups of A and B. Group A received film of OLJ and group B received dexamethasone film. The patients were referred to the clinic at the days zero, three and six, for examination.

Results:

The results showed that the drug had acceptable stability in formulation over 4 weeks and over 90% of the drug was stable in the sheets. The clinical trial showed that the amount of the pest on the third and the sixth day in the receiving group of the OLJ was decreased by 12.32% and 70.4%, while in the control group (dexamethasone receptor) was 44.37% and 42.44% respectively. Also pain reduction in the group of OLJ in the third and the sixth day was 55.58%, and 100%, while in the dexamethasone group was 44.35%, 97.83% respectively.

Conclusions:

Among patients with oral pets who used olive leaves, the rate of pain reduction is higher than dexamethasone. Due to the fact that the leaves of the olive tree do not have a specific side effects and are acceptable in terms of apparent, medicinal properties and stability, they can be used at industrial scale in the treatment of pests.

Keywords: Oleuropein

N-acetylcysteine for the management of acute and chronic pulmonary complications of sulfur mustard; from bench to bedside

Seyed Ruhollah Musavinasab*, Iman Karimzadeh, Majid Shohrati , Mostafa Ghanei

P172

Authors' Affiliations:
Department of Clinical Pharmacy, Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract Presenter:
Seyed Ruhollah Musavinasab

****Correspondance:***
Seyed Ruhollah Musavinasab

Coauthors:
Iman Karimzadeh
Majid Shohrati
Mostafa Ghanei

Introduction:

Sulfur mustard exposure, as the most widely used chemical weapon, can lead to acute and long-term pulmonary complications via various pathways, such as triggering an imbalance between the oxidant and antioxidant system. Currently, there is no validated antidote, chemoprophylaxis and curative modality for pulmonary toxicities secondary to sulfur mustard exposure.

The aim of this literature review is to collect available experimental and clinical data on the efficacy of N-acetyl cysteine (NAC), as a prominent antioxidant agent, in the prevention and/or treatment of sulfur mustard-induced acute and chronic pulmonary toxicities.

Methods:

A literature search was performed by the relevant keywords like ''N-acetyl cysteine'', ''Sulfur mustard'' and ''Lung injury'' in databases such as Scopus, Medline, Embase and ISI Web of Knowledge. No time limitation was considered. Exclusion criteria were Non-English and/or Persian language articles and congress abstracts. Nineteen articles were selected for review.

Results:

Fifteen out of 16 in vitro and experimental studies concluded that oral, intravenous, intraperitoneal and intra-tracheal administration of NAC is effective in the management of sulfur mustard-induced acute lung injury, in a time-dependent manner, via direct scavenging, inhibition of oxidative stress, inflammatory responses and apoptosis. In addition, oral NAC alone (1200 or 1800 mg/day for 4 months) or at a dose 600 mg/day for 6 months in combination with clarithromycin (500 mg/day) have led to improvements of clinical and para clinical pulmonary parameters (FEV1, FVC and FEV1/FVC ratio) of patients with bronchiolitis obliterans due to sulfur mustard, through undetermined mechanisms despite a gap of 18 years between exposure and treatment.

Conclusion:

Despite limitations of relevant experimental and clinical studies, NAC can be considered as a candidate agent for prevention (e.g., 4800 mg/day) and/or treatment of sulfur mustard-induced acute lung injuries, as well as its long-term pulmonary toxicities, especially bronchiolitis obliterans due to its demonstrated effectiveness, favorable safety profile and low-cost. However, the optimal dose, time of initiation, route and duration of administration of NAC for these purposes remain unknown and need more clinical studies

Keywords: N-acetylcysteine, early lung injuries, late lung injuries, sulfur mustard gas, prophylaxis, treatment

Development of Medication Safety Standards in Selected Hospitals in Iran

Fatemeh Izadpanah*, S. Nikfar, F. Bakhshi, M.Zargaran

P173

Authors' Affiliations:
Food & Drug Administration of I.R.I, Tehran, Iran

Abstract Presenter:
Fatemeh Izadpanah

****Correspondance:***
Fatemeh Izadpanah

Coauthors:
S. Nikfar
F. Bakhshi
M.Zargaran

Introduction:

Correct and smart use of drugs can have a significant impact on health promotion. However, medication errors are common and can lead to financial costs and human suffering while they are almost preventable. It is essential to note that the use of drugs for treating diseases is not always a safe practice.

Methods:

10 10 hospitals were selected for the implementation of medication safety standards. A checklist of medication safety standards was prepared and the selected hospitals were assessed.

(Table 1)

Medications safety standards	Percentage of hospitals progress
Drugs with similar names and forms	96.5%
High-risk medications	98%
Medication reconciliation	63%
Medication errors	96%
Safe injection	80%
Lifesaving drugs for each specialty	89%

A guideline which was aimed to show how to implement the standards, were sent to the selected hospitals. Seven hospitals implemented medication safety standards.

Results:

Comparing the initial and final status of hospitals in terms of the implementation of medication safety standards, it seems that on average hospitals improved their status from 42.5% to 87.5%.

Conclusion:

High-risk drugs are more hazardous for patients with chronic diseases who are exposed to poly-therapy; hence, the list of high-risk medications should be prioritized. It is suggested that the general lists and guidelines will be announced by the Ministry of Health.

Another way to reduce the risks of high-risk? medications is to use medication reconciliation forms which must be completed carefully while transferring the patients between different wards. To increase medication safety, in some cases such as reducing medication errors, motivational strategies can be used.

Keywords: patient safety, medication satandard, pharmacist, medication error

Study of Consumption Pattern of Vancomycin in Imam Khomeini Hospital in Sari, Spring of 2017-2018

Tannaz Dehpouri, Zahra Bagherzadegan, Ebrahim Salehifar*

P174

Authors' Affiliations:
Mazandaran University of Medical Science, Iran.

Abstract Presenter:
Tannaz Dehpouri

****Correspondance:***
Ebrahim Salehifar

Coauthors:
Zahra Bagherzadegan
Ebrahim Salehifar

Introduction:

The indiscrimmate use of board spectrum antibiotics is a universal dilemma. This study was done to manage the Vancomycin usage in different parts of Imam Khomeini Hospital in Sari.

Methods:

This study was conducted in Spring 2017 compared to Spring 2018 at Imam Khomeini Hospital, North of Iran, based on recorded reviews of hospitalized patients, considering National guidelines for rational use of costly antibiotics. The Defined Daily Dose (DDD) recommended by World Health Organization (WHO) was used as an identical measurement unit in this study. The total number of hospitalized patients was extracted from hospital's Health Information System (HIS) considering the day/beds of patients over specific timespan.

Results and Discussion:

According to spring 2017 calculations, total Hospitalized patients were 26,301 and 24,912 in spring 2018. At the other hand, total number of admitted patients was 9,842 in spring 2017 and 8,761 in Spring 2018. Calculations show that relevant DDD values in spring 2017 and spring 2018 were 7.6 and 7.2 respectively. Checking DDD values of following wards: Gynecology (0.86 to 0.34), Neurosurgery (16.30 to 1.12), ICU3 (41.68 to 19.62), NICU (6.35 to 3.96), Vascular surgery (272.22 to 166.92), Emergency (3.04 to 2.03), Oncology (17.90 to 8.99), Gastroenterology (2.08 to 0.79), and Oncosurgery (216.66 to 55.64) showed that DDD values reduced in Spring 2018 Comparing to Spring 2017. The calculations showed that DDD values in some sections in 2018 were higher than the values in 2017. Related wards were included: Internal section (4.82 to 6.29), Surgery ward (2.55 to 2.57), ICU1 (16.68 to 33.67), ICU2 (29.23 to 41.65), Orthopedy (8.40 to 9.62), and pediatric section (0.13 to0.57). The highest rate of DDD in 2018 was for vascular ward (166.92) and the lowest value was for Gynecology ward (0.34). 272.22 was the highest DDD rate, found in vascular surgery ward, and lowest rate was 0.13 found in Pediatric ward in 2017.

Conclusion:

The conducted survey result's at the mentioned hospital in spring 2018 based on protocols showed that rational prescribing and Vancomycin usage in different wards affected positively on antibiotic usage rate and reducing DDD value from 7.6 to 7.2.

Keywords: Vancomycin, Defined Daily Dose, Rational Use

Evaluation of the impact of patients' drug information about injectable multiple sclerosis medication in adverse drug events

Fatemeh Ali Aghdam

P175

Authors' Affiliations:
13Aban Pharmacy, Tehran, Iran.

Abstract Presenter:
Fatemeh Ali Aghdam

****Correspondance:***
Fatemeh Ali Aghdam

Introduction:

Multiple sclerosis (MS) is one of the most common inflammatory diseases of the central nervous system and is the main cause of impotence in young adults. The chronic nature of the disease makes it highly difficult for patients to adhere to treatment. Intolerance or discontinuation of treatment can increase the incapacity and duration of hospitalization. Accordingly, our goal in this study is to identify the essential aspects of educating and counseling, to cover the needs of patients by evaluating their mistakes in the field of drug use, storage and management of complications. They and their opinions are in need of information or advice.

Methods:

This cross-sectional study was performed on 384 patients with MS. Referring to 13 Aban pharmacy and Sina hospital clinics who were taking injectable MS medications including interferon beta or GlatiramerAcetat. The information in this study was recorded by a questionnaire completed by a researcher.

Results:

The level of information was generally better in women(p=0.028). Also patients living in Tehran were more likely to have higher levels of information probably due to better access to educational resources(p=0.024). Although level of education and degree of patients was not related, attending classes of the MS community and companies significantly affected patients'knowledge (p0.001).

Conclusion:

Generally, patients' knowledge about their injectable drug is very low and in areas such as drug storage, missed doses, administration and management of adverse effects and drug interactions are problematic and require comprehensive training and counseling. Therefore, organizing counseling and educational classes at the beginning of treatment and then periodically to alleviate patients' information is essential and can improve the quality of life of the patients and the acceptance of treatment.

Keywords: Multiple Sclerosis, Drug information, Patient education, Interferon beta, Adverse drug events

Does Atorvastatin Help Prevent Classic Migraine Attacks? A Triple-Blind Controlled Clinical Trial

Reza Ganji*, Mehdi Sayyah, Nazanin Rostami

P176

Authors' Affiliations:
Department of clinical pharmacy, school of pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract Presenter:
Reza Ganji

Correspondance:
Reza Ganji

Coauthors:
Mehdi Sayyah
Nazanin Rostami

Introduction:

Headache is one of the disabling nervous disorders which sub distally affects the quality of life. Only 13% of patients with a migraine sufficiently respond to conventional preventive treatments. Findings show that migraine patients may suffer from vasomotor dysfunction. statins have been proven to have pleiotropic effects, such as the improvement of vascular function by promoting the function of vascular endothelium. Therefore, this group of drugs may improve the prevention of migraine attacks in patients with a classic migraine.

Method:

The present research was a triple-blind controlled clinical trial, which was conducted on patients with a classic migraine. To this end, 68 patients with a classic migraine were randomly assigned to two groups of placebo and test (20-mg atorvastatin). Patients in the placebo group received tablets of 500-mg sodium valproate and placebo and those in the test group were treated with tablets of 500-mg sodium valproate and 20-mg atorvastatin tablets once a day for two months. After 8 weeks, patients were re-evaluated and the data were analyzed using statistical tests.

Results:

The results of dependent t-test showed that there was a significant difference between the pretest and posttest in the pain severity in both placebo and test groups (p=0.000). The pretest mean score of pain severity was equal to 7.903 in the placebo group and 7.849 in the test group. These figures were obtained 5.871 and 3.273 in the posttest, respectably. Dependent t-test also indicated that there was a significant difference between the pretest and posttest in terms of the number of migraine attacks in both placebo and test groups (p=0.000). The pretest mean number of migraine attacks was equal to 4.61 in the placebo group and 4.67 in the test group. These figures reduced to 3.61 and 1.61 in the posttest, respectively.

Conclusion:

The study findings suggested that the 20 mg per day dose of atorvastatin can help reduce the number of attacks and pain severity in patients with a migraine. In addition, this drug does not cause considerable side effects and leads to a high level of patient satisfaction.

Keywords: Headache, Migraine, Atorvastatin, Sodium valproate, statin

Evaluation of the antibiotics susceptibility of Acinetobacter baumannii isolated from patients admitted to ICU department of Imam Hossein Hospital

Pardis Nazirzade, Arash Mahboubi*, Mohammad Sistanizad*

P177

Authors' Affiliations:
Department of Clinical Pharmacy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Department of Pharmaceutics, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Pardis Nazirzade

****Correspondance:***
Arash Mahboubi
Mohammad Sistanizad

Introduction:
Bacterial antibiotic resistance is the emerging worldwide health problem. Among Gram-negative bacteria Acinetobacter baumannii, has great importance due to its high mortality and high frequency of antibiotic resistance. The incidence of multidrug-resistant Acinetobacter baumannii(MDR A. baumannii) is increasing worldwide and lead to nasociminal infections and mortality.
The aim of this study was to evaluate the susceptibility of clinically isolated Acinetobacter baumannii from patients admitted to ICU department of Imam Hossein Hospital to Colistin, Ampicillin Sulbactam, Cefepime, Gentamicin, Tazocin, Amikacin, Ciprofloxacin, Ceftazidime, Co Amoxiclav, Imipenem, Meropenem, Ceftriaxone, and Levofloxacin.
Method:
68 clinical isolated samples were evaluated and identified by microbiological method by using TSI, SIM, SC, Urea Broth for detection of Acinetobacter baumannii. The susceptibility of the isolated species was determined by disk diffusion according to CLSI method. The sensitivity to the antibiotics were reported based on the growth inhibition zone diameter.
Result:
35 specimens of 68 clinically isolated bacteria were identified as Acinetobacter baumannii (51.47%).
The susceptibility rates of strains to Ampicillin Sulbactam, Cefepime, Gentamicin, and Tazocin were 42.86%, 8.58%, 5.72%, and 2.85% respectively. The results showed that 97.14% of isolates were susceptible to Colistin. All isolates were resistant to Amikacin, Co Amoxiclav, Ceftriaxone, Ciprofloxacin, Imipenem and Meropenem.
Conclusion:
The result of the present study showed incidence of the resistance of Acinetobacter baumannii isolated to the various classes of antibiotics used in hospital acquired infections.
The results of this study showed that the only effective antibiotic against these isolates is Colistin which have many side effect including acute renal failure (33% to 60%), nephrotoxicity (18% to 26%) and neurotoxicity (7%). These results are warning for non-appropriate use of the antibiotics.

Keywords: Acinetobacter baumannii, Disk diffusion, Antibiotic susceptibility, Colistin

Comparison of Oral and Injected Vitamin D3 Effects on the Reduction of Statin-Induced Myopathy: Single Blind Randomized Controlled Clinical Trial

Mobina Tahmasebi Vand, Ahmad Sa'dinpour, Nikoo Sadat Masousomi, Reza Ganji*

P178

Authors' Affiliations:
Pharmacy, International Unit, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract Presenter:
Mobina Tahmasebi Vand

****Correspondance:***
Reza Ganji

Coauthors:
Ahmad Sa'dinpour
Nikoo Sadat Masousomi

Introduction:

Statin inhibits HMG-CoA reductase enzyme, that cause lower cholesterol level in plasma, but use of this drugs have been side effects that one of them is myopathy disorders. Difference methods have been suggested to reduce these disorder. As vitamin D is effective in reducing muscle and inflammatory diseases, this study examines the therapeutic effect of vitamin D on statin-induced myopathy.

Method:

This study was Single Blind Randomized Controlled Clinical Trial and performed on patients with statin-induced myopathy. Forty-three Patients were divided two group by random block method, the first group were administered 50,000 units Perl of vitamin D3 orally for 8 weeks the next group doses of 300,000 IU amp vitamin D3 per month. A questionnaire to collect information were considered included the McGill Pain Management (MPQ) in six therapeutic hypnosis sessions were conducted for the experimental group and for statistical analysis of data from analysis of covariance was used to help software SPSS22.

Results:

The results showed that vitamin D resulted in significantly reduced, pain perception, Emotional perception of pain, pain Assessment, Various pains and pain Management by Which was statistically significant (p 0/05). Serum levels of vitamin D and VAS (visual analogue scale) levels increased after oral and injected vitamin D (P = 0.001).

Conclusion:

As a result, it can be said that Vitamin D is an effective intervention in the management of pain and decrease side effect in patients with Statin-Induced Myopathy and can be used as a noninvasive way health care team is available.

Keywords: Myopathic Condition, HMG-CoA Statins, Vitamin D3

Comparison of the effect of oral strip and pearl of vitamin D in patients with vitamin D deficiency in a single-blind clinical trial

Nikoo Sadat Masoumi, Aryan Yousefi, Mobina Tahmasebi Vand, Reza Ganji*

P179

Authors' Affiliations:
Pharmacy, International Unit, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract Presenter:
Nikoo Sadat Masoumi

****Correspondance:***
Reza Ganji

Coauthors:
Aryan Yousefi
Mobina Tahmasebi Vand
Reza Ganji

Introduction:

Evidence suggests that vitamin D deficiency is associated with various diseases. Since the difference in the supplementary formulation can help to quickly cure and compensate for this deficiency, this single-blind clinical trial examined the effect of vitamin D oral strip and pearl in patients with vitamin D deficiency.

Materials and Methods:

This single-blind, randomized clinical trial was conducted on patients with vitamin D deficiency for two months in Golestan Hospital in 2012. In all patients, the level of tests, including vitamin D, is measured both at the beginning of the study and at the end of the study (after eight weeks). For 30 patients, 50,000 units of vitamin D (ergocalciferol) are administered orally once weekly for eight weeks (control group) and for 30 others, 2,000 units of the vitamin D oral strip are administered daily for eight weeks. Patients with insufficient levels will also be treated for at least four weeks. Finally, the results of patients' trials will be reviewed before and after eight weeks of receiving the drug and the data will be classified based on information such as serum vitamin D level and the calcium level and compared and analyzed using the statistical methods.

Results:

There was a significant difference between serum vitamin D levels before and after consumption in both groups receiving strip and pearl in non-diabetic patients, all patients and also patients with an insufficient level of vitamin D (p=0. 001), but there was no significant difference between the two groups of pearl and strip.

Conclusion:

Finally, it seems that the difference in the supplemental form and the hepatic first-pass did not affect the level of serum vitamin D, and both pearl and oral strip forms were equally effective.

Keywords: Diabetes Mellitus, Vitamin D, Oral Strip and Peral

Evaluation of Pain Management Efficacy in Critically Ill Intubated Patients in a Referral Teaching Hospital

Ali Ebrahimi, Sarah Mousavi*

P180

Authors' Affiliations:
Pharmacy student, Pharmacy student's Research Committee, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract Presenter:
Ali Ebrahimi

***Correspondance:**
Sarah Mousavi

Introduction:

Pain assessment, reassessment, and documentation was lacking in our intensive care unit (ICU). The aim of this study is to evaluate current pain assessment and management in critically ill patients with its goal to describe pain management episodes according to behavioral pain scale (BPS) and describe the effectiveness of analgesics according to the recommendation of guidelines.

Methods:

In this prospective study, a sample of 60 intubated critically ill patients was selected from intensive care units (ICUs). The researcher evaluates patient' pain severity using BPS tool in patients receiving analgesics according to nurses' note. Adults ventilated ≥2 days and received analgesics were included. At each time of analgesic administration, the BPS score was recorded and this process was repeated 72 hours later. The appropriateness of pharmacologic interventions was assessed according to the society of critical care medicine guideline. Based on this guideline only patients with BPS score >5 should receive analgesics.

Results:

The most prescribed analgesic was morphine sulfate (48.3%) followed by fentanyl (23.3%). 55% of analgesics at day 1 and 25% at day 3 were prescribed appropriately according to the guideline recommendation and BPS score. Morphine was the most effective drug (17 patients out of 29). Despite a BPS score less than 5, 26 patients received analgesics.

Discussion and Conclusion:

Self-report pain assessment scales may be inappropriate when critically ill patients are incapable of adequate communication because of sedation or mechanical ventilation. Lacks of established pain protocol in our setting leads to inadequate pain control and overuse of analgesics. Development of a protocol or adherence to international guidelines is mandatory for rational use of analgesics, better pain controling in patients, and reducing the risks of medical errors and treatment failures.

Key words: Pain management, Pain assessment, Critically ill, Intubated patients

Evaluation of polypharmacy and drug interactions frequency in patients admitted to the emergency department in Golestan teaching hospital of Ahvaz jundishapur university of medical sciences

Mobina Tahmasebi Vand*, Hassan Barzegari, Mandana Izadpanah, Soheil Roshan Zamiri

P181

Authors' Affiliations:
Hassan Barzegari Department, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract Presenter:
Mobina Tahmasebi Vand

****Correspondance:***
Mobina Tahmasebi Vand

Coauthors:
Hassan Barzegari
Mandana Izadpanah
Soheil Roshan Zamiri

Introduction:

Drug interactions are one of the major concerns in the health care setting.

Patients admitted to the emergency department due to overcrowding, stress, insufficient number of healthcare professionals, high turnover of patients, and communication failure among multiprofessional teams are at increasing risk for occurring of drug interactions.In emergency departments, health care professionals must offer immediate care to critical patients, so medications may be added to complex treatment regimens without the benefit of screening for drug interactions.The pharmacists play several roles in pharmacotherapy, such as revising prescriptions to investigate drug interactions and writing recommendations, which must contribute to patient's safety. regarding the high prevalence of polypharmacy in emergency department, we decided to evaluate polypharmacy and drug interactions in emergency departments.

Method:

This retrospective study was done for 3 months from March to June 2018 at Golestan hospital, an educational hospital affiliated to Ahwaz Jundishapur University of Medical Sciences. Data including patients' demographics, medication dose, drug interactions, dose adjustments were collected in patients with hospital stayed longer than 24 hours. The analysis of drug interactions was performed using the Lexicomp and Micromedex applications.All of interactions were classified according to severity as severe, moderate, mild, and without interactions.

Result:

The number of medication in each medical record ranged from 2 to 19 and the average per prescription was 8.4. finally, total of 228 potential drug interactions were identified in 55 patients. Among detected interactions, 4 interactions were severe ,39 interactions were moderate, 145 interactionS were mild, and 6 ones showed no interaction. The castp and FTsite servers were used for predicting interactive sites of proteins. The information of interactive pocket was used for fimbriae subunits and chaperone docking.

Keywords: drug interaction, polypharmacy, emergancy department

Adherence to ASCO, the latest clinical recommendations, for prophylaxis of acute chemotherapy-induced nausea and vomiting in Iran

Azadeh Moghaddas*, Mahbobeh Ebrahimi, Valiollah Mehrzah

P182

Authors' Affiliations:
Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract Presenter:
Azadeh Moghaddas

****Correspondance:***
Azadeh Moghaddas

Coauthors:
Mahbobeh Ebrahimi
Valiollah Mehrzah

Introduction:

In spite of advances in the management and prevention of chemotherapy-induced adverse effects, chemotherapy-induced nausea and vomiting (CINV) still remains as one of the scariest? Adverse effects. There is a paucity of data on the adherence to clinical guidelines for prophylaxis of CINV in clinical practice. Therefore, we assessed the adherence to the 2017 American Society of Clinical Oncology (ASCO), latest clinical recommendations, for management of acute CINV at our institution.

Methods and Results:

During a 6-months cross-sectional study on outpatient's cancer patients, we collected data from the relevant baseline characteristics of patients. From the written prescription documents during temporary hospitalization, we collected all the prophylactic orders for management or prevention of acute CINV (within 24 h after administration of chemotherapy) including doses and schedules of drugs used for prophylaxis of acute CINV.

Between September 2017 and April 30, 2018, 139 patients had the inclusion criteria. 20% of patients encountered severe chemotherapy-induced nausea during 6-24 hours after chemotherapy. The severity of chemotherapy-induced vomiting was significantly higher after 2 hours of chemotherapy administration (P 0.001). The emetogenic potential of chemotherapy was high in 39 (28.1%) patients, moderate in 70 (50.35%) patients; low in 25 (18%), and minimal in 5 (3.6 %) patients.

The most prescribed prophylactic regimens for management of CINV in our institute were the combination of aprepitant, granisetron, dexamethasone and metoclopramide (51.8%). According to compatibility with ASCO guideline, selection of different regimen for prophylaxis of acute CINV in our center was compliant in 0 %, 78%, 96% and 60% of high, moderate, low and minimal emetogenic potential of chemotherapy respectively.

Conclusions:

Although our center is a referral and university-affiliated center, the adherence to the ASCO clinical recommendations for prophylaxis of CINV at our institution was poor due to lack of prescribing olanzapine and over prescription of serotonin, neurokinin antagonists and dopamine antagonists.

Keywords: Chemotherapy-induced nausea and vomiting, American Society of Clinical Oncology, Guideline

Investigating the Effect of thiosemicarbazones complex Ni on Expression Changes of Mir34a in controlling of Notch signaling pathway in jurkat E6.1.

Fatemeh Ghorbani*, Golnaz Asadi Tehrani, Sina Mirzaahmadi

P183

Authors' Affiliations:
Islamic Azad University, Zanjan, Iran.

Abstract Presenter:
Fatemeh Ghorbani

****Correspondance:***
Fatemeh Ghorbani

Coauthors:
Golnaz Asadi Tehrani
Sina Mirzaahmadi

Introduction:

Acute lymphoblastic leukemia (ALL) is a type of cancer that usually starts with bone marrow. All is the most common cancer in children. In recent years, a lot of attention has been paid to finding new anti-cancer compounds containing metallic ions. dipyridine ketone-derived thiosemicarbazone is a strong and selective anticancer agent that overcomes drug resistance and is currently undergoing pre-clinical progress. Antimicrobial activity of this new thiosemicarbazone by (1) ribonucleotidereductase inhibition (2) oxidation-reduction activities of thiosemicarbazone complexes with iron (fe) and copper and nickel and the formation of cytotoxic free radicals are very effective and is one of the drugs used to treat various types of leukemia. The aim of this study was to evaluate the changes in the expression of mir34a gene on the Notch signalling pathway in acute lymphoblastic leukemia of the jurkat E.6.1 cell line under treatment with thiosemicarbazone nickel.

Methods:

Different does of Ni were investigated with MTT test. then, the Thiosemicarbazones Ni drug was prepared at concentrations (0.5 and 1 macromolar) and the jurkat E6.1 cancer cells were treated with the thiosemicarbazoneni after the cell passage in groups and time (72 hours). miRNA extraction and cdna synthesis were performed and the expression of the miRNA mir34a and mir199(housekeeping gene), was evaluated by realtimepcr. Finally, the results were analyzed by relative quantitative measurement and rest software.

Results:

The results of this study showed that mir34a showed a significant increase (p 0.001) during 72 hours of treatment with nickel in concentrations (0.5 and 1 macromolar), and the highest increase in expression at a concentration of 1 macromolecular was observed

Conclusions:

Given the results, it has been found that doses of 0.5 and 1 Ni in 72 hours are the optimal doses and time of the effect of this complex. The results of this study can be used to control and treat optimal treatment of leukemia in humans by identifying molecular pathways in the function of the chemotherapy drugs used, as well as introducing new drugs and preventing uncontrolled growth of jurkat cancer cells.

Keywords: Acute lymphoblastic leukemia, Thiosemicarbazones Ni, Mir34a

Impact of seminar-based training on ICU nurses to reduce medication errors rate

Nazafarin Hatami-Mazinani, Motahareh Mahi-Birjand, Afsaneh Vazin*

P184

Authors' Affiliations:
Student Research Committee, Department of Clinical Pharmacy, Faculty of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract Presenter:
Nazafarin Hatami-Mazinani

***Correspondance:**
Afsaneh Vazin

Coauthors:
Motahareh Mahi-Birjand
Afsaneh Vazin

Introduction:

There are inherent risks, both known and unknown, associated with the therapeutic use of drugs. Medication errors are among the most common medical errors in the hospitals. Our aim was to detect prescription, administration and transcription errors by a non-disguised direct observation after a course of seminar-based training for nurses involved in administrating and transcribing process. The study was placed in a medical ICU, in a teaching hospital in Shiraz, Iran.

Methods and Results:

A pharmacy student was assigned to train nurses in the following subjects. 1. Incident of medication error in current ICU 2. I.V drug preparation and administration techniques 3.Protocols for administration of drugs in patients who have N-G tubes 4.Drug-Drug compatibilities. After finishing the trainings the whole process of 307 drug doses were observed.(in a 3 different shifts).data were collected and analyzed. Results: The 307 drug doses were observed. 204 doses (66.45%) were given to male patients and 103 doses (33.55%) were given to Females. 325 errors (105.86%) were detected.

Conclusions:

The evaluation clearly shows training nurses can reduce administration technique errors. And presence of a pharmacist could prevent a large number of medication errors.

Keywords: Administration errors, Medication errors, Clinical Pharmacist, Training, ICU

Evaluation of Some Medication Errors in Internal Wards of Imam Sajjad Ramsar Hospital in the spring and summer of 2017

Saeed Raoof Asli, Setareh Ghorbanian Khorshidi, Nematollah Ahangar, Shahram Ala*

P185

Authors' Affiliations:
Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran

Abstract Presenter:
Saeed Raoof Asli

****Correspondance:***
Shahram Ala

Coauthors:
Setareh Ghorbanian Khorshidi
Nematollah Ahangar
Shahram Ala

Introduction:

The medication error refers to any preventable event that results in inappropriate drug therapy or injury to the patient, while medication is under the control of the medical staff and the patient. Studies show that 20% of the total medical errors occur due to medication errors that result in an annual loss of at least 100,000 people in the United States. So Drug errors can be named as one of the challenges and criteria for patient safety assessment in the treatment system.

Methods and Results:

This is a descriptive cross-sectional study and the population consisted of 200 records of the patients admitted to the internal department of Sajjad Ramsar Hospital. Collected data included demographic data from patients, records of drug records in the patient's case, drug orders transferred to the patient's kardex medicine, and Medscape was used to determine drug interactions and severity of complications.

For this study, a total of 112 pharmacologic drugs were identifie and 1888 prescriptions for 200 patients were administered. Of the 1720 drug registrations registered by doctors, 223 drug errors were documented by the physician and 36 errors were recorded by nurses in the implementation of drug and drug control orders. The highest number of errors occurred by the medical team was 86.1%. The contribution of the nursing team to the transcription error and the implementation of the orders was 13.9%. Doctors' mistakes were 11%, and the incidence of errors for them and for nurses was 1.2%. Patient sharing was 16.8% on average and a total of 166 drug interactions were observed. There was a significant relationship between the number of drug items and the increase in the number of hospital days with drug interactions (p 0.05).

Conclusions:

Most of the errors among all errors incidence occurred in the contribution of the physicians' team and the overall incidence of errors occurred in the contribution of nurses to the doses of drugs transferred to the patient's kardex. The results of this study indicate high interactions in the internal wards, which makes clear the necessity of carrying out more extensive studies.

Keywords: Drug error, Internal medicine, Drug order

Investigation analgesic effect of curcumin topical formulation compared with diclofenac gel on patients with primary knee osteoarthritis: a randomized double blind trial

Zahra Azadbakht, Sara Ataei*

P186

Authors' Affiliations:
Department of clinical pharmacy, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran

Abstract Presenter:
Zahra Azadbakht

Correspondance:
Sara Ataei

Introduction:

Osteoarthritis is the most common form of arthritis, affecting millions of people worldwide. It occurs when the protective cartilage on the ends of the bones wears down over time. The purpose of this study is to compare the effects of two different topical treatment of osteoarthritis; curcumin ointment 10% and diclofenac sodium gel 1% on osteoarthritis patients**.**

Methods and Results:

Topical curcumin ointment 10% prepared in the base of vaseline. In this randomized and double-blind trial, 60 men and women aged > 40 years diagnosed with primary OA in the knee were randomly classified into two groups of 30. Each formulation were placed in similar tubes and encoded with A and B. group A were given diclofenac gel and group B were given curcumin ointment. Each group must be self-applied their own formulations 4 times daily for 2 weeks. The intensity of pain was recorded once before treatment and then after that and measured by the visual analogue scale (VAS). At the end of the study, recorded points were evaluated and statistically analyzed and superior treatment was suggested. To prove that the curcumin ointment has not any skin irritation, the Draize test on rabbit skin was performed during 72 hour.

The mean and SD of pain in people suffered from primary knee osteoarthritis in group B was 2.6±1.1 and in group A was 4.1±1.7. So reduction in curcumin group was more than diclofenac group ($P \leq 0.05$). No irritation was observed during Draize test. So the formulation was suitable for skin administration.

Conclusions:

Both Diclofenac gel and curcumin ointment were effective in pain intensity reduction, but the curcumin was more effective.

Keywords: Primary knee osteoarthritis, Curcumin ointment, Pain reduction

Evaluation of consumption rate and direct cost of parenteral antibiotics before and after Health Revolution Program at the Namazi hospital in Shiraz

Atefeh Jalali, Fatemeh Soleymani, Nikoo Sakhajoo, Iman Karimzadeh*

P187

Authors' Affiliations:
Pharmaceutical Strategic Studies Office

Abstract Presenter:
Atefeh Jalali

****Correspondance:***
Iman Karimzadeh

Coauthors:
Fatemeh Soleymani
Nikoo Sakhajoo
Iman Karimzadeh

Abstract:

The excessive use of anti-microbial medicines over the past few decades has led to an ever-increasing spread of microbial resistance, reducing the efficiency of anti-microbial drugs, and the costly and time-consuming treatment for infectious diseases. The purpose of this study is to investigate the effect of Health Revolution Program on the number of use and direct cost of injectable antibiotics at the Namazi Hospital within the six-year period.

Forty-four injectable anti-microbial drugs administered at the Namazi teaching hospital in Shiraz were considered. They were divided into three groups of antifungals, antibacterials, and antiviruses based on the Anatomical/Therapeutic/Chemical (ATC) classification codes. Four indexes, including (1) total consumption rate, 2) per capita consumption, 3) total cost, and 4) per capita rial, were measured annually to assess the changes in the process of prescribing antimicrobials. Defined daily dose (DDD) for each medication was also calculated. These data were extracted from the hospital pharmacy electronic database.

The most costly and commonly administered anti-microbials after the Health Revolution Program was voriconazole and vancomycin, respectively. General surgery, cardiac surgery, and adult emergency were the 3 most common hospital wards that anti-microbials were administered. After the project, total consumption, per capita consumption, total cost, and per capita rial of all anti-microbials increased by 13.31%, 1.39%, 142.63%, and 146%, respectively. The increases in per capita consumption, total cost, and per capita rial were statistically significant (P 0.001). In comparison to the period before health revolution program, the DDD of studied antimicrobials was also raised significantly after the project (P 0.001). In contrast to antibacterials, total consumption, per capita consumption, total cost, and per capita rial of antiviral and antifungal agents did not increase significantly.

Our results indicated an overall increase in both the consumption rate and direct cost on anti-microbials, as well as a strong tendency to use expensive anti-microbials after the implementation of the Health Revolution Program. Since previous studies have shown a high percentage of irregular consumption and administration of antimicrobials in Iran, more comprehensive studies are needed to investigate the utilization pattern of these agents to prevent the spread of microbial resistance.

Keywords: Parenteral antibiotics, Health Revolution Program, Direct Cost

Formulation and evaluation of physicochemical properties of amitriptyline oral strip

Sara Zahedi*, Mahdieh Paluni, Mehdi Rezaeifar, Mehdi Ansari, Maryam Kazemipour

P188

Authors' Affiliations:
Kerman University of Medical Sciences Faculty of Pharmacy

Abstract Presenter:
Sara Zahedi

Correspondance:
Sara Zahedi

Coauthors:
Mahdieh Paluni
Mehdi Rezaeifar
Mehdi Ansari
Maryam Kazemipour

Introduction:

Amitriptyline is a tricyclic antidepressant that is connected to the anesthetic sites of the surface of the sodium channel. Due to its mechanism of action, it can be used as an analgesic for oral wounds, aphthous, and pain. The purpose of this investigation is formulation and evaluation of physicochemical properties of amitriptyline oral strip.

Methods:

First, a mixture of the polymer and plasticizer was prepared in water. Then, amitriptyline was added to the mixture and hemogenized completely. The remaining ingredients of the formulation were added. Following spreading the mixture on a glass plate, it was dried and cut in order to obtain trans-parent thin films of the drug. Finally, physic-chemical characteristics such as surface pH, solubility, fragility, uniformity, and the stability of the drug were measured and evaluated.

Results:

The results showed that this formulation is suitable for preparation of flexible and isolated films with acceptable thickness of 0.02 mm and surface pH at 4. Stability tests showed at least 96.9% of the drug was stable in films kept in the oven at 40°c.

Conclusions:

This research was capable of providing amitriptyline oral films with suitable appearance and pharmaceutical properties, acceptable stability, rapid dissolution, and high bioavailability.

Keywords: Amitriptyline, oral thiln film, Formulation

Comparing Cardiac Troponin Levels after Anesthesia using Sevoflurane and Isoflurane in patients undergoing cardiac surgery: a systematic review and meta-analysis

Nashmil Ghadimi*, Hossein Hosseinifard, Sara Kaveh, Rasoul Azarfarin

P189

Authors' Affiliations:
Rajaei Cardiovascular Medical & Research Center, Iran University of Medical Sciences Tehran, Iran.

Abstract Presenter:
Nashmil Ghadimi

****Correspondance:***
Nashmil Ghadimi

Coauthors:
Hossein Hosseinifard
Sara Kaveh
Rasoul Azarfarin

Introduction:

Cardiac troponin is a very important and special indicator of heart cell injury and necrosis. Higher troponin levels in blood correlate with greater risk of heart damage. This study aimed to compare the troponin levels after anesthesia using sevoflurane and isoflurane in patients undergoing cardiac surgery.

Methods:

We searched EMBASE, PubMed, and Cochrane CENTRAL databases for randomized controlled trials and related websites were identified by using the search Mesh terms ''sevofurane,'' ''isofurane,'' ''randomized controlled trials, ''and '', cardiac enzymes.'' The final search date was December 2, 2018.Two investigators independently reviewed each article for data extraction and quality of studies, evaluating the quality of articles with the Cochrane checklist, with RevMan software version 5.3. In order to compare the effects of sevoflurane and isoflurane on the amount of blood troponin at the time of ICU admission and in 6, 12, 24, and 48 hours after entering the ICU, the difference in mean of Troponin level at any time relative to the baseline value for each study was measured, and then combined with the meta-analysis of the results. The combination of the results from the random-effects model was used. The heterogeneity of the studies was measured by the Cochran (Q) and I2 statistics. In this study, four studies were finally included in the meta-analysis analysis.

Results:

In the selected studies, a total of 184 patients were treated with sevoflurane and 184 patients were treted with Isoflurane. The mean age of the subjects in the sevoflurane and Isoflurane group was 45.89 and 45.79, respectively. The heterogeneity between the studies was (Q=134.32, DF=3, I2=97.77). The results of meta-analysis showed that pooled mean difference ± SD in troponin levels (ng/mL) at the time of ICU admission between the two groups were (-0.19±0.05 ng/mL, p0.001), 6h (0.12±0.07, p=0.10), 12h (0.06±0.18, p=0.74), 24h (1.14±0.13, p0.001), and 48h (0.53±0.15, p0.001).

Conclusions:

This meta-analysis showed that blood troponin levels were significantly lower in patients, who underwent cardiac surgery and received sevoflurane than those who inhaled isoflurane at the time of admission in ICU and 24 and 48 hours after admission.

Keywords: Troponin, Sevoflurane, Isoflurane, Cardiac surgery

Cobb Syndrome (Spinal Cord Arteriovenous Malformation): A Systematic Review from Pathogenesis to Treatment, from Bench to Bed

Elmira Niknami, Sorour Jafari, Sara Darjazini, Ali Saffaei , Zahra Sahraei*

P190

Authors' Affiliations:
Pharmacy Students' Research Committee, School of Pharmacy, Isfahan University of Medical sciences, Isfahan, Iran.

Student Research Committee, Faculty of pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

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

Abstract Presenter:
Elmira Niknami

****Correspondance:***
Zahra Sahraei

Coauthors:
Sorour Jafari
Sara Darjazini
Ali Saffaei
Zahra Sahraei

Introduction:

Cobb syndrome is a vascular skin nevus with an angioma in spinal cord and it is associated with skin and nervous complications. In this rare and life-threatening syndrome early diagnosis and treatment is essential to save patients' life. Up to yet there was not any certain consensus regarding this syndrome's treatment. Hence, it is necessary to conduct a review on published case reports for Cobb syndrome's treatment. The aim of this study was to evaluate the Cobb syndrome treatment through a systematic review

Methods:

In this systematic review which was done in 2018 October, three medical databases including PubMed, Google Scholar and Scopus were searched with appropriate keywords based on MeSh database. The articles were screen 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 selected articles qualified through Jaddad scale by independent investigators. The main therapeutic strategies extracted from remained articles. This systematic review was based on standards of PRISMA guideline.

Results:

In this review 172 article were found in mentioned databases. Duplicated articles were removed by EndNote software and 77 articles remained. In first step 7 article were excluded due to irrelevant title and non-English language and 70 article remained. In second step the Abstracts reviewed carefully and 40 articles removed. Finally, after evaluating the full texts, 10 articles entered to final evaluation. This 10 articles were about the pathogenesis and treatment of Cobb syndrome. This syndrome has an unknown pathogenesis that is attributed to a malformation in spinal cord which cause angiogenic and inflammatory factors in spinal cord and blood vessel wall. This can lead to tangled and unstable blood vessel which can fail appropriate oxygen and nutrition delivery to skin cells and cause skin lesions. The treatment principle in in three approaches, including non-pharmacologic, systemic treatment and, topical treatment.

Discussion and Conclusion:

Pharmacologic treatments including resection surgery, embolization, and radiotherapy used to remove blood vessel malformation. For systemic treatment Corticosteroids can use as monotherapy or as pre-embolization treatment. For topical treatment, normal saline and topical antibiotics can use to manage the wound clinical condition. This treatment have been successfully improved patients signs and symptoms in many cases.

Keywords: Cobb syndrome; Treatment; Cutaneomeningospinal Angiomatosis; Pathogenesis

Evaluation of efficacy and safety of topical naloxone in control of chronic pruritus in patients with neurodermatitis

Yasaman Kiani Doust, Nazanin Rostami Charati, Yunes Panahi*

P191

Authors' Affiliations:
Department of Clinical Pharmacy, Pharmaceutical Branch, Islamic Azad University of Medical Science, Tehran, Iran

Abstract Presenter:
Yasaman Kiani Doust

****Correspondance:***
Yunes Panahi

Coauthors:
Nazanin Rostami Charati
Yunes Panahi

Introduction:

Pruritus is considered the most common and hardest skin condition to treat. Recent pathophysiological studies have found a number of therapeutic approaches, such as μ-opioid receptors (MOR) receptor antagonists to treat the condition in patient with neurodermatitis. The effectiveness of systemic administration of MOR receptor antagonists for the control of pruritus is well established. However, it has been suggested that topical administration of MOR receptor antagonists, such as Naloxone®, can be more effective to control pruritus, with lower cost and lesser side effects. The objective of this study was to compare the efficacy of combination of oral intake of antihistamine and topical application of Naloxone with oral administration of antihistamine and placebo in patients with neurodermatitis.

Methods:

A total of 45 patients (24 males and 30 females) with clinical symptoms of neurodermatitis (pruritus), who met the selection criteria assigned for the study, were enrolled in a randomised control trial (RCT) at Baqiyatallah Hospital (Tehran, Iran). After the initial diagnosis of pruritus by study dermatologist and obtaining their consents, cases were randomly allocated into two groups. Patients in the control group received an oral antihistamine cetirizine 10 mg/day

and those in the treatment group were treated with oral antihistamine cetirizine 10

mg/day) and topical application of Naloxone twice daily in the morning and afternoon. A survey was conducted to collect the demographic, skin and health conditions data. The dermatological life quality index (DLQI) and pruritus scores (5-D itch scale) quaternaries were designed to capture the data on severity of disease in both groups before (days 0) and after treatment (day 56).

Results and conclusions:

The average age of cases in this study was (42.52 ±13.9). There was no significant difference in average age of patients in treatment (40.9 ±15.7) and control (43.8±13.4) groups (P>0.05). Dermatological life quality index significantly reduced from 17.97±13.4 on day 0 (before treatment) to

7.88 ± 8.29 after treatment (P=0.001) in treatment group. However, there was no significant difference before (17.0 ± 5.0) and after antihistamine intake (15.2 ± 5.5) in the control group (P=0.172).

Similarly, pruritus scores significantly differed before (34.17±7.87) and after treatment (18.54±9.06) with oral demonstration of antihistamine and topical application of Naloxone in treatment group (P=0.001). Whereas, pruritus scores didn't differ before (38.26 ± 7.42) and after (36.63 ± 10.48) oral administration of antihistamine alone (P=0.239). Results of this study suggest that combination of oral antihistamine and topical application of Naloxone is more effective to control pruritus and can improve the health condition of patients with pruritus compared to those who only used antihistamine.

Keywords: Itch, Neurodermatitis, Naloxone, Pruritus

Evaluation of Efficacy and Safety of Topical Naloxone Ointment on Controlling of Chronic Pruritus caused by Chemical Injuries

Nazanin Rostami Charati, Yasaman Kiani Doust, Yunes Panahi*

P192

Authors' Affiliations:
Department of Clinical Pharmacy, Pharmaceutical Branch, Islamic Azad University of Medical Science, Tehran, Iran

Abstract Presenter:
Nazanin Rostami Charati

***Correspondance:**
Yunes Panahi

Coauthors:
Yunes Panahi
Yasaman Kiani Doust

Introduction:

One of the most harmful complications of chemical warfare injuries is chronic pruritus, which has led to a decrease in the quality of life of these patients. There is no definitive treatment for the elimination of this type of itching, and the compounds that are used only reduce and control the annoying symptoms. Since in the pathophysiology of this, opioid receptors (MOR) have a significant role in causing itching, the naloxone (a competitive antagonist of opioid receptors (MOR)) was used locally in these patients. The purpose of this study was to evaluate the efficacy and safety of topical naloxone in controlling chronic pruritus in a chemical victim.

Method and materials:

Seventy volunteers were diagnosed with chronic pruritus caused by chemical weapon by Dermatologist of Dermatology Clinic of Baqiyatallah Aj Hospital after considering the criteria for entering and leaving the study and obtaining conscientious informed consent and justification were randomly divided into two groups of case and control. The study was performed in a double blinded study. In addition to standard treatments (oral antihistamines), group A and group B received medication. Patients use medication twice a day for eight weeks. At the beginning of the study, the informed consent form and three DLQI questionnaires, Pruritic Score and demographic data were completed. After four and eight weeks, the patient was contacted and at the end of the study, the questionnaires were completed again to evaluate the effect of the medicine.

Results:

57 male patients with an average age of 53.3 ± 5.9 were at least 34 and had a maximum of 63 years, mean age in the treatment group was 51.4 ± 5.9 and 55.5 ± 5.1 in the control group. The result of the score of DLQI questionnaire in the case group was 24.7 ± 4.4 before treatment and after treatment was 13.7 ± 7.5 with Pvalue 0.001 and in the control group, the score before treatment was 25.6 ± 4 and after treatment, 22.5 ± 6.7 with a Pvalue 0.120 . The result of the Pruritic score questionnaire in the case group was 32.2 ± 9.8 before treatment, and after treatment, it was 21.1 ± 10.2 with a Pvalue of 0.001 and in the control group, the score before treatment was 36.4 ± 8.4 and after treatment, 32.6 ± 11.3 with Pvalue 0.220.

Keywords: Naloxone, chemical injury, pruritus

Evaluation of licorice solution in the treatment of recurrent aphtous ulceration: a randomized, double blinded clinical trial

Zahra Kiani*, Narjes Akbari, Neda Asadimehr

P193

Authors' Affiliations:
Birjand University of Medical Sciences, Birjand, Iran.

Abstract Presenter:
Zahra Kiani

****Correspondance:***
Zahra Kiani

Coauthors:
Narjes Akbari
Neda Asadimehr

Introduction:

Recurrent aphthous stomatitis (RAS) is the most common pathological lesion in the oral mucosa, with an incidence rate of 5-50%. This study aimed to compare the efficacy of diphenhydramine solution (DS) and diphenhydramine containing 5% of glycyrrhizaglabra extract (DSG) in the management of RAS.

Methods:

This was a double-blind, randomized, clinical trial recruiting 70 RAS patients who had no systemic diseases. Participants were randomly assigned into DS and DSG groups (n = 35 per group). The severity of pain was assessed at the baseline and after 2, 3, and 5 days of intervention using visual analog scale (VAS). Also, the duration of wound healing was measured by photography. The data were analyzed in SPSS software version 18 using descriptive and inferential statistical tests.

Results:

Both solutions had significant effect on pain score but pain score on DSG (7.96 on the first day versus 0.28 5th day) was significantly lower than DS group (8.56 on the first day versus 2.53 5th day). The mean wound healing duration in the DSG group was 1.6 days less than in the DS group, and there was a significant difference between the two groups concerning the mean wound healing duration (p = 0.000).

Conclusions:

DSG appears to be more effective than DS alone in RAS treatment.

Keywords: Recurrent aphthous stomatitis, diphenhydramine, glycyrrhiza glabra

Evaluation of the pattern of human albumin utilization in a teaching hospital of Tabriz University of Medical Sciences, Iran

Manizheh Karimi*, Bohlol Habibi Asl, Taher Entezar maleki,
Hamid Tayyebi-Khosroshahi

P194

Authors' Affiliations:
Department of Pharmacognosy, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.

Abstract Presenter:
Manizheh Karimi

****Correspondance:***
Manizheh Karimi

Coauthors:
Bohlol Habibi Asl Taher Entezar maleki
Hamid Tayyebi-Khosroshahi

Introduction:

Albumin is a protein colloidal solution with limited availability and high cost. It imposes a high cost to the health system. It should be used in such approved indications as Abdominal Paracentesis, spontaneous bacterial peritonitis extensive burn and nephrotic syndrome.

The aim of this study was to evaluate the pattern of albumin use in Tabriz Shahid Madani Hospital.

Material and Methods:

This study was an observational retrospective research on drug utilization. All patient that were prescribed albumin during the study period (from 96/10/1 to 97/3/31) were evaluated. The information necessary to evaluate the pattern of Albumin usage was determined according to the Ministry of Health's guideline.

Results:

The total 681 vials of Albumin were prescribed for 80 patients during the study period.

Only 62.2% of patients had Medical records and patient history based on the Ministry of Health's guideline. The most common reasons to prescribe albumin were hypoalbuminemia (7.5%) volume expansion after the heart surgery (27.5%), paracentesis (5%), bacterial peritonitis (1.25%).

Conclusion:

The results showed that based on the guidelines, the most prescriptions of albumin in this hospital have not been written appropriately. Therefore, educational programs on using guidelines may help reduce albumin usage.

Keywords: Pattern of usage, Albumin, Shahid Madani Hospital, Tabriz

Inappropriate disk selection for isolated pathogens: a call to action

Sara Raziee*, Lida Shojaei, Foroud Shahbazi,
Farzaneh Korani, Farshid Raeisi

P195

Authors' Affiliations:
Students Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Sara Raziee

Correspondance:
Sara Raziee

Coauthors:
Lida Shojaei
Foroud Shahbazi
Farzaneh Korani
Farshid Raeisi

Introduction:

The results of antibiotic susceptibility pattern help physician to select the appropriate antibiotic for pathogens. The aim of our study was to evaluate the appropriateness of disk selection for isolated bacterial.

Methods:

From June2017 to March 2018 all specimens received at the laboratory of the heart center were studied, retrospectively. Disk diffusion method in the Muller Hinton Agar medium were used for determination of antimicrobial susceptibility pattern of isolates. The antibiogram result for each isolate was assessed based on The Clinical & Laboratory Standards Institute disk selection guide.

Results:

The mean age of our recruited patients was 63.73±16.24 years and the most of them were female (84/153, 54.9%). Of 153 samples, 100 (65.4%) were from urine, 42 (27.5%) from tracheal and the others (7.2%) from the blood. The most of the specimens (74/153, 48.4%) were received from coronary care units. Escherichia coli was the most frequent isolates (65/153, 42.48%) followed by Klebsiella spp. (32/153, 20.92%). The inappropriate antimicrobial disks selection was occurring among in 34.73% and 68.09% of isolated Escherichia coli and Klebsiella spp. respectively. The resistance rates of two later pathogens to third generation cephalosporins, aminoglycoside and carbapenem were 42.19%, 26.23%, 16.67% for Escherichia coliand 63.64%, 31.03%, 50% for Klebsiella spp. respectively.

Conclusion:

Wrong disk selection was common in the present study. Establishment and implementation of the Clinical & Laboratory Standards Institute guideline could be helpful for appropriate disk selection.

Keyword: antibiogram, appropriateness, disk diffusion, CLSI

Electrochemical sensor for trace determination of diclofenac sodium drug in real samples and drug residues using ZnFe2O4 nanoparticles modified carbon paste electrode

Arezou Rashidipour, Ebrahim Nabatian, Saeid Ahmadzadeh*

P196

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences

Abstract Presenter:
Arezou Rashidipour

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Ebrahim Nabatian

Introduction:

Diclofenac sodium (DICLS) is a nonsteroidal anti inflammatory drug (NSAID) that is widely prescribed for the treatment of rheumatoid arthritis, osteoarthritis, musculoskeletal injuries, and post-surgery analgesia in human and veterinary medicine. It is also extensively used in eye surgery, where on-line monitoring is necessary. DICLS is a potent inhibitor of cyclooxygenase (COX) enzymes for avoiding the production of prostaglandins. DICLS is well absorbed after oral administration with extensive hepatic metabolism. DICLS has been found to increase the blood pressure in patients with Shy–Drager syndrome and diabetes mellitus. On the other hand, DICLS may cause life-threatening heart or circulation problems such as heart attack and stroke, especially if the patient uses it long term. The determination of small amounts of DICLS in pharmaceutical preparations is very important for medical and pharmaceutical needs where it is used for the treatment of various diseases. Therefore it is vital to develop a simple, fast, selective, and cost-effective method for determining the trace amounts of diclofenac in different pharmaceutical formulations. The current work deals with a new approach for the quantitative determination of DICLS using electrochemical methods.

Methods and Results:

ZnFe2O4/NPs/1B3MITFB/MCPE prepared by mixing of 0.1 g of 1B3MITFB, 0.9 g of the paraffin oil, 0.1 g of ZnFe2O4/NPs, and 0.9 g of graphite powder. Then the ingredients mixed well for 1 h until a uniformly wetted paste was obtained. A portion of the paste was filled firmly into one glass tube as described above to prepare ZnFe2O4/NPs/1B3MITFB/MCPE. The electrochemical investigations carried out using square wave voltammetry (SWV) and cyclic voltammetry (CV) techniques. The obtained results revealed that the electro-oxidation peak current was proportional to the KA concentration in the range of 1-500 μM with the detection limit of 0.5 μM.

Conclusions:

The proposed method was successfully applied to the determination of DICLS in pharmaceutical samples. The excellent properties of the ZnFe2O4/NPs/1B3MITFB/MCPE make it promising for application as a real sample analysis.

Keywords: Diclofenac sodium, Quantitative electrochemical determination, Modified carbon paste electrode, Ionic liquid, ZnFe2O4 nanoparticles

Novel adsorption materials based on polyamide-graphene composite for efficient removal of amoxicillin from aqueous solution; experimental and computational aspect of adsorption process

Omid Paknia, Maryam Dolatabadi, Amir Basiri, Saeid Ahmadzadeh*

P197

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Omid Paknia

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi
Amir Basiri

Introduction:

Amoxicillin (AMX) is a semisynthetic b-lactam antibiotic commonly used in the humane treatment and veterinary practice and it has been employed in several studies as a model compound representing the antibiotics family (1, 2). Due to its chemical composition, pharmacological characteristics and environmental toxicity, it is known as one of the main pollutants to be persistent in the aquatic environment. Although the concentration of the residual antibiotics in the aquatic and terrestrial environment is generally not high, they are considered to be emerging micro pollutants because of their immediate and potential threats to the environment and living bodies. Therefore, it is significantly important to remove such compounds from the waste streams prior to their discharge into the aquatic environment (2, 3).

Methods and Results:

The effect of operating parameters in the adsorption process such as initial concentration of amoxicillin, pH solution, adsorbent dosage, and reaction time was investigated. Response surface methodology (RSM) was used to optimize the parameters and suggested model was analyzed using ANOVA. The results showed that optimum conditions for removal of AMX were the adsorbent dose of 0.75 g L-1, pH of 9.5, initial AMX concentration of 14.0 mg L-1, and reaction time of 65.5 min. The initial concentration of antibiotic had the greatest influence on AMX adsorption among other variables. Langmuir model (R2=0.965) was chosen as an efficient model. Kinetic models such as first and second order models were studied for analysis of experimental mechanism data and the second order model (R2=0.950) was chosen as an efficient model. According to this isotherm model, the maximum adsorption capacity of the polyamide-graphene composite was 89.5 mg g-1. Along with experimental work, the computational aspect of the adsorption process investigated.

Conclusions:

The experimental results of adsorption tests performed according to a central composite design were worked out by response surface methodology. A quadratic model allowed correlating the independent variables, namely the contact time, pH, initial AMX concentration and adsorbent dosage, to the AMX removal selected as a response.

Keywords: Amoxicillin, Adsorption, Polyamide-graphene composite, Isotherm, Kinetic.

Experimental and theoretical approach for high efficiency removal of tetracycline from hospital wastewater using ultrasonically synthesized zinc hydroxide nanoparticles

Mohammad Mahdi Poustchin, Maryam Dolatabadi, Amir Basiri, Saeid Ahmadzadeh*

P198

Authors' Affiliations:
Deputy of Research, Kerman University of Medical Sciences, Kerman, Iran

Abstract Presenter:
Mohammad Mahdi Poustchin

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi
Amir Basiri

Introduction:

Tetracycline antibiotics (TC) are widely used to treat and prevent human diseases and promote the growth of livestock and aquaculture animals. The medical investigations have revealed that TC is poorly absorbed in the digestive tract of human and animals and excreted in stool and urine as a mixture of the parent compound and metabolites (1). The release of antibiotics and their metabolites into the aquatic environment increases the risk of developing resistance in human bacteria and veterinary pathogens. TC usually are detected in soils, surface waters, groundwater, and even in drinking water due to their low removal rates in water and wastewater treatment plants. Aqueous containing this class of chemicals need to be treated using an efficient process in order to protect human and the environment against their adverse effects (2, 3).

Methods and Results:

This study was carried out experimentally in a laboratory scale. The effect of main variables including initial TC concentration, solution pH, adsorbent dosage and reaction time on the adsorption process investigated. The design and process optimization performed using Design Expert 7 software. Isotherm and kinetics of the adsorption process studied. Optimization showed the highest removal efficiency is obtained as 91.8% at TC initial concentration of 9.4 mg L-1, pH 5.5, adsorbent dose 2.3 g L-1, and contact time 43.5 min. The maximum adsorption capacity was found to be 218 mg g-1. The adsorption process for TC removal followed the Langmuir isotherm with (R2=0.980) and second-order kinetic model (R2=0.995). Experimental and computational aspect of adsorption process investigated.

Conclusions:

The study showed that ultrasonically synthesized zinc hydroxide nanoparticles (USZHN) could be efficient for TC removal from hospital wastewater, even in field samples. USZHN as adsorbent could be regenerated for further TC removal experiments. However, we need to increase its adsorption capacity by, for example, increasing its porosity.

Keywords: Tetracycline, Zinc hydroxide nanoparticles, Kinetic, Isotherm, Hospital wastewater

Modeling of fluoxetine removal from wastewater using photo electro-Fenton process; Performance and mechanism

Omid Paknia, Maryam Dolatabadi, Saeid Ahmadzadeh*

P199

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran

Abstract Presenter:
Omid Paknia

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi

Introduction:

Fluoxetine hydrochloride (FLX) (C17H18F3NO) is a selective serotonin reuptake inhibitor, one of the most frequently prescribed drugs to treat depression, eating disorders, and obsessive-compulsive disorder (1). FLX is a chiral compound and the commercially available drug is marketed as a racemic mixture. FLX and its principal metabolite norfluoxetine (NFLX) are detected in surface waters due to their incomplete metabolization after therapeutic use and due to incomplete elimination in wastewater treatment plant (2). The occurrence of FLX in surface waters and in aquatic organisms has raised concern as ecotoxicological effects to aquatic organisms have been reported.

Methods and Results:

The current work deals with investigating the potency and efficiency of photo electro Fenton process in the successful removal of FLX from wastewater using response surface methodology based on central composite design. Analysis of variance (ANOVA) was applied to verify the significance of independent variables solely and their interactions (3). Development model using ANOVA and response optimization revealed that maximum FLX removal efficiency of 91.4 % occurred at the current density of 8.5 mA cm-2, initial FLX concentration of 32 mg L-1, pH of 4.5, the reaction time of 85 min. However, according to the obtained results, a reverse proportion between the initial FLX concentration and pH solution with removal efficiency was observed. The normal plot of residuals demonstrated that the linear curve of normal probability versus the internal residuals was reasonably close to a straight line with the correlation coefficient of 0.987.

Conclusions:

The photo electro Fenton process as an environmentally friendly treatment method was optimized and applied successfully for efficient removal of FLX pollutant from wastewater samples using response surface methodology in the current work.

Key Words: Fluoxetine, Removal, Photo electro Fenton process, Modeling

Selective electrochemical sensing of chlorpromazine hydrochloride using carbon paste electrode modified with ionic liquid and CdO nanoparticles; experimental and theoretical approach

Mohammad Mahdi Rezaeifar, Maryam Dolatabadi, Saeid Ahmadzadeh*

P200

Authors' Affiliations:
Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Mohammad Mahdi Rezaeifar

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi

Introduction:

Chlorpromazine hydrochloride (CPH), which is used as an anti-anxiety, anti-depression, and sedative drug, is one of the most commonly used drugs in the treatment of acute and chronic mania such as schizophrenia and psychosis. Among other uses of CPH is its use in the treatment of severe hiccups, tetanus, vomiting, and nausea. Additionally, in patients hospitalized after surgery it is used as a sedative and shock-reducing drug. Current paper deals with fabrication of electrochemical nanostructured sensor as an accurate and rapid tool with high sensitivity for the reliable determination of CPH in both pharmaceutical and urine samples.

Methods and Results:

To evaluate the analytical applicability of CdO /NPs/1B3MITFB/MCPE for determination of CPH in real samples such as drug, urine, and serum. A sensitive modified carbon paste electrode (MCPE) employing CdO nanoparticle (CdO /NPs) and 1-butyl-3-methylimidazolium tetrafluoro-borate (BMITFB) ionic liquid was developed for trace level analysis of CPH in the current work using square wave voltammetry (SWV) and cyclic voltammetry (CV) techniques. Under the optimum conditions in voltammetric determination, the oxidation peak current was proportional to the CPZ concentration in the range of 0.1–350 µM with the detection limit of 0.07 µM. The synthesized CdO nanoparticles were characterized by different methods such as SEM, XRD, and EDAX. By applying non-equilibrium Green's function (NEGF) formalism combined with first-principles of density functional theory (DFT), the electron transport properties of the CPH based on conjugated orbitals were investigated.

Conclusions:

In the present study, 1-butyl-3-methylimidazolium tetrafluoro-borate modified CdO/NPs carbon paste electrode was used to investigate the electrochemical behaviors of NE in the aqueous solution. The modified electrode CdO/NPs/1B3MITFB/MCPE showed great improvement in comparison with the traditional carbon paste electrode.

Keywords: Chlorpromazine hydrochloride, Quantitative electrochemical determination, Modified carbon paste electrode, Ionic liquid

Synthesis and cytotoxicity evaluation of N-(5-(4-chlorophenyl) oxazol-2-yl) benzamide derivatives with potential anticancer effects

Ali Asghar Varavni, Mojgan Nejabat , Mohammad Ramezani, Fatemeh Soltani, Mona Alibolandi, Farzin Hadizadeh, Alireza Aliabadib*

P201

Authors' Affiliations:
Students Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Ali Asghar Varavni

****Correspondance:***
Alireza Aliabadib

Coauthors:
Mojgan Nejabat
Mohammad Ramezani
Fatemeh Soltani
Mona Alibolandi
Farzin Hadizadeh

Introduction:

Cancer is a general term for a group of more than 100 diseases in which cells from any part of the body begin uncontrolled proliferation. Nowadays, cancer is an important public health problem in all countries. For decades, conventional chemotherapy has been the most common type of anticancer pharmacotherapy. Cancer chemotherapy has been one of the major advances in area of medicine in the last few decades. However, the drugs administered in chemotherapy have a narrow therapeutic index and therefore high incidence of undesired side effects

Materials & Methods:

۴′-Chloroacetophenone was treated with N-bromo-succinimide (NBS) and p-toluene sulfonic acid (PTSA) in methanol (Scheme 1). The reaction mixture was refluxed for 20 h and then by extraction procedure the intended product (2) was collected. Compound 2 was treated with urea to afford aminooxazole derivative 3. Obtained derivative 3 was reacted with various derivatives of benzoic acid in the presence of DCC and HOBt to achieve final derivatives 4a-4l. MTT assay was done against three cancerous cell lines containing MCF7 (breast cancer), PC3 (prostate carcinoma) and A431 (epidermoid carcinoma) in comparison with doxorubicin as reference drug.

Results & Discussion:

All synthesized compounds were identified using spectroscopic techniques like 1HNMR, IR and MS. The synthesized derivatives were afforded with high yield. Tested derivatives exhibited significant anticancer activity in vitro compared to doxorubicin in MTT assay especially against MCF7 and PC3. Some of the tested derivatives demonstrated nanomolar potency towards these cells. Nitrated derivatives showed remarkable activity towards MCF7 whereas fluorinated compounds were so active against PC3 cells.

Conclusion:

Oxazole derivatives that were synthesized and their related anticancer activities were evaluated in vitro could be proposed as potential lead compounds for development of novel antineoplastic drugs.

Keywords: Synthesis, Oxazole, Cytotoxicity, Anticancer

Synthesis of Novel Isothiocyanate Derivatives of Noscapine and Their Antiprotozoal Activity

Kosar Babanezhad Herikande*, Peyman Salehi, Morteza Bararjanian, Samad N. Ebrahimi, Marcel Kaiser

P202

Authors' Affiliations:
Shahid Beheshti University of Medical Science, Tehran, Iran.

Abstract Presenter:
Kosar Babanezhad Herikande

****Correspondance:***
Kosar Babanezhad Herikande

Coauthors:
Peyman Salehi
Morteza Bararjanian
Samad N. Ebrahimi
Marcel Kaiser

Abstarct:

Noscapine is a naturally occurring alkaloid with phthalideisoquinoline scaffold that was isolated from Papaver somniferum [1]. In this paper, the synthesis of five α-amino and isothiocyanate derivatives of lactone ring reduced N-nornoscapine (3) [2] is reported. The anti-parasite activity of the products was investigated against Trypanosoma b. rhodesiense, Trypanosoma cruzi, Leishmania donovani axenic amastigotes and P. falciparum. All compounds showed good activity against Trypanosoma b. rhodesiense (1.0IC506.5 µM and 0.5SI29.3). All iso thiocyanate derivatives were active against L. donovani (0.8IC501.3 µM and 0.8SI18.4) and nine compounds displayed high anti-plasmodial activity (1.1IC502.7 µM and 1.4SI14.5). Molecular docking was carried out on trypanothione reductase (TbTR, PDB ID: 2WOW) [3] and UDP-galactose 4' epimerase (TbUDPGE PDB: 1GY8) [4] as targets for studying the probable mechanism of action. Compounds 7e and 6d showed excellent docking scores with -8.39 and -8.32 kcal/mol for TbTR and TbUDPGE, respectively.

Keywords: Noscapine, Isothiocyanate, Docking

Computational and experimental approach for fabrication of voltammetric modified sensor; Determination of domperidone

Anna Etemadifar, Ebrahim Nabatian, Amir Basiri, Saeid Ahmadzadeh*

P203

Authors' Affiliations:
Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Anna Etemadifar

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Ebrahim Nabatian
Amir Basiri

Introduction:

Domperidone (DMP) is a peripheral selective dopamine D2 receptor antagonist that was developed by Janssen Pharmaceutical and is used as an antiemetic, gastroprokinetic agent, and galactagogue. It may be administered orally or rectally, and is available in the form of tablets, orally disintegrating tablets (based on Zydis technology), suspension, and suppositories. The drug is used to relieve nausea and vomiting; to increase the transit of food through the stomach (by increasing gastrointestinal peristalsis); and to promote lactation (breast milk production) by release of prolactin. DMP can be used to relieve gastrointestinal symptoms in Parkinson's disease; it blocks peripheral D2 receptors but does not cross the blood–brain barrier in normal doses (the barrier between the blood circulation of the brain and the rest of the body) so has no effect on the extrapyramidal symptoms of the disease. In addition to this, DMP may enhance the bioavailability (effect) of levodopa (one of the main treatments in Parkinson's disease).

Methods and Results:

Electrochemical investigations revealed a well-defined irreversible oxidation peak for DMP over a wide concentration range from 2.0 µM to 140 µM in 0.1 M phosphate buffer solution (pH 6.0). The limit of detection was found to be 1.2 µM. The electron transport properties of DMP based on conjugated orbitals investigated employing non-equilibrium Green's function formalism combined with first-principles of density functional theory.

Conclusions:

A simple and precise analytical approach developed for determination of DMP in biological and pharmaceutical samples using carbon paste electrode (CPE) modified with 1-Ethyl-3-methylimidazolium tetra fluoroborate as ionic liquid and ZnFe2O4 nanoparticle. 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.

Keywords: Domperidone, Modified carbon paste electrode, Voltammetric determination, Ionic liquid

Enhanced adsorption onto modified carbon nanotubes for removal of ranitidine from hospital wastewater: Strategies and Challenges

Motahareh Sadegh Zadeh*, Maryam Dolatabadi, Amir Basiri, Saeid Ahmadzadeh

P204

Authors' Affiliations:
Kerman University of Medical Science, Kerman, Iran.

Abstract Presenter:
Motahareh Sadegh Zadeh

****Correspondance:***
Motahareh Sadegh Zadeh

Coauthors:
Maryam Dolatabadi
Amir Basiri
Saeid Ahmadzadeh

Introduction:

Ranitidine is classified as a drug of high environmental concern due to its existence in a variety of aquatic environments (1). One example was its identification in effluents, in several water treatment plants in Italy, with a mean concentration of 288.2 ng dm-1. Investigations demonstrate that even under optimum conditions, the ranitidine is only partially biodegradable, with an efficiency of 71% of degradation within 28 days. As a consequence, ranitidine is not biodegradable in water treatment plants, with the accumulation of water surfaces, where sunlight can change partially its structure, which can generate persistent and toxic photoproducts (2). Thus, it is a critical issue to remove ranitidine effectively from hospital wastewaters before discharging them.

Methods and Results:

Response surface methodology (RSM) under central composite design (CCD) category of Design Expert 7 software was used to achieve efficient removal of ranitidine. The main objective of the CCD method is to optimize the response surface and quantify the relationship between the controllable input parameters and the obtained response surfaces (3). The effect of various variables including; pH solution (3-11), adsorbent dosage (5-20 mg L-1), initial ranitidine concentration (100-100 mg L-1), and reaction time (5-60 min) investigated to achieve the best removal condition. Optimization showed the highest removal efficiency is obtained as 97.4% at ranitidine initial concentration 42.0 mg L-1, pH 9.5 adsorbent dose= 8.5 mg L-1, and reaction time 30 min. The modified carbon nanotubes with phosphoric acid could reduce ranitidine in wastewater. The equilibrium data were better fitted to the Langmuir model (R2= 0.9891), while the model of second-order could well describe the kinetics of adsorption (AIC values of -8.2).

Conclusions:

The adsorption process applied successfully for ranitidine removal from hospital wastewater and the predicted model for treatment of synthetic wastewater is in satisfactory agreement with removal efficiency of real hospital wastewater treatment.

Keywords: Ranitidine, Modified carbon nanotubes, Hospital wastewater, Kinetic, Isotherm.

Adsorption kinetics, isotherms, and thermodynamic studies for ibuprofen adsorption from synthetic wastewater using modified kaolin; Experimental and theoretical investigation

Motahareh Sadegh Zadeh*, Maryam Dolatabadi, Saeid Ahmadzadeh

P205

Authors' Affiliations:
Kerman University of Medical Science, Kerman, Iran.

Abstract Presenter:
Motahareh Sadegh Zadeh

Correspondance:
Motahareh Sadegh Zadeh

Coauthors:
Maryam Dolatabadi
Saeid Ahmadzadeh

Introduction:

The residues of pharmaceutical compounds especially non-steroidal anti-inflammatory drugs (NSAIDs) in water effluents have gained increasing interest during the last decade due to their potential to cause adverse ecological effects. NSAIDs beneficial effect on human health, however, is accompanied by a great concern regarding their fate on the environment especially once released through urine, feces and toilet flushing in water (1, 2). Ibuprofen (IBU) is a common example of NSAIDs found in effluents especially in water leaving sewage treatment plants at significant concentrations e.g. 10 ng L-1 to 169 µg L-1. Therefore, treatment of IBU from aqueous media is crucial.

Methods and Results:

Central composite design was used to enhance the removal efficiency of IBU by optimizing the experimental conditions under response surface methodology. The experiment was done under 5 levels of various operational parameters. The initial concentration of IBU was varied among 1 to 5 mg L-1, the temperature, pH solution, modified kaolin as adsorbent, and reaction time. The adsorption and further reaction of molecules simulated (3). Adsorption process was applied successfully with removal efficiency of 99.5% under optimal conditions of initial IBU concentration of 4.2 mg L-1, pH of 6.5, the temperature of 25°C, the adsorbent dosage of 0.5 g L-1, and reaction time of 50 min. Regression analysis showed the good fit of the experimental data to the second-order polynomial model with coefficient of determination (R2) value of 0.968, adjust correlation coefficient (Adj.R2) value of 0.930 and predicted correlation coefficient (pred. R2) value of 0.908. The kinetics of the process followed the second-order model and the isotherm of the process best fitted by the Langmuir adsorption model.

Conclusions:

According to the obtained results, adsorption process using modified kaolin with surfactant was found to be an efficient technique for or treatment of IBU from synthetic wastewater. The theoretical results confirmed the obtained experimental data.

Keywords: Ibuprofen, Adsorption process, Modified kaolin, Synthetic wastewater.

Kojic acid-derived integrase inhibitors as novel anti-HIV-1 agents: synthesis, molecular modelling and bioactivity

Hajar Sirous-Najafabadi*, Afshin Fassihi, Simone Brogi,
Giuseppe Campiani, Zeger Debyser

P206

Authors' Affiliations:
Bioinformatics Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract Presenter:
Hajar Sirous-Najafabadi

***Correspondance:**
Hajar Sirous-Najafabadi

Coauthors:
Afshin Fassihi
Simone Brogi
Giuseppe Campiani
Zeger Debyser

Abstract:

The HIV-1 establishes one of the most life-threatening opportunistic infections in human hosts which is spreading rapidly. All FDA-approved anti-HIV drugs have some inevitable drawbacks such as emergence of multi-drug-resistance to HIV strains, drug toxicity, the patient's ability to conform to the prescribed therapy?? and costs. there is a solid ground behind the substantial worldwide research to develop new, more potent and less toxic anti-HIV agents. Among recent progress in anti-HIV drug design, considerable emphasis is given to HIV-1 integrase (HIV-1 IN) as a legitimate drug target [1, 2].

As a continuation of our recent efforts in developing integrase inhibitors (INIs) [3, 4], we described the design, synthesis and biological evaluation of a series of novel derivatives based on 3-hydroxy-pyrane-4-one (HP) scaffold. The design of compounds was based on the minimal structural requirements for binding to HIV-1 IN active site including a metal binding group and the hydrophobic aromatic moiety (Figure). These compounds were prepared using commercially available Kojic acid as the starting material. An in-depth computational analysis was performed using a novel HIV-1 IN/DNA binary 3D model as well as quantum polarized ligand docking (QPLD) protocol for investigating the binding mode of the newly conceived molecules in complex with IN. The 3D- model was generated using the proto-type foamy virus (PFV) DNA as a structural template, positioning the viral poly desoxy ribonucleic chain into the HIV-1 IN homology model. Moreover, synthesized compounds were biologically screened for in vivo anti-HIV-1 activity, cellular toxicity, in vitro HIV-1 IN and HIV-1 IN strand transfer inhibitory activities.

Bioassay results indicated that most of HP analogues possessed favorable inhibitory activities against HIV-1 IN with low micro-molar IC50 values. Particularly two halogenated derivatives offered the best biological activities in terms of reduced toxicity (CC50 >250 and 195.5 µM) and optimum inhibitory activities against HIV-1 IN (IC50=0.37 and 0.7 µM) and HIV-1 in cell culture (IC50=1.72 and 1.95 µM). These observations were in good accordance with free binding energy results estimated from molecular modelling experiments. Overall, findings of present study well endorsed the capability of HP as a valuable scaffold for design and development of effective HIV-1 INIs.

Keywords: HIV-1, Integrase, molecular modelling, kojic acid

Sensitive determination of clozapine employing ionic liquid carbon paste electrode modified by magnetic nanoparticles

Mohammad Sadegh Hamzeh Nejadi

P207

Authors' Affiliations:
Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, P.O. Box 76175-493, Kerman, Iran.
Student Research Committee, Kerman University of Medical Sciences, P.O. Box 76175-493, Kerman, Iran. c Department of Chemistry, Faculty of Sciences, Shahid Bahonar University of Kerman, P.O. Box 76175-133, Kerman, Iran.

Abstract Presenter:
Mohammad Sadegh Hamzeh Nejadi

****Correspondance:***
Mohammad Sadegh Hamzeh Nejadi

Introduction:

Clozapine in patients with schizophrenia and schizoaffective disorder may decrease the rate of suicidal behavior. Clozapine is associated with a relatively high risk of low white blood cell count (agranulocytosis), a condition of suppressed immunity which may cause death? To decrease this risk, regular blood test is recommended. Other serious risks include seizures, inflammation of the heart, high blood sugar levels, and, in older people with psychosis as a result of dementia, an increased risk of death. Common side effects include drowsiness, decreased or increased saliva production, low blood pressure, trouble seeing? (visual disorder), and dizziness. The potentially permanent movement disorder tardive dyskinesia occurs in about 5% of people. Its mechanism of action is not entirely clear.

Methods and Results:

Square wave volta metric technique was employed for the analysis of clozapine. The working electrode namely carbon paste electrode (CPE) modified with CdO nanoparticle and 1-butyl-3-methylimidazolium tetrafluoroborate as a binder. Electro-oxidative behavior of clozapine on the surface of modified electrode was investigated, which indicated that the nanostructured modified electrode could efficiently promote electro catalytic oxidation of clozapine. The catalytic oxidation signal demonstrated a wide linear range from 5.0 to 120.0 µM towards clozapine with a satisfactory detection limit of 2.0 µM. The developed modified CPE applied for quantitative determination of clozapine in biological and pharmaceutical samples.

Conclusions:

A fast, selective, highly sensitive and simple electrochemical strategy developed for quantitative analysis of clozapine employing the described modified carbon paste electrode.

Keywords: Clozapine, CdO nanoparticle, Voltammetric sensor, Modified carbon paste electrode

A novel strategy for the treatment of acetaminophen from the hospital wastewater using modified carbon nanotube: Theoretical and experimental view

Mohammad Sadegh Hamzeh Nejadi

P208

Authors' Affiliations:
Student research committee, Kerman University of Medical Sciences, Kerman, Iran. Department of Chemistry, Shahid Bahonar University of Kerman, Kerman, Iran. Environmental Science and Technology Research Center, Department of Environmental Health Engineering, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. d Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran. Pharmaceutics Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran

Abstract Presenter:
Mohammad Sadegh Hamzeh Nejadi

****Correspondance:***
Mohammad Sadegh Hamzeh Nejadi

Introduction:

Acetaminophen is one of the most heavily used medicines even without medical prescription? (OTC) and it was found that nearly 58-68% of acetaminophen (AC) is excreted from the body and eventually discharged into municipal wastewater systems. Presence of AC leads to diseases and problem such as critical liver injury and hepatocyte necrosis. Moreover, protein denaturation, lipid peroxidation, and DNA damage and even mortality by AC overdose were reported due to its toxicity. Therefore, its removal from water sources as an emerging contaminant is greatly desired.

Methods and Results:

The effects of variables such as initial AC concentration, pH, adsorbent dosage, and reaction time on AC removal were studied using central composite design (CCD) and the optimum experimental conditions were found with desirability function combined response surface methodology (RSM). The significance of the independent variables and their interactions are tested by analysis of variance (ANOVA) with a 95% confidence level. The maximum removal rate was achieved at the initial AC concentration of 5.6 mg L-1, pH 4.8, adsorbent dosage 120 mg L-1 within the reaction time of 25 min. The equilibrium data for AC adsorption were better fitted to the Freundlich model (R2= 0.905), while the model of pseudo-second-order could well describe the kinetics of adsorption (AIC values of -14. Analysis of variance (ANOVA) revealed that all of the main effects found are statistically significant on the AC removal. Probability F-values (F = 65.91) and correlation coefficients (R2 = 0.9545) indicate that model fits the experimental data well.

Conclusions:

The removal efficiency decreases by increasing initial concentrations. This indicates that the initial influent concentration is an important parameter for studying the fate of hospital wastewaters.

Keywords: Acetaminophen, Treatment, Hospital wastewaters, Central composite design.

Development of a voltammetric sensor based on electropolymerized-molecularly imprinted polymer (MIP) for dopamine measurement

Arezou Rashidipour, Ebrahim Nabatian, Majid Rezayi, Saeid Ahmadzadeh*

P209

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences

Abstract Presenter:
Arezou Rashidipour

****Correspondance:***
Saeid Ahmadzadeh

Coauthors:
Ebrahim Nabatian
Majid Rezayi

Introduction:

Dopamine (DA), a neurotransmitter presents in the brain and plays a very important role in the functioning of the central nervous system, cardiovascular, renal, and hormonal systems as well as in drug addiction and Parkinson's disease. Abnormal levels of DA in human body fluids often lead to various neurological disorders including Parkinson's disease and schizophrenia. Dopamine is available as an intravenous medication, which acts on the sympathetic nervous system, to produce effects such as increasing heart rates and blood pressure. However, unusual level of the dopamine in our human body will lead to neurodegenerative disorders, such as schizophrenia, senile dementia, Parkinsons's disease, and HIV infection. The quantified detection of DA is clinically important for the diagnosis and treatment of neurological diseases. Therefore, due to the importance of DA, its accurate determination in pharmaceutical and clinical samples is greatly demanded. Current work deals with fabrication of electrochemical molecularly imprinted polymer (MIP) sensor as an accurate and rapid tool with high sensitivity for reliable determination of DA in pharmaceutical preparations.

Methods and Results:

All chemicals used were analytical reagent grade purchased from Merck. A Differential pulse voltammetric (DPV) method for the trace analysis of DA was developed in the current work. Electro-oxidation behavior of DA on the modified electrode was investigated which indicated that the modified electrode could efficiently promote electrocatalytic oxidation of DA. At pH 7.0, the catalytic oxidation signal exhibited a wide linear range with a low detection limit. The Gr/PPy-MIP/GCE was also used for quantitative determination of DA in biological and pharmaceutical samples.

Conclusions:

A fast, selective, high sensitive, and simple electrochemical strategy was developed for trace analysis of DA in pharmaceutical and biological samples using the constructed electrode. The excellent properties of the Gr/PPy-MIP/GCE make it promising for application as a real sample analysis.

Keywords: Dopamine analysis, molecularly imprinted polymer, Electrochemical sensor, Modified electrode

Fast and complete removal of the penicillin from hospital wastewater using electrocoagulation process

Amir Emad Kheirieh, Saeid Ahmadzadeh, Maryam Dolatabadi*

P210

Authors' Affiliations:
Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Amiremad Kheirieh

****Correspondance:***
Maryam Dolatabadi

Coauthors:
Saeid Ahmadzadeh
Maryam Dolatabadi

Introduction:

Penicillin is one of the most important groups of β-lactam antibiotics, which are commonly used as the raw material to produce a variety of semisynthetic penicillin. This group is highly effective and still widely used in both veterinary applications and in human medicine. Therefore, its indiscriminate might release to the environment and eventually reduce its efficiency in these fields by increasing the penicillin resistance in human and animal pathogens (1, 2). These results indicated that antibiotics cannot be completely eliminated during biological treatment and they are emitted into receiving water systems. Therefore, antibiotic removal from wastewaters before discharging into the biological treatment process and receiving water systems is very important.

Methods and Results:

In the current work response surface methodology (RSM) under CCD category was used as a set of mathematical and statistical techniques for analysis and modeling the obtained results. Experiments were done under five levels of various operational parameters (3). The reactor setup equipped with two iron plate electrodes located in the center of the electrocoagulation cell with immersed dimensions of 6×1×0.2 cm. The maximum removal rate of penicillin achieved at the pH 9.2, the current density of 6.4 mA cm-2 and initial concentration of 3.4 mg L-1 within the reaction time of 10 min. Analysis of variance (ANOVA) suggested that the effect of mentioned operating parameters was statistically significant on the Penicillin removal. The obtained results revealed reasonable energy consumption of 0.315 kWh m-3 for removing penicillin from hospital wastewater.

Conclusions:

The obtained results revealed that electrocoagulation process as a powerful and environmentally friendly emerging technique can be applied for efficient treatment of wastewater sample in the current work.

Keywords: Penicillin, Removal, Electrocoagulation, Hospital wastewater.

A comparative QSAR analysis, molecular docking and in silico-screening studies of 4-thiazol-N-(pyridin-2-yl) pyrimidin-2-amine derivatives as highly potent and selective inhibitors of CDK4 and CDK6

Zohre Mirveis*, Vahid Jaderi, Hanie Abasi, Masood Fereidoonnezhad

P211

Authors' Affiliations:
Department of Medicinal Chemistry, Student Research Committee, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran

Abstract Presenter:
Zohre Mirveis

****Correspondence:***
Zohre Mirveis

Coauthors:
Vahid Jaderi
Hanie Abasi
Masood Fereidoonnezhad

Introduction:

Initiation of S phase of the cell cycle is regulated by Cyclin D dependent kinases (CDK4 and CDK6). Several studies has reported that in 90% of cancers the CDK4/6-Rb-E2F pathway is disrupted. Mice lacking these kinases are viable and inactivation of the CDK4/6 genes only affects the proliferation of specific cell types, suggesting that CDK4/6 are required for the mitotic cell cycle. Therefore, CDK4/6 can be rational targets for designing small molecules as therapeutic agents in cancers.

Methods and Results:

In this study, a series of4-thiazol-N-(pyridin-2-yl) pyrimidin-2-amine with potent activity as CDK-4/6 inhibitors were applied to quantitative structure–activity relationship (QSAR) analysis. A collection of chemometrics methods such as multiple linear regression (MLR), factor analysis–MLR (FA-MLR), principal component regression(PCR), and partial least squared combined with genetic algorithm for variable selection (GA-PLS) were applied to make relations between structural characteristics and kinase inhibitory in this compounds. The initial conformation of the CDK4/6 was taken from PDB (ID-4:2euf and ID-6:512s). The Molecular docking simulations were carried out by means of an in house batch script (DOCKFACE) for automatic running of 4.2 and AutoDockVina. Autodock results were visually evaluated, and the top ranked binding energies (kcal/mol) in AutoDockdlg output file were considered as response in each run. The molecular docking study showed hydrogen binding interactions between Asp163, Val101, Thr107 and Glu99of the active site with heterocyclic ring of these compounds. Some ionic and π–π binding interactions were also observed. The validity of docking protocol was completely acquired using Receiver Operating Characteristic (ROC) and enrichment factor (EF). Based on the resulted QSAR model, an in silico-screening study was conducted and new potent lead compounds based on new structural patterns were designed.

Conclusions:

The reliability, accuracy and predictability of the proposed QSAR models were evaluated by various criteria, including cross-validation, the root mean square error of prediction (RMSEP), root mean square error of cross-validation (RMSECV), validation through and Y-randomization. Finally, some compounds were introduced as logical candidates for novel anticancer agents.

Keywords: Cyclin D dependent kinases (CDK4 and CDK6) inhibitors, QSAR, Molecular docking.

Design, synthesis, molecular docking studies and biological evaluation of new N-thiazolidine-2,4-dione derivatives as potential anticancer agents

Seyed Reza Beheshti*, Ahmadreza Bekhradnia, Katayoun Morteza Semnani, Malihe Akhavan

P212

Authors' Affiliations:

Mazandaran University of Medical Sciences, Iran.

Abstract Presenter:
Seyed Reza Beheshti

Correspondance:
Seyed Reza Beheshti

Coauthors:
Ahmadreza Bekhradnia
Katayoun Morteza Semnani
Malihe Akhavan

Introduction:

N-Heterocycles are some of the most important building blocks in organic and medicinal chemistry. Among these 2,4-thiazolidinedione derivatives are important class of nitrogen containing heterocyclic compounds 1 that have absorbed a great interest in medicinal chemistry because of their broad spectrum of biological activities such as antimicrobial, ant obesity, anti-inflammatory, antioxidant, antiproliferative, antitumor activities 2,3. The goal of this investigation was synthesis, molecular docking studies, and then investigating their anticancer activity.

Methods:

The reaction of chloroacetic acid and thiourea derivatives were resulted the desired thiazolidinedione in the presence of hydrochloric acid and in reflux condition. Consequently, the new synthesized thiazolidinedione derivatives were condensed by benzo pyrazine aldehydes and substituted benzyl halides in DMF via multi-component reaction (MCR). All crude resulted products were washed with water and recrystallized in appropriate solvent.

Results:

New synthesized compounds were prepared in high yields and elucidated on the basis of elemental analyses as well as FTIR, Mass and 1H NMR, 13CNMR spectroscopy. The MTT assay of synthesized hybrids showed effective anti-cancer activity against to MCF-7 cell line.

Discussion and Conclusion:

In summary, we have disclosed a clean and efficient procedure for the synthesis of new thiazolidine-2, 4- dione derivatives which were condensed by aromatic aldehydes. All compounds were screened against MCF-7 and HTC-116 cell lines using MTT assay method

Keywords: Thiazolidine-2, 4- dione, Anticancer activity, MTT assay, multi-component reaction (MCR)

Synthesis, docking and acetylcholinesterase inhibitory evaluation of 2-(2-(4-(2-phenylacetyl) piperazin-1-yl) ethyl)-1H-benzo[de]isoquinoline-1,3(2H)-dione derivatives as potential anti-alzheimer agents

Hossein Malekshahi, Seyedeh Rana Mousavi, Ahmad Mohammadi-Farani, Alireza Aliabadi*

P213

Authors' Affiliations:
Students Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Hossein Malekshahi

****Correspondance:***
Alireza Aliabadi

Coauthors:
Seyedeh Rana Mousavi
Ahmad Mohammadi-Farani

Introduction:

Alzheimer's disease (AD) is a neurodegenerative disorder in elderly patients. Decrease in cholinergic neurotransmission is the main known cause in the pathophysiology of the disease. Improvement and potentiation of the cholinergic system could be beneficial for treatment of the AD. Acetylcholinesterase inhibitors such as donepezil can enhance the duration of action of acetylcholine (Ach) and therefore, through this mechanism improve the symptoms of AD.

Methods:

According to the various biological activities of naphthalimides, we decided to design and synthesize a new series of anticholinesterase agents containing naphthalimide substructure. According to the scheme 1, intended derivatives were synthesized via condensation of aminoethylpiperazine and naphthalene-1,8-dicarboxylic anhydride. Then, various phenylacetic acid derivatives were utilized to prepare the final compounds 4a-4o. Acetylcholinesterase inhibitory potency of the synthesized compounds was tested by Ellman's protocol. Moreover, molecular docking was also performed for seeking the likely binding mode and interactions.

Results:

All synthesized derivatives obtained with a moderate yields. Spectroscopic data such as 1HNMR, IR and MS were applied to characterize the final compounds. The tested derivatives demonstrated potent inhibitory activity towards AChE compared to donepezil. Interestingly, some of the tested compounds demonstrated remarkable inhibitory potency towards AChE. Compound 4i with para substitution of the chlorine moiety was the most active derivative (IC50 = 0.11±0.02) in this series compared to donepezil (IC50 = 0.14±0.02) as reference drug. Molecular docking also confirmed the obtained data.

Discussion and Conclusion:

The naphthalimide derivatives synthesized in the current project could be proposed as potential lead compounds for inhibition of AChE.

Keywords: Naphthalimide, Acetylcholinesterase, Alzheimer

Synthesis of bio Nano hydrogel based on Arabic gum and magnetic Ni-Fe bimetals nanoparticles coated with silica gel and its swelling ratio and drug delivery

Sajjad Partovi*, Milad Khojaste Mehr, Mohmmad Mehrshaad, Behrooz Maleki, Hashem Akhlaghi, Mahnaaz Ghezi, Elham Bahman

P214

Authors' Affiliations:
Islamic Azad University, Sabzevar Branch, Iran.

Abstract Presenter:
Sajjad Partovi

****Correspondance:***
Sajjad Partovi

Coauthors:
Milad Khojaste Mehr
Mohmmad Mehrshaad
Behrooz Maleki
Hashem Akhlaghi
Mahnaaz Ghezi
Elham Bahman

Abstract:

In this study a novel bio-nanohydrogel with magnetic properties was prepared that it can be used in drug delivery. To reach this goal natural polymer Arabic gum was selected as base hydrogel and for possessing magnetic properties, magnetic nanoparticles were combined with this hydrogel. To gain this goal, multistage synthesis was designed. Sol-gel method was used for preparation of magnetic nanoparticles. Then the surface of the prepared nanoparticles was covered by silica and in the next stage vinyl groups were deposited on the nanoparticles to be ready to attach to Arabic gum. Arabic gum bio-polymer also underwent modifications and hydroxyl groups were replaced with vinyl ending groups. Finally, a reaction was carried out in which, in the presence of suitable initiator and cross-linker, gum Arabic was attached to the magnetic nanoparticles. At any synthesis steps, the product was identified by infrared spectroscopy analysis. The morphology of the magnetic nanoparticles and the final product was evaluated by scanning electron microscopy with field emission SEM.

keywords: Nano hydrogel, Arabic gum, magnetic Ni-Fe bimetals, nanoparticles

Design, Synthesis, Cytotoxicity and In-Vitro DNA Interaction of Bis-Azolyl-Thio-Alkanes

Mahtab Karbasian*, Sara Rasoul-Amini

P215

Authors' Affiliations:
Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences

Abstract Presenter:
Mahtab Karbasian

Correspondance:
Mahtab Karbasian

Coauthors:
Sara Rasoul-Amini

Abstract:

In order to find out novel lead compound as efficient candidate for anticancer agents, several cytotoxic azolyl-alkyl-quinolines I and quinolones II were designed (1) and evaluated through computational studies for their potential of DNA interaction (2,3) and MTT assay for their cell toxicity (3,4).

The computational results confirmed that the designed structures have the capability of DNA interacting via intercalation, minor groove binding, and also the capability of considerable cytotoxicity comparing to control drugs (doxorubicin and mitoxantrone). Some of the previously reported structures were evaluated for them in-vitro DNA interaction using spectrophotometric techniques (ultraviolet and fluorescence).

Following the previous studies, novel bis-azolyl-thio-alkanes III were designed based on insertion of bio/isosteric groups as flat aromatic groups in two terminal portions of the structure and thio-alkyl (-S-(CH2) n-) as linker providing optimum length between aromatic portions.

In the present study, six recently reported 5a, b bis-azole III (azole: benzothiazole, methyl-thiadiazole; n=4-6) were evaluated for their cytotoxicity against MCF7 as breast cancer cell, HepG2 as hepatocyte cancer cell line, and HEK293 as normal cell line comparing to the two control drugs using MTT assay. The compounds III were also assessed for their potential of in-vitro DNA interaction against ct-DNA (42%GC) using spectroscopic techniques (ultraviolet and fluorescence) in titrimetric experiment.

The MTT experiments illustrated considerable potency of the test compounds (in the concentration range of 10.3 – 10.7 mM) against the two cancer cell lines showing less cytotoxicity on the normal cell line comparing to the reference drugs (in the concentration range of 3×10-7 -3×10-9 M). The in-vitro DNA interaction studies confirmed the potential of DNA interaction through stepwise changes in spectroscopic pattern.

The obtained results encourage us to continue in-vitro experiments on the designed derivatives to find out structure activity relationship to introduce the efficient lead cytotoxic structure.

Keywords: azole, cytotoxicity, DNA, MTT, spectrophotometric

N1-(isoquinolin-5-yl)-N2- phenylpyrrolidine-1, 2-dicarboxamide derivatives as TRPV1 antagonists: 2D-QSAR & 3D-QSAR and molecular docking studies

Sina Hoseinizare*, Maryam Motehayer, Masood Freidoonnezhad

P216

Authors' Affiliations:
Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract Presenter:
Sina Hoseinizare

****Correspondance:***
Sina Hoseinizare

Coauthors:
Maryam Motehayer
Masood Freidoonnezhad

Introduction:

Transient receptor potential vanilloid 1 (TRPV1) is an ion channel expressed on sensory neurons triggering an influx of cations, which is selectively activated by a wide range of exogenous & endogenous stimuli ligands. Activation of this channel is associated to chronic inflammatory pain and peripheral neuropathy. Therefore, inhibitingTRPV1 function represents a strategy for the treatment of a variety of disease states, particularly in the management of chronic intractable pain. Recently, N1-(isoquinolin-5-yl)-N2- phenylpyrrolidine-1, 2-dicarboxamide derivatives were introduced as novel analgesic agents.

Methods:

GRIND-based 3D-QSAR models were conducted using Pentacle software. A collection of 2D chemometrics methods such as multiple linear regression (MLR), principal component regression (PCR), and genetic algorithm-PLS (GA-PLS) were applied on this compounds. The initial conformations of the TRPV1 were taken from PDB ID: 5IS0. The Molecular docking simulations were carried out using Auto Dock 4.2 and Vina. Protein ligand interactions fingerprints (PLIF) studies were done using preAuposSOM, AuposSOM 2.1 web server and Dendroscope 3.2.10.

Results:

The best multiple linear regression equation was obtained from GA-PLS which predicts 89% of variances. Autodock results were visually evaluated, and the top ranked binding energies (kcal/mol) in AutoDockdlg output file were considered as response in each run. The molecular docking study revealed that the important amino acids inside the active site of the cavity that are responsible for essential interactions were Tyr511, Met547 and Ile573. In addition, the pyrolidine group was forming primary hydrophobic interactions with the residue Ile569. The ALMOND procedure of 3D-QSAR model correctly predicted the activity of the studied compounds and graphically showed the best structurally requirement for TRPV1 antagonists.

Discussion and Conclusion:

The PLIF method makes it possible to study the effect of different starting states of the structures on generated poses as well as their corresponding vector of contacts towards TRPV1. Based on the resulted QSAR model and PLIF studies an in silico-screening study was also conducted and new potent lead compounds based on new structural patterns were designed that can inhibit TRPV1 function represents a strategy for the treatment of chronic intractable pain.

Keywords: 3D QSAR, Transient receptor potential vanilloid type 1.

Design, docking study and synthesis of para-substituted 1,2,4-oxadiazole derivatives as cholinesterase inhibitors

Maryam Nazari*, Sayyed Abbas Tabatabai

P217

Authors' Affiliations:
School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Maryam Nazari

Correspondance:
Maryam Nazari

Coauthors:
Sayyed Abbas Tabatabai

Introduction:

Alzheimer's disease (AD) is a degenerative disorder of the nervous system caused by decrease in cholinergic neurotransmitters such as acetylcholine (ACh). Cholinesterase inhibitors can increase both the level and duration of action of ACh by inactivation of cholinesterase enzyme. Among FDA approved medicines Donepezil still plays an important role in the treatment of AD for several reasons which are recited: fewer side effects than other anti-AD drugs, absence of dose-dependent hepatotoxicity, longer half-life (70-80h) and 100% oral relative bioavailability. According to our endeavors to develop new AChE inhibitors we designed and synthesized novel donepezil-like compounds which had benzyl piperidine fragment as same as donepezil and a ring of 1,2,4-oxadiazole in the place of indanone moiety of donepezil.

Method:

Ethyl-4-piperidine carboxylate was N-alkylated with benzyl bromide to obtain yellow oil and the various amidoximes were prepared from the reaction of proper benzonitriles with hydroxylammonium chloride in alkaline media. The final products were afforded by the treatment of yellow oil with synthesized amidoximes in the presence of sodium ethoxide under reflux in dry Ethanol.

Result:

In this research, some novel compounds bearing benzyl piperidine and well known 1,2,4-oxadiazole ring were designed. Docking studies showed these compounds fitted properly in the active site of cholinesterase enzyme with favorable affinities which were comparable with donepezil as standard compound. These structures were synthesized with acceptable yield and structurally elucidated by IR, NMR and Mass spectra.

Conclusion:

Based on the structure activity relationship (SAR) of the cholinesterase inhibitors, para-substituted 1,2,4-oxadiazole derivatives as novel cholinesterase inhibitors were designed, synthesized and approved by IR, NMR and Mass spectra.

Keywords: Alzheimer's disease. Cholinesterase inhibitor. 1,2,4-oxadiazole. Synthesis.

Design and synthesis of novel chromonenone-3-arylisoxazole-5-carboxamides as cholinesterase inhibitors

Arezoo Rastegari*, Mina Saeedi, Roshanak Hariri, Tahmineh Akbarzadeh

P218

Authors' Affiliations:
Department of Medicinal Chemistry, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Arezoo Rastegari

****Correspondance:***
Arezoo Rastegari

Coauthors:
Mina Saeedi
Roshanak Hariri
Tahmineh Akbarzadeh

Introduction:

Alzheimer's disease (AD) is a progressive and erosive neurodegenerative disorder [1]. Various factors are responsible for the development of AD. One of the most important reasons is the reduction of cholinergic activity at certain points of the brain [2]. Therefore, the most rational method for the treatment of AD is the increase of the level of acetylcholine (ACh) in the brain by blocking the AChE which is responsible for the hydrolysis of ACh. Herein, we designed and synthesized novel chromenone-isoxazole hybrids as cholinesterase (ChE) inhibitors.

Methods:

Required starting materials were obtained by the reaction of various derivatives of acetophenone and diethyl-oxalate. Reaction of the latter compounds and hydroxylamine hydrochloride, produced ethyl 5-aryl isoxazole-3-carboxylate derivatives. Hydrolysis of these compounds using KOH in methanol led to the formation of the corresponding acid. On the other hand, the reaction of 7-hydroxy-coumarine and 1-fluoro-4-nitrobenzene in a basic condition afforded related compound which tolerated reduction using NH4Cl and Zn to obtain the corresponding amine. Reaction of acid derivatives and synthesized amine in the presence of EDCI and HOBt in dry acetonitrile afforded final products. All compounds were evaluated for their in vitro AChEI and BChEI inhibitory activity based on modified Ellman's method [3]. Also, the most potent derivative was evaluated for its BACE1 inhibitory as well as metal chelating ability.

Results:

Among all synthesized compounds, 5-(3-nitrofenyl)-N-(4-((2-oxo-2-chromosome-7-yl) oxy) phenyl) isoxazole-3-carboxamide (A) showed the most AChEI activity (IC50 = 1.23 µM). It also showed moderate inhibition toward BACE1 (48.46 % at concentration of 50 µM) and good metal chelating ability toward Fe2+, Cu2+, and Zn2+ ions.

Conclusion:

In conclusion, most of synthesized compounds showed good AChEI activity and the best AChEI activity was distinguished by compound A (IC50=1.23 µM). Furthermore, 5-(3-chloro-phenyl)-N- (4-((2-oxo-2-H-chromen-7-yl) oxy) phenyl) isoxazole-3-carboxamide (B) depicted the best BChEI activity (IC50 = 9.71 µM). Comparing our results with those reported in the literature associated with hybridization of isoxazole and chromenone moieties confirmed the necessity of the presence of carboxamide moiety as well as the arrangement of isoxazole and coumarin scaffolds to obtain desired biological activity [4,5].

Keywords: Alzheimer's disease, Beta secretase (BACE1), Cholinesterase, Chromenone, Isoxazole

Design, Synthesis and docking study of novel 1,3- benzdiazinane- 4- one derivatives as anti-HIV-1 agents

Nassim Faraji Jalali*, Tannaz Zebardast, Zahra Hajimahdi , Afshin Zarghi

P219

Authors' Affiliations:
Department of Pharmaceutical Chemistry, Faculty of Pharmacetical Chemistry, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Abstract Presenter:
Nassim Faraji Jalali

****Correspondance:***
Nassim Faraji Jalali

Coauthors:
Tannaz Zebardast
Zahra Hajimahdi
Afshin Zarghi

Introduction:

The causative agent of AIDS as a deadly disease is the human immunodeficiency virus type 1 (HIV-1). Drugs used against the virus have limitations such as high costs, side effects, and more importantly, drug resistance. For this reason, achieving newer compounds with different structures is essential in the treatment of AIDS. Since the integrase enzyme is an essential enzyme for replication of virus, it is nowadays taken into consideration for anti-HIV drug discovery. In this study, various 1,3- benzdiazinane- 4- one derivatives were designed based on HIV-1 integrase inhibitors pharmacophores.

Material and Methods:

Target compounds were prepared by one-pot multicomponent reaction. The isatoic anhydride and 2-aminobenzimidazole were reacted in toluene in the presence of KAl(SO4)2.12H2O (alum) as catalyst under reflux condition for 4 hours, and then the methyl benzaldehyde derivatives were added to the reaction contents and after 50 hours the resulting products were obtained. A molecular modeling study using the later crystallographic data available for PFV (prototype foamy virus) integrase was also performed to explain the probable mechanism of action of synthesized compounds.

Results:

Target compounds were synthesized and purified using different crystallization and chromatography methods. The structure of the synthesized compounds was confirmed by IR, LC-MS (ESI), and 1H-NMR. Docking study revealed that the compounds were well placed in the active site of the enzyme and connected through the nitrogen and carbonyl groups to the magnesium ions, and through the tolyl group to the hydrophobic pocket in the active site. In addition, the binding mode of designed compounds is similar to those of the integrase enzyme inhibitors such as Raltegravir.

Conclusion:

We designed and synthesized novel 1,3- benzdiazinane- 4- one derivatives based on HIV-1 integrase inhibitors pharmacophores. Structure of synthesized compounds was confirmed by IR, LC-MS (ESI), and 1H-NMR. Docking study showed that the anti-HIV activity of these compounds might involve a metal chelating mechanism. The anti-HIV activity of novel compounds is under investigation.

Keywords: Docking study, Synthesis, 1,3- Benzdiazinane- 4- one, Integrase, Anti-HIV

Design, molecular modeling and synthesis of the phenyliminothiazolidinone derivative as HIV-1 integrase inhibitors

Haniyeh Bahrambeigi*, Mahboubi Rabbani, Zahra Hajimahdi, Afshin Zarghi

P220

Authors' Affiliations:
Shahid Beheshti University of Medical Science, Tehran, Iran.

Abstract Presenter:
Haniyeh Bahrambeigi

****Correspondance:***
Haniyeh Bahrambeigi

Coauthors:
Mahboubi Rabbani
Zahra Hajimahdi
Afshin Zarghi

Introduction:

In 2017, 940000 people died from HIV-1 related globally. Nowadays, there are effective anti-HIV-1 drug therapy regimens but the necessity of developing newer agents to combat with this infective germ is growing, because of drug - resistance issue. One of the most important key - enzymes of HIV-1 virion is HIV-1 integrase enzyme (IN). Inhibition of this enzyme could stop the life cycle of the virus because HIV-1 integrase mediates the linkage of viral DNA to host DNA in the infected cell which is a critical step in the process of viral DNA replication and so the virus proliferation. Integrase has two metal ions and a chelating motif can bind to it by using a coordinate covalent bond; when this occurs, the enzyme function is blocked.

Methods:

To synthesize these new phenyliminothiazolidinone analogs, phenyl isothiocyanate was reacted with aniline in dried THF as the solvent. Then, diphenylthiourea intermediate was reacted with ethyl chloroacetate in absolute ethanol in the presence of anhydrous sodium acetate as the catalyst to thiazolidinone intermediate. After all, the final products were synthesized by the reaction of the thiazolidinone intermediate with different aromatic aldehydes.

Results:

Target compounds were synthesized and purified using different crystallization and chromatography methods. The structure of the synthesized compounds was confirmed by IR, LC-MS (ESI), and 1H-NMR. A molecular modeling study using the later crystallographic data available for PFV (prototype foamy virus) integrase was performed to explain the probable mechanism of action of synthesized compounds. The docking scores showed that the designed molecules have an acceptable binding affinity.

Discussion and conclusion:

In this study, we designed and synthesized a novel series of phenyliminothiazolidinone derivatives as new HIV-1 integrase inhibitors based on our knowledge about HIV-1 Integrase Inhibitors' SAR. According to this knowledge, thiazolidinone derivatives could play as the chelating motif. Addition of arylidene group, may potentiate the anti-HIV-1 effects through an auxiliary attachment. The anti-HIV-1 effects assay is under evaluation.

Keywords: Synthesis, anti-HIV-1 activity, Phenyliminothiazolidinones, Docking

Design, synthesis and molecular modeling studies of novel 3-benzimidazolyl-2,3-dihydroquinazoline-4-one derivatives as anti-HIV-1 agents

Fateme Karimi*, Tannaz Zebardast, Zahra Hajimahdi, Afshin Zarghi

P221

Authors' Affiliations:
Department of pharmaceutical Chemistry, Faculty of pharmaceutical chemistry, Tehran Medical Sciences, Islamic azad University, Tehran, Iran

Abstract Presenter:
Fateme Karimi

****Correspondance:***
Fateme Karimi

Coauthors:
Tannaz Zebardast
Zahra Hajimahdi
Afshin Zarghi

Introduction:

Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS) as a fatal disease requiring serious cure. Antiretroviral therapy has limitations such as high cost, side effect, and more importantly pharmacological resistance. So there is a demand for novel drugs from alternative scaffolds. HIV-1 integrase is an essential enzyme which catalyzes the insertion of viral DNA into the host cellular DNA. In this study, novel derivatives of 3-benzimidazolyl-2,3-dihydroquinazoline-4-one scaffold were designed regarding HIV-1 integrase inhibitors pharmacophores.

Material and Methods:

Final products were synthesized by one-pot multicomponent reaction. The isatoic anhydride and 2-aminobenzimidazole were refluxed in toluene in the presence of KAl(SO4)2.12H2O (alum) as catalyst for 4 hours, and then the methoxybenzaldehyde derivatives were added to the reaction contents. The reaction was continued till 50 hours, and the resulting products were obtained using crystallization and chromatography methods. A docking study using the later crystallographic data available for PFV (prototype foamy virus) integrase was also performed to explain the probable mechanism of action of target compounds.

Results:

Target compounds were designed and synthesized using pharmacophore groups of HIV-1 integrase. The structure of the synthesized compounds was confirmed by IR, LC-MS (ESI), and 1H-NMR. Docking study showed that the compounds were well placed in the active site of the enzyme and connected through the nitrogen and carbonyl groups to the magnesium ions, and through the methoxyphenyl group to the hydrophobic pocket in the active site. In addition, the binding mode of designed compounds is similar to those of the integrase enzyme inhibitors such as Raltegravir.

Conclusion:

Novel 3-benzimidazolyl-2,3-dihydroquinazoline-4-one derivatives were designed and synthesized, and structure of synthesized compounds was confirmed by IR, LC-MS (ESI), and 1H-NMR. Molecular modeling study displayed that the anti-HIV activity of these compounds might involve a metal chelating mechanism. The anti-HIV activity of novel compounds is under investigation.

Keywords: Molecular modeling study, Synthesis, 3-benzimidazolyl-2,3-dihydroquinazoline-4-one, Integrase, Anti-HIV

Study of removal of some drug compounds from serum samples using silica modified mesoporous as adsorbent

Haniyeh Ranjkesh Zade, Mohammad Reza Vardast

P222

Authors' Affiliations:
Department of Medicinal Chemistry, School of pharmacy, Urmia University of Medical Sciences, Urmia, Iran

Abstract Presenter:
Haniye Ranjkeshzadeh

****Correspondance:***
Mohammad Reza Vardast

Introduction:

In this study, the mesoporous silica structure was used to remove some drug compounds. Mesoporous materials have cavities with diameters between 2 and 50 nanometers. SBA-15, a new nanoporous with hexagonal structure, high pore size and thermal stability, has opened a promising new window towards solid acids. So far, the SBA-15 has been used as a carrier of natural and synthetic drugs, and the merger of acid groups into SBA-15 pores has recently been investigated. The combination of graphene oxide (GO) with SBA-15 has been used as a modified mesoporous silica adsorbent. Graphene oxide is a two-dimensional, monolayer, hexagonal and crystalline structure, with oxygen groups on its plates. Graphene oxide has the ability to interact better with materials, which allows the covalent bonding of plates Link to polymers or other materials.

Methods and Results:

The hexagonal mesoporous operating agent SBA-15 with a size of 60-70 angstroms cavities was synthesized using a silicon-based silicon TEOS active surface-active plunger P123 surface material at low concentration and in the shortest possible time. GO and SBA-15 were combined to achieve a modified mesoporous silica adsorbent. The size, morphology, composition and properties of the nanocomposite were studied by Scanning electron microscopes (SEM), Fourier transform infrared spectroscopy (FT-IR), X-Ray Diffraction (XRD). The drugs used for this absorbent include Amiodarone and Diltiazem. Which was finally measured using a liquid chromatography apparatus. Blood plasma samples used for examining the applicability of the proposed method showed an excellent rate of drug absorbance from our samples.

Conclusions:

SBA-15 nano silicate adsorbent modified with Graphene oxide due to its extensive surface and efficient absorbent functional groups can be used to remove some of the drugs from human serum samples.

Keywords: SBA-15, Graphene oxide, Liquid chromatography, Drug.

Structure activity relationship of Pseudomonas exotoxin A, a new medical approach for cancer therapy

Zeinab Amiri Tehranizadeh, Mohammad-Reza Saberi

P223

Authors' Affiliations:
Department of Medicinal Chemistry, School of Pharmacy, Mashhad University of Medical Sciences, Iran

Abstract Presenter:
Zeinab Amiri Tehranizadeh

****Correspondance:***
Mohammad-Reza Saberi

Abstract:

Recombinant immunotoxins are a class of medicines which consist of an antibody or itsfused fragments to a toxic moiety. The most famous toxic moieties are based on Pseudomonas exotoxin A (PE), Diphtheria toxin (DT) and ricin. Denileukindiftitox is the first immunotoxin which was initially approved in US in 1999 and targets interleukin 2 (IL2) receptors and redirects its cytotoxic effects by part of DT. Truncated PE has shown a significant decrease in tumor sizes in vitro. However, one of the major obstacles of immunotoxins in cancer therapy is immunogenicity and size of the toxic moiety. In this study, we tried to solve the mentioned problems by reducing the size of PE toxin and introducingseven-point mutations to reduce the immunogenicity of the immunotoxins. For this purpose, we took advantage of protein 3D structure modeling of immunotoxins targeting HER2 receptors by Modeler 9.2. Final constructs were refined and evaluated. The accepted structures were introduced to Gromacs software. Stability analysis of the constructs wasreported as RMSD. Residual fluctuations were surveyed during the time of simulation by principle component analysis (PCA). Introduction of B-cell epitope mutations (R505A, R427A, R490A, R467A, D463A, R538A and R456A) were analyzed structurally. The interaction of the truncated toxin with their native ligand (NAD) was reported by docking and MD simulations. Finally, the best structures based on stability and maximum catalytic activity were selected for further studies.

Keywords: Immunotoxin, Pseudomonas exotoxin A, Cancer, SAR, Gromacs, targeting

Homology modeling molecular dynamics simulation and docking studies of formyl peptide receptor like 1a potential target against Alzheimer's disease

Hamid Nadri*, Amirhossein Sakhteman, Alireza Moradi, Bahar Pakseresht

P224

Authors' Affiliations:
Department of medicinal chemistry, faculty of pharmacy and pharmaceutical sciences research center, shahid sadoughi university of medical sciences, Yazd, Iran

Abstract Presenter:
Hamid Nadri

***Correspondance:**
Hamid Nadri

Coauthors:
Amirhossein Sakhteman
Alireza Moradi
Bahar Pakseresht

Introduction:

FPRL-1 is a class A of GPCR receptors. 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.

Methods:

With the aid of templates retrieved from I-TASSER server, we were able to perform homological 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_α 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.

Conclusion:

The best model built by modeler 9v12. ROC value of this receptor was 0.9 which indicated the high quality of the best model. As retrieved by the results of this study, the best frame extracted was frame 169. This study can lead to further studies regarding the design of novel antagonists to treat Alzheimer's Disease.

Keywords: FPRL-1, Alzheimer's Disease, Docking studies, Molecular Dynamics Simulation

Synthesis of cyanodihydropyrone derivatives from resorcinol and evalution of their antiplatelet aggregation activity

Mahvand Oraji, Salimeh Amidi, Marjan Esfahanizadeh, Farzad Kobarfard*

P225

Authors' Affiliations:
shahid Beheshti university of medical science

Abstract Presenter:
Mahvand Oraji

Correspondance:
Farzad Kobarfard

Coauthors:
Salimeh Amidi
Marjan Esfahanizadeh

Introduction:

Patients with Cardiovascular disease have an increased risk of mortality and functional limitation. In recent years, antiplatelet therapy for prevention of cardiovascular disease has been a routin protocol. However, the present antiplatelet drugs in clinic suffer from same side effects and same patients are refractive to their effects. Therefore, new antiplatelet agents are in demand. Studies on phenolic compounds such as resveratrol and nitril derivatives have revealed the antiplatelet activity of these functional groups. Therefore, the synthesis of cyanodihydropyrone derivatives of resorcinol was selected as the main objective of the present study (1, 2).

Methods:

Resorcinol, malononitrile, and various substituted aromatic aldehydes in presense of piperidine and ethanol were heated under refluxed for 4-6hr. In vitro antiplatelet activity of the prepared compounds was evaluated using arachidonic acid (AA) and adenosine diphosphate (ADP) as platelet aggregation inducers.

Results:

The structure of the obtained derivatives were characterized by IR, 1HNMR, and ESI-MS. All the reactions gave high yields. Antiplatelet activity of the prepared compounds was evaluated according to born method.

Discussion and Conclusion:

All derivatives showed better activity against the aggregation induced by arachidonic acid than the aggregation induced by ADP. Those compounds which showed (>90%) inhibition were selected for IC50 determination and compounds with higher water solubility showed lower IC50 values.

Keywords: Antiplatelet activity, Cyanodihydropyrone, Phenolic compounds, Arachidonic acid

Pharmacophore-Based Virtual Screening: An Efficient Rational Approaches to Discovery of New Tubulin Inhibitors

Elmira Amini, Shohreh Mohebbi, Massoud Amanlou, Hafezeh Salehabadi*

P226

Authors' Affiliations:
Department of Medicinal Chemistry, School of Pharmacy, Zanjan University of Medical Sciences, Zanjan, Iran

Abstract Presenter:
Elmira Amini

****Correspondance:***
Hafezeh Salehabadi

Coauthors:
Shohreh Mohebbi
Massoud Amanlou

Introduction:

Microtubules (MTs) are protein biopolymers that formed in cylindrical structures by polymerization of α/β tubulin heterodimers (1). MTs are essential players in many cellular processes, including maintenance of cell shape, intracellular transport, mitosis, cell signaling, and cytokinesis. Polymerization of MTs is a key step in G2-M phase in cell cycle. Cell division can be prevented by disturbing the tubulin system dynamics. Therefore, tubulin inhibitors could be considered as potential anticancer agents (2). Computer-aided drug design (CADD) as a systematic and economical tool is proven to have a high potential to identify new lead compounds especially with the aim of challenging drug targets (3). Molecular docking is a computationally inexpensive approaches that can predict the orientation of ligand in protein binding site. Today, docking-based virtual screening on libraries of compounds has been commonly used as a direct and rational drug discovery method. Here we applied pharmacophore-based virtual screening on ZINC database, and docking studies to identify new tubulin inhibitors.

Methods:

The crystal structure of tubulin-colchicine domain, with the PDB ID of 1sa0 was derived from Protein Data Bank (www.rcsb.org). Three pharmacophore models were generated from the tubulin-colchicine complex crystallographic structure (PDB code: 1sa0) using Ligand Scout 3.12. Virtual screening of ZINC database (over 35 million purchasable compounds) has been done and models were assigned individually as filters for screening. Afterwards, collected compounds from ZINC database were followed by docking studies.

Results and Discussion:

The key interactions between the selected ligands from ZINC database and tubulin were meticulously investigated in detail by molecular docking studies. Finally, eight ligands were selected by limiting on the binding free energy to -7 kcal.mol-1 and having an appropriate orientation in active pocket of tubulin.

Conclusion:

In the present study, a structure-based virtual screening of the ZINC database was performed to identify new tubulin inhibitors as anticancer agents. Molecular docking studies identified the binding modes of most active compounds and also indicated that the potency of the compounds could be improved by better positioning of the compounds into the protein pockets. These compounds can be used and optimized for future drug development.

Keywords: Tubulin, Inhibitor, Molecular docking, Pharmacophore model, Virtual screening

Vilazodone-Tacrine hybrids as potential anti alzheimer: QSAR, molecular docking and Molecular Dynamic (MD) simulation studies

Hanieh Abbasi, Zohre Mirveis, Ayyub Mojaddami*

P227

Authors' Affiliations:
Department of Medicinal Chemistry, Student Research Committee, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract Presenter:
Hanieh Abbasi

***Correspondance:**
Ayyub Mojaddami

Coauthors:
Zohre Mirveis
Ayyub Mojaddami

Introduction:

Alzheimer's disease (AD) is a type of functional impairment of the brain, which gradually degrades the mental abilities of the patient. Given the importance of this disease the goal pursued in this study was to inhibacetylcholinesterase (AChE) and butyl cholinesterase (BuChE) receptors in order to obtain new drug candidates for the disease.

Methods and Results:

In this study, more than 60 Vilazodone-Tecrin hybrid species have been designed to inhibitAChE and BuChE. A series of chemical methods such as multiple linear regression (MLR), MLR analysis factor (FA-MLR), the main component regression (PCR) and the least square with genetic algorithm for variable selection (GA-PLS) were used to create relationships between structural features in these compounds and their AChE/ BuChE inhibitory. Docking analysis against hAChE (PDB ID: 1ACJ), hBuChE (PDB ID: 4BDS) was conducted using Autodock 4.2 and Vina. MD simulations were performed using the GROMACS program, utilizing the GROMOS force field 53A5.

The results of Docking show that the most important amino acids in the active site cavity are PheA330, TrpA84 for AChE and Trp82 for BuChE. The best regression equation was obtained from GA-PLS which predicts 90% of variances. MD simulation showed the protein binding mechanism of ligand at molecular and atomic level as well as the equilibrated binding conformation of compounds on both targets.

Conclusions:

The validity and predictability of the molecular docking as well as QSAR were completely evaluated. Based on the results of molecular docking, and the best QSAR model, an in silico-screening study was also conducted and new potent lead compound based on new structural patterns were proposed as a good candidate with potent anti-Alzheimer activity for synthesis.

Keywords: Anti Alzheimer, cholinesterase inhibitors, Molecular Docking, QSAR.

Design and synthesis of novel Integrase Inhibitors from substituted quinoline series and computational study of their interaction with the enzyme

Amineh Sadat Tajani, Farzin Hadizadeh, Mohammadreza Saberi*

P228

Authors' Affiliations:
Mashhad University of Medical Sciences

Abstract Presenter:
Amineh Sadat Tajani

****Correspondance:***
Mohammadreza Saberi

Coauthors:
Farzin Hadizadeh

Introduction:

The human immunodeficiency virus, (HIV) which belongs to Retroviridae family, infects vital immune cells and causes a failure in one of the most important defensive barriers of the immune system that makes the body become more susceptible to opportunistic infections. The prolonged incubation period of the virus and the unawareness of the patient provide the possibility for transmission to others. Early diagnosis and appropriate pharmacotherapy may prevent the progression of the disease and infection. Integrase enzyme inhibitors, as reproduction inhibition agents, are one of the possible pharmacotherapies that have been used in treatment of HIV infection. In this study we aim to design, synthesize and software analyze of new quinoline based compounds (simulation) with integrase inhibition ability.

Materials and Methods:

The synthesis begins with the interaction between four aniline derivatives and acetic anhydride which turns in to four acetanilide components. Then after drying the previous products, 2-chloroquinoline-3-carbaldehyde compounds synthesized through Vilsmeier-Haak Reaction. The structure of these derivatives were analyzed with IR and NMR methods. Subsequently the final products formed by the reaction with ethanolamine to form imine bond following by IR and NMR evaluations. The GOLD docking software was used to evaluate enzyme inhibition activity of the products. Co-crystal enzyme (5ClTEP) was the standard compound in this method

Conclusion:

According to the docking data, comparable inhibition activity of the designed molecules and the co-crystal molecule was observed even though some ligand modification could improve the ligand-protein interaction.

Keywords: human immunodeficiency virus, Integrase inhibitors, quinoline based compounds, the GOLD software, Docking

Synthesis, docking and acetylcholinesterase inhibitory evaluation of phthalimide and naphthalimide derivatives incorporated piperidine and piperazine moieties as potential anti-alzheimer agents

Mina Rajabian, Ahmad Mohammadi-Farani, Alireza Aliabadi*

P229

Authors' Affiliations:
Kermanshah University of Medical Sciences, Kermanshah, Iran.

Abstract Presenter:
Mina Rajabian

****Correspondance:***
Alireza Aliabadi

Coauthors:
Ahmad Mohammadi-Farani

Introduction:

Alzheimer's disease (AD) is a neurodegenerative disorder in elderly patients. Decrease in cholinergic neurotransmission is the main known cause in the pathophysiology of the disease. Improvement and potentiation of the cholinergic system could be beneficial for treatment of the AD. Acetylcholinesterase inhibitors such as donepezil can enhance the duration of action of acetylcholine (Ach) and therefore, through this mechanism improve the symptoms of AD.

Methods:

According to the various biological activities of phthalimide and naphthalimide derivatives, we decided to design and synthesize a new series of anticholinesterase agents containing phthalimide and naphthalimide based substructure. According to the following schemes, intended derivatives were synthesized via an aldol condensation reaction. Then, acetylcholinesterase inhibitory potency of the synthesized compounds was tested by Ellman's protocol. Moreover, molecular docking was also performed for seeking the likely binding mode and interactions.

Results:

Synthesized compounds were characterized by spectroscopic methods and their binding mode were observed in silico. Some of the synthesized derivatives show better acetylcholinesterase activity compared to donepezil. Compound H2 (naphthalimide based) exhibited the highest inhibitory potency (IC50=0.83µM) compared to donepezil. Furthermore, docking study confirmed same binding mode as donepezil for all of the synthesized compound.

Discussion and Conclusion:

Phthalimide and naphthalimide derivatives demonstrated outstanding acetylcholinesterase inhibitory activity. In conclusion, the synthesized compounds could be suggested as new anti-acetylcholinesterase lead compounds. More experimental investigations are needed to prove this statement in the future.

Keywords: Synthesis, Phthalimide, Acetylcholinesterase, Alzheimer

Synthesis, docking and acetylcholinesterase inhibitory evaluation of benzamide derivatives with probable anti-alzheimer effects

Negin Tamasoki, Ahmad Mohammadi-Farani, Alireza Aliabadi*

P230

Authors' Affiliations:
Kermanshah University of Medical Sciences, Kermanshah, Iran.

Abstract Presenter:
Negin Tamasoki

****Correspondance:***
Alireza Aliabadi

Coauthors:
Ahmad Mohammadi-Farani

Abstract:

Alzheimer's disease (AD) is a common neurodegenerative disorder in geriatric patients. Attenuation of the cholinergic neurotransmission has been known as the main reason in the etiology of the disease. Potentiation of the cholinergic system could be an effective therapeutic strategy of the AD. Inhibitors of the Acetylcholinesterase such as donepezil and galantamine can enhance the duration of action of acetylcholine (Ach). So, through this mechanism symptoms of AD will be improved. According to the positive background of the benzamide derivatives as acetylcholinesterase inhibitors, we have decided to design and synthesize a new series of anticholinesterase agents. According to the scheme 1, intended derivatives were synthesized. Then, acetylcholinesterase inhibitory potency of the synthesized compounds was tested by Ellman's protocol. Moreover, in silico inhibition was also explored using molecular docking by ArgusLab software for seeking the likely binding modes and interactions.

Keywords: Benzamide, Synthesis, Acetylcholinesterase, Alzheimer

Synthesis and cytotoxicity evaluation of 2-(4-((1,3-Dioxoisoindolin-2-yl) methyl) phenyl)-N-phenylthiazole-4-carboxamide derivatives as apoptosis inducers with potential anticancer effects

Ghazal Mahmoudi, Leila Hoseinzade, Alireza Aliabadi*

P231

Authors' Affiliations:
Kermanshah University of Medical Sciences

Abstract Presenter:
Ghazal Mahmoudi

****Correspondance:***
Alireza Aliabadi

Coauthors:
Leila Hoseinzade

Introduction:

Cancer is a group of diseases in which cells can be aggressive, invasive and/or metastatic. These three malignant properties of cancer differentiate them from benign tumors, which are self-limited in their growth and do not invade or metastasize. Despite advances in diagnosis and treatment, overall survival of patients still remains poor and discovery of new anticancer agents feel deeply needed.

Materials & Methods:

Chemistry: According to the scheme 1, synthesis of phenylthiazole derivatives bearing phthalimide moiety was done. The aniline derivatives were reacted with obtained acidic compound 5 to achieve final derivatives 6a-6m.

MTT assay: Cytotoxicity of synthesized compounds was evaluated against cancer cell line (PC3, HT-29, SKNMC) in vitro using MTT assay and structure activity relationships were defined. Activation of caspase 3 was also explored.

Results & Discussion:

All synthesized compounds were characterized by spectroscopic methods. Remarkable cytotoxic activity as well as caspase activation was observed. The reference drug exhibited on IC50 2.1µM whereas para nitro which was identified as the most active compound, exhibited an IC50 value of 1.2µM on three cell lines.

Conclusion:

Phenylthiazole derivatives demonstrated outstanding cytotoxic activity. Besides, tested compounds showed a potent caspase 3 activation and apoptosis induction.

Keywords: Cytotoxicity, Anticancer, Synthesis, Phenylthiazole, Naphthalimide

Synthesis, docking and acetylcholinesterase inhibitory evaluation of N-(2-(Piperidin-1-yl) ethyl) benzamide derivatives as potential anti-alzheimer agents

Farzaneh Moradi, Ahmad Mohammadi-Farani, Alireza Aliabadi*

P232

Authors' Affiliations:
Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Farzaneh Moradi

****Correspondance:***
Alireza Aliabadi

Coauthors:
Ahmad Mohammadi-Farani

Abstract:

Alzheimer disease (AD) an age-related neurodegenerative disorder is a common form of dementia [1]. Based on the cholinergic hypothesis potentiation of the cholinergic system can attenuate and improve the symptoms especially cognitive decline [2]. Acetylcholinesterase (AChE) inhibitors potentiate of the cholinergic system by increasing the half-life of the acetylcholine in synaptic cleft fortify the cholinergic neurotransmission [3]. In the current project, a new series of benzamide derivatives 4a-4l (scheme 1) bearing piperidinyl moiety were designed regarding

Pharmacophore. Then, the synthesis of the related derivatives was carried out and corresponding anti-acetylcholinesterase activity was evaluated. Moreover, in silico investigation of the most potent compound was also explored using ArgusLab software. Interestingly, some of the tested compounds demonstrated remarkable inhibitory potency towards AChE. Further experiments as well as in vivo investigation of potent compounds can be performed as potential lead compounds to develop new anti-Alzheimer agents.

Keywords: Synthesis, acetyl cholinesterase, benzamide, Alzheimer

Design, Synthesis, Radiolabeling and Biological evaluation of 99mTc-HYNIC-GPRPILE and 99mTc-HYNIC-GPLGAAD Peptides as fibrin imaging agent

Sara Hadadi, Sara Sheybani, Sedigheh Rezaeianpour, Soraya Shahhosseini*

P233

Authors' Affiliations:
Pharmaceutical Chemistry and Radiopharmacy Department, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Sara Hadadi

****Correspondance:***
Soraya Shahhosseini

Coauthors:
Sara Sheybani
Sedigheh Rezaeianpour

Introduction:

Today, Thrombosis is a serious risk factor for both thromboembolic diseases (such as DVT, PE) and cancer. Fibrin is a major constituent of clots and is present in all types of thrombi, but absent in circulation. Fibrin is a highly sensitive and specific target for molecular imaging of thrombi. In the present study, we have developed two linear fibrin-binding peptides for thrombus imaging. Peptides were synthesized, radiolabeled with 99m-Tc and their stability in normal saline and human plasma, LogPand their affinity to fibrin and bio distribution in Balb/c mice were determined.

Methods:

HYNIC-Gly-Pro-Arg-Pro-ILe-Leu-Glu and HYNIC-Gly-Pro-Lys-Gly-Ala-Ala-Asp peptides were synthesized using a standard Fmoc strategy and radiolabeled with 99m-Tc. The stability of the radiolabeled peptides in human plasma and normal saline as well as partition coefficient (LogP) were determined. The affinity of radiopeptides were determined in saturation binding assays. The bio distribution of radiopeptides were determined in normal Balb/c mice.

Results:

HYNIC-GPRPILE calculated for C41H65N13O11: 915.5; found m/z = 916.5 [M + H] +. Analytical RP-HPLC: Rt = 10min; 85 % A, 15 % B., LogP=-1.83±0.31. HYNIC- GPLGAAD calculated forC31H47N11O11:749.3; found m/z=750.3 [M + H] +. Analytical RP-HPLC: Rt = 8min; 85 % A, 15 % B, LogP=-2.58±0.51. The optimal labeling conditions were 20 µg peptide, 80 °C, pH 5–6 and incubation time 30 min. The radiochemical purity of radiolabeled peptides was more than 95%. The stability of peptides in human plasma at 37 °C were 95 % after 6 hrs. Radiopeptides showed high affinity to fibrin and pattern of bio distribution was the same as a hydrophilic peptide.

Conclusions:

Based on the results, radiopeptides are good candidates for in vivo studies.

Key words: Thrombosis, HYNIC, Fibrin, 99m-Tc, DVT

Synthesis of PH-sensitive Boronated chitosan-Urocanic acid nanoparticles to use in BNCT

Fatemeh Dousti*, Mahboubeh Rostami, Farshid Hassanzadeh, Yaser Kasehsaz

P234

Authors' Affiliations:
Isfahan University of Medical Science

Abstract Presenter:
Fatemeh Dousti

****Correspondance:***
Fatemeh Dousti

Coauthors:
Mahboubeh Rostami
Farshid Hassanzadeh
Yaser Kasehsaz

Introduction:

High-grade gliomas, and specifically glioblastoma multiform are still extremely resistant to all current forms of therapy (1). BNCT is based on the nuclear capture and fission reactions that occur when the stable isotope 10B is irradiated with low-energy (0.025 eV) thermal neutrons, this results in the production of high-linear energy transfer (LET) alpha particles (4He) and recoiling lithium (7Li) nuclei. In theory, α particles can selectively destroy tumor cells and spare adjacent normal cells. In order to be successful, 20 µg/g of 10B per weight of tumor must be selectively delivered to the tumor cells (2, 3). The present study was aimed to increase the delivery of 10B to glioma cells by synthesis of a pH-sensitive targeted Boronated chitosan-Urocanic acid nanoparticles.

Methods:

At the first to improve the water solubility of chitosan, imidazolium chloride was applied for modification. In the second step, to prepare a pH-sensitive system, Urocanic acid was grafted onto the CS using EDC/NHS strategy at room temperature. To make the targeted system, BPA was attached to the main body of the CS. BPA loaded CS-NPs were prepared by a simple dialysis method by TPP crosslinking. The release profile of BPA from the prepared nanoparticles at acidic pH (5.7) and physiological pH (7.4) was evaluated. The size and zeta potential of the prepared nanoparticles were studied by direct light scattering instrument.

Results & Discussion:

The FT-IR and NMR spectra confirmed the structure of the modified systems. The quantity of BPA loaded in NPs was about 80 %. About 70% of loaded BPA was released at acidic condition after 24h. It seems that release follows a swelling-controlled mechanism. Our preliminary study thus provided clear evidence for the successful preparation of BPA loaded with novel pH-sensitive chitosan-urocanic acid NPs. The results of this study are promising to introduce a novel boronated nanocarrier to BNCT studies.

Keywords: Chitosan, Nano particles, 4-borono-L-phenylalanine(BPA), PH-sensitive, boron neutron capture therapy (BNCT)

Fabrication of an electrochemical sensor for direct determination of doxorubicin anticancer drug in human plasma

Motahare Atefinezhad, Fereshteh Chekin*

P235

Authors' Affiliations:
Department of Pharmacy, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran

Abstract Presenter:
Motahare Atefinezhad

****Correspondance:***
Fereshteh Chekin

Abstract:

Doxorubicin (DOX), 2R,4S)-4-(3-Amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyloxy)-2 ydroyl-1,2,3,4-tetrahydro-2,5,12-trihydroxy-7-methoxynaphthacene-6,11-dione, is an anthracycline antibiotic produced by Streptomyces peucetius varieta caesius, which is one of the most important anticancer drugs currently used in clinic because of its broad spectrum antineoplastic activity [1–4]. A novel simple method for direct detection of clinical drug doxorubicin (DOX) was developed by the chitosan and nitrogen doped porous reduced graphene oxide modified glassy carbon electrode (CS-NdprGO/GCE) in clinical blood samples. The electrochemical behavior of DOX was observed at CS-NdprGO/GCE by cyclic voltammetry (CV). The electrochemical oxidation peak current was greatly increased because of CS-NdprGO nanocomposite. Under optimized conditions, the oxidation peak current of DOX measured by differential pulse voltammetry (DPV) exhibited a good linear property with the increasing of the concentration in the range of 0.01 μM to 15 μM. The detection limit was founded to be 10 nM. Furthermore, the CS-NdprGO/GCE was successfully used to monitor the clinical DOX pharmacokinetic with good results.

Keywords: Doxorubicin, Electrochemical sensor, Chitosan, Nitrogen doped porous reduced graphene oxide

Design and synthesis of novel aminobenzothiazole derivatives linked to biphenyl acetic acid as dual inhibitor of acetyl cholinesterase and β-secretase

Zahra Abdolahi, Alireza Moradi, Hamid Nadri*

P236

Authors' Affiliations:
Shahid Sadoughi University of Medical Sciences

Abstract Presenter:
Zahra Abdolahi

****Correspondance:***
Hamid Nadri

Coauthors:
Alireza Moradi

Introduction:

Alzheimer's disease (AD) is an age-related neurodegenerative disorder characterized by progressive memory loss and cognitive impairment. It is one of the several neurodegenerative disorders occurring as a result of programmed cell death known as apoptosis. The key events in the progression of AD are the sequential cleavages of β-amyloid precursor protein (β-APP) by β-site APP-cleaving enzyme 1 (BACE-1 or memapsin-2) and degradation of acetylcholine (Ach) by acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) at synaptic cleft. From the therapeutic point of view, BACE-1 and cholinesterase appear to be promising drug targets, which stimulated the design and synthesis of BACE-1 and cholinesterase (ChE) inhibitors.

Herein we designed and synthesized a series of compounds possessing both benzothiazole and aryl-carboxylic acid linked with amino acid moieties

Results and Discussion:

From the data evaluated, all compounds exhibited superior activity against BuChE compared with AChE. The Compound 4f exhibited the best activity against both AChE (67.8±2.6 % inhibition at 50 µM) and BuChE with IC50 value of 0.330±0.006 µM. Compound 4b, 4e and 4h were tested against BACE1, out of which 4b showed 33.1±0.6 % inhibition at 100 µM. These finding revealed that both aryl carboxylic acid moiety and benzothiazole group were modulating the activity. The structure of the synthesized compounds was elucidated using IR and NMR spectroscopy. The docking studies were performed to determine the binding mode of the compounds in the active site of BuChE. It was shown that the hydrophobic contacts were predominant in ligand-enzyme interaction.

Keywords: Alzheimer's disease, acetylcholinesterase, BACE-1, benzothiazole, biphenyl acetic acid

Synthesis, docking and acetylcholinesterase inhibitory evaluation of (E)-3-(4-(diethylamino) phenyl)-1-phenylprop-2-en-1-one derivatives with probable anti-alzheimer effects

Razie Azizifar, Ahmad Mohammadi-Farani, Alireza Aliabadi*

P237

Authors' Affiliations:
Students Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Razie Azizifar

****Correspondance:***
Alireza Aliabadi

Coauthors:
Ahmad Mohammadi-Farani

Introduction:

Alzheimer's disease (AD) is a neurodegenerative disorder in elderly patients. Decrease in cholinergic neurotransmission is the main known cause in the pathophysiology of the disease. Improvement and potentiation of the cholinergic system could be beneficial for treatment of the AD. Acetylcholinesterase inhibitors such as donepezil can enhance the duration of action of acetylcholine (Ach) and therefore, through this mechanism improve the symptoms of AD. According to the various biological activities of phthalimide, we decided to design and synthesize a new series of anticholinesterase agents containing phthalimide based substructure.

Methods:

According to the scheme 1, intended derivatives 6a-6o were synthesized and subsequently the corresponding acetylcholinesterase inhibitory potency of the synthesized compounds was tested by Ellman's protocol. Moreover, molecular docking was also performed for seeking the likely binding mode and interactions.

Results:

All synthesized derivatives obtained with moderate yields. Spectroscopic data such as 1HNMR, IR and MS were applied to characterize the final compounds. The tested derivatives demonstrated potent inhibitory activity towards AChE compared to donepezil. Molecular docking also confirmed the obtained data.

Discussion and Conclusion:

Fortunately synthesized compounds 6a-6o demonstrated potent anti-cholinesterase activity. Some of them exhibited more activity than donepezil. Overall, phthalimide based compounds studied in this research could be proposed as potential lead compound for development of novel anti-Alzheimer drugs.

Keywords: synthesis, phthalimide, acetylcholinesterase, alzheimer

A Facile Four-component Synthesis of Pyrazolophthalazines Using and Efficient Ionic Liquid Catalyst and investigation their antioxidant activity

Zahra Isazadeh, Manouchehr Mamaghani Zahra Isazadeh*

P238

Authors' Affiliations:

Abstract Presenter:
Zahra Isazadeh

***Correspondance:**
Manouchehr Mamaghani
Zahra Isazadeh

Introduction:

An efficient process for the synthesis of pyrazolophthalazine derivatives was developed by using tetrabutylammonium bromide (TBAB) as ionic liquid catalyst in excellent yields (88-95%).

Most of the significant developments against disease have been made by designing and testing new structures, which are often heteroaromatic derivatives. In addition, over 80% of the top small molecule drugs by U.S. retail sales in 2010 contain at least one heterocyclic fragment in their structure. Therefore, researchers are on a continuous pursuit to design and produce better pharmaceuticals, pesticides, insecticides, rodenticides, and weed killers by following natural models. A significant part of such biologically active compounds is composed of heterocycles. Moreover, phthalazine derivatives possess a versatile pharmacological properties including anticonvulsant, vasorelaxant, and cardiotonic activities.

Methods and Results:

We state here an efficient process for the synthesis of pyrazolophthalazine derivatives by a four-component reaction of equimolar amounts of phthalic anhydride, hydrazine hydrate, arylaldehydes, and malononitrile in the presence of 20% tetrabutylammonium bromide (TBAB) ionic liquid as catalyst. This protocol furnishes the desired products in excellent yields (88-95%). (Scheme 1)

The main objective of the research work was to devise a convenient and green protocol forthe synthesis of pyrazolophtalizines as biologically important heterocycles by using easilyavailable and recyclable catalyst.

In this process the synthesis of pyrazolophthalzine derivatives has been carried out by the reaction of equimolar amounts of phthalic anhydride, hydrazine hydrate, malononitrile, and aryl aldehyde in the presence of 20% TBAB at 78 °C. The products were purified by chromatographic methods and the structures of all products were established by spectroscopic methods.

Conclusions:

The protocol described here produced the desired pyrazolophthalazines in excellent yields (88-95%) and lesser reaction times. The catalyst was reused at least 5 times without appreciable reduction in catalytic activities.

Keywords: phthalazine, pyrazolophthalazine, TBAB

Novel trans-Thiolate derivatives of platinum (II) as potential anticancer agents: synthesis and biological evaluation

Faezeh Mirzaei*, Masood Fereidoonnejhad, Hamid R Shahsavari

P239

Authors' Affiliations:
Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract Presenter:
Faezeh Mirzaei

Correspondance:
Faezeh Mirzaei

Coauthors:
Masood Fereidoonnejhad
Hamid R Shahsavari

Introduction:

In recent years, cycloplatinated (II) complexes have been attracted growing attention for their possible use as anticancer drugs. These complexes possess strong σ(Pt-C) bonds what increase their stability in physiological conditions and avoiding off-target reactions; therefore, simplify the potential therapeutic applications.

Methods and Results:

In this study, a series of trans-thiolate derivatives of Pt (II) complexes were synthesized. All complexes were fully characterized by NMR spectroscopy and X-ray diffraction method. BioLegend's PE Annexin V Apoptosis Detection Kit with 7AAD was used to specifically determine the dose-dependent apoptotic effect of these complexes on cancerous cells. Comet assay was used as a valuable method to predict the genotoxic effect of compounds on cancerous cells. Quantitation of DNA content using flow cytometry or cell cycle analysis, was also applied to assess the mechanisms of anti-proliferative effects of these anticancer agents.

Treatment of breast cancer cells (MCF-7) results in the appearance a relatively long tail following the electrophoresed cells in the concentration of 10 µM, which shows strong genotoxic ability of compounds. In case of concentration of 50 µM, no nucleus has been remained and just a blurry tail of degraded DNA could be seen. Apoptosis results showed that with the increase in the concentration, the percentage of the cells in early apoptotic phase significantly elevates. Complex 2b exhibited high potency in inhibiting cell proliferation and significantly higher in vitro cytotoxic activity against A549 (lung), SKOV3 (ovarian), and MCF-7 (breast) cancer cell lines, compared to cisplatin.

Conclusions:

Comet assay revealed that, following the DNA damage, the migration of chromosomal DNA from the nucleus increases and resembles the shape of a tail or comet. These observations collectively showed that these compounds intensely targeted genome content of cancerous cells. On the other hand, apoptosis observation indicated that these compounds, are able to effectively induce apoptosis in cancerous cells in a dose dependent manner. It also implies that anti-proliferative/cytotoxic effect observed of compounds in cytotoxic assay, could be mediated partly through inducing apoptosis in cancer cells.

Keywords: platinum (II) complexes, anticancer, comet assay, Apoptosis

RSM Analysis on in Silico in Vitro Binding of Apixaban to Factor Xa

Reza Mamizadeh Arkhazlo*, Nima Razzaghi-Asl

P240

Authors' Affiliations:
Student Research Committee, School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

Abstract Presenter:
Reza Mamizadeh Arkhazlo

***Correspondance:**
Reza Mamizadeh Arkhazlo

Coauthors:
Nima Razzaghi-Asl

Introduction:

Apixaban is an orally bioavailable anticoagulant drug, used for the treatment of venous thromboembolic events, recurring deep vein thrombosis. Response surface method (RSM) is an efficient computational technique for simultaneous estimation of factor effects on response, the issue not covered in traditional one-factor-at-each-time approaches. In the present project Apixaban, a factor Xa inhibitor, was subjected to analysis of variance (ANOVA) incorporated into RSM statistical package. The aim was to estimate the interactive effectiveness of selected factors for in silico target binding accuracies with regard to validated experimental binding affinities towards factor Xa and interpretation of data.

Methods:

RSM was applied to model the influence of six independent factors on docking accuracies of Apixaban with regard to validated experimental binding affinities. Three distinctive levels (-1, 0, and +1) were dedicated for each factor under study and ANOVA was performed for each endpoint (response) on the basis of Box-Behnken matrix, including 62 independent runs. Responses were defined as the differences between in silico and in vitro data in terms of binding to factor Xa. All statistical analyses were performed via Box-Behnken method, incorporated into Design-Expert (DOE) software-v.7. Docking simulations were done by AutoDock4.2.

Results:

ANOVA results exhibited that quadratic model was significant and could best describe the relationship among dependent variables (ΔnH: difference of hydrogen bonds within in silico and in vitro modes & ΔnHyd: difference of hydrophobic contacts within in silico and in vitro modes) and independent ones (A: Translation distance for drug, B: initial drug conformation, C: quaternion degrees for drug, D: torsion degrees for drug, E: grid box size, F: target conformation and G: grid spacing) with R2 values of 0.9282 and 0.8202, respectively. Model F-values were found to be 24.90 and 3.47, which indicated that in both cases the models were significant. The obtained models for ΔnH and ΔnHyd in terms of significant factors and their coded levels were as follows:

$\Delta n\_H=1.96+0.042B+1.17C+0.12D-0.46F+0.13G-0.25CD-0.25CG-0.25DG$

$\Delta n\_Hyd=7.37-0.17B+0.12D+0.12E-0.54F+0.58G+0.75BE-0.25CD-0.75DG+0.75EG+1.75FG$

As can be understood from the model terms, the most significant terms for predicting hydrogen bonds was quaternion for degrees for drug, whereas in the case of hydrophobic bonds, grid spacing (distance between autogrid adjacent points) was most determinant in predicting hydrophobic contacts. Moreover, factor F (target conformation) and factor G (grid spacing) indicated significant interaction in the second model. The most significant interactive terms for first model were found to be C×D, C×D, and D×G. Moreover, desirable solutions to achieve minimized responses (minimum differences between in silico and in vitro results) were offered.

Conclusions:

The optimized docking technique provided a convenient and efficient method toward comparative qualitative/quantitative exploration of Apixaban binding to its target. The outputs of this study provide optimization of effective factors for the development of in silico-in vitro correlation.

Keywords: Response Surface Method, Docking, Factor Xa, Apixaban

Analysis of configuration, structural patterns and functional groups diversity among US FDA approved drug

Elham Heidarian, Salimeh Amidi, Farzad Kobarfard*

P241

Authors' Affiliations:
Department of Chemical Medicine of Shahid Beheshti Pharmacy School, Tehran, Iran.

Abstract Presenter:
Elham Heidarian

****Correspondance:***
Farzad Kobarfard

Coauthors:
Salimeh Amidi

Introduction:

The relationship between structural features of a chemical compound and medicinal chemistry. Chemical characteristics of a compound further determines its ADMET properties and eventually affects its drug ability.

SAR studies have been the subject of a plethora of screntifie articles in medicinal chemistry.

However, millions of compounds are synthesized every year by chemists as a drug candidate but just a few of them are qualified as a medication which could be used in clinic.

A holistic approach to the structural features of those medications which are officially approved as drugs, could reveal the secret patterns of these molecules which are the winners of the race to be a drug.

The present study was aimed at the analysis of electronic configuration, structural patterns, and functional groups diversity among the globally approved drugs which are currently in use.

The outcomes could be used for future designs of drug candidates as well as drug repositioning approaches.

Methods and Results:

Chemical structures of US-FDA approved drugs were analyzed from five points of view, i.e type and number of functional groups, type and number of aromatic rings, and the presence or absence of acidic and/or basic functional groups.

The total numbers of loan pairs of electrons and total number of electrons in π-system

Results:

Statistical analysis of the results revealed the following facts;

The top five most frequent functional groups among the FDA approved drugs are:

Amin (65.1%)

Halogen (38.99%)

Amid (33.39%)

Alcohol (32%)

Ether (29.68%)

Calculating in 1159 US_FDA approved drugs with the molecular weight less than 600 D.

_ the most frequent rings are heterocyclic rings**.**

_ the most often number of electrons in π-system is in Amins.

Numbers of loan pair electrons were calculating in 1159 US_FDA approved drugs with the molecular weight less than 600 D.

Some other interesting structural features were also determining among the drugs studied in the present project.

Keywords: functional groups, electrons pattern, electronic configuration

Investigating the Electrochemical Behavior of the hawthorn using with cyclic voltammetry and squar wave voltammetry methods

Kosar Shirazi, Seyed Mohammad Shoaei*

P242

Authors' Affiliations:
Department of Chemistry, Zanjan branch, Islamic Azad University, Zanjan, Iran

Abstract Presenter:
Kosar Shirazi

Correspondance:
Seyed Mohammad Shoaei

Introduction:

In recent years, more attention has been devoted to herbal medicines. Many compounds with therapeutic effects has been extracted from the herbs. The aim of this study is to evaluate the antioxidant and the antimicrobial effect of hawthorn. Also we have investigated atioxidan capacity hawthorn using with cyclic voltammetry and squar wave voltammetry methods. Effect of pH and some metal on the antioxidant capacity has been studied (Fe3+, Ca2+, Cd2+,Co2+ and Cr3+). The kinetic data were extracted from cyclic voltammograms with the help of digital simulation. The homogeneous and heterogeneous rate constants were estimated by comparing the experimental cyclic voltammetric responses with the digital simulated results.

The products used are often derived from C. monogyna, C. laevigata, or related Crataegus species, "collectively known as hawthorn", not necessarily distinguishing between these species. The dried fruits of Crataegus pinnatifida are used in traditional Chinese medicine, primarily as a digestive aid. A closely related species, Crataegus cuneata is used in a similar manner. Other species are used in herbal medicine where the plant is believed to strengthen cardiovascular function.

Methods and Results:

We have investigated atioxidan capacity hawthorn using with cyclic voltammetry and squar wave voltammetry methods. The kinetic data were extracted from cyclic voltammograms with the help of digital simulation. The homogeneous and heterogeneous rate constants were estimated by comparing the experimental cyclic voltammetric responses with the digital simulated results.

Conclusions:

The reduction of hawthorn is pH independent and occurs at very high potentials, which means that it can be studied only at pH values higher than 7. The use of buffer electrolyte in a mixed acetonitrile/water solvent proved very convenient for preventing strong adsorption of the analyte on the electrode surface and enabling better repro- ducibility and sensitivity. Adsorptive linear sweep square wave voltammetry permitted accurate quantification of hawthorn in commonly used pharmaceutical drugs in the micromolar range after a very simple and rapid sample treatment. Good precision was obtained .This electroanalytical method can be used for determination of thera- peutic doses of hawthorn in biological fluids if coupled with high performance liquid chromatog- raphy (HPLC) with electrochemical detection.

Keywords: Antioxidant, Electrochemical, Cyclic Voltammetry, squar wave voltammetry

Synthesis, Molecular docking studies Structural determination and biological evaluation of Novel pyrazolo [4, 5-b] quinoxaline bearing Hydantoin as a potential anticancer agent

Zahra Keshavarzian, Malihe Akhavan*

P243

Authors' Affiliations:
Mazandaran University of Medical Science, Mazandaran, Iran.

Abstract Presenter:
Zahra Keshavarzian

***Correspondance:**
Malihe Akhavan

Introduction:

Among heterocyclic anticancer compounds, quinoxalines and Hydantoin are the most prominent since they constitute important classes of natural products and synthetic pharmaceuticals.1 In general, they are used as valuable intermediate and building blocks in pharmaceutical synthesis. Thus, much attention has been paid to the synthesis of quinoxaline derivatives, bearing Hydantoin either by classic methods or by multicomponent reactions. 2, 3

Methods:

The title compound was prepared through a three- step procedure. Firstly, equimolar amounts of D-glucose and o-phenylenediamine were reacted with phenyl hydrazine in the acetic acid, to form the pyrazolo[4,5-b] quinoxaline derivative.

The second step involved oxidation of the resulted compound by use of sodium metaperioddate

Finally, the related aldehyde was condensed by Hydantoin to yield the corresponding 3-alkylidene parasol [4, 5-b] quinoxaline.

Results:

The desired compound was successfully obtained by the aforementioned procedure and its production was confirmed using NMR, IR, and mass spectroscopy. The MTT assay of this synthesized hybrid showed promising and effective anticancer activity against MCF-7 and HTC-116 cell lines. Molecular docking demonstrated the title compound can be considered a notable group of inhibitors for 3E33.

Keywords: Anticancer activity

Development of a validated and sensitive HPLC method for determination of α-phenyl cinnamonitrile in plasma as a new antiplatelet agent.

Elahe Sadeghi Bojd, Zahra Abbasian , Farzad Kobarfard, Simin Dadashzadeh*

P244

Authors' Affiliations:
Department of medicinal chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Department of Pharmaceutics, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Elahe Sadeghi Bojd

Correspondance:
Simin Dadashzadeh

Coauthors:
Zahra Abbasian
Farzad Kobarfard

Introduction:

Cardiovascular disorders are the main cause of mortality all around the world (1). Prevention and treatment of these types of disorders have been always a challenge for health care professionals. Platelets have an essential role in heart diseases. There are different types of antiplatelet agents, such as aspirin and clopdiogrel that have shown some adverse effects (2). Therefore, there is a need for further efforts to find new antiplatelet agents. A-phenyl cinnamonitrile has shown potent platelet aggregation inhibitory effect against arachidonic acid-induced aggregation (3). As a continuation of the quest to find an optimum anti-platelet drug candidate,the present study was aimed at pharmacokinetic study of this compound in rats. A high performance Liquid chromatography (HPLC) method has been developed and validated for determination of α-phenyl cinnamonitrile in rat plasma.

Methods:

The sample preparation procedure involved liquid-liquid extraction following extraction of analyte and Internal Standard (IS) (4-chloro-α-phenyl cinnamonitrile) from plasma by tert-butyl methyl ether. The separation was carried out using reversed-phase conditions on a C8 column with an isocratic mobile phase consisting of deionized water and acetonitrile (30:70, v/v) at a flow rate of 1.0 ml/min by UV detection at 309 nm.

Results:

The retention times of analyt and IS were 6.05 and 7.05 min, respectively. A linear response was observed over a concentration range of 50-1500 ng/mL. The recovery was more than 75%. Precission and accuracy were calculated as ≤12% and 95-110% respectively and lower limit of quantification (LLOQ) was 50 ng/ml. The assay was successfully applied to determine the pharmacokinetic parameters in rat after IV administration of the analyte at 3 mg/kg.

Conclusions:

The reported assay method showed good characteristics of linearity, sensitivity, accuracy, selectivity, and precision that made it suitable for ADME studies as part of drug development process.

Keywords: α-phenyl cinnamonitrile, HPLC, pharmacokinetic studies

"Study the kinetics of Vinorelbine release in simulated blood human environment using modified Iron Oxide with Poly (lactic acid)."

Sara Shirinzad*, Mahshid Nikpour Nezhati, Homayon Ahmad Panahi

P245

Authors' Affiliations:

Islamic Azad University of Central Tehran Branch, Tehran, Iran.

Abstract Presenter:
Sara Shirinzad

***Correspondance:**
Sara Shirinzad

Coauthors:
Mahshid Nikpour Nezhati
Homayon Ahmad Panahi

Introduction:

The criteria for Fe3O4 -NPs to be used as drug delivery vehicle are discussed in order to find their optimum condition in drug delivery application. Many researches showed the promising results of Fe3O4 -NPs aginst cancer cells via in vitro studies. For MNPs coating, natural polymers like collagen and chitosan, or synthetic materials, such as TEOS (tetraethyl orthosilicate), polyethylene glycol, and dextran can be used. Various functional groups like aldehyde (-CHO), amine (-NH), and hydroxyl (-OH) can be conjugated to these silica-coated particles for different biomedical and biochemical purposes. The antibody-conjugated chitosan-SiO nanocarriers could be excellent materials for pH-responsive tumor-targeted drug delivery. Polymeric nanoparticles can provide sustained, controlled, and targeted delivery of anticancer drugs. Poly (lactic acid) (PLA) is an FDA-approved biodegradable polymer with low toxicity, excellent biocompatibility, and bio absorbability in vivo.

Methods and Results:

Fe3O4 nanoparticles were synthesized by stober process, TEOS (Sigma Aldrich), Chitosan (Sigma Aldrich), Poly lactic Acid (Sigma Aldrich)

The Fe3O4 nanoparticles as core and TEOS-Chitosan-PLA nanoparticles as shells were produced and their size measured with SEM.

Conclusions:

These NPs showed a pH responsive drug release profile. It was observed that the rate and amount of drug released from the NPs were higher at pH=8. All these characteristics demonstrated that the pH-responsive NPs could be promising drug-delivery carriers for cancer therapy.

Keywords: Nanoparticle, Drug delivery, Iron Oxide, Anti-cancer, Polymeric

Monoamin Oxidase Inhibitory Activity of Curcumin and Its Derivatives: In Silico Approach

Hamidreza Nazemi, Mahmoud Mirzaei*

P246

Authors' Affiliations:
Isfahan pharmacy Students' Research Committee, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract Presenter:
Hamidreza Nazemi

Correspondance:
Mahmoud Mirzaei

Introduction:

Depression is one of the most common mental disorders that decreases the personal mood and interferes with many daily activities. In many cases, patients do not respond to known anti-depressant agents and they experience serious side effects (1). Therefore, it is important to always look for more efficient and safer anti-depressants. Decades of studying on natural products and their effects on depression have shown promising results (2). Curcumin has proven to have potential positive effects on depression (3) but its poor pharmacokinetics and bioavailability led scientists to find more stable forms and better derivatives (4). This work will try to find some better alternatives for Curcumin.

Methods:

3D structures of 259 compounds including Curcumin, its derivatives and some of known MAOI drugs like Moclobmide have been obtained from ChmeSpider and then they have been optimized by the B3LYP/3-21G* of Gaussian package. Then, 2BXR has been obtained from PDB and it has been prepared by Discovery Studio to be included in molecular docking by AutoDock software. The results of binding energies (Eb (and interacting amino acids have been evaluated from the outputs.

Results:

147 Curcumin derivatives were found to show better Ebs than Curcmin itself (Eb = -9.78). Among these compounds, 75 compounds had logP lower than 5. Among these 75 compounds, best compounds were compounds with ChemSpider ID respectively 23319790, 338352, and 1267000. We found also similar surrounding amino acids for best Curcumin derivatives and reference compounds.

Conclusions:

Quantitative and qualitative evaluation of Curcumin, its derivatives and known MAOIs indicated that some Curcumin derivatives with low Eb and logP have this potential to be seen as next anti-depressant candidates. Therefore, further studies are required regarding pharmacokinetic and safety profiles of these compounds to reach more efficient and safer drugs.

Keywords: Anti-depressants, Curcumin, MAOI, Docking

Radio protective effects of lentil sprouts against X-ray radiation

Mohammadmehdi Gravandi*, Kambiz Varmira, Kamran Mansouri

P248

Authors' Affiliations:
Student Research Committee, Faculty of Pharmacy, Kermanshah University of medical sciences

Abstract Presenter:
Mohammadmehdi Gravandi

****Correspondance:***
Mohammadmehdi Gravandi

Coauthors:
Kambiz Varmira
Kamran Mansouri

Introduction:

Lentils have an excellent nutrition profile and favorable levels of antioxidants. Factors like temperature,light intensity,duration of germination and elicitation agents are affecting the contents of lentil sprouts. Ionizing radiation (IR) is the main source of radical production in human body but there are considerable advantages for diagnostic and therapeutic applications; thus, it is impossible to neglect application of clinical rays.

Methods and Results:

Radioprotective efficacy of lentil (Lens culinaris) sprouts against X-ray radiation-induced cellular damage. Lentil seeds were dark germinated at low temperature and the sprout extract was prepared in PBS. Free radical scavenging of extract was evaluated using 2,2-diphenyl-1- picrylhydrazyl (DPPH) assay and then the radioprotective potency of extract (0 to 1000 µg/mL) on the lymphocyte cells was determined by lactate dehydrogenases assay. Moreover, micronuclei assay was assessed using the cytokinesis-block technique. The irradiations were performed using 6 MV X-ray beams. The value of IC50 for DPPH assay was 250 µg/mL. The median lethal dose for radiation was determinate at 5.37 Gy. Pretreatment with lentil sprout extract at 1000 µg/mL reduced cytotoxicity at 6 Gy total concentration from 70% to 50%. The results of micronuclei assay indicated that cells were resistant to radiation at concentrations of 500-1000 µg/mL of exogenous lentil sprout extract. The value of median effective concentration for micronuclei assay was 500 µg/mL MN assay has been applied in the toxicological study to screen for genotoxic compounds. The study determined that exogenous lentil sprout extract protected lymphocyte cells from death and DNA doublestrand break formation induced by radiation.

Conclusions:

Our data showed that extract of total lentil sprout have more antioxidant activity than Haghparast et al. / RPS 2017; 12(1): 38-4544 radicle part. The LDH assay showed thatextract concentration at 1000 µg/mL protected 20% of cells against X-ray irradiation at 6 Gy total dose. A similar trend was observed in protection of different concentration using MN assay. In conclusion, these results suggest that lentil sprout extract has a moderate protective effect against irradiation.

Keywords: Radioprotective agents

Determination of methamphetamine enantiomers in sample seized in Tehran

Reza Mobaraki*, Alireza Khajehamir, Farzad Kobarfard

P249

Authors' Affiliations:
Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Reza Mobaraki

****Correspondance:***
Reza Mobaraki

Coauthors:
Alireza Khajehamir
Farzad Kobarfard

Introduction:

Methamphetamine and its derivatives are among the most frequent illicit drugs which are currently being used. Methamphetamine is made in clandestine labs using different starting materials and reagents. Since methamphetamine is a chiral compound, it is expected that a mixture of two stereoisomers of this compound is obtained and depending on the method of synthesis, different enantiomeric ratio will be produced. Therefor determination of enantiomeric ratio for the seized samples could be used for determination of their origin and their possible propinquity.

Methods and Results:

GC-MS method: The samples were extracted by ethyl acetate after dissolution in water, then derivatized with (S)-(−)-N-(Trifluoroacetyl) pyrrolidine-2-carbonyl chloride (l-TPC) and injected into the GC-MS instrument. Since (l-TPC) is a chiral derivatizing agent, the two diastereomers which were obtained after derivatization were separated on a HP-5 GC column

Polarimetry method: The samples were dissolved in water and their optical rotation was determined by polarimetry.

In all samples, two enantiomers were separated, and d (+) enantiomer was more than the l (-) enantiomer.

The optical activity of the samples was also dextrorotatory.

Conclusions:

Considering that different enantiomeric ratio was obtained for the seized samples, it could be speculated that different methods are being used in clandestine labs for the synthesis of methamphetamine. The similarity of the seized samples in enantiomeric ratio could be used by law enforcement authorities to find the distribution networks which are involved in distributing methamphetamine in Tehran.

Keywords: Methamphetamine, enantioseparation, GC-MS

Determination of Illicit Drugs in Paper Currency of Iran

Seyedeh Zahra Takrimi Niyarad, Kimia Tabib, Salimeh Amidi, Farzad Kobarfard*

P250

Authors' Affiliations:
Department of Medicinal Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Seyedeh Zahra Takrimi Niyarad

***Correspondance:**
Farzad Kobarfard

Coauthors:
Kimia Tabib
Salimeh Amidi

Introduction:

Prevalence of illicit drug usage in different societies is unclear and the researchers use indirect ways to obtain these data; assessment of banknotes' pollution with illicit drugs is a solution for this problem. These data also give information about the extent of illicit drugs usage because using cash is one of the most usual ways for buying illicit drugs. In different countries several investigations have been carried out in this field such as detection of cocaine and cannabis (Marijuana) on United States' currency, illicit drugs and their metabolites contamination on banknotes of the Slovakia, Czech Republic and Austria and methamphetamine contamination on bills in the Metropolitan Area but in our country there is no information about this important issue (1-4).

Methods:

A total of 180 bills were collected from various places in Tehran and analyzed. Each bill was soaked in a 0.1M HCl and was shaken for 90 minutes on an orbital shaker, after shaking the pH of solution raised to 12 by adding a 2M NaOH and extracted with 2ml of $CHCl_3$. After evaporation of $CHCl_3$, methanol was added to the residue to extract the desired material. The methanolic solutions were analyzed by gas chromatography-mass spectroscopy (GC/MS) (4).

Results:

The negative control sample had peaks that showed the presence of color; but these peaks did not exist in samples that are collected. Intentionally contaminated banknotes with methamphetamine was prepared by gently rubbing 10µg of the compound on the banknotes and they were used as positive samples. In the first part of our study a GC/MS method was used without prior derivatization of the extracts from banknotes. No contaminated banknote was found among samples. Therefore, a method based on derivatization with dansyl chloride was developed and used for further investigation.

Conclusions:

The present study showed that the use of GC/MS technique can be a good method for identifing and determination of illicit drugs on banknotes. However due to the diversity of the physicochemical properties of illicit drugs, a total extraction with methanol and derivatization of the extract seems to be more suitable for these type of studies.

Keywords: Banknotes, Gas chromatography-mass spectroscopy (GC/MS), illicit drugs, Paper currency

Computational studies on the B36 as potential carriers in drug delivery systems for isoniazid drug

Sepideh Ahmaditabar, Mozhgan Sabzehzari*

P251

Authors' Affiliations:
Faculty of Pharmacy, Jundishapur University of Medical Sciences, Ahwaz, Iran

Abstract Presenter:
Sepideh Ahmaditabar

Correspondance:
Mozhgan Sabzehzari

Abstract:
Recently, efforts have been made to find an appropriate carrier to deliver the drug, but it still needs further studies. Nanostructures have found numerous applications researches on the development of a drug carrier based on the nanostructures has been rapidly grown? Isoniazid (iso) isrecommended as first-line anti-tuberculosis drugs, which has high effectivity and strong antibacterial action. However, drug resistance is a common problem during long-term therapy, which causes treatment failure leading to progressive disease. Delivery of isoniazid directly to the target site using specific nanocarriers may be a potential strategy to reduce its side effects as well as toxicity. Therefore, it is necessary to investigate the delivery of isoniazid using B_36 in order to perform further pharmacological studies.

Keywords: Drug delivery, isoniazid drug, B_36 fullerenes, DFT

B36 fullerene as a promising carrier for gemcitabine anti-cancer drug delivery: DFT studies

Sepideh Ahmaditabar, Mozhgan Sabzehzari*

P252

Authors' Affiliations:
Faculty of Pharmacy, Jundishapur University of Medical Sciences, Ahwaz, Iran

Abstract Presenter:
Sepideh Ahmaditabar

Correspondance:
Mozhgan Sabzehzari

Abstract:
Chemotherapeutic agents of choice are 5-fluorouracil, gemcitabine, and erlotinib. Gemcitabine has been approved by the FDA for use as a single agent for the first line treatment of both locally advanced and metastatic cases of pancreatic cancer. Although this chemotherapeutics have direct effects on cancerous tissues, the toxicities in normal tissues are usually dose-limiting factors in successful chemotherapeutic regimes. Recently, some efforts have been performed to find an appropriate carrier to deliver the drug, but it still needs much further studies. Nanostructures have found numerous applications and researches on the development of a drug carrier based on the nanostructures has been rapidly grown. These researches tempted us to investigate the ability of B36 fullerene as a carrier for gemcitabine drug (1-3).

Keywords: B36 fullerenes, gemcitabine, drug delivery, DFT

3D-QSAR and molecular docking studies on potent anticancer agents

Tooba Abdizadeh*, Farzin Hadizadeh

P253

Authors' Affiliations:
Clinical Biochemistry Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran

Abstract Presenter:
Tooba Abdizadeh

***Correspondance:**
Tooba Abdizadeh

Coauthors:
Farzin Hadizadeh

Abstract:

Cancer, the uncontrolled, rapid and pathological proliferation of abnormal cells, is one of the most life-threatening diseases and causes of death worldwide [1]. Numerous drugs have been used for cancer treatment but have severe side effects. Consequently, increasing interest has been devoted to the design and discovery of more effective anticancer agents with promising activity and high therapeutic index in current medicinal chemistry. The design of anticancer inhibitors is an ongoing topic in drug design [2-3]. In the present study, 3D-QSAR and molecular docking were used to provide a theoretical basis for finding highly potent anticancer drugs. QSAR was used to generate models and predict the anti-cancer inhibitory activities, in order to rationalize their selectivity towards anticancer, using the Sybyl program (x1.2 version). Benzamides derivatives as selective anticancer agents were selected as our data set, which was split randomly into training and test sets. Docking was carried out using the MOE software. Partial least square was used as QSAR model-generation method. External validation and cross-validation (leave-one-out and leave-10-out) were used as validation methods. Both CoMFA (q2, 0.589; ⟦ r⟧_ncv^2, 0.934) and CoMSIA models (q2, 0.601; ⟦ r⟧_ncv^2, 0.917) for training set yielded significant statistical results. The predictive ability of the derived models was examined by a test set of 15 compounds and external validation results displayed⟦ r⟧_pred^2 and r_m^2 values of 0.730 and 0.621 for CoMFA and 0.712 and 0.636 for CoMSIA, respectively. The obtained models showed a good predictive ability in both internal and external validation and could be used for designing new benzamides derivatives as potent anti-cancer agents in cancer treatment.

Keywords: anticancer, CoMSIA, benzamides, docking, CoMFA

Electrochemical Behavior of Palm sap at a Glassy Carbon Electrode and its Analytical Application

Hamideh Ghorbani, Seyed Mohammad Shoaei*

P254

Authors' Affiliations:
Department of chemistry, Zanjan branch, Islamic Azad University, Zanjan, Iran

Abstract Presenter:
Hamideh Ghorbani

***Correspondance:**
Seyed Mohammad Shoaei

Introduction:

Palm sap is quite nutritious and highly prone to fermentation. The unfermented juice could be an ideal health drink. Palm sap's quality profile and fermentation chemistry help to predict its shelf life and potential safety. There is demand from farmer–producer companies and food processing industries to develop bottling technology and a transportation/distribution protocol for palm sap similar to common soft drinks. Different techniques were followed for bottling palm sap, but none proved successful at the pilot level or commercial scale. To develop a systemic preservation technique, it is crucial to understand the biochemical composition, fermentation chemistry, and existing preservation methods and their disadvantages. This review mainly focuses on the chemical, microbial, volatiles, and flavor changes of palm sap. In addition to a detailed discussion on contemporary sap preservation techniques, this paper also addresses the effect of pasteurization in combination with preservatives, such as nisin, sodium benzoate, chitosan, potassium sorbate, sorbic acid, citric acid, and sodium metabisulfite, on the shelf life of sap, challenges to preserving palm sap, and future directions for preservation methods

Analysis of herbal medicine is an important technique, and it offersmany applications in biochemical, pharmaceutical and clinical research.

Methods and Results:

The electrochemical behavior of the Palm sap was studied in 0.1 mol. L-1 buffer electrolyte in a mixed acetonitrile/water solvent (pH= 4.0) by cyclic voltammetry (CV) at a glassy carbon electrode. In CV, two oxidation peaks (P1 and P2) with Ep1 = 0.12Vand Ep2 = 0.55 V appeared at a scan rate of 0.05 Vs-1, and a new electroanalytical method for this herbal drug was established according to the oxidation peak P2. The peak currents have a linear relationship with Palm sap concentration in a range from 9.0 × 10-7 to 2.0 × 10-5 mol L-1. Using the established method, Palm sap in a herbal drug was determined without pre-separation with satisfactory results. Moreover, the electrode dynamics parameters were also investigated by electrochemical techniques and the possible electrode reaction mechanism was deduced.

Keywords: herbal medicine, Palm sap, Electrochemical, Dynamics parameters, Analysis

Development and validation of measurement method for methadone isomers using high performance liquid chromatography in human plasma samples

Marzieh Faraz*, Hashem Montaseri, Faegheh Baha-al-Dini bigi Zarandi

P255

Authors' Affiliations:

Department of Quality Control and Pharmaceutical Department, Faculty of Pharmacy, Shiraz University of Medical Sciences

Abstract Presenter:

Marzieh Faraz

****Correspondance:***
Marzieh Faraz

Coauthors:
Hashem Montaseri
Faegheh Baha-al-Dini bigi Zarandi

Abstract:

A sensitive, simple, fast, applicable, and validated HPLC analytical method was developed and applied for determination of R and S isomers of methadone in plasma samples.

A HPLC system consist of Shimadzo Controller unit, Pumps and UV detector (λ=210 nm) was used. AGP, chiral column was used for separation and quantification of methadone enantiomers in plasma samples.

The retention time, LOD and LOQ for methadone enantiomers in final developed chromatographic methods were 9.8 min for R, and 11.8 min for S, and 2 and 5 ng/ml for enantiomers.

Standard curves were obtained for R and S methadone (5-50 ng/ml, r2= 0.999). The average of inter and intra-day variation were 3.1 and 2.6 for isomers.

Specific extraction methods were developed using solvent- solvent extraction method for methadone enantiomers. The extraction ratio for isomers in blood was 84%.

The blood concentration of methadone and its enantiomers in blood samples, (collected from patients under treatment in MMT program) was measured using Our HPLC method. Our results showed that unfortunately only 45% of patients have the safe, nontoxic, and therapeutic plasma concentrations of R methadone and 30% needs to be monitor for toxicity and 15% are in toxic concentration and 10% are in lethal concentration.

Therefore, due to interpersonal diversity of enantioselective metabolism and pharmacokinetic of methadone, and in order to increase the safety and efficacy of methadone therapy, it is highly recommended that TDM of methadone is done for all patients in MMT program in our country.

Keywords: enantioselective HPLC, chiral AGP column, methadone enantiomer, plasma concentration

Synthesis of alpha, beta-unsaturated carboxylic acid derivatives and evaluation of their antiplatelet aggregation activity

Sahra Feyzi, Marjan Esfahanizadeh, Zohreh Soleymani, Farzad Kobarfard*

P256

Authors' Affiliations:
Students Research Committee, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Sahra Feyzi

****Correspondance:***
Farzad Kobarfard

Coauthors:
Marjan Esfahanizadeh
Zohreh Soleymani

Introduction:

Cardiovascular disease is still the main cause of morbidity and mortality in the world. Platelet activation is known to play a significant role in its initiation, progression and complications, and for this reason direct antiplatelet therapy is a major focus in the management of cardiovascular risk. However, in addition to platelet activation, factors such as decreased antioxidant status and increased reactive oxygen species, inflammation, dyslipidemia and sedentary lifestyle are also associated with poor cardiovascular outcomes.

Platelet aggregation inhibitors, which are currently in use suffer from some side effects and inefficiency in some of the patients. Therefore, new antiplatelet agents are on demand. The present study was aimed at the synthesis and evaluation of a group of α-β-unsaturated carboxylic acid derivatives.

Methods:

A solution of benzaldehyde derivatives, phenylacetic acid and trimethylamine in acetic anhydride was stirred at 90°C for 6 hr. The reaction mixture was worked up to obtain the desired α-β-unsaturated carboxylic acids in a satisfactory purity.

Results:

The structure of the obtained derivatives was characterized by IR, 1HNMR and ESI-MS. All the reactions gave 63% yields. Antiplatelet activity of the prepared compounds was calculated as percent inhibition against the aggregation induced by arachidonic acid (AA) and adenosine diphosphate (ADP).

Conclusions:

Different activities observed for the compounds with various substituents on the phenyl ring. Those compounds with higher water solubility (lower lipophilicity) showed higher antiplatelet activity. A few compounds showed IC50 values lower than 100 µM.

Keywords: Antiplatelet activity, α-β-unsaturated carboxylic acid

Synthesis and biological activity of some benzochromenoquinolinones: Tacrine analogues as potent anti-Alzheimer's agents

Roshanak Hariri*, Mohammad Mahdavib, Seyedeh Sara Mirfazli, Najmeh Edraki, Tahmineh Akbarzadeh, Mina Saeedi

P257

Authors' Affiliations:
Department of Medicinal Chemistry, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Roshanak Hariri

****Correspondance:***
Roshanak Hariri

Coauthors:
Mohammad Mahdavib
Seyedeh Sara Mirfazli
Najmeh Edraki
Tahmineh Akbarzadeh
Mina Saeedi

Abstract:

Alzheimer's disease (AD) is a well-known neurodegenerative disorder affecting millions of old people worldwide and the corresponding epidemiological data emphasize the importance of the disease. As AD is a multifactorial illness, various single-target directed drugs that have been reached to clinical trials, have failed. Therefore, various factors associated with outset of AD have been considered in targeted drug discovery. In this work, various benzo-chromeno-quinolinones were synthesized and evaluated for their cholinesterase and metal-chelating properties. Among the synthesized compounds, 14-amino-13-(3-nitrophenyl)-3,4-dihydro-1H-benzo [6,7] chromeno [2,3-b] quinoline-7,12(2H,13H)-dione (6m) depicted the best inhibitory activity towards acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) with IC50s = 0.861 and 6.028 µM, respectively. Also, it showed metal chelating ability toward Cu2+, Fe2+ and Zn2+. In addition, docking study demonstrated desirable interactions of compound 6m with amino acid residues characterizing AChE and BChE.

Keywords: Alzheimer's, Benzochromenoquinolinones, Cholinesterase, Docking study, Tacrine

New, green and highly efficient procedure for the synthesis of valsartan, as an effective antihypertensive drug

Babak Pourrostam*, Mohammad Mahdavib, Seyedeh Sara Mirfazli,
Najmeh Edraki, Tahmineh Akbarzadeh, Mina Saeedi

P ۲۰۸

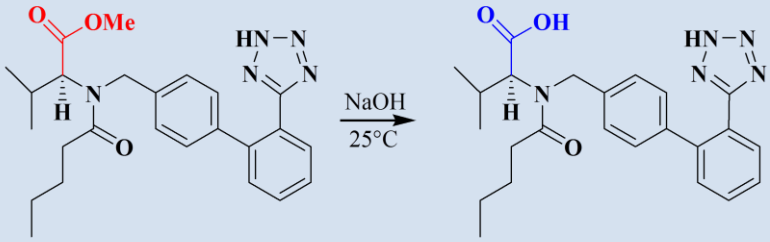
Authors' Affiliations:
Antibiotic Sazi Iran Co

Abstract Presenter:
Babak Pourrostam

****Correspondance:***
Babak Pourrostam

Coauthors:
Yadollah Nasiri
Marzieh Sadat Shahabi

Abstract:
Valsartan is mainly used for treatment of high blood pressure, congestive heart failure, and to increase the chances of living longer after a heart attack. Owing to its ability to inhibit the angiotensin-converting enzyme, it is widely used for the treatment of hypertension and related diseases and conditions. As an angiotensin II receptor antagonist, valsartan avoids the side-effects of calcium antagonists, and shows high stability [1].
Valsartan is one of the most commonly used cardiovascular drugs which its consumption process has noticeably grown in our country and achieved from 2 to 27 tons per year over the past five years.
So far, the active ingredient of this drug was imported from other countries and there was no domestic manufacturer in the country.
Some of problems associated with previous synthetic processes described in the literature are such as use of highly toxic, low purity and an overall low yield of valsartan. [2]
For the first time in Iran, in Antibiotic Sazi Iran Company, valsartan was produced from basic hydrolysis of valsartan methyl ester at 25 ˚C in the presence of NaOH in aqueous solution without any organic solvent. (Scheme 1)



Scheme **1**: Synthetic procedure for the manufacture of valsartan

Prepared valsartan was then characterized by Fourier transform infrared (FTIR) spectroscopy, ^{1}H-NMR and ^{13}C-NMR spectroscopy and HPLC. All of these analyses confirmed synthesis of valsartan. Unique technical knowledge, higher yield than competitor companies, appropriate product quality based on pharmacopoeia, better purity than existing processes and green synthetic procedure are the advantages of present protocol.

Keywords: Valsartan, Valsartan Methylester, Cardiovascular drugs, Hydrolysis

High pressure homogenization as the suitable method for preparation of Nigella sativa oil emulsions in treatment of eczema

Sepideh Forooghi*, Fereshteh Golfakhrabadi, Lana Tamadon, Mahsa Maleki

P260

Authors' Affiliations:
pharmacy student, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Abstract Presenter:
Sepideh Forooghi

****Correspondance:***
Sepideh Forooghi

Coauthors:
Fereshteh Golfakhrabadi
Lana Tamadon
Mahsa Maleki

Introduction:

Nigella sativa (family: Ranunculaceae) seed oil has been used as a natural remedy for various skin disorders for centuries in many cultures. In recent years' studies in emulsions has increased due to their stability and potential applications in food, cosmetic, and pharmaceutical industries. An emulsion is a mixture of two or more liquids that are normally immiscible. Eczema is a group of conditions in which the skin becomes red, itchy, and inflamed. Current treatment strategies including topical corticosteroids are now restricted due to their side effects. Herbal treatments are used traditionally for eczema but their applications are not validated by controlled clinical trials. The aim of this study is to formulate a stable N. sativa water-in-oil (W/O) emulsion for treating eczema.

Methods and Results:

Cold press method was employed to extract the oil from seeds of N. sativa. The emulsions were prepared by two step method. In the first step, the pre-mixture containing definitive amounts of the N. sativa oil, surfactant, and co-surfactant were dispersed in water and then mixed using ultra homogenizer. In the second step, the final emulsion was obtained after passing through high-pressure homogenizer. The influence of emulsifying conditions including emulsifier' and co-surfactant' type and concentration, homogenizer pressure, and number of cycles on the properties and stability of the emulsions were studied. Particle size analyzing and stability studies were used for investigation of the formulations. All the formulations contain 10% of N. sativa oil. The emulsions with Tween 20 (10%) as the surfactant and ethanol (5%) as the co-surfactant were much more stable. Different pressures of high pressure homogenizer results in the emulsions with different particle size and stability. The process using 100 MPa pressure and 3 cycles passing, yielded in smallest particles in uniform distribution. Coalescence and creaming destabilization were not significant in these formulations. Changing in particle size and also any phase separation does not occur after 3 weeks storage at 40 ˚C and 25 ˚C.

Conclusions:

The O/W emulsions prepared in this study represented good characteristics with physicochemical potency for using in patients suffering from eczema in future.

Keywords: Nigella sativa, Eczema, Emulsions, Seed oil

Preparation and characterization of simvastatin-succinyl chitosan-citicoline nanoparticles via ionotropic gelation technique

Negin Mozafari, Soleiman Mohammadi-Samani,
Fatemeh Farjadian, Amir Azadi*

P261

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract Presenter:
Negin Mozafari

***Correspondance:**
Amir Azadi

Coauthors:
Soleiman Mohammadi-Samani
Fatemeh Farjadian

Abstract:

With the aim of improving the effect of simvastatin on Alzheimer's disease, the conjugated form of simvastatin-succinyl chitosan-citicoline was synthesized as discussed before (1). In order to improve drug delivery, nanoparticle of this conjugated form was prepared (2). To receive this purpose, polyanions like tri poly phosphate (TPP) can be used. The aim of this study is preparing nanoparticles of simvastatin-succinyl chitosan-citicoline with ionotropic technique and comparing with the unremarkable conjugated form. For this purpose, 0.36 w/v concentration of the simvastatin-succinyl chitosan-citicoline solution in sodium acetate buffer (pH=5.46) which is equivalent to 0.18 w/v concentration of chitosan was prepared. Concurrently, 1.5% w/v of TPP solution was prepared and then added drop by drop to the conjugated solution (1:7). Dynamic light scattering showed that the nanoparticles of conjugated form were 196 nm with a polydispersity index of 0.153. Spherical shape of nanoparticles was obtained from transmission electron microscopy. The maximum percentage of hemolysis test was 10%. The conjugated form had still some free amine groups. Then in order to achieve the nanoparticles, the ionotropic technique was used in which chitosan can connect to TPP and makes a gel structure (3). Unlike microscopic result of unremarkable conjugated form which showed aggregation in the sample, nanoparticles of conjugated form were separated from each other. The percentages of hemolysis test of all concentrations were in acceptable range and much lower than the percentages of unremarkable form. For this reason, it can be concluded that the nanoparticles of conjugated form had more stability than the unremarkable form.

Keywords: simvastatin, citicoline, ionotropic, Alzheimer's disease

Development of a Rapid and Sensitive In-house Reversed-Phase High-performance Liquid Chromatography Method for the Quantification of Propofol in Plasma

Kamyar Keshavarz F., Mona Rajabi, Saeed Oraee-Yazdani, Farshad H. Shirazi*

P262

Authors' Affiliations:
Pharmaceutical sciences Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Kamyar Keshavarz F.

****Correspondance:***
Farshad H. Shirazi

Coauthors:
Mona Rajabi
Saeed Oraee-Yazdani

Abstract:

Propofol (2,6-diisopropylphenol) is one of the most widely used anesthetic agents not only for the induction and maintenance of anesthesia but also for prolonged sedation of patients in ICU. Despite some serious adverse effects such as PRIS (Propofol infusion syndrome) associated with high dose and prolonged use of this drug, pharmacological merits of quick onset of action, rapid and complete recovery even after prolonged use has made this drug a favoured choice. Rapid and complete recovery are the consequences of drug biodistribution and biotransformation by liver Cytochrome P enzymes. Eventually, distinct individuals show variable responses (eg. Adverse effects) to the same dose of propofol (1.2). Hence, to evaluate the inter-individual pharmacokinetics of this agent, the monitoring of its serum concentration seems necessary. To achieve this goal, an in-house reversed-phase high-performance liquid chromatography method which is quick and sensitive was developed. To achieve the standard curve, 0.4 ml of human plasma was spiked with various concentrations of propofol (50µl) and a fixed concentration (0.25µg/ml) of thymol (internal standard, 50µl). After vortexing, plasma was precipitated by adding 0.5 ml of precipitation solution comprised acetonitrile and perchloric acid (67:33) and then centrifuged. Supernatant was directly injected (20µl injection volume) to the C18 column (250mm×4.6mm, filled with 5µm particles). Mobile Phase was a mixture of acetonitrile and water (78:22) at pH=4 adjusted by glacial acetic acid. Propofol was detected by fluorescence detector with excitation and emission wavelengths of 276 nm and 310 nm respectively (3,4). The standard curve was linear (r2>0.99) in the range of 0.7 - 1.7 µg/ml and the coefficient of variation was less than 15%. Limit of quantification was 0.4 µg/ml.

Keywords: Propofol, HPLC

Formulation and physiochemical evaluation of Omeprazole mucoadhesive paste

Negar Khosravi

P263

Authors' Affiliations:

Kerman University of Medical Sciences, Iran.

Abstract Presenter:
Negar Khosravi

Correspondance:
Negar Khosravi

Introduction:

Omeprazole(OMP) is a proton pump inhibitor used for treatment of the symptoms of gastro esophageal reflux and combination therapy in Helicobacter pylori infection. There are different dosage forms of OMP available and each one have their own limitations such as difficulty of use for children and elderly, high first pass effect and interactions with food.

To bypass first pass metabolism and to increase bioavailability of drug, also to present a formulation friendly to children and adults, in this project we try to present oral mucoadhesive paste of OMP.

Methods:

Oral mucoadhesive paste is a combination of Na-CMC, Gelatin and Pectin in Plasti base gel. Plasti base gel is obtained by rapidly cooling the hot LDPE mixture in liquid paraffin. Ten formulations with different percentages of these components were prepared, the formulations were evaluated for appearance, particles, uniformity and thumb test. Five selected formulations were evaluated for adherence and occlusivity. One final formulation was selected for release evaluation.

For analyzing OMP, UV spectrophotometry method was used .In this procedure NaOH 0.1 N was used as solvent and then the absorbance was read at 290 nm .Calibration curve was drown in 5-25µg/ml range. Accuracy and precision were calculated. The drug content and the release profile (franz diffusion cell) were evaluated.

Results and Conclusion:

According to the results, it was determined that omeprazole can be formulated in mucoadhesive paste base. The best formulation showed an instant followed by a plateau release at about 45%.

Keywords: Mucoadhesive, Omeprazole, physicochemical evaluation

Formulation and Charactrization of Fe/Al as Dapsone in Vitro Efficient Delivery

Baharalsadat Ahmadi Moosavi, Abbas Pardakhty, Mehdi Ranjbar*

P265

Authors' Affiliations:
Student research committee, Kerman University of Medical Sciences, Kerman, Iran

Abstract Presenter:
Baharalsadat Ahmdimoosavi

****Correspondance:***
Mehdi Ranjbar

Coauthors:
Abbas Pardakhty

Abstract

Dapsone is a synthetic derivative of diamino-sulfone with anti-inflammatory and anti-bacterial properties. In recent research, sulphone compounds have attracted considerable attention due to versatile bioactive, acidic and anti-inflammatory properties bioactive [1]. Nanotechnology with the important strategy in preparation of new structures such as LDHs, exhibited diagnosis possibility at the cellular which this may significantly improve the diagnosis different concentrations of drugs? The chemical composition of LDH is generally expressed as [M(II)1-xM(III)x(OH)2]. Y-. zH2O, where M(II) is divalent metal cation, M(III) is trivalent metal cation, 'Y' is interlayer anionic species, 'n' is charge on interlayer anion, 'x' and 'y' are fraction constants. By virtue of this unique structure, LDHs have been widely explored as inorganic composite materials for drug/gene delivery, demonstrating controllable drug release and excellent biocompatibility. Compared to bulk LDHs, monolayer LDH (MLDH) nanosheets exhibit much higher specific surface and more combinative sites, leading to greatly enhanced surface activity for drug loading [3]. 0.495 (M) Mg(NO3)2·6H2O and 0.165 (M) Al(NO3)3·9H2Owere dissolved in 250ml ofwater to synthesize Fe/Al LDHwithMg: Al ratio of 3:1. To maintain the pH of the mixed precursor solution at 8, ammonia was dropwise added to itwith constant stirring for 24 h. The appearance of a white gelatinous precipitate indicated the formation of Fe/Al-LDH. The precipitate was collected by centrifugation and repeatedly washed by redispersing it in water followed by centrifugation (at 3000 rpmfor 5 mins) to remove excess nitrate anions. The washed LDH precipitate was then oven dried at 100C to getMgAl-LDH nanopowder. Subsequently, 2 g sodium salicylate was dissolved in 50 ml water of pH 7.5, and the solution was added to100 ml aqueous suspension in 0.0025(M) HNO3 and 0.75 (M) NaNO3 containing 1 g LDH. The pH of the LDH-salicylate mixture was raised to 9 by drop-wise addition of 0.01M NaOH. In the present study, salicylate intercalated Fe/Al-LDH nano hybrids were synthesized using the co-precipitationmethod. Successful intercalation of Salicylate in the interlayer space of Fe/Al-LDH was confirmed by XRD data and FTIR Spectroscopy of the intercalated nano hybrid. Salicylatewas loaded to the extent of 30wt.% in the LDH Salicylate formulation. The cumulative release profile of Salicylate in PBS (pH = 7.4) medium revealed nearly 80% release in 24 h at 37 °C, and the entire drug was released over a period of 48 h.

Keywords: Antioxidant, Optical properties, Layered Double Hydroxide, Drug delivery

Morphine extraction and removal from aqueous media by multiwall carbon nanotubes

Faezeh Shakermahani, Shekofeh Hassanzadeh, Maryam Kazemipour, Mehdi Ansari*

P266

Authors' Affiliations:
Pharmaceutics Research Center, Kerman University of Medical Sciences, Kerman, Iran. 2. Faculty of Sciences, Kerman Branch, Islamic Azad University, Kerman, Iran

Abstract Presenter:
Faezeh Shakermahani

Correspondance:
Mehdi Ansari

Coauthors:
Shekofeh Hassanzadeh
Maryam Kazemipour

Introduction:

Morphine belongs to a group of medications known as narcotic analgesics which will be prescribed for patients with cancer, kidney stone and sever traumatic pains [1]. The main goal of this study is to separate morphine in-vitro inoculated with it by carbon nanotubes and finding a safe, cheap and quick way for separating organic materials [2]. A goal which results in making filters for separating morphine from blood in patients with medication toxicity.

Methods:

Morphine concentration was determined by spectrophotometric method that was developed and validated in this study. Removing morphine from aqueous media was performed by both continuous and equilibration method. Concentration 100 mg/l of morphine was used for experiments. Factors affecting the absorption of morphine such as pH of the solutions, type and amount of the absorbent, absorbent capacity, temperature, contact time, and interferences were studied. Absorption results were fitted to either of Langmuir, Frundlich, and D-R isotherms to find the best isotherm and subsequently define the absorption mechanisms.

Results:

More than 80% of the morphine content of the solutions was removed by first pass through the column containing MWCNTs at pH 5.5. Morphine extraction in different temperatures showed that it is more extracted at lower temperature. Adsorption of morphine will come through plateau up to 40 minutes. Morphine absorption by 0.05 g of each of the adsorbents including MWCNTs, Fullerene C60, and activated charcoal were 100.0, 13.7, and 52.8%, respectively. It can be concluded that MWCNTs adsorb morphine much more than Fullerene and activated charcoal. Effect of adsorbent amount on the adsorption efficiency was also studied and it showed that amount absorbed were 80% and 93.7% for 0.1 and 0.2 g of adsorbent, respectively. Adsorption capacity of MWCNTs for adsorption of morphine was 71.3mg/g. Regeneration of the MWCNTs by NaOH 0.1 N showed better effect than neutral or acidic solutions.

Conclusion:

Generally, it can be concluded that carbon nanotubes have high level of adsorption for morphine so that one gram of it can adsorb 71.30 mg of morphine so it seems that it plays a significant role in removing toxicity.

Keywords: Morphine, Carbon Nanotube, Extraction, Removal

Development and validation of a new RP-HPLC method for simultaneous quantitation of Insulin and Pramlintide in a noninvasive and intelligent drug delivery system

Maryam Haghighi*, Jaber Emami

P267

Authors' Affiliations:
Isfahan university of medical sciences, Isfahan, Iran

Abstract Presenter:
Maryam Haghighi

****Correspondance:***
Maryam Haghighi

Coauthors:
Jaber Emami

Abstract:

A simple and rapid RP-HPLC method was developed and validated for simultaneous quantitation of Insulin and Pramlintide, two peptides which are secreted from pancrease and they are responsible for tuning blood glucose levels in healthy people. This isocratic RP-HPLC separation was achieved on a C18 µ-Bondopack column (250mm*4.6mm) using mobile phase of water: acetonitril solution (65:35 v/v) containing 0.1% Trifluroacetic acid at flow rate of 1ml/min and column temperature of 30˚C. Detection of both peptides was done by UV detector operated in single wavelength of 214nm. The achieved method was validated for specificity, linearity, precision, accuracy, robustness and limit of quantitation. Linearity was obtained in the concentration range of 45 to 300 µg/ml of insulin and 1.5 to 10 µg/ml of pramlintide (determined concentrations for standard curve was prepared according to native concentrations of these two peptides in body). The results of the analysis were validated statistically and recovery studies confirmed the accuracy and precision of the proposed method. The method was found to be simple, specific, precise, accurate and reproducible. The method was applied to determine loading capacity, entrapment efficiency and in-vitro release profile of a smart insulin/pramlintide delivery system for diabetic patients.

Keywords: Diabetes, Diabetes, Pramlintide, RP-HPLC, Smart drug delivery.

Enhanced degradation of the antibiotic sulfamethoxazole using heterogeneous electro-Fenton

Amir Emad Kheirieh, Maryam Dolatabadi, Saeid Ahmadzadeh*

P268

Authors' Affiliations:
Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Amiremad Kheirieh

***Correspondance:**
Saeid Ahmadzadeh

Coauthors:
Maryam Dolatabadi

Introduction:

Sulfonamides are synthetic antimicrobials, developed in the early 1900s. They work by providing a bacteriostatic effect on bacteria, first delay the reproduction of bacteria cells, and then prevent the cells from growing by inhibiting the production of folic acid, which is required for cell growth. Sulfamethoxazole (SMZ) is the most widely prescribed antibiotics in the US and other developed countries, and hence frequently detected in the environment (1, 2). The detection of the chemicals in treated drinking water and wastewater treatment plant effluent indicates that SMZ is not effectively removed during conventional water and wastewater treatment. Thus, it is an emerging issue to remove SMZ effectively from wastewaters before discharging them.

Methods and Results:

The central composite design was used to enhance the removal efficiency of SMZ by response surface methodology (RSM). The experiments were done under four levels of various operational parameters (3). The initial concentration of SMZ was varied among 5 to 50 mg L^{-1}, the current density ranging from 1 to 5 mA cm^{-2}, H_2O_2 ranging from 1000 to 2000 µL L-1, and reaction time ranging from 5 to 20 minute. The best removal efficiency of 96.4% found under the optimal operating condition of initial SMZ concentration 37.5 mg L-1, current density 3.0 mA cm^{-2}, H_2O_2 560 µL L-1, and reaction time of 10.0 min. the quadratic effect of H2O2 dosage and current density significantly improved the SMZ removal efficiency. However, according to the obtained results, a reverse proportion between the initial SMZ concentration and PH solution with removal efficiency was observed. The rate of the oxidation process of SMZ reduced by increasing the amount of H_2O_2 and Fe^{2+} ions, which might be due to reducing the amount of hydroxyl free radicals involved in the scavenging reaction.

Conclusions:

The kinetics investigations revealed that for the batch treatment system in the current work, the second-order model best fitted to the examined kinetics models. The amount of electrical energy consumption per each cubic meter of the treated wastewater was found to be 0.370 $kWh.m^{-3}$.

Keywords: Sulfamethoxazole, Heterogeneous electro-Fenton process.

Synthesis of novel nano sized technetium-99m– (chitosan-glutamine) conjugate as liver targeted contrast agent towards molecular SPECT/CT imaging

Maryam Nejati, Mehdi Shafiee Ardestani*

P269

Authors' Affiliations:
Faculty of Pharmacy, International Campus, Tehran University of Medical Sciences International Campus (TUMS-IC), Tehran, Iran

Abstract Presenter:
Maryam Nejati

Correspondance:
Mehdi Shafiee Ardestani

Abstract:

Medical diagnosis is always known as a complex process which relies ultimately on human perception and intellect to get information from different sources, sorting through many possible actions, and finally considering the best treatment for an individual patient. A lot of methods are developed aiming more accurate diagnosis and a better care as result, which molecular imaging is counted as one of the most important ones so far. The goal behind molecular imaging is to visualize biological processes non-invasively. Although molecular imaging modalities, such as PET and SPECT offer potential to detect diseases at molecular and cellular changes level, they suffer from a poor spatial resolution. Therefore, the current trend is to use dual modality systems which the combined strengths of morphological/anatomical such as CT and molecular imaging modalities are utilized. Advances in SPECT instrumentation, CT technology, and radiopharmaceutical development have led to SPECT/CT beyond its current level of performance.

In this study, chitosan and glutamine based biocompatible nanoparticles were synthesized prior to labelling with technetium-99m to introduce an efficient contrast agent (99mTc-chitosan-glutamine) for liver imaging. Furrier transform infrared spectroscopy (FTIR) and proton nuclear magnetic resonance (1H-NMR) applied to confirm conjugation. For further information, the chitosan-glutamine nanoparticles were characterized using scanning electron microscopy (SEM) and dynamic light scattering (DLS). 99mTc-chitosan-glutamine showed 90% radio chemical purity using TLC chromatography. In-vivo radiopharmaceutical studies were carried out by injection of 99mTc-chitosan-glutamine to mice followed by scanning the organs of interest using SPECT/CT technique. The whole body imaging process has conducted at three different times after injection, 15min, 60min and 120min. Consequently, the SPECT/CT results provided high activity level (%ID/g=29.74±7.42) at 120min for liver which statistically, had a significant difference compared to other organs. Thus, it is acceptable that 99mTc-chitosan-glutamine can be used as a candidate in liver targeting contrast agent via SPECT/CT. further? the targeting behavior of nano-conjugate on liver cells, the MTT results showing the more toxicity on cancerous Hep-G2 cell line than chitosan individually therefore it is encouraging to use this nano-conjugate as a drug carrier to improve liver drug delivery as well.

Keywords: Molecular imaging, Chitosan-Glutamine, SPECT/CT, Radiopharmaceutical, Technetium

Formulation and in Vitro Evaluation of Patches of Donepezil with Eudragit Polymers

Soghra Nosrati Fahim*, Seyed Alireza Mortazavi, Zahra Jafari Azar

P270

Authors' Affiliations:
Azad University of Medical Science, Tehran, Iran.

Abstract Presenter:
Soghra Nosrati Fahim

****Correspondance:***
Soghra Nosrati Fahim

Coauthors:
Seyed Alireza Mortazavi
Zahra Jafari Azar

Introduction:

Alzheimer disease is the most common cause of dementia that slowly destroys memory and? thinking skills. In this disease we have decreased amount of substance called acetylcholine (Ach). According to the studies Ach has important role in memory formation. One way to increase endogen Ach is inhibition of acetylcholinesterase enzyme. Donepezil hydrochloride is a reversible inhibitor of this enzyme that is used in moderate to severe stages of Alzheimer. Transdermal patch is a new dosage form which is prepared by polymers, plasticizer and permeation enhancers that can make continues release. This pattern of release is very important in control of symptoms of Alzheimer, because of decreased side effects and stable blood drug concentration. Transdermal patches can be better than oral tablets because they can release the donepezil during 24 hours and it can be suitable for patients who cannot swallow. The aim of this study was formulation of patches of donepezil with Eudragit polymers.

Methods:

In this study, circular patches of donepezil with 3 cm diameter was prepared by solvent evaporation method using Eudragit as polymer that make matrix of patches, PEG400 (polyethylene glycol) and PG (propylene glycol) and glycerin as plasticizer. These materials were used with different percentages and various combination of each groups. After formulations, different physicochemical tests were performed. As fallows weight, thickness assay, folding endurance, dissolution and skin permeation were done on all the formulations.

Results:

The best formulations were carried out in Eudragit S100 and PEG400 and glycerin and Eudragit S100 and PG and glycerin.

Conclusions:

Eudragit S100 is the best polymer that can control the release and the formulation which have appropriate physicochemical properties and skin permeation.

Keywords: Formulation, Donepezil, Patch, Eudragit, In vitro study

Investigation of Intestinal Permeability of Anti-Cancer Agent, Paclitaxel

Anis Shahnaei*, Hadi Valizadeh

P271

Authors' Affiliations:
Tabriz University of Medical Sciences, Tabriz, Iran.

Abstract Presenter:
Anis Shahnaei

Correspondance:
Anis Shahnaei

Coauthors:
Hadi Valizadeh

Introduction:

PTX is a cytotoxic chemotherapy agent which is administered intravenously. This route may enhance hypersensitivity and drug reactions in some patients (1) so, many researches have been focused on oral use of PTX. PTX is in the fourth class of biopharmaceutical classification system (BCS) and has low permeability and solubility (2, 3). In the present study, the intestinal permeability of paclitaxel (PTX) in male wistar rats by using Single Pass Intestinal Perfusion (SPIP) method was assessed. We hypothesized that PTX is a substrate for permeability glycoprotein (P-gp), therefore verapamil (VPL) was used in PTX's solutions to inhibit P-gp and enhance permeability of PTX into the intestine.

Materials and methods:

PTX solution and PTX in combination with VPL were perfused separately by a syringe pump into the cannulated intestine with SPIP method and samples were taken and analyzed by High Performance Lipid? Chromatography (HPLC) method and permeability coefficients (P eff) were calculated. For correcting water efflux through the rat intestine, Phenol Red (PR) solution were utilized.

Results:

The effect of increasing the concentration of PTX and PTX + VPL on its intestinal permeability and absorption were assessed by P eff of solutions. P eff of PTX solutions were 1.57E-04 ± 6.84E-05, 3.40E-05 ± 2.90E-05 and 7.56E-05 ± 2.51E-05 for 2.5, 5, and 10 µg/mL concentrations respectively. P eff of PTX + VPL solutions were 3.19E-04 ± 3.62E-06, 3.40E-04 ± 5.81E-05 and 2.36E-04 ± 8.97E-05 for 2.5, 5, and 10 µg/mL concentrations respectively. Repeated measure analysis was used by a general linear model to investigate the difference between PTX and PTX +VPL solutions while the concentration was increased. The difference between P eff of PTX and P eff of PTX + VPL was statistically significant (p = 0.000) (Figure of Abstract).

Conclusion:

PTX has limited intestinal absorption. Increasing the concentration of oral solutions of PTX could not increase its intestinal permeability. VPL could inhibit activity of P-gp. Thus, addition of VPL to PTX could potentially increase intestinal permeability of PTX.

Keywords: paclitaxel, verapamil, permeability glycoprotein, intestinal permeability, SPIP

Investigation of using pectin and chitosan as the main excipients for ibuprofen pellets

Foroogh Kalantari*, Ladan Nejati, Pooria Taghavimoghadam, Neda Bavarsad, Abbas Akhgari

P272

Authors' Affiliations:
Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract Presenter:
Foroogh Kalantari

****Correspondance:***
Foroogh Kalantari

Coauthors:
Ladan Nejati
Pooria Taghavimoghadam
Neda Bavarsad
Abbas Akhgari

Introduction:

Pellets are one of the solid dosage forms that have attracted a lot of attention today. These advantages include less size dispersion and high absorption. Pectin and chitosan can be effective as excipients in the pellet formulation. The aim of this study was using polysaccharides, pectin, and chitosan in pellet formulation and also to evaluate the probable interactions of these cationic and anionic polysaccharides with each other and with Ibuprofen in the pellet formulation.

Methods:

Different formulations containing ibuprofen, microcrystalline cellulose, and various ratios of chitosan: pectin were designed. The pellets were prepared by extrusion - spheronization method and dissolution studies for all formulations in phosphate buffer (pH=6.8) were carried out using basket model (50rpm) at 37°C within 8 hours. DSC1 and FTIR2 analysis, porosity, and density measurements and MDT3 calculations were also performed.

Results:

All prepared formulations had acceptable sphericity. Pellets produced by MCC did not disintegrate in dissolution liquid, while incorporation of pectin and chitosan in the formulations significantly increased the disintegrating during release test. The results of dissolution profiles showed that formulation F1 (containing 70% MCC4 and 30% drug) exhibited the lower drug release compared to the other pellets (containing MCC, pectin, chitosan and drug).

Based on DSC and FTIR analysis, no interactions between carboxyl group of pectin and NH_4^+ group of chitosan were observed.

Conclusions:

The results of the study showed that Pectin and chitosan, as natural, biocompatible, easy processing, low price, and available polysaccharides can be effective substituents for MCC in the formulation of ibuprofen pellets, while drug release profile is not effective enough.

Keywords: Ibuprofen, Microcrystalline cellulose, Polysaccharide

Cold atmospheric plasma in treatment of Trichophyton Rubrum

Atena Shapourzadeh, Mehdi Razzaghi-Abyaneh, Seyed- Mohammad Atyabi*

P273

Authors' Affiliations:
Islamic Azad University Damghan Branch, Damghan, Iran

Abstract Presenter:
Atena Shapourzadeh

****Correspondance:***
Seyed Mohammad Atyabi

Coauthors:
Mehdi Razzaghi-Abyaneh
Seyed- Mohammad Atyabi

Abstract:
In this research the effect of cold atmospheric plasma which contains helium and oxygen gases on growth rate of Trichophyton rubrum and also the activity of the produced kratinase enzyme and ergostrol have been analyzed. The mechanism contains two gas capsules and a power supply including electrodes which works with a radio frequency of 15 MHz and a voltage 10 kv. With utilizing the radio waves, the electric extraction begins and produces various active chemical types which spread rapidly outside the mechanism. The central electrodes accelerate the free electrons with the aid of radio frequency. These high-energy electrons under the non – elastic effect of charged particles cause the stimulation of molecule, atoms, free radicals and paired electron-ion. When the electric is being evacuated with the aid of new compounds, the ions and electrons disappear. There are a lot of causes for ringworm disease but one of them is the famous fungi called Trichophyton rubrum. Various ways have been used to treat with these fungi but they mostly take time. We have decided to create a new way for treating these fungi. The samples of the mentioned fungi are gathered from patients who referred to Pasture Institute of Iran. The samples have been cultured in SDA (saburo dextrose agar) medium. Afterwardes, culturing the positive rubrum samples inside the tubes of SDA plus chloramphenicol after 7-14 days keeping in 28 °C, We prepared the suspension cellular samples with density of 106 cell/ml and poured 100 microliters of it in a 96-well plates. Afterwards, samples have been treated with cold atmospheric plasma in the 90, 120, 150, and 180 seconds. The results are reported in charts, graphs, and pictures. The result obtained that the plasma flow indicates a significant difference in growth inhibition of Trichophyton rubrum, the fungus walls ergosterol, and keratinase enzyme activity.

Keywords: Atmospheric cold plasma, Trichophyton rubrum

Anti-psoriatic and toxicity evaluation of nanoliposomal methotrexate in imiquimod induced mice model

Mahdiyeh Bahramizadeh*, Mahmood reza Jaafari

P274

Authors' Affiliations:
Mashhad University of Medical Science, School of Pharmacy, Mashhad, Iran.

Abstract Presenter:
Mahdiyeh Bahramizadeh

****Correspondance:***
Mahdiyeh Bahramizadeh

Coauthors:
Mahmood reza Jaafari

Abstract:

Methotrexate (MTX) is one of the most effective drugs in the treatment of psoriasis. Since the systemic use of this drug has different adverse effects, the use of methotrexate is limited to patients who have not responded to the local treatment or when more than 20% of the body surface is involved. Therefore, it seems that topical use of methotrexate due tofewer side effect provides wider?? Application of this drug.

In this study we investigate the effectiveness and toxicity of topical nanoliposomal methotrexate (LM) on imiquimod (IMQ)-induced psoriasis like dermatitis in mice model. After shaving dorsal skin of the BALB/c mice, IMQ was used topically for 12 consecutive days. The onset of treatment with 8 different treatment groups including different concentration of LM started on the 5th day simultaneously.

Other groups were received PBS, hydrogel of MTX, simple liposome and lotion of betamethasone (as positive group). Appearance observation, histopathological examination and analysis of blood samples were collected and recorded in three time points. LM reduced inflammation and thickness score dose-dependently and significantly compared to the group receiving injected MTX. Whereas other groups didn't show dramatic decrease in these score at the same time interval. No liver, kidney, pulmonary and bone marrow toxicity were observed in the mice that received the LM. The results of this study showed that topical nanoliposomal MTX could be a topical option for the treatment of psoriasis with less toxicity.

Keywords: nanoliposome, methotrexate, topical, psoriasis, animal-model

Comparison the Effects of Nano-Curcumin and Curcumin on Liver Function in Sub Acute Paraquat Poisoning in Male Rat

Alireza Pelarak*, Yasaman Behnamfar, Akram Ranjbar

P275

Authors' Affiliations:
Student Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

Abstract Presenter:
Alireza Pelarak

****Correspondance:***
Alireza Pelarak

Coauthors:
Yasaman Behnamfar
Akram Ranjbar

Introduction:

Paraquat is one of the most common herbicides used in agriculture that can cause severe toxicity in humans and animals. In this study, we compared the effects of nano-curcumin and Curcumin on the liver tissue oxidation in subacute toxicity with paraquat.

Methods:

36 male albino Wistar 8 weeks? Were randomly divided into 6 groups. (n=6)

Group 1: receives normal saline

Group 2: receives Paraquat at a concentration of 5 mg / kg,

Group 3: receives Curcumin 30 mg / kg,

Group 4: receives Nanocorcinum 30 mg / kg,

Group 5: receives Curcumin + Paraquat at 5 mg / kg simultaneously,

Group 6: receives nano-corcomin + paraquat at a concentration of 5 mg / kg simultaneousl.

This treatment is continued for 7 days. At the end of the course, the serum and liver tissue samples were collected from all rats. Total Anti oxidation Capacity (TAC), Lipid Peroxidation (LPO), Thiol groups (SH), Liver enzymes (ALT, AST and ALP) were evaluated by spectrophotometry. Histopathological evaluation is also performed on the liver tissue. The value of p0.05 was considered significant.

Results:

In paraquat poisoned groups compared to healthy control group, Liver tissue damage, Lipid Peroxidation(LPO) and Liver enzymes (ALT,AST and ALP) were increased and Total Anti oxidation Capacity(TAC) and Thiol groups(SH) were decreased significantly(p=0.05). In treated groups compared to control poisoned group Lipid Peroxidation (LPO), Liver enzymes (ALT, AST, and ALP) and Liver tissue damage were decreased significantly and Total Anti oxidation Capacity (TAC) and Thiol groups (SH) were increased significantly.

Conclusions:

Curcumin and nano-curcumin decreased oxidative stress and liver tissue damage that caused by the conditions?? Poisoning with paraquat.

Keywords: Paraquat, curcumin, nano-curcumin, liver

Chitosan-modified PLGA nanoparticles tagged with CD8AP17s aptamer for targeted delivery of tacrolimus to T cells

Atena Mansouri, Khalil Abnous, Mona Alibolandi, Seyed Mohammad Taghdisi, Mohammad Ramezani*

P276

Authors' Affiliations:
Nanotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

Students Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Atena Mansouri

****Correspondance:***
Mohammad Ramezani

Coauthors:
Khalil Abnous
Mona Alibolandi
Seyed Mohammad Taghdisi
Mohammad Ramezani

Abstract:

TAC is an inhibitor of calcineurin which ultimately inhibits the production of IL-2, an essential component for the proliferation of T cells. Todays, calcineurin inhibitors such as TAC are the basis of most immunological suppression protocols after organ transplantation. Targeted delivery of TAC can reduce its side effects while reducing its required therapeutic dose. This study introduces a targeted delivery platform via chitosan-modified PLGA nanoparticles conjugated electrostatically with CD8AP17s aptamer to deliver TAC into T cells (MOLT-4 cells) which express CD8 as the target of aptamer. Also, Jurkat (CD8-) cell line was chosen as non-target cells to investigate the effects of the designed delivery system in-vitro. The particle size and zeta potential of the TAC-PLGA-CS-Apt nanocomplex were 345 nm and 13.7 mV, respectively. Release study showed an efficient TAC release from complex in citrate buffer (pH 5.5). The MTT assay showed that TAC-PLGA-CS-Apt nanocomplex was highly selective toward MOLT-4 cells. Complex increased the cellular uptake of TAC in MOLT-4 cells (target) while reducing its cytotoxicity in Jurkat cells (non-target). Our study showed that complex nanoconjugate could efficiently deliver TAC into MOLT-4 cell.ls as a model of CTL and it could be considered as a potential candidate for TAC delivery.

Keywords: Tacrolimus, Chitosan, CD8AP17s, PLGA, aptamer

Evaluation of Curcumin nano-micelle on proliferation and apoptosis of HT29 and Hct116 colon cancer cell line

Ramin Ataee*, Hamid Reza Mohammadi, Mohammad Shokrzadeh, Omid Akbari-Dafsari, Mona Modanlou, Abbas Mohammadpour, Nahid Amani

P277

Authors' Affiliations:
Pharmaceutical Sciences Research Center, Mazandaran University of Medical Sciences,Sari Iran

Abstract Presenter:
Ramin Ataee

****Correspondance:***
Ramin Ataee

Coauthors:
Hamid Reza Mohammadi
Mohammad Shokrzadeh
Omid Akbari-Dafsari
Mona Modanlou
Abbas Mohammadpour
Nahid Amani

Introduction:

Curcumin is a natural polyphenolic substance with anti-oxidative, anti-inflammatory and anti-cancer? Properties. Its therapeutic potential is substantially hindered by the rather low water solubility, rapid metabolism and low bioavailability, hence the need for suitable carriers. In the present study we aimed to evaluate anti proliferative and apoptotic effects of polymeric micelles of curcumin on two colorectal cancer cell lines.

Methods and Results:

Cancer cells HT29, HCT116 cells were exposed to different concentrations of nanocurcumin (1, 50, 100, 250 and 500 µg/ml). After 48 hours of incubation, cell viability was evaluated by MTT assay. Also, Annexin V-FITC and Propidium iodide staining were performed by flowcytometry for evaluation of apoptosis.

According to MTT assay results, IC50 value of nanocurcumin in HT29 andHCT116 was obtained; 70.63 and 123.9 µg/ml, respectively. We also found that nanocurcumin was able to induce significant apoptosis in cancer cells which was comparable with cisplatin.

Conclusions:

These results revealed remarkable anti-proliferative and apoptotic effects of polymeric nanomicelles curcumin in colorectal cancer cell lines.

Keywords: Curcumin, Nano-Micelle, Colon Cancer, Apoptosis, proliferation

One-pot synthesis of some new Triazolyl-Flavanone derivatives using CuI nanoparticles as catalyst

Mahsa Maleki*, Amanollah Zarei Ahmady, Mosadegh Keshavarz, Maryam Kardani

P278

Authors' Affiliations:
Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Abstract Presenter:
Mahsa Maleki

****Correspondance:***
Mahsa Maleki

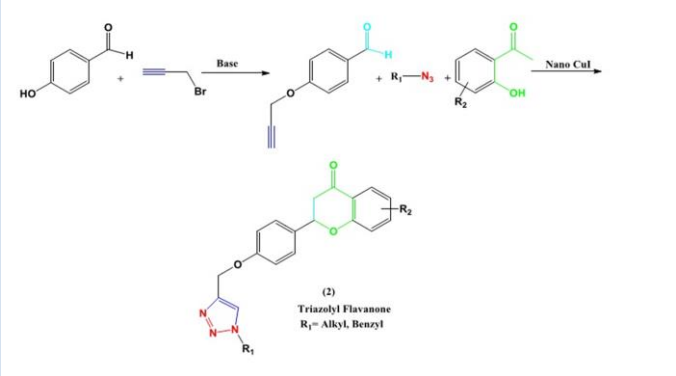
Coauthors:
Amanollah Zarei Ahmady
Mosadegh Keshavarz
Maryam Kardani

Abstract:

Nowadays nanocatalysts have been introduced as effective and suitable alternatives for classic catalysts. The high surface-to-volume ratio of nanoparticles significantly enhances catalytic properties and selectivity of the reactions, while their fundamental properties and heterogeneity are maintained. The goal of this project is to synthesize new derivatives of bifunctional compounds called Triazole Flavonone, which due to the presence of two pharmacophores on one molecule, show pharmacological properties of both pharmacophores simultaneously.

Initially, copper iodide nanoparticles were prepared and catalyzed reaction between proparginated 4-hydroxybenzaldehyde, alkyl azide and 2-hydroxy acetophenone, then Triazole-Flavonone were prepared (scheme 1).

Notably, in this synthesis, copper iodide nanoparticles used as catalyst for two cycloadditions of flavonene and triazole.



Keywords: Triazolyl-Flavanone, nanoparticles, catalyst

Development and characterization of electrospun diclofenac nanofibers as a novel fast dissolving drug delivery system for rapid pain relief

Nima Sharifi*, Azadeh Haeri, Maryam Torshabi, Seyed Alireza Mortazavi

P279

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Department of Dental Biomaterials, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Nima Sharifi

****Correspondance:***
Nima Sharifi

Coauthors:
Azadeh Haeri
Maryam Torshabi
Seyed Alireza Mortazavi

Introduction:

Efficacy and onset of pain relief are critical in acute pain management which are limited in the standard and conventional dosage forms. Designing fast action analgesics could improve clinical outcomes and reduce excessive dosing (1). Additionally, mouth-dissolving formulations are beneficial for patients with difficulty in swallowing (2). As one of novel drug delivery system, nanofibrous mats could provide quick disintegration and onset of action due to fibril nanostructure and high surface area. Diclofenac sodium is a nonsteroidal anti-inflammatory drugs (NSAIDs), commonly used for the management of mild-to-moderate pain (3) and in this study, it is incorporated into electrospun nanofibers.

Methods and Results:

Three fast dissolving mats of diclofenac sodium were prepared by electrospinning of aqueous solutions of polyvinylalcohol (PVA, 12% w/v), polyvinylpyrrolidone (PVP, 10% w/v), and polyethylenoxide (PEO, 8% w/v) polymers. For comparison, three film formulations were prepared by solvent casting method by the same drug to polymer ratios of nanofibers. The morphology and diameter of the mats were evaluated using scanning electron microscopy (SEM) and atomic force microscopy (AFM). Diclofenac content uniformity was assessed using UV at 275 nm wavelength. The disintegration test and dissolution kinetics of nanofiber mats and films were evaluated in simulated saliva.

The SEM and AFM observation showed very uniform and bead-free fibers with average diameters within the range of ~300-600 nm for all three nanofiber formulations. Drug content in nanofibers and films was 97-100% and 88-100%, respectively. Disintegration times of PVA-, PVP-, and PEO-based nanofibers were 0.33 sec, 1.2 sec, and 10 secs, respectively. After 5 min incubation in simulated saliva, percentages of drug released were 87%, 96%, and 86% for PVA-, PVP-, and PEO-based nanofibers, respectively. All nano formulations showed shorter disintegration time and higher release rate compared to film formulations. Among nanofibers prepared from different polymers, PVP nanofibers exhibited short disintegration time (1 sec) with almost complete drug release in 5 min.

Conclusions:

PVP based electrospun diclofenac nanofiber is a promising oral fast dissolving system which could provide rapid analgesic action even in children, older people, and patients with dysphagia.

Keywords: nanofibers, electrospinning, diclofenac sodium, fast dissolving system, oral film

The effect of cold atmospheric plasma for drug powders sterilization

Seyed Alireza Atyabi*, Mohammad Sadegh Khosravi, Mesbahodin Salami, Seyed Ali Nojoumi

P280

Authors' Affiliations:
Tehran University of Medical Science, Tehran, Iran.

Abstract Presenter:
Seyed Alireza Atyabi

****Correspondance:***
Seyed Alireza Atyabi

Coauthors:
Mohammad Sadegh Khosravi
Mesbahodin Salami
Seyed Ali Nojoumi

Abstract:

Cold atmospheric plasma (CAP) has a great potential for sterilization in the pharmaceutical industry, by deactivation of bacteria, fungus, microbe, and other microorganisms where conventional methods are not applicable. The CAP acts under atmospheric conditions at 37°C. Only a small fraction of gas atoms and molecules, which are the main carriers of heat, collide with electrically generated highly energetic electrons. This results in further excitation, ionization, and dissociation, while the plasma remains "cold". Therefore, we investigate here whether CAP is able to denature/modify protein to investigate the sterilization of the raw material containing protein. The aim of this study is analyzing cold atmospheric plasma effect on pharmaceutical products specially protein complexes.

Different proteins were treated with CAP jet in Helium gas for 60, 90, and 120 seconds. The antimicrobial effects on Gram-negative and Gram-positive bacteria of clinical relevance, as well as the fungus Candida albicans and Trichophyton rubrum, were tested. All micro-organisms disappeared, and analyzing the structural changes of protein using circular dichroism (CD) and fluorescence. The results of the CD showed that the classical spiral structure of the protein in the treatment solution has not changed. Our results showed that the CAP can be used for protein sterilization without any change in stability and activity of them.

Keywords: Cold atmospheric plasma, Protein, sterilization

Computational study of the thermodynamic and physicochemical properties of doxorubicin lipophilic derivatives regarding to their anticancer effects

Hoda Jalali, Malahat Rezaee , Ali Asghar Rastgari*

P281

Authors' Affiliations:
Department of Molecular and Cell Biochemistry, Faculty of Biological Science, Falavarjan Branch, Islamic Azad University, Isfahan, Iran

Abstract Presenter:
Hoda Jalali

****Correspondance:***
Ali Asghar Rastgari

Coauthors:
Malahat Rezaee
Ali Asghar Rastgari

Introduction:

The incidence of cancer has grown dramatically in recent decades. Doxorubicin is one of the medicines used to treat various types of cancers. It is very hydrophilic with a very short half-life. Due to its high solubility, it is necessary to increase the dose of doxorubicin for penetration into the cells. It causes some problems for the patients such as destruction of healthy cells, and consequently the weakening of the patient's physical strength. An important way to prevent these problems is to use doxorubicin lipophilic derivatives. Computational simulation can be a suitable method to design lipophilic derivatives of the drug and study their thermodynamic and physicochemical characteristics.

Methods and Results:

In this study, Hyperchem was used as a strong Software. The conjugates of fatty acid-doxorubicin (derivatives of doxorubicin) were simulated by the software in a manner similar to the use by Chhikara et al. (2011) in an experimental study. Nine derivatives of doxorubicin were designed and free energy changes (ΔG), log P value, hydration energy, polarty, and volume of doxorubicin derivatives were calculated and compared.

As the main results we can refer to: 1) Free energy changes (ΔG) related to doxorubicin derivatives gradually were decreased with increasing the chain length of attached fatty acyl groups, 2) There was a gradual increase in the amount of log P, hydration energy, polarty, and volume of doxorubicin derivatives to increase in chain length of the fatty acid moiety. Also, it was concluded that efficient effect of Doxorubicin acyl conjugates, in particular FA.5Doxo and FA.6Doxo, could be due to their higher half-life and suitable thermodynamic and physicochemical properties.

Conclusions:

According to the results, it can be concluded that Doxorubicin Fatty Acyl Conjugates (FA.5Doxo and FA.6Doxo) are not pre-drugs and can be used as drugs for the treatment of cancer. Considering the achievements in this study, it is suggested that anticancer drugs could be designed based on the modeling characteristics to increase the treatment efficiency.

Keywords: Doxorubicin, HyperChem, Anticancer

Study on the effects of drug physicochemical properties in drug delivery to burnt tissue through microneedle

Erfan Fattahi, Hamidreza Moghimi*, Fatemeh Ghorbani-Bidkorbeh*

P282

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Shaheed Beheshti Medical University, Tehran, Iran

Abstract Presenter:
Erfan Fattahi

Correspondance:
Hamidreza Moghimi
Fatemeh Ghorbani-Bidkorbeh

Abstract:
Burns which are one of the devastating forms of trauma can be caused by different ways like heat, electricity, chemicals, and even radiation. Due to drug delivery difficulties, management of healing burn wound is the most challenging issue. Among intervention methods for treatment, transdermal therapy has received maximum compliance of a patient because of its elementary, non-invasive approach, and safety. Here, we used a new approach of transdermal drug delivery using microneedle (MN). This is a new drug delivery system and new treatment modality, which can transfer drugs to the lower layers by increasing skin permeability. The aim of this study was evaluation of the effects of drug size in drug absorption into burnt tissue. Hydrophilic model drugs; Diclofenac (small molecule) and Vancomycin (large molecule) were employed and their permeation through human third degree burn scars was studiedstudied in-vitro using static diffusion cells (Franz cell) at 32° C for 24 hours. After applying microneedle on the burn skin, which was fixed on Franz cell, drug saturation solution was defined as donor phase and sampled every two hours. To determine drug concentration in the receptor phase, UV spectrophotometry method at specific wavelengths was used. The results showed that microneedle application on the burnt skin had important role in increasing the absorption of drugs, as Diclofenac and Vancomycin were absorbed 238.8%, 129.81%, respectively, more than ordinary drug application (without microneedle). Drug absorption increase was even more significant in the case of crosswise microneedle application. Therefore, it can be concluded that microneedle application on the skin changes the skin barrier properties. Microneedle has been employed to deliver a model of large or small hydrophilic drugs into the skin. Importantly, this is a one-step delivery strategy for the drug delivery hydrophilic agents. Therefore, it represents a significant progression in exploitation of MN for successful transdermal delivery of a much wider range of drugs.

Keywords: Burn-eschar, Drug Delivery, Microneedle, Diclofenac, Vancomycin

Prediction of new Hsp70 inhibitors based on quinazoline scaffold by virtual screening method

Fatemeh Mozaffariyan, Monir Bazmi, Maryam Abbasi*

P283

Authors' Affiliations:
Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

Abstract Presenter:
Fatemeh Mozaffariyan

***Correspondance:**
Maryam Abbasi

Coauthors:
Monir Bazmi
Maryam Abbasi

Introduction:

Heat shock proteins (Hsps) are an extremely evolutionarily preserved group of chaperone proteins. Hsps are categorized into families by their molecular weights: Hsp100, 90, 70, 60, 40, and small Hsps. Hsp70 plays many roles in cellular processes including the correct folding of denatured proteins to avoid their aggregation and ubiquitination. Following the cellular stresses, the expression levels of Hsp70 are increased, thus inhibition of Hsp70 would be a good treatment for cancer disease. Many compounds (natural and synthetic) have introduced as Hsp70 inhibitors, among these, we chose quinazoline as lead compound for virtual screening studies.

Methods and Results:

1000 compounds with quinazoline scaffold were chosen from ZINC (www.zinc.docking.org) database that were filtered using Lipinski's rules. First, docking validation was performed by re-docking co-crystallized ligand with Hsp70 protein (PDB ID: 4IO8) by AutoDock 4.2. Then, virtual screening was done. All of the results were sorted in terms of the binding energy and orientation of ligands in the active site of the Hsp70 protein. The best ligands according to the binding energy and the essential interactions with the active site were chosen.

Conclusions:

The findings indicated that new quinazoline compounds were perched in Hsp70 active site and we can introduce them as new Hsp70 inhibitors for future studies.

Keywords: Hsp70 inhibitor, Docking, Virtual screening

Synthesis of N-arylsulfonyl hydroxy proline derivatives as potential carbonic anhydrase II inhibitors.

Hanieh Rahimi, Reza Khodarahmi, Hadi Adibi*

P286

Authors' Affiliations:

Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Chemistry, Islamic Azad University, Tehran

Medical Branch, Tehran Iran Pharmaceutical Sciences Research Centre, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran
Medical Biology Research Centre, Faculty of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Hanieh Rahimi

***Correspondance:**
Hadi Adibi

Coauthors:
Reza Khodarahmi

Introduction:

Primary arylsulfonyl chloride the most efficient metal binding group to design inhibitors for the metallo-enzymes carbonic anhydrases (CA, EC 4.2.1.1), being its structural features ideal for the binding to the ion present at the bottom of the active site cavity and the residues nearby. A series of hydroxyl proline and arylsulfonylchloride were synthesized, then the compounds were characterized by NMR, IR, MS techniques. Human CAII was purified from expired packed red blood cells. The inhibitory activities of the synthesized compounds against CAII were then assessed using DNSA as the fluorescent active probe and measuring the enzyme esterase activity and the inhibition parameters (IC50, Ki values) were calculated. Some of compounds had micromolar affinity for CAII. Furthermore, SAR analyses were done for the test compounds.

Methods and Results:

The tested compounds were synthesized via the reaction of hydroxy proline and arylsulfonyl chlorides in CHCL3 in the presence of NH3 and H2O at 0 °C.

Results: The results show our compounds have inhibition activity to carbonic anhydrase. The most potential compound was (HR9) (IC50=6.491uM).

Conclusions:

In summary, we have synthesized and evaluated a novel series of hydroxyproline derivatives with potential inhibitor carbonic anhydrase effects. The results obtained showed the test compounds had IC50 more than the control drug.

Keywords: carbonic anhydrase II inhibitors, Hydroxyproline

Green Synthesis and Detection of Bi (OH)3/Chitosan Nanostructures by Hydrothermal Synergistic Method to Investigate the Antimicrobial Effects

Fatemeh Mehrabbi, Mohammad hasan Moshafi, Mehdi Ranjbar*

P287

Authors' Affiliations:
Student research committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Fatemeh Mehrabbi

****Correspondance:***
Mehdi Ranjbar

Coauthors:
Mohammad hasan Moshafi

Abstract:

Due to the direct action mechanism against bacteria, nanostructures can remain relatively effective against bacterial resistance mechanisms, which could be considered as futuristic alternatives to antibiotics. Nanostructures commonly used for this purpose include metals, metal oxides, and organic nanostructures, which have different powers to fight microbes, as well as physicochemical properties and their mechanism of action. Although most nanostructures are produced by generating free species Oxygen has its own antimicrobial effects, some of them work through their physical structures or create metal ions. In the last two decades, the use of metallic nanoparticles in the diagnosis of diseases, drug delivery systems, and especially as antimicrobial agents, has been particularly noted [1]. In another study on metal nanoparticles, AgO and ZnO composite resin nanoparticles on Streptococcus mutans and Lactobacillus sp were used and the final result was obtained that these nanoparticles showed good antimicrobial activity against two microbes that are present in the oral cavity [2]. In another study, E. coli, B. subtilis and S. aureus were used to study the antibacterial effect of CuO nanoparticles with a particle size of 20-30 nm, and the result of this experiment showed a very toxic effect on the tested microorganisms [3]. A solution of 5% by weight of bismuth nitrate dissolved in a 1: 2 ratio of distilled water and ethanol to a mono-molar solution of profit is added. The resulting mixture is heated at 30 ° C for 30 minutes with the aid of a magnetic stirrer and simultaneously on the heater to remove the organic solvent phase on the refrigerant system. Then, the process of coordination and nucleation in the aquatic environment is achieved by adjusting profits. The solution is then centrifuged through the filter and is washed several times with water and ethanol and dried at 50 ° C in the vacuum oven. During the process of proportional to precipitation, we will increase the natural stabilizer of lactose. Then, in order to form the nanocomposite, 50 milligrams of chitosan precipitate was dissolved in 20 ml of dimethyl sulfoxide twice, distilled into an additional superconducting balloon and the reaction mixture was heated to 120 microns for exposure to microwave radiation. Antibacterial activity of Bi (OH)3/Chitosan nanocomposites was performed on 12 bacterial isolates include Escherichia coli, Klebsiellapneumoniae ,Pseudomonas aeruginosa, Serratiamarcescens , Salmonella typhi, Acinetobacterbaumannii, Citrobacterfreundii, Proteus mirabilis, Staphylococcus aureus, Bacillus cereus and Bacillus subtilis.The bacteria were propagated on nutreint Agar (Merck, Germany) at 37°C, and maintained at 4°C .In this work, research into the extent of preventing microbial growth is investigated after the construction of nanoparticles in the size and dispersion of the microbes. After making nanoparticles and investigating nanostructures on bacterial strains, we found that 32% of nanoparticles prevent the growth of bacteria in the control.

Keywords: Antibactrial, Bi (OH)3/Chitosan, Antioxidant, Nanostructures.

Hyaluronic acid/Chitosan-coated nanoliposome as targeted Inulinase carrier against A549 lung cancer cell line

Soheil Abbaspour-Ravasjani*, Maryam Mohammadi, Mahdi Zeinali, Behrooz Shokouhi , Hamed Hamishehkar

P290

Authors' Affiliations:
Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Abstract Presenter:
Soheil Abbaspour-Ravasjani

****Correspondance:***
Soheil Abbaspour-Ravasjani

Coauthors:
Maryam Mohammadi
Mahdi Zeinali
Behrooz Shokouhi
Hamed Hamishehkar

Introduction:

Inulinases (EC: 3.2.1.7) are well-known hydrolyzing enzymes that have been considered in biotechnology and food industries to hydrolyze inulin and polymers containing fructose. According to previous studies, the anti-cancer activity of Inulinase have been approved. Over the years, vesicular systems such as liposomes have gained noteworthy interests in pharmaceutical, biotechnological, and medicine fields due to their natural ingredients and biodegradability. Liposomes are formed by the self-assembly of phospholipid molecules in aqueous solutions which can entrapped both hydrophilic and lipophilic substances. The liposomal membrane can be modified by polymeric layers to create the positive charges on their surface and increase their electrostatic intractions with negatively charged ligands. Chitosan as linear polysaccharide is widely applied in the biomedical and biotechnological fields due to its biocompatibility, biodegradability, and non-toxicity. It has been demonstrated that the coating of liposome with chitosan (chitosome) can improve the structural properties of liposomes and increase their targeting efficiency. Among the several targeting agents, hyaluronic acid (HA) has been extensively applied as an active targeting ligand to treat the lung cancer. Therefore, the objectives of the current paper are to (i) prepare the HA targeted chitosome, (ii) study the characteristic features of the synthesized formulasions, (iii) immobilize the inulinase on HA targeted chitosome, and (IV) Investigate the in-vitro anti-cancer activity of nano formulations by assessment of their cellular cytotoxicity, apoptosis, and DNA fragmentation.

Methods and Results:

Liposome was produced by thin layer hydration-sonication method. Chitosome was prepared by adding 0.1% chitosan to prepared liposome under continues stirring. The conjugation ofenzyme and HA to the surface of the chitosome was performed via electrostatic interaction. The average size of liposomes, chitosome, and inulinase immobilized on HA targeted chitosome were 80.2, 141.3, and 163.1 nm, respectively. The zeta potentioal measurements showed -12.1, +43.1, and -3.2 mV for mentioned groups. The in-vitro anti-cancer activity of nano formulations showed that the targeted inulinase presented the higher cell cytotoxicity and apoptotic effects as compared to free and non-targeted inulinase.

Conclusions:

The results of this study revealed that the targeted delivery of the inulinase can improve the cell cytotoxicity, cell uptake, and apoptosis rate.

Keywords: Liposome, Target Therapy, Cancer, Inulinase, A549

Investigating the anti-bacterial effects of *Mentha Longifolia* encapsulated in G2 dendrimer on E. Coli Staphylococcus aureus and Escherichia coli bacterium

Sahar Javadi, Roya Karimipourkashani, Mehdi Shafiee Ardestani*

P291

Authors' Affiliations:
Tehran University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Sahar Javadi

Correspondance:
Mehdi Shafiee Ardestani

Coauthors:
Roya Karimipourkashani

Abstract:

Regarding the recent developments in nanotechnology and tendency to use natural preservatives, the aim of this research was to determine the chemical compositions and antimicrobial effects of *Mentha longifolia* essential oils encapsulated in G2 dendrimer against Staphylococcus aureus and Escherichia coli bacterium. In this research, G2 dendrimer nanoparticles as a new generation of dendrimers were synthesized and conjugated with *Mentha longifolia* essential oils. The essential oils of *Mentha longifolia* were soaked and prepared by Clevenger and after drying they were encapsulated into G2 dendrimers. Its compounds were determined by GC-Mass spectroscopy, then the antimicrobial effects of *Mentha longifolia*- G2 dendrimer mixture were studied on a gram-positive bacterium, Staphylococcus aureus and a gram negative one, Escherichia coli. The results obtained from MIC, DLS, and FTIR analysis showed that *Mentha longifolia*- G2 dendrimer nano-composition was a new structural construct that had high usability and strong antimicrobial effect on Staphylococcus aureus and Escherichia coli bacteria.

Keywords: G2 dendrimer, Mentha longifolia- G2 dendrimer, Staphylococcus aureus, Escherichia coli, Antimicrobial effect

Fabrication of hollow poly acrylic acid nano gels via emulsion polymerization as a model for loading of drugs

Sorosh Ziarati, Majid Karimi, Faranak Mahdavi, Elham Askarizadeh*

P292

Authors' Affiliations:
Department of applied chemistry, faculty of pharmaceutical chemistry, Tehran medical sciences Islamic Azad University, Tehran, Iran.

Abstract Presenter:
Sorosh Ziarati

**** Correspondance:***
Elham Askarizadeh

Coauthors:
Majid Karimi
Faranak Mahdavi

Abstarct:

Today, studies on the controlled release of drugs and other bioactive agents from drug-delivery systems have attracted considerable attention. In this method, chemical or biological active agents are delivered to the intended target at the appropriate speed and for the desired duration.

Polymer carriers are one of special importance among numerous methods for obtaining systems in which drug is released at variable speeds. In fact, polymers are the most important tools for preparing novel drug-delivery systems due to their unique properties, including substance permeability, control mixing with other substances, easy manufacture, and biocompatibility.

Of various types of polymers used for this purpose, hydrogels have attracted considerable attention. Hydrogels are completely permeable to hydrophilic active agents with a high molecular mass. This property in addition to the high biocompatibility of hydrogels has motivated studies on these polymers for using in the slow release of proteins such as insulin, aprotinin, tumor antigens, and luteinizing hormone. Furthermore, hydrogel membranes have numerous applications as carriers of water-insoluble drugs such as steroids.

One of the common in situ synthesis methods in polymerization is emulsion polymerization which is divided to mini, nano, micro and Pickering emulsion. Pickering emulsions is a suspension polymerization method by using solid particles as stabilizer to fabricate polymer beads. This method is a straight forward method for fabrication micro and nano spheres hybrid polymer. These compounds have different applications, especially in drug delivery, food industry, and purification of cosmetic materials.

In this study by using the method of in situ Pickering miniemulsion polymerization, poly acrylic acid (PAA) hollow nanogels are synthesized. With regards to extensive studies of PAA abilities in drug loading and drug delivery, the ability of produced nanogels in drug loading are investigated in different pH. The BSA protein is used as drug model. The Bradford assay is applied to determine the ability of nanogels in drug loading. The PAA nanogels were characterized by scan electron microscopy (SEM), DLS, and Infrared spectroscopy. Uv-Vis spectrophotometer was applied in Bradford method. The data shows that the maximum BSA loading capacity can reach as high as 200% in pH=5.

Keywords: nano gels, Hollow poly acrylic acid, drug loading

Bile salt-based self-emulsifying drug delivery system for oral delivery of tamoxifen citrate

Armin Jalili, Marjan Daeihamed*

P293

Authors' Affiliations:
School of Pharmacy, Guilan University of Medical Sciences

Abstract Presenter:
Armin Jalili

****Correspondance:***
Marjan Daeihamed

Introduction:

Tamoxifen (TMX) is a selective estrogen receptor modulator and the first choice in breast cancer prevention and treatment (1). It has a weak alkali (pka 8.8) with a lipophile structure and low solubility in water (2). It also undergoes to hepatic first-pass metabolism and is a substrate of P-glycoprotein-mediated efflux (3). So its oral bioavailability is low and needs to be improved (4). Different lipid-based formulations have been suggested to increase oral absorption (5). Self-emulsifying drug delivery systems (SEDDS) are because of the lipid-based formulations which are made up of oil, surfactant, and the drug without aqueous phase and form emulsions upon contact with the gastrointestinal fluids and under peristaltic-like movements (6). Surfactants are essential components of SEDDSs, however; they may cause digestive irritations and systemic toxicities. Bile salts have been used for oral delivery of many lipophilic drugs. In this study, bile salt-based SEDDSs are studied for the first time as a safe and effective alternative for oral drug delivery of Tamoxifen.

Methods:

The Solubility of TMX in different excipients were measured. Nanoemulsions were prepared by the spontaneous emulsification method (aqueous titration). Various oils, surfactants, and co-surfactants were screened for their ability to form nanoemulsions. The pseudo-ternary phase diagrams were constructed in order to obtain the most appropriate composition of SEDDS formulation. The optimum formulation was prepared and the globule size, cloud point, stability, and release studies were conducted.

Results:

Among different studied oils (sesame oil, oleic acid, isopropyl myristate, and triacetin), triacetin showed 11-fold(?) more solubility than water and a larger micro/nano-emulsion region on pseudo-ternary phase diagrams with various ratios of Tween 80, polyethylene glycol 400, isopropyl alcohol (IPA), and sodium taurocholate (Tau). Adding bile salts to the formulation widened the region of formulation. The ternary phase diagrams showed that among 1-5% Tau in IPA, PEG 400 showed proper emulsification region and formulation properties.

Discussion and Conclusion:

Bile-salt based SEDDSs are suggested for the first time as a new oral delivery system for TMX and could enhance the solubility of TMX.

Keywords: bile salt, microemulsion, self-emulsifying drug delivery system (SEDDS), tamoxifen

POSS Complexation for brachytherapy applications

Sana Pirmardvand Chegini, Mohammad Imani, Mojgan Zandi, Parvin Shokrollahi*

P294

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy and Novel Drug Delivery Systems Research Centre, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract Presenter:
Sana Pirmardvand Chegini

****Correspondance:***
Parvin Shokrollahi

Coauthors:
Mohammad Imani
Mojgan Zandi

Introduction:

Nowadays, one of the concerns in medical world is cancer and no certain cure has been found for it. Several methods including chemotherapy and radiotherapy are used to control the progress of the disease and reduce its effects. Radiotherapy by radiation source aims to destroy cancer cells with minimal destruction in healthy tissues. Brachytherapy is a type of radiotherapy that the radiation sources (lanthanide metals) are placed inside or next to the cancerous tissue which requiring treatment and is used as an effective treatment for some types of cancers. This method can be done involving the radioactive source in a polymeric matrix that is placed near the cancerous tissue.

The problem with the usage of these metals are inorganic compounds in comparison with polymer substrates have high surface energy so this compound didn't distribute very well in the polymer matrix. The metal which used as active drug in a complex structure could have better distribution in the polymer so attempted to synthesize a large complex of metal with a suitable ligand to overcome this problem.

Method:

Selecting the appropriate ligand with organic substitutes and type of metal-containing complexes trapped in the polymer matrix, can help to improve the distribution of active metal. In this study, polyhedral oligomeric silsesquioxane-triol (POSS) with incomplete cage structure and organic chain for the formation of metal complex was used. FTIR, UV spectrophotometry, TGA, fluorescence spectroscopy, and photoluminescence were used to characterization.

Result and discussion:

FTIR, UV spectrophotometry, TGA, fluorescence spectroscopy, and photoluminescence confirmed synthesis of metal-POSS complex. POSS with general formula RnSinO1.5n, has a silicon cag, and hybrid organic – inorganic properties. EDAX results shown uniform distribution of complex in polymer matrix. Finally, complex composites (5wt%) with polyurethane based on polycaprolactone and hexamethylendiisocyanat were prepared and sent for cytotoxicity tests. Test results showed no cytotoxicity effect on L929 cells.

Keywords: Brachytherapy, cancer, POSS, complexation

Preparation and optimization physicochemical characteristics of Dex-plga nanomicelles loaded Hydrocortisone as a drug delivery system

Shifteh Malek Hosseini*, Leila Behboud

P295

Authors' Affiliations:
Student Research Committee, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran.

Abstract Presenter:
Shifteh Malek Hosseini

Correspondance:
Shifteh Malek Hosseini

Coauthors:
Leila Behboud

Introduction:

Glucocorticosteroids are a product of the adrenal cortex and perform a staggering number of physiological effects essential for life. Hydrocortisone is a low potency glucocorticoid which its clinical use is largely predicated on its anti-inflammatory and immunosuppressive properties [1]. Polymers incorporated with therapeutics can be bioactive to provide their own therapeutic benefits or biodegradable to improve release kinetics and prevent carrier accumulation [2]. Poor water solubility is the major defect of this drug that causes manifestation of side effects. The polymeric self-assembled nanoparticles offers some unique advantages, including core-shell morphology, site-specific drug delivery, and avoids unwanted side effects. Moreover, micelles remain stable in blood circulation for prolonged period of time [3]. Dextran is widely used for various biomedical applications due to their water solubility, prolonging the half-lives of drugs, and biocompatibility. Because of this reasons, loading of Hydrocortisone into Dextran-PLGA micelles can decrease its side effects.

Materials and methods:

Dextran-PLGA copolymer incorporating Hydrocortisone was synthesized to make polymeric micelles for drug delivery. Physicochemical properties of the fabricated system were evaluated with FT-IR, NMR, TEM, and critical micelle concentration of the fabricated system and drug release was determined.

Results:

In this study we prepared Hydrocortisone encapsulated polymeric micelle of PLGA grafted Dextran copolymer. Chemical bonding of Dextran-PLGA was confirmed with FT-IR and NMR. Critical micelle concentration of polymer for micelles was 50 □g/ml. The average particle size was around 300 nm with appropriate size distribution and their morphology showed spherical shapes.

Discussion and Conclusion:

We rendered dextran using PLGA copolymer as a hydrophobic domain, that is, PLGA acts as a drug incorporation site with biodegradability and dextran main chain acts as a hydrophilic outer-shell of the nanoparticles. Hydrocortisone bonds to hydrophobic PLGA in the core of the micelle and Dextran as a hydrophilic polymer on the surface of the micelle leads to dissolution of the micelle in body's fluids and allows the micelles to bypass the reticuloendothelial systems. This model of drug delivery leads to decrease in drug side effects and better compliance of patients and can be used in many inflammatory diseases as a drug delivery system. Nanomicelles, Hydrocortisone, Drug delivery systems.

Keywords: Nanomicelles, Hydrocortisone, Drug delivery systems

A simple preparation method for quercetin nanoparticles via thin film sonication: effect of surfactant type and sonication time

Pegah Cheshmehnoor, Simin Dadashzadeh, Noushin Bolourchian, Azadeh Haeri*

P296

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Pegah Cheshmehnoor

Correspondance:
Azadeh Haeri

Coauthors:
Simin Dadashzadeh
Noushin Bolourchian

Introduction:

Quercetin is a bioflavonoid with various beneficial properties including cardiovascular protection, anti-diabetic, anti-inflammatory, and anti-infective activities (1). However, its oral bioavailability is limited due to its poor aqueous solubility and slow dissolution rate (2). Various formulation strategies have been proposed for bioavailability improvement of hydrophobic drugs such as micro/nano-sizing, solid dispersion and physical form changes (3). In the present study, nano-sizing of quercetin powders was performed using a cost-effective method.

Method:

Nanoparticles were prepared using the thin-film hydration method and subsequent sonication. Mixtures of quercetin and surface modifiers (either poloxamer 407, poloxamer 188, Brij 35 or Brij 78) in 1:1.5 weight ratios were dissolved in ethanol. The thin film was formed via a rotary evaporator. The film was then hydrated and bath-sonicated. To evaluate the effect of bubbling on particle size during film hydration, citric acid and sodium hydrogen carbonate were added to the film forming materials and hydration medium, respectively. Quercetin nanoparticles were analyzed for particle size and polydispersity index (PDI).

Results:

By using various surfactants and 30 min sonication, four quercetin nanoformulations were prepared with the Z-average and PDI of 242-500 nm and 0.1-0.3, respectively (Figure 1). Smaller nanoparticles were achieved by poloxamer surfactants. Increasing sonication time to 45 min did not further decrease Z-average except for poloxamer 188 containing formulations. CO2-assisted nanoparticles were found to be higher in particle size and PDI with all four surface modifiers (Figure 1). By using poloxamer 188 and 45 min sonication, optimized quercetin nanoparticle with particle size of 233 ± 21 nm and PDI of 0.22 ± 0.04 was achieved.

Conclusion:

The thin-film hydration method and subsequent sonication seems to be a promising approach for fabrication of quercetin nanosuspensions.

Keywords: quercetin, nanoparticles, simple thin film method, CO2 assisted method

Synthesis of nanocrystalline Cellulose as novel superdisintegrant for pharmaceutical tabletting excipients

Shabnam Sheikhy, Hamed Hamishehkar, Ali Akbar Safekordi, Khosro Adibkia, Shabnam Sheikhy*

P297

Authors' Affiliations:
Department of Science and Research branch, Islamic Azad University, Tehran, Iran.

Abstract Presenter:
Shabnam Sheikhy

****Correspondance:***
Shabnam Sheikhy

Coauthors:
Hamed Hamishehkar
Ali Akbar Safekordi
Khosro Adibkia

Abstract:

Disintegrant is one of the most important components in a typical tablet dosage form. It is responsible for ensuring the breakup of the tablet matrix upon ingestion. In new tablet formulation replacing the disintegrant with fewer amount of super disintegrants for the break-up of the tablet matrix upon ingestion of the tablet especially in fast dissolving tablet so that the information provided could be help to tablet formulation development.

Cellulose, the most ancient and important natural polymer, has a long history of appli¬cation in the pharmaceutical industry, which can be used in practically as a tablet coating when blended with different tablet excipients for oral administration.

In nanoscience and nanotechnology, the synthesis and modification of nanomaterials with well-defined structure and functionalities have attracted growing interest due to their many potential applications. Synthesis of nanocrystalline cellulose from micro crystalline Cellulose as superdisintegrant in order to decrease disintegration time lead to faster influence as a disintegrant. cellulose nanofibers (CNFs) can be formed by the treatment of cellulose with strong acids.

Tablets prepared with microcrystalline cellulose (MCC) and tablets prepared with sodium starch glycolate (SSG) were used as negative and positive controls, respectively. Dissolution study results indicated that tablets include NCC as disintegrate showed better disintegration and dissolution behaviors. In vitro dissolution testing are designed to standardize drug release. Thus, the obtained release data can show the cumulative percentage of zolpidem released from the formulated tablets with MCC, SSG, and NCC. It is clear that the dissolution of zolpidem has improved considerably in the tablet formulation containing NCC.

It was concluded that the novel synthesized super disintegrant has an appropriate potential for the application in the formulation of fast dissolving tablets.

Keywords: nanocrystalline Cellulose, Superdisintegrant, Zolpidem, rapidly dissolving tablet

Effects of Morphine-loaded Molecularly Imprinted Polymer(MIP) nanocarriers on neurite elongation in PC12 cells

Iman Godazi Langroudi*, Hossein Zhaleh, Reza Tahvilian , Fereshte Bagheri

P298

Authors' Affiliations:
Kermanshah university of medical science, Faculty of Pharmacy

Abstract Presenter:
Iman Godazi Langroudi

****Correspondance:***
Iman Godazi Langroudi

Coauthors:
Hossein Zhaleh
Reza Tahvilian
Fereshte Bagheri

Introduction:

Morphine is a Mu opioid drug that has some controversial roles on neuronal cells. Former data suggest that Morphine induces apoptosis in neural cells but some newer studies imply that this drug may stimulate neuronal elongation on central nervous system cells. To evaluate these effects of Morphine, molecularly imprinted nanocarriers(MIP) of Morphine were made and the effects of Morphine and MIP Morphine nanocarriers were evaluated on PC12 cells in different concentrations.

Methods:

PC12 cells were cultured in DMEM culture medium. The treatments were divided to 2 groups which were Morphine and MIP Morphine. There were 8 different concentrations in each group, including: (I) culture without any treatment in each group (control), (II) 1µM treat, (III) 100nM treat, (IV) 10nM treat, (V) 1nM treat, (VI) 100PM treat, (VII) 10PM treat, and (VIII) 1PM treat. The proliferation and cell viability of PC12 cells were assessed by MTT and LDH tests, respectively. The same treatments were done for measuring the length of neurons either (TNL test).

Results:

In Group 1, Morphine in treatment III to VIII was not toxic and increased the proliferation of cells compared with control treatment (p0.05). Morphine in treatment II was toxic and decreased the cell viabilty and proliferation of cells compared with control treatment (p0.05). In Group 2, MIP in treatments IV to VIII were not toxic and increased the proliferation of cells compared with control treatment (p0.05). MNP in treatments II and III were toxic and decreased the cell viabilty and proliferation of cells compared with control treatment (p0.05) and this behavior maybe because of the better penetration of nanocarriers than the Morphine alone. It was observed that the length of neurons increases in treatments IV to VIII in both groups but the MIP Morphine group treatment does it faster than the Morphine alone.

Conclusion:

It can be concluded that the MIP Morphine nanocarriers at low concentrations can increase the length and proliferation of PC12 cells faster, and also they are not toxic to cells.

Keywords: Morphine, PC12 cells, Molecularly Imprinted Polymer, Nano carriers

Study of Drug Distribution and Release Mechanisms in Naproxen Loaded Solid Lipid Nanoparticles

Azin Ezzati, Bahar Hajinejad, Zahra Jafariazar, Seyyed Alireza Mortazavi, Fatemeh Ghorbani Bidkorpeh*

P299

Authors' Affiliations:
School of Pharmacy, Islamic Azad University of Medical Sciences, Iran.

Abstract Presenter:
Azin Ezzati

****Correspondance:***
Fatemeh Ghorbani Bidkorpeh

Coauthors:
Bahar Hajinejad
Zahra Jafariazar
Seyyed Alireza Mortazavi

Abstract:

In 1990s, Solid Lipid Nanoparticles were introduced as an innovative alternative to novel drug delivery in nano dimensions.SLN is generally composed of solid lipid(s) and surfactant (s), and stabilizer, where the active pharmaceutical ingredient is loaded at the intervals between the components of the lipid matrix. Distribution of drug in different SLNs can vary. Ingeneral, there are 3 types of distribution in these compounds:1) Solid Solution 2) Drug-enriched Shell 3)Drug-enriched Core.Our purpose is to investigate the type of distribution and kinetic model and the release mechanism in Nap-SLN. Methods: Based on our previous studies, 3 formulations were prepared by using probe sonication method, all of them containing 5% (w/w) lipid phase,3.5% (w/w) aqueous phase and 0.14% (w/w) naproxen: FA) GMS/WITEP:1/1 ,FB) GMS/WITEP:7/3 , FC) GMS/WITEP: 9/1.Immediately after preparation particle size was measured using the DLS device and by using dialysis bag,release test was performed in phosphate buffer medium with pH = 6.8. Finally,by using mathematical calculations,the type and kinetic model of release were investigated. In the zero order model,first order model,Higuchi model and Korsmeyer-peppas model ,the correlation coefficients (R2) in FA-B-C were (0.8973- 0.9608-0.9843),(0.9594-0.9404-0.9652),(0.9962- 0.9689-0.9924) and(0.9638-0.9966-0.7747), respectively. The particle size in FA-B-C was 94.9-118-268 (nm), respectively. The percentage of cumulative concentrations of free drug in phosphate buffer after 4 hours, were respectively:85.12% -77.46% -56.91%. By studying the correlation coefficients obtained in 3 formulations,it was concluded that the kinetic of the release follows the Higuchi model.But by examining the results obtained as the n-peppascoefficient,it was founded that the mechanism of release follows the Anamalous Transport which simultaneously incorporates Fickian and Non-Fickianrules.For these formulations,where 0.4n0.9,release would be a combination of diffusion and erosion.Furthermore,by examining the release of the formulations within 24 hours,we found that due to the rapid release of the naproxen from the SLN within 4 hours,the major percentage of naproxen was successfully loaded in the SLN shell,which is why it tends to release more quickly and specifies that the drug distribution type in the SLN is Drug-Enriched Shell.Finally, the datademonstrated that the increase in the percentage of GMSincreases the particle size and naproxen tendency to be in the core of SLN, therefore, drug release will be slower.

Keywords: Solid Lipid Nanoparticle, Naproxen, Drug distribution mechanism, Kintic of release, Drug release mechanism.

Investigation and comparison of physicochemical properties of PCL/PVA and PCL/Collagen Co-axially elctrospinning nanofibers

Mazdak Limoee, Pouran Moradipour, Leila Behbood*

P300

Authors' Affiliations:
Students Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Mazdak Limoee

***Correspondance:**
Leila Behbood

Coauthors:
Pouran Moradipour

Introduction:

Recently, an improved electrospinning method called coaxial electrospinning has become popular. It is a new approach using a special spinneret composed of two coaxial capillaries that can electrospin two different polymer solutions concurrently to fabricate ultrafine fibers with special core/shell structure. This fibers can be used as a scaffold in wound healing (1). The hydrophilic core has a great potential to dissolve biomolecules such as peptide and protein and the hydrophobic shell as a frame, enhance stability and sustained drug release (2). The core-shell nanofibers were almost used for peptide-based drugs (3). In this study peptide loaded PCL nanofibers were studied and compared to physicochemical properties of two kind of nanofibers containing Poly-caprolactone (PCL)/ Polyvinylalcohol (PVA) and PCL/Collagen.

Methods:

Three solutions of PCL 9%w/w in mixture Dichloromethane/ Ethanol (60:40), PVA 7% w/w in distilled water and collagen 70% w/w in distilled water were prepared. Core-shell fibers were generated with core-shell nozzle with size 14 and 18 gauge using The PCL solution as shell and each of PVA and Collagen as core. In this study voltage was changed from 8 to 20 K volts and flow rate between core and shell solution (1:1, 1:3, 1:5) to find the optimized fibers. Afterwards, Lysozyme Mw=14.4KD as a peptide model dissolved in core solution (600ng/5mg) and released peptide in phosphate buffer PH=7.4 was evaluated. The kinetics of release was calculated by mathematical models for zero-order kinetic, first-order kinetic, and Higuchi kinetic. The physicochemical properties of fibers were investigated by different analysis such as TEM and FTIR.

Results:

In low voltage 8-12 K volts and flow rate 1:1 didn't make any fibers. The optimum voltage was 16 K volts and the optimum flow rate was 1:3In spite of the PCL/PVA fibers, the PCL/collagen fibers had good stability in aqueous solution with no disintegrations. FTIR showed no incompatibilities with polymers. Peptide release was sustained in 30 days and in first 7 days did not have any release. TEM image showed core-shell structure of PCL/Col nanofibers.

Conclusions:

The PCL/Collagen fibers had better physicochemical properties than PCL/PVA fibers and therefore, more suitable for bioengineering scaffold. The scaffold is suitable for long-term drug/ peptide-based drugs delivery.

Keywords: Co-axially electrospinnng, Collagen, Nanofibers, Polycaprolactone

Development of solid lipid nanoparticles of moxifloxacin HCL for ocular delivery

Seyedeh Negin Kassaee, Mohammad Mehdi Mahboobian

P301

Authors' Affiliations:
Department of Pharmaceutics, School of Pharmacy, Hamadan University of Medical Sciences, Hamadan, Iran

Abstract Presenter:
Seyedeh Negin Kassaee

****Correspondance:***
Mohammad Mehdi Mahboobian

Introduction:

Moxifloxacin HCL (MOX) is a broad-spectrum fourth-generation fluoroquinolone for treatment of bacterial conjunctivitis and keratitis. The objective of the present study was to use nanotechnology to improve MOX ocular bioavailability. Based on this strategy, solid lipid nanoparticles (SLNs) of MOX for ophthalmic delivery was prepared and evaluated.

Methods:

MOX-SLNs were prepared with glycerol monostearate as a lipid and poloxamer 188 and tween 80 as surfactants using solvent emulsification/evaporation technique. Different formulations were characterized by measuring particle size, polydispersity index (PDI), zeta potential and drug entrapment efficiency (EE %). Optimized formulation was selected for in-vitro release and ex-vivo cornea permeation using excised bovine corneas fixed onto Franz diffusion cells.

Results:

According to the results, various SLN formulations with suitable properties such as nano-size particles less than 500 nm and entrapment efficiency more than 80% were achieved by using high speed homogenizer and solvent emulsification /evaporation technique. Optimized formulation showed sustained drug release pattern. In comparison to free drug solution, SLN sample exhibited superior penetration across isolated bovine cornea indicating its potential enhanced corneal penetration properties.

Discussion and Conclusion:

Our findings revealed that MOX could be incorporated efficiently into lipid based nanoparticles with ideal properties for ophthalmic delivery. By enhancing MOX permeation through excised bovine cornea, it seems SLN could be a promising strategy for improvement of ocular bioavailability of MOX.

Key Words: Moxifloxacin HCL, Solid lipid nanoparticles, Ocular delivery.

Co-delivery of paclitaxel and etoposide via amphiphilic PEG-PLGA nanoparticles: Artificial neural network modeling and physicochemical characterization

Hassan Maleki, Mehdi Adabi , Amir Amani, Masood Khosravani*

P302

Authors' Affiliations:
Department of Medical Nanotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

Abstract Presenter:
Hassan Maleki

****Correspondance:***
Masood Khosravani

Coauthors:
Mehdi Adabi
Amir Amani
Masood Khosravani

Abstract

Poly (ethylene glycol) (PEG) and poly (lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) comprising etoposide (ETP) and paclitaxel (PTX) drugs were designed and fabricated by nanoprecipitation technique to avoid the therapeutic limitation. The effects of defined parameters on the nanoparticles (NPs) size have been investigated to form PTX/ETP-NPs with expected characteristics by means of artificial neural networks (ANN) modeling. The resultant NPs were spherical and the mean size was about 150 nm along with ideal drug loading and encapsulation ratio. Besides, a number of characterization methods confirmed that the drugs were successfully dispersed as an amorphous phase in the NPs matrix without any change in the chemical structures. Consequently, it can be concluded that the encapsulated drugs in NPs can improve the solubility, stability, and bioavailability of the drugs in a controlled-release pattern which would be beneficial for the well-organized cancer therapy.

Keywords: PEG-PLGA, Co-delivery, Etoposide, Paclitaxel, Artificial neural network modeling.

Lipoic Acid Niosomes: Preparation and Pharmaceutical evaluation

Mohammad Amin Raeisi Estabragh, Mohammad Farajli Abbasi, Abbas Pardakhty*

P303

Authors' Affiliations:
Pharmaceutics Research Center, Neuropharmacology Institute, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Mohammad Amin Raeisi Estabragh

****Correspondance:***
Abbas Pardakhty

Coauthors:
Mohammad Farajli Abbasi

Introduction:

Alpha-lipoic acid (ALA) is well-known as a potent antioxidant. ALA has been suggested for prevention and treatment of hypoxic-related diseases as well as improving diabetic peripheral neuropathy, cardiovascular disease and stroke damage. Niosomal formulation of ALA may enhance its penetration into target organs, for example brain. Initially we prepared and characterized niosomes of ALA for further in vivo studies.

Methods and Results:

For preparation of niosomes Span® 20, 40 and 60 (Sorbitan esters), Tween® 20, 40 and 60 (ethoxylated derivatives of sorbitan esters) and cholesterol in different molar ratios were prepared by film hydration method by using Experimental Design software. Selected niosomes were passed through polycarbonate membranes by liposome extruder for reducing the vesicular size ranges. Morphology, size analysis, drug release profile, encapsulation efficiency and vesicular stability were evaluated.

All used surfactant-combinations formed multi lamellar vesicles (MLVs). Single mode size distribution, high encapsulation efficiency (more than 80%), good stability of vesicles depicted as unchanged size during 6-month storage in refrigerator and diffusion based release profiles were shown for the most of prepared niosomal formulations.

Conclusions:

Niosomal formulation of ALA compromises a good option for new drug delivery system which further studied in animal models can prove or reject its applicability in CNS hypoxic models such as stroke.

Keywords: Alpha-Lipoic Acid, Niosomes, Stability, Size analysis

Synthesis and characterization of a novel chitosan-fatty acid derivative for drug delivery

Salar Kazemi*, Mohsen Aminide, Maryam Yousefif,
Morteza Rafiee Tehranig, Zohreh Mohammadic

P304

Authors' Affiliations:
Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
School of Chemical Engineering, College of Engineering, University of Tehran, Tehran, Iran.

Abstract Presenter:
Salar Kazemi

****Correspondance:***
Salar Kazemi

Coauthors:
Mohsen Aminide
Maryam Yousefif
Morteza Rafiee Tehranig
Zohreh Mohammadic

Abstract:

Within the past 20 years, chitosan has gained more attention because of its unique characteristics [1]. Chitosan is a natural mucoadhesive, biodegradable, biocompatible and nontoxic polymer which has been applied in pharmaceutical industry [2]. Among several unique effects of chitosan, it has low efficiency in protein, gene or drug delivery [3]. Therefore, developing new chitosan derivatives is an essential need in this field. In present study, thiolated chitosan-fatty acid was synthesized and optimized as a new chitosan derivative, using two methods. A natural saturated fatty acid was used mainly due to its good antibacterial property and its effect on enhancing drug bioavailability when used as delivery system [4], [5]. In addition, the modification of chitosan by covalent attachment of thiol group displaying higher mucoadhesive and permeation-enhancing property [6], [7]. This novel chitosan derivative was characterized by means of FTIR, 1H NMR, TGA and Nano Zetasizer. According to FTIR spectra, the presence of the amide bond could be referred to the enhancement peak at 1736 cm-1 related to attaching fatty acid to chitosan. Also, two weak bands at about 1500 cm-1 are attributed to the stretching vibration of thioglycolic acid carbonyl group. H1 NMR results revealed that degree of fatty acid substitution in chitosan was about 32% and both substitution reactions were successfully performed. TGA results showed that decomposition of the new derivative occurred in three stages. Zeta potential of thiolated chitosan-fatty acid polymer was about +41 that is suitable for delivery applications. These findings confirm that this new derivative can be introduced as a suitable polymer for biomedical purposes.

Keywords: chitosan, new derivative, synthesis, fatty acid

Chitosan nanoparticles as an epidermal growth factor delivery system

Samaneh Montazeri*, Zohreh Mohammadi, Mahboobeh Nazari, Hanieh Jafary

P305

Authors' Affiliations:
Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran
Nanobiotechnology Research Center, Avicenna Research Institute, ACECR, Tehran, Iran.
School of Pharmacy-International campus, Iran University of Medical Sciences, Tehran, Iran.
Monoclonal Antibody Research Center, Avicenna Research Institute, ACECR, Tehran, Iran.

Abstract Presenter:
Samaneh Montazeri

****Correspondance:***
Samaneh Montazeri

Coauthors:
Zohreh Mohammadi
Mahboobeh Nazari
Hanieh Jafary

Introduction:

Recombinant human epidermal growth factor (rhEGF) is essential in cellular signaling for migration, proliferation, differentiation and maturation and known to stimulate cell proliferation and accelerate wound healing (1). Since, maintaining of effective topical concentrations of EGF at the wound site is very difficult, development of a suitable delivery system for EGF is necessary. Suitable delivery of therapeutic as well as functional (rhEGF) is largely required in the pharmacological and regenerative medicine (2). The aim of this study was to develop chitosan nanogels containing EGF for increasing the growth factor stability in environmental conditions as well as its long and effective release with the aim of using in dermal formulations.

Methods:

Stability of rhEGF in different pHs and temperatures was evaluated by Bio photometer. The effects of stabilized EGF on growth rate of human melanoma skin cancer Cells (A375) was determined by xtt method. Release pattern of rhEGF from the chitosan nano gel was measured by HPLC technique

Results:

Nanogels containing EGF in ratios of 2:1 and 6:1 (chitosan to protein) revealed favorable stability in different pHs and also could preserve the biological activity of epidermal growth factor. The cell viability studies indicated significant growth induction in both ratios, while stability of protein by both of these nanogels was well preserved. Moreover, they were able to release 80% and 60% of the protein after 24 hours.

Conclusions:

According to the findings of this study, chitosan nanogels in optimal ratios can release EGF in a rational manner and can be considered as suitable candidates for preparation of dermal formulations, with regenerative purposes.

Keywords: drug delivery system, chitosan, EGF

Doxorubicin and TRAIL plasmid co-delivery to colon cancer cells using modified PAMAM dendrimer

Maryam Hashemi*, Elham pishavar

P306

Authors' Affiliations:
Nanotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Maryam Hashemi

Correspondance:
Maryam Hashemi

Coauthors:
Elham pishavar

Abstract:

Although cancer is an extremely complex disease involving multiple signaling pathways, cancer treatment will be attainable in the future. One strategy is combination therapy involving both gene therapy and chemotherapy, which has resulted in enhanced anti-cancer effects and reduced cytotoxicity. Polyamidoamine dendrimer (PAMAM) has attracted considerable attention because of its potential applications ranging from drug delivery to molecular encapsulation and gene therapy. In this study, PAMAM G5 modified with cholesteryl chloroformate and alkyl-PEG was applied for co-delivery of doxorubicin (DOX) and Tumor TRAIL plasmid into colon cancer cells, in vitro and in vivo. The results showed DOX was efficiently encapsulated in modified carrier with loading level a

about 90 %, and the resulting DOX-loaded PAMAM containing plasmid encoding TRAIL showed much stronger antitumor effect than PAMAM-DOX and PAMAM-TRAIL plasmid. On the other hand, the obtained results demonstrated that the treatment of mice bearing C26 colon carcinoma with this developed co-delivery system significantly decreased tumor growth rates. Thus, this modified PAMAM G5 can be considered as a potential carrier for co-delivery of drug and gene in cancer therapy.

Keywords: Combination therapy, Doxorubicin, Polyamidoamine, Cholesterol, TRAIL plasmid

Ring-Opening Polymerization of Poly (D, L-lactide-co-glycolide)-poly (ethylene glycol) Diblock Copolymer Using Supercritical CO2

Farzin Hadi Zadeh*, Hossein Kamali, Elham Khodaverdi

P307

Authors' Affiliations:
School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract Presenter:
Farzin Hadi Zadeh

****Correspondance:***
Farzin Hadi Zadeh

Coauthors:
Hossein Kamali
Elham Khodaverdi

Abstract:

Ring-opening polymerization of PLGA-PEG diblock copolymers was studied using supercritical CO2 (SCCO2). The results of the SCCO2 method were compared with a melting procedure using a three-necked flask. A pressure of 317 bar, temperature of 132 ° C, and time of 14 h resulted in the maximum molecular weight (10138 g/mol) and yield (91.62 w/w %); these results were significantly higher than those for the melting method (Mw = 6664.5 g/mol, yield = 78.56 w/w %). Furthermore, the reaction time for achieving maximum Mw and yield via SCCO2 (14 h) was lower than with the melting method (24 h). The lactide-to-glycolide molar ratio and percent by weight of methoxy PEG matched well with the initial value when SCCO2 was used. The melting temperature (Tm), critical micelle concentration (CMC), and particle size in SCCO2 were higher than the melting method, as the obtained molecular weight of SCCO2 was higher.

Keywords: Ring-opening polymerization, PLGA-PEG, SCCO2, Melting method

Preparation and characterization of sustained release sirolimus nanofibers as a potential local vascular drug delivery system

Rozhin Talimi, Shahram Rabbani, Simin Dadashzadeh, Azadeh Haeri*

P308

Authors' Affiliations:
Faculty of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran.

Abstract Presenter:
Rozhin Talimi

****Correspondance:***
Azadeh Haeri

Coauthors:
Shahram Rabbani
Simin Dadashzadeh

Introduction:

Coronary artery bypass surgery (CABG) is one of the main surgical revascularization methods for treatment of coronary artery disease. However, vascular restenosis, occurring 1 to 12 months after CABG, diminishes the overall efficacy of surgical bypass and long term patency of vascular interventions (1, 2). Sirolimus is a potent immunosuppressive agent with beneficial effect in preventing restenosis following vascular interventions (3). In this study, to deliver sirolimus locally, electrospun polycaprolactone (PCL) nanofibers were prepared as a promising platform due to several advantages such as biocompatibility, biodegradability, high drug loading, and controlled release properties.

Methods:

Sirolimus loaded ultra-fine nanofiber PCL mats at two drugs. Polymer (D: P) weight ratios (1:5 and 1:10) were successfully prepared by electrospinning from 10% (w/w) PCL solution. Nanofibers were characterized by drug content, scanning electron microscopy (SEM), atomic force microscopy (AFM) observations, Fourier transform infrared spectroscopy (FTIR), mechanical strength, and X-ray diffraction (XRD). The releasing characteristics of sirolimus nanofibers were determined by dialysis bag method in normal saline solution at 37 °C for 120 hours.

Results:

Sirolimus was successfully loaded into nanofibers with average drug content of 162.44 and 87.30 µg/mg for 1:5 and 1:10 (D: P weight ratio) fibers(?), respectively. The SEM and AFM images displayed very uniform and bead-free fibers with average diameters within the range of 384 to 510 nm. XRD data exhibited decreased drug crystallinity during the electrospinning process; however, no interaction between drug and polymer was detected by FTIR analysis. Sirolimus release from PCL nanofibers was 67% and 46% over 120 h for fibers with 1:5 and 1:10 D: P weight ratios, respectively.

Conclusion:

These results suggested that the electrospun PCL based sirolimus nanofibers can serve as an effective controlled release drug delivery system to prevent restenosis after CABG.

Keywords: Nanofibers, sirolimus, polycaprolactone, vascular stenosis, controlled release nanosystem

Synthesis of thermo-sensitive boronated chitosan-poly (N-isopropylacrylamide) NPs to use in BNCT

Monireh Soleiman-beigi*, Farshid Hassanzadeh, Mahboubeh Rostami, Yaser Kasesaz

P309

Authors' Affiliations:
Master of Science student of Medicinal Chemistry, Department of Medicinal Chemistry, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Science, Isfahan, Iran

Abstract Presenter:
Monireh Soleiman-beigi

****Correspondance:***
Monireh Soleiman-beigi

Coauthors:
Farshid Hassanzadeh
Mahboubeh Rostami
Yaser Kasesaz

Introduction:

Glioma stem cells in the quiescent state are resistant to clinical forms of therapy. An almost inevitable glioma recurrence is due to the persistence of these cells. The high linear energy transfer associated with BNCT could kill quiescent and proliferative cells [1]. BNCT is a targeted therapy in which cancer cells accumulate boron and are subsequently irradiated with neutrons. During this process in which 4He and 7Li are emitted when 10B reacts with thermal neutrons releasing energy. In order to be successful, a sufficient amount of 10B must be selectively delivered to the tumor [2, 3]. The most important purpose of the study is to synthesize boronated CS-NPs which can deliver a high boron payload to the tumors.

Methods:

At the first to improve the thermos responsivity of chitosan, poly (N-isopropylacrylamide) was applied to modification. In the second step, to modify the water solubility, Succinic acid moieties were grafted onto the CS. To make the targeted system, BPA was attached to the main body of the CS. BPA loaded CS-NPs were prepared by a simple dialysis method by TPP crosslinking. The release profile of BPA from the prepared nanoparticles at temperatures ranging from 37 to 42 ºC. The size and zeta potential of prepared nanoparticles were studied by direct light scattering instrument.

Results & Discussion:

The FT-IR and NMR spectra confirmed the structure of modified systems. The quantity of BPA loaded in NPs was about 88 %. About of 81% of loaded BPA was released at 39 ºC after 24h. It seems that release follows a swelling-controlled mechanism. Our preliminary study thus providing clear evidence for the successful preparation of BPA loaded with novel thermo-sensitive chitosan-poly(N-isopropylacrylamide) NPs. The results of this study are promising to introduce a novel formulation of a highly stable boronated nanocarrier of BPA with extensive physico chemical characterization to BNCT studies.

Keywords: Chitosan, Thermo-Sensitive, nanoparticles(NPs), boron neutron capture therapy, BNCT

Formulation and Charactrization of Niosomal/Cu Nanaparticles: Optical and Delivery Study

Zohreh Asadi-korom, Abbas Pardakhty, Mehdi Ranjbar*

P310

Authors' Affiliations:
Student Research Committee, Kerman University of Medical Sciences, Kerman, Iran.

Abstract Presenter:
Zohreh Asadi-korom

****Correspondance:***
Mehdi Ranjbar

Coauthors:
Abbas Pardakhty

Introduction:

Recently many researchers have studied the capabilities of vesicular system for local antibiotics delivery. There are some advantages including penetration enhancement, better efficacy, controlled release and reduced toxicity. One of the highly studied vesicular systems is "niosomal" formulations which we focus on in this research. One such class of nanomaterials are metal oxide (MeO) and metal sulfide (MeS) nanoparticles (NPs), ranging in size from 1 to 100 nm and available in different shapes and sizes. Metallic nanoparticles have an antibacterial effect, in addition to the inhibitory effect of the particle, due to its small size, large surface area and large outer surface area. Scientists believe that nanoparticles can be used as an appropriate alternative bio chemical. With the development of nanotechnology over the last decade, golden opportunities have been created to discover the antibacterial effects of metallic nanoparticles. There has been an immense extension of nanomaterial applications and uses as a result of basic and applied research from scientists all over the world. [1-3].

Methods and Results:

In this study, non-ionic surfactant vesicles containing ofloxacin (OFX) was prepared by film hydration method. Different kinds of sorbitan esters (Span 20,40, 60 and 80), polysorbates (Tween20,40, 60 and 80) and poly oxyethylene alkyl ethers (Brij52,72 and 95) with cholesterol were used in vesicular formulations. In vitro characterization of niosomes including microscopic observation, release of OFX, size analysis, and encapsulation efficiency calculation were studied. OFX concentration was measured by second derivative UV spectroscopy at 250 nm.

Conclusions:

All used surfactants formed round MLVs (multilamellar vesicles) except Span/Tween 80. Log-normal size distribution was observed for all prepared niosomes. Vesicles were stable with minimum size change during 2-month storage at 4-8 C. Maximum encapsulation efficiency percent of OFX were 70 and 63%, respectively. Biphasic release profiles of both compounds were obtained and the release data was best fitted with Baker-Lonsdale release kinetic model.

Keywords: Nanostructures, Drug delivery, Ofloxacin, Optical properties

Paclitaxel and Doxorubicin Molecular Dynamics Study: A Novel Cancer Drug Delivery by Carbon Nanotube, Fullerene, and Graphene Oxide

Mohammad Dahri Dahroud, Milad Rezaian, Mohammad Khedri, Hossein AkbariAliabad, Reza Maleki*

P311

Authors' Affiliations:
Pharmaceutical Strategic Studies Office, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract Presenter:
Mohammad Dahri Dahroud

***Correspondance:**
Reza Maleki

Coauthors:
Milad Rezaian
Mohammad Khedri
Hossein AkbariAliabad

Abstract:

Nowadays, investigating various methods to achieve effective cancer therapy is one of the consequential research in medicine and pharmacy. Nano-based drug delivery is a progressive field in breast cancer therapy. In current work, we have analyzed the pH sensitive co-release/adsorption of doxorubicin (DOX) and paclitaxel (PAX) by N-isopropylacrylamide (PIN) in conjugation with three Nano-carrier; carbon nanotube (CNT), fullerene and graphene oxide (GO). Molecular dynamic performance is the cornerstone of this simulation study. Three agents were studied and analyzed by figures; Interaction energies, hydrogen bond, and Radius of gyration. Results show that, having compared CNT whit GO and Fullerene, CNT is the best carrier for DOX and PAX release and adsorption. It's able to adsorb the drugs in physiological pH and release it in the cancer acidic microenvironment. Studying the number of hydrogen bonds discovered that PIN formed many hydrogen bonds with water, causing in high hydrophilicity of PIN, therefore building it more established in the circulation while avoiding from its gathering. We also revealed that, CNT and PIN would assemble an appropriate conjugation for the delivery of DOX and PAX, because PIN makes plentiful hydrogen bonds and CNT makes constant interactions with these drugs.

Keywords: nano-carrier, doxorubicin, paclitaxel, N-isopropylacrylamide, molecular dynamics

Paclitaxel and Doxorubicin Molecular Dynamics Study: A Novel Cancer Drug Delivery by Carbon Nanotube, Fullerene, and Graphene Oxide

Seyed Behnam Farmanara, Mohammad Hassan Moshafi, Abbas Pardakhty*

P312

Authors' Affiliations:
Kerman University of Medical Sciences School of Pharmacy-Pharmaceutics Research Center

Abstract Presenter:
Seyed Behnam Farmanara

***Correspondance:**
Abbas Pardakhty

Coauthors:
Mohammad Hassan Moshafi

Introduction:

Recently many researchers have studied the capabilities of vesicular systems for local antibiotics delivery. There are some advantages including penetration enhancement, better efficacy controlled release and reduced toxicity.

Methods:

In this study non-ionic surfactant vesicles were prepared by film hydration method. Different kinds of sorbitan esters (span 20, 40 and 60) and polysorbates (tween 20, 40 and 60) and cholesterol were used in vesicles formulations. In vitro characterization of niosomes including size distribution measurement by laser light scattering method, evaluation of release of azithromycin phosphate in normal salin and UV absorbtion of azithromycin by Sulfuric acid 27 normal.

Results and discussion:

Log-normal size distribution was observed for all prepared noisome formulations. Release of azithromycin phosphate was best fitted by Baker & Lonsdale and Peppas models indicating a diffusion based release of antibiotic. Release of encapsulated azithromycin in vesicular systems was more than free drug. Morphological study of vesicles by optical microscopy revealed different shape and size niosomes which were more as MLVs (Multilamellar Vesicles). High vesicular stability revealed the ability of azithromycin niosomes for topical controlled release of this antibiotic.

Key words: Azithromycin, Noisome, Diffusion cell

Chitosan-alginate nano-carrier for transdermal delivery of pirfenidone in idiopathic pulmonary fibrosis

Marzieh Abnoos, Mojdeh Mohseni, Roya Ilka, Bita Mehravi*

P314

Authors' Affiliations:
Iran University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Marzieh Abnoos

****Correspondance:***
Bita Mehravi

Coauthors;
Mojdeh Mohseni
Roya Ilka

Introduction:

This research was carried out to investigate the feasibility of transdermal delivery of pirfenidone (PFD) using chitosan-sodium alginate nanogel carrier system.

PFD is a pyridone compound with anti-inflammatory and anti-fibrotic effects and US FDA approved for treating idiopathic pulmonary fibrosis (IPF). Presently, PFD is administered orally and this has limitations including first pass metabolism and gastrointestinal irritation. The aim of this study is to limit pharmacotherapeutic setbacks of PFD.

Methods and Results:

CHI-SA nanoparticles were synthesized using the pre-gelation method. In order to characterize nanoparticles Scanning electron microscopy (SEM), transmission electron microscopy (TEM), dynamic light scattering (DLS), and Fourier-transform infrared spectroscopy (FTIR) analyses were used. Drug encapsulation and release manner were studied using UV spectroscopy. Ex vivo permeation examinations were performed using Franz diffusion cell and fluorescence microscopy. The results indicated that nanoparticles have spherical morphology and the average particles size was 80 nm. In-vitro drug release profile represents sustained-release during 24 h and the loading capacity and efficiency were 50% and 94%, respectively. In addition, the skin penetration of PFD loaded in nanoparticles was significantly increased as compared to PFD solution.

Conclusions:

The synthesized nanoparticles can be developed as a potential transdermal delivery system.

Keywords: Nanocarriers, pirfenidone, pulmonary fibrosis.

Optimization of Curcumin Loaded Phospholipid Nanoparticles Using a Two-Level Factorial Design

Seyedeh Sara Akhlaghi, Sonia Alavi , Simin Dadashzadeh, Azadeh Haeri*

P315

Authors' Affiliations:
Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract Presenter:
Seyedeh Sara Akhlaghi

***Correspondance:**
Azadeh Haeri

Coauthors:
Sonia Alavi
Simin Dadashzadeh

Abstract:

Curcumin (CUR) is a polyphenolic compound with highly potent antioxidant, anti-inflammatory and antiproliferative properties [1]. However, poor absorption and rapid systemic elimination limit its clinical use. Therefore, numerous approaches have been made to improve the bioavailability of CUR [2]. Phospholipid nanoparticles are the most promising nanocarriers, owing to their biocompatibility, biodegradability and non-toxicity [3]. The objective of this study was to determine key formulation parameters of CUR phospholipid nanoparticles using 2-level factorial design.

CUR nanoparticles were prepared using triglyceride, egg phosphatidylcholine (EPC) and glycerol or fructose solution by high-shear homogenization method. Briefly, a 24 full-factorial design with center points was employed to evaluate the main factors that affect nanoparticles' size and entrapment efficiency (EE). Four independent variables including total lipid, triglyceride to EPC ratio, medium type and percentage were studied and 22 different formulations were designed by Design Expert® software. The effect of d-α-tocopheryl polyethylene glycol 1000 succinate (TPGS) enrichment on formulation characteristics was also evaluated. Nanoformulations were characterized regarding mean diameter, polydispersity index (PDI), zeta potential, release profile, morphology and Fourier Transform Infrared (FTIR) analysis.
All studied parameters had a significant effect on the EE. It was found that the optimum EE could be obtained at higher total lipids and glycerol percentage in medium and lower triglyceride to EPC ratio. TPGS enrichment almost doubled CUR entrapment. Z-average diameter of the optimized formulation (prepared with total lipid content of 100 mg, triglyceride to EPC ratio of 1, glycerol as medium and 10% TPGS) was 58.6±0.6 nm with a PDI of 0.18±0.01 and drug entrapment of ~69%. The optimum formulation showed a sustained release pattern, releasing about 80% within 2 weeks incubation in 37 °C. FTIR revealed successful encapsulation of CUR without any interaction with nanoparticle components. AFM results showed spherical shaped nanoparticles.

In this study, 2-level factorial design was successfully applied to optimize CUR lipidic nanoparticles. Addition of TPGS further improved EE of the optimized formulation.

Key Words: Curcumin, phospholipid based nanoparticles, 2-level factorial design, sustained release

Thermoresponsive Injectable Hydrogel for Controlled Release of Curcumin

Maryam Babaei, Mohammad Ramezani, Mona Alibolandi*

P316

Authors' Affiliations:
Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Maryam Babaei

***Correspondance:**
Mona Alibolandi

Coauthors:
Mohammad Ramezani

Abstract:

Nowadays thermo responsive in-situ forming injectable hydrogels, a cutting edge polymer network have received special attention as sustained delivery carriers that can provide spatial and temporal control over the release of loaded bioactive or therapeutic agents [1]. Comprehensive research over the years demonstrated that curcumin and other curcuminoid derivatives possess anticancer properties and suppress the proliferation and survival of many type of invasive cancers cells such as colon and breast cancer. However, despite the unique properties of these traditional therapeutic agents,the clinical application of curcumin isdiminished due toits extremely low solubility and poor physio-chemical stability in aqueous media, and consequently low bioavailability[2].

In current project curcumin nanoparticle loaded in thermosensitive biodegradable hydrogel composed of poly (ε-caprolactone-co-lactide)-b-poly (ethylene glycol)-b-poly (ε-caprolactone-co-lactide)) was prepared [3] and applied in treatment of glioma. The main objective of this study is to develop a biodegradable long persistence injectable hydrogel that can leverage therapeutically beneficial outcomes of curcumin and surmount the impediments and improve the efficacy of this anti-cancer drug in clinical usage. Compared to free curcumin, our formulation shows advantages such as, prolonged release time and lower burst release. Also the synthesized polymer exhibited short term gelation time as a function of temperature.

Keywords: hydrogel, curcumin

A novel hybrid theranostic system for colon adenocarcinoma

Mahsa Shahriari*, Mona Alibolandi, Mohammad Ramezani, Khalil Abnous

P317

Authors' Affiliations:
Pharmaceutical Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran.

Abstract Presenter:
Mahsa Shahriari

****Correspondance:***
Mahsa Shahriari

Coauthors:
Mona Alibolandi
Mohammad Ramezani
Khalil Abnous

Abstract:

Gold NPs have great potential in biomedical applications. PAMAM dendrimers are spherical, hyper branched macromolecules, which, along with stabilizing metal nanoparticles such as gold NPs, can encapsulate therapeutic molecules. The aim of the current study was to investigate the theranostic capability of curcumin-loaded dendrimer gold hybrid structure. Dendrimer-gold hybrid structure was synthesized by complexing $AuCl4^-$ ions with PEGylated amine-terminated generation 5 poly (amidoamine) dendrimer. The resultant hybrid system was loaded with curcumin. The curcumin-loaded PEGylated Au dendrimer was further conjugated to MUC-1 aptamer in order to target the colorectal adenocarcinoma in vitro and in vivo. Obtained results demonstrated that the targeted theranostic agent was accumulated in HT29 and C26 cells in vitro and showed higher cellular cytotoxicity in comparison with non-targeted system. On the other hand, in vivo experiment demonstrated the potential of the targeted theranostic system in CT-scan tumor imaging as well as cancer therapy. Findings from this study suggested that MUC-1 targeted curcumin-loaded PEGylated Au dendrimers, along with demonstrating high therapeutic index against colorectal cancer adenocarcinoma, have good X-ray attenuation and thus are desirable probes for CT imaging.

Keywords: PAMAM, curcumin, colorectal cancer, theranostic, CT scan

Oral delivery of insulin using Casein-based hydrogel: in vitro and in vivo evaluation

Ali Aliabadi, Bahman Khameneh, Sepehr Maftouhian, Farzin Hadizadeh*

P318

Authors' Affiliations:
Department of Medicinal Chemistry, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract Presenter:
Ali Aliabadi

****Correspondance:***
Farzin Hadizadeh

Coauthors:
Bahman Khameneh
Sepehr Maftouhian
Farzin Hadizadeh

Abstract:

Hydrogels are drug delivery systems which have favorable properties in comparison to other systems and the enzymatic cross-linked casein hydrogel is one of them that has received great attention in the recent years. In the present study, in vitro and in vivo evaluations of the enzymatic cross-linked casein hydrogel containing insulin were investigated. differential scanning calorimeter; Scanning electron microscopy; X-ray diffraction and Atomic force microscopy methods were used in order to investigation the properties of the hydrogels. The rheological and releasing behaviors at different environments were also investigated. CD test was used to identify the secondary structure of insulin protein and the hypoglycemic effects of the formulation were evaluated in the diabetic rats. Hydrogel had a three-dimensional porous structure which is desirable for insulin loading. In vitro release studies showed slow releasing of insulin in acidic media, but releasing in neutral and alkaline environments was rapid. Hypoglycemic effects of the insulin-containing hydrogel were investigated by oral administration and the results showed decreasing of the glycaemia levels. According to the results, the enzymatic cross-linked hydrogel can be considered as a favorable formulation for oral delivery of insulin.

Keywords: Hydrogel, Casein, Hypoglycemic activity

Comparison of electrospun and solvent cast Eudragit RL100 films as ophthalmic drug delivery of Ketorolac tromethamine by suitable polymeric nanofibers

Shahla Mirzaeei*, Shiva Taghe

P319

Authors' Affiliations:
Pharmaceutical Sciences Research Center, School of Pharmacy, Kermanshah University of Medical Sciences, Kermanshah, Iran

Abstract Presenter:
Shahla Mirzaeei

****Correspondance:***
Shahla Mirzaeei

Coauthors:
Shiva Taghe

Introduction:

The delivery of an effective eye medicine has been a problem so far. The rapid removal of ordinary liquid drops is still an unresolved problem in the delivery of the eye medicine. Due to the small diameter of the nanofibers, the super-high level, a significant amount of drug can be placed in a very small piece of nanofibers. Nanoelectronic plates can effectively turn into the corneal area in the cholusic area. Ketorolac tromethamine (KT) for topical use in preventing eye inflammation after surgery, reducing postoperative pain, reducing conjugate, without altering corneal opacity. Eudragit RL100 is the biodegradable and biocompatible in nature. Slow degradation rate of Eudragit RL100 makes it suitable for fabrication of nanofibers patch for prolonged drug delivery. The purpose of this study is to create a chain of Eudragit RL100 nanofibers and film inserts using Ketorolac tromethamine, which is used to treat inflammation.

Methods:

Nanofibers solutions were obtained upon the composition of Eudragit with ketorolac Solved in methanol under magnetic stirring at room temperatures. Preparation of the nanofibers was carried out using a customized electrospining system. Films prepared by solvent casting technique. Samples characterized on the basis of morphology, entrapment efficiency, percentage moisture absorption, percentage moisture loss, thickness, folding endurance and drug release behavior, etc.

Results and Discussion:

The smooth surface of NFs would be favorable for the ocular use compared to non-homogenous and rough surface films. The rough surface of films was also evident from the SEM image. Films were found to be brittle and posed difficulty in handling. On the contrary, NFs possessed good folding endurance and this makes the insert safe and comfortable for ocular use. The inserts were found to be sterile for up to 30 days. The KET loaded NFs exhibited sustained release of the drug for more than 144 hours and could be used as a suitable alternative for treating of external infections of the eye.

Conclusions:

Based on the results obtained, we conclude that nanofibers are better than Films obtained by solvent casting technique and could be utilized as a potential delivery system for treating anterior segment ocular diseases.

Keywords: Nanofibers, Ocular drug delivery, Electrospinning, Ketorolac tromethamine

Preparation and characterization of cisplatin loaded magnetic chitosan nanoparticle

Newsha Fallah*, Fatemeh Ghorbani Bidkorbeh, Farshad H. Shirazi, Seyed Alireza Mortazavi

P320

Authors' Affiliations:
Department of pharmaceutics, Faculty of pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Shahid Beheshti University of Medical Science, Tehran, Iran

Abstract Presenter:
Newsha Fallah

****Correspondance:***
Newsha Fallah

Coauthors:
Fatemeh Ghorbani Bidkorbeh
Farshad H. Shirazi
Seyed Alireza Mortazavi

Abstract:

Magnetic nanoparticles have been one of the most innovative drug delivery systems in recent years. The capability of localized drug release, inducing hyperthermia in the targeted area using an external magnetic field, and their intrinsic potential for having the role of contrast agent for magnetic resonance imaging has turned these particles into an ideal theranostic system. In this study, iron oxide nanoparticles were covered by chitosan as a biodegradable polymer with a core-shell structure and tripolyphoshphate (TPP) was used as final cross linking agent in order to form a nano sized drug carrier. Due to wide range of use and tendency for reducing the side effects by localized delivery, cisplatin was chosen as model drug. Synthesis of magnetic nanoparticles was conducted with co-precipitation method and chitosan coat was made with cross linking method. At first, chitosan was dissolved in acetic acid solution, then dry iron oxide nanoparticles were added to chitosan for magnetic stirring during 24 h ours in order to adsorb the polymer on the surface of nanoparticles. Cisplatin was first loaded on the TPP with stirring time of 24 hours, and then drug-cross-linker complex was added to chitosan magnetic nanoparticles using magnetic stirring. The iron oxide nanoparticle particle size was in range of 40-70 nm with PDI of 0.12 and the final nanocarrier size was estimated between 350-500 nm with PDI of 0.18 measured by zeta-sizer. The entrapment efficiency and drug release rate was calculated using dialysis membrane in normal saline based on cisplatin calibration curve. The results showed that the cisplatin entrapment efficiency was about 77% in pH = 6.9 and that 91% of loaded drug was released after 24 hours. The morphology of nanoparticles was illustrated by atomic force microscopy (AFM) and also resulted size of nanoparticles were confirmed. In conclusion based on the reported results, the chitosan coated magnetic nanoparticles demonstrated a great potential for better delivery of cisplatin.

Keywords: Nanocarrier, Magnetic nanoparticle, Cisplatin, Chitosan

Synthesis and preparation of oral delivery systems based on folic acid-targeted resveratrol-loaded nanoparticles

Mahshid Naserifar, Mohammad Ramezani, Hossein Hosseinzadeh, Mona Alibolandi*

P321

Authors' Affiliations:
Pharmaceutical Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Iran.

Abstract Presenter:
Mahshid Naserifar

****Correspondance:***
Mona Alibolandi

Coauthors:
Mohammad Ramezani
Hossein Hosseinzadeh
Mona Alibolandi

Introduction:

Resveratrol (trans-3,5,4'-trihydroxystilbene), which is obtained from the seeds and skins of red grapes is known as a powerful antioxidant, and has several properties, including antimicrobial, anticancer, and anti-inflammatory effects. Resveratrol belongs to a class of polyphenolic compounds.

Resveratrol possesses an ideal therapeutic effect, while after oral administration it shows very short plasma half-life of about 8 minutes. Then, in different ways, including cyp3A4 liver enzyme, it is metabolized, and its potency is reduced. The aim of the current study was to prepare a PLGA-based resveratrol nanoparticles (NPs), which targeted with FA in order to protect resveratrol from fast degradation, modify its pharmacokinetics properties, and increase the intestinal permeation.

Method:

First, the carboxylic acid group of folic acid was activated by EDC and NHS, then aminated by ethylene diamine. The PLGA is activated by EDC and NHS and reacted with aminated folic acid. Resveratrol was encapsulated in PLGA and FA-conjugated PLGA. The amount of encapsulated resveratrol was analyzed through RP-HPLC at 310 nm. The size and morphology of the prepared nanoparticles were investigated using DLS and SEM, respectively. The release of the prepared formulation was evaluated at HCl 0.1 N for 2 h and PBS pH 7.4 for 48 h in order to mimic stomach and intestinal condition, respectively. Caco-2 cells were used for transwell permeability experiment.

Result:

Regarding the results, the prepared formulation showed high encapsulation efficiency of 87.7% ±1.571623 and 50.1% ±1.2459 and loading content of 52% and 38% for the not-targeted and targeted nanoparticles, respectively. In vitro release experiment showed that the prepared formulation was able to maintain a 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 54.03%±0.2344 and 92.10%±0.1778 for the non-targeted and targeted formulations, respectively.

Conclusion:

It could be concluded that the prepared formulation could provide the versatile platform for oral delivery of resveratrol.

Keywords: Resveratrol, PLGA, Folic Acid, Oral drug delivery

Cost evaluation of Chemotherapy for 5 Common Cancers in Isfahan, Iran

Mohammadreza Amirsadri*, Amirhoushang Zargarzadeh, Farimah Rahimi, Fatemeh Jahani

P323

Authors' Affiliations:
Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences

Abstract Presenter:
Mohammadreza Amirsadri

****Correspondance:***
Mohammadreza Amirsadri

Coauthors:
Amirhoushang Zargarzadeh
Farimah Rahimi
Fatemeh Jahani

Introduction:

Cancer is the third leading cause of death in Iran, and its treatment is overly costly. The cancer treatment costs are rising annually, and increased price of chemotherapy drugs is the main influential factor. The present study aimed to evaluate the chemotherapy costs for 5 common cancers in Isfahan, Iran.

Method:

The data were collected from the records available at the Cancer Registration Center in the Health Deputy of Isfahan University of Medical Sciences and from the chemotherapy drugs distributing pharmacies in Isfahan. The data were analyzed using SPSS software.
Results: The results showed that breast, skin, colorectal, Stomach and thyroid cancers with 5,481 cases were the most common cancers in 2015; and the highest and the lowest amount of money spent on chemotherapy drugs pertained to colorectal cancer with 110,510,720 IRR per patient a year and to thyroid cancer with 40,791,123 IRR per patient a year. Regardless of the cancer type, the mean total costs of chemotherapy drugs for a patient were estimated to be 96,307,145 IRR in 2015. It is predicted that this figure rises to 113,173,024 IRR in 2018.

Conclusion:

Cost of chemotherapy for 5 common cancers is high and estimated to increase by averagely?? 113,173,024 IRR in 2018 per patient. Evaluation of these costs will help the government make better policies and expand the coverage of health insurance.

Keywords: Cost Analysis, Chemotherapy, Cancer.

Study of prescribing pattern of drug and per capita drug before and after family medicine program in health centers of Guilan province

Hamid Ghahremani Saghir*, Ali Naghi Karimi, Mehran Ehsani, Farshid Asoudeh , Mohammad Abbasi

P324

Authors' Affiliations:
Gilan University of Medical Sciences, Rasht, Iran

Abstract Presenter:
Hamid Ghahremani Saghir

****Correspondance:***
Hamid Ghahremani Saghir

Coauthors:
Ali Naghi Karimi
Mehran Ehsani
Farshid Asoudeh
Mohammad Abbasi

Introduction:

The family medicine program has been implemented in villages of the country since 2005. The purpose of this study was to evaluate the drug use and determine drug indicators before and after the implementation of the program.

Materials and Methods:

This study was a descriptive-analytic study that was carried out in all health care centers of Guilan province in 2015. In this study, we reviewed the prescriptions and prescription drugs and the price of copies as well as the income and allocation figures Cities and financial documents were collected and analyzed during the year2004 (year before the program), and 2011 (six years later), and 2015 (extension of the program on population below 20 thousand).
Results: The number of sentences was increased by 0.91 in 2011 compared to 2004. The number of copies issued in 2004 equaled 288.0 (28.8 per 100 population) and in 2011 it was 644. 0 (64 per 100 people). Hence, the per capita edition of the edition in 2011 was more than 2.2 times higher than in 2004. The per capita cost of drug per person in 2004 was 3775 rials and in 2011 was equivalent to 17,201 Rials. However, the per capita pharmaceutical costs per person in 2011 were 4.5 times higher than the cost of drug per year in 2004.

Conclusion:

Increasing the per capita rate of prescription drugs in the areas where family medicine programs are implemented suggests increasing the facilities for patients and patients to the units providing rural health services. On the other hand, the decrease in the average number of prescriptions issued by family physicians indicates compliance with the principles of rational prescribing.

Keywords: Prescription Indicators, Family medicine Program, Per capita drug, Justice in the distribution of resources, Drug management and equipment

Antibiotic prescription patterns in health centers by Guilan Family physicians, Iran

Hamid Ghahremani Saghir*, Ali Naghi Karimi, Mehran Ehsani, Farshid Asoudeh , Siavash Nadem, Mohammad Abbasi

P325

Authors' Affiliations:
Gilan University of Medical Sciences, Rasht, Iran

Abstract Presenter:
Hamid Ghahremani Saghir

****Correspondance:***
Hamid Ghahremani Saghir

Coauthors:
Ali Naghi Karimi
Mehran Ehsani
Farshid Asoudeh
Siavash Nadem
Mohammad Abbasi

Introduction:

Inappropriate use of antibiotics is a global public health challenge and has been associated with antibiotic resistance. WHO reports show that efforts to promote rational antibiotic use in developing countries are poor. With the growing number of infections with antibiotic-resistant bacteria, rational drug use becomes imperative and studies that promote rational drug use are highly necessary. The aim of this study was to determine the pattern of administration of antibiotics in Guilan'sfamily physicians from the years 2014 to 2018.

Materials and Methods:

A cross- sectional retrospective study was conducted from July 2014 to September 2018 in which the family physicians surveyed3235597 prescriptions collected from 194 urban and rural comprehensive health centers from 16 counties of Guilan province. The percentage of prescriptions with antibiotics and antibiotic groups consumed by male and female family physicians was evaluated by using the Pharmaceutical Management Software of Guilan Provincial Health Department(PMSG).

Results:

Of the 3235597 Prescriptions processed, 872700 Prescriptions (17.7%) had at least one antibiotic. cephalosporin and penicillin groups had the highest administration rates. Among 5 most-consuming drugs, Cefixime was ranked third with 17.5%.

Conclusion:

The prescription and irrational use of antibiotics is a global and regional problem that can be solved by continuouslyeducating medical groups on rational administration prescribing and correct use of them and adequate training for the general public and culturalization to the properuse of antibiotic drugs. The findings have important policy implications for recommendations on the utilization of antibiotics in Iran.

Keywords: Antibiotic prescriptions, Rational antibiotic use, Family physicians, Microbial resistance, Pharmacoepidemiology

The synergism effect of probiotic Nis-Lact-Bif on diarrheagenic E. coli and Campylobacter jejuni

Hamid Reza Ebrahimi Nezhad*, Davoud Esmaeili

P326

Authors' Affiliations:
Student of pharmacy, Department Pharmaceutics, in Baqiyatallah university of medical science, Iran

Abstract Presenter:
Hamid Reza Ebrahimi Nezhad

****Correspondance:***
Hamid Reza Ebrahimi Nezhad

Coauthors:
Davoud Esmaeili

Introduction:

Probiotics are resident bacteria that live in or on human body as beneficial microorganisms which confer health benefits on the host. Nowadays, repeated antibiotic use or misuse, causes antibiotic resistance and detrimental effects on normal microbial flora. Great potential for prophylaxis and treatment of a range of microbial infections, make probiotics an effective remedy for this problem. The aim of this study was to investigate the antibacterial synergism of Lactobacillus spp., Bifidobacterium spp. and Escherichia coli strain Nissle 1917 (ECN) on clinical sample of diarrheagenic E.coli and Campylobacter jejuni.

Methods:

A paper disk diffusion technique used to evaluate the antibacterial activity. Sterile 6 mm paper disks were saturated with probiotic suspensions made by settling probiotic medications into distilled water. three kind of disks were prepared. One disk for Lactobacillus spp. and Bifidobacterium spp., another disk for ECN and third disk were also made by mixing probiotics. Clinical sample of diarrheagenic E. coli and Campylobacter jejuni were cultivated on separated Muller Hinton agars and disks were placed on the inoculated Muller Hinton agars. The plates were incubated with a microaerophilic gas pack inside an anaerobiosis jar, for 24 h at 37°C.

Results:

The zone of inhibition (ZOI) of bacterial growth were measured. All pathogenic microorganisms showed sensitivity to the probiotic disks. The combined disk had a better effect against pathogens.

Conclusion:

A considerable synergistic effect of probiotic strains was observed and it meant that combined strains can be more efficient against intestinal pathogens.

Keywords: probiotic, Lactobacillus. Bifidobacterium, Escherichia coli Nissle 1917, diarrhea, Campylobacter jejuni, E. coli