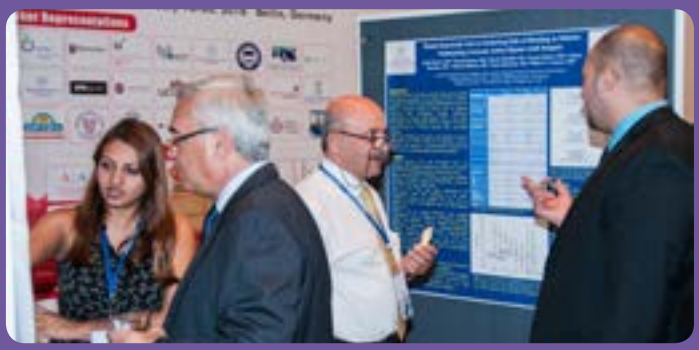

9TH ANNUAL EUROPEAN PHARMA CONGRESS

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Posters

Hicham H Khodr et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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The recovery of Oxyhaemoglobin in haemolysate by Desferal (DFO) and Defriprone (L1) that are currently in clinic use for the treatment of transfusional iron overlaod in beta thalassemia major patients

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The development of potent metal chelators has a great benefit in medicine, agriculture and industry. Surprisingly, the clinically use of defriprone (L1) in synergism with desferal (DFO) as potent metal chelators for the treatment of iron (III) overload in thalassemic patients, has additional clinical applications such as inhibiting prostate cancer proliferation at clinically relevant doses and plasma concentrations. Furthermore, the bidentate ligand L1 and hexadentate ligand DFO exhibit a great effect by recovering the oxyhaemoglobin from the iron-mediated oxidative damage on oxy-haemoglobin in haemolysed red blood cells after five minutes of iron addition (data not published yet). In this work, physical and chemical properties (pKas and β) values of L1 and DFO were used to theoretically show the potential of DFO over L1 in complexing iron (III). These simulations might offer an insight into which compound recovers faster the oxidative damage from oxyhaemoglobin that occurs in blood haemolysate associated with an accumulation of iron (III). This study shows that 0.5 mM DFO recover 95% of the oxidative damage of oxyhaemoglobin faster than that of 0.5 mM L1. This was measured by monitoring the absorbance in the visible region between 500 nm and 800 nm of the oxyheamoglobin with varying concentrations of iron (III) from 50 μM to 250 μM in 50 increment steps at physiological pH using 50 mM phosphate buffer in the presence and absence of L1 and DFO. The potential medical application of these compounds would be useful to prevent oxidative damage that occurs as a result of red blood cell haemolysis with the commensurate release of oxy-haemoglobin, that contributes to acute and chronic vascular disease, inflammation, thrombosis, and renal impairment.

Biography

Hicham H Khodr obtained his PhD in NMR studies of ligand-Ferritin interaction. He is an expert in NMR spectroscopy and programming. He had developed an autotitration system at King's College London Pharmacy, UK. This system enables us to study the physicchemical properties of many compounds that of agriculture and clinical uses. Furthermore, he worked with Prof. Hider group at KCL, Pharmacy in the area of synthesis and characterization of new candidate compounds as pro drug for the treatment of b-thalassemia major. His major target is to develop new candidate compounds (bidentate and tetradentate) for preventing the oxidative damage in red blood cell haemolysis as well as for the treatment of β-thalassemia major.

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Maria P et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Expression of antimicrobial peptide Hcap18/LL-37 following non-viral delivery of plasmid DNA encoded by CAMP gene in human fibroblasts and keratinocytes

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Skin wounds caused by burns have high global incidence. Autologous tissue recovery in these lesions is ineffective, due to affected area low vascularization and the susceptibility of the patients to infections caused by multi-resistant microorganisms, resulting in a high mortality rate. Non-viral vectors continue to be an attractive alternative to viral vectors due to their safety, ease of preparation and scale-up. These systems could represent a strategy to treat or improve skin wounds by genetically modifying own patients cells. In this work, we have developed a system of non-viral transfection of human keratinocytes and fibroblasts, consisting in a polymer/plasmid DNA complex (polyethyleneimine/CAMP modified Lenti-IRES bicistronic vector with tRFP), known as polyplexes in order to overexpress the antimicrobial peptide hCAP 18-LL37, which has been shown to exhibit a broad spectrum of antimicrobial activity as well as additional defensive roles such as regulating the inflammatory response and promoting re-epthelialization and wound closure. By measuring the amount of free pDNA, the formation and stability of the complexes were determined. Transfection efficiency in 2D cultures was evaluated by flow cytometry. Quantification of mRNA by RT-qPCR demonstrated the expression of the CAMP gene in transfected keratinocytes and fibroblasts; this suggests that the antimicrobial peptide hCAP18 / LL-37 are being expressed at higher levels than those of the same non-transfected cells. These are promising results for the use of polyplexes in the transfection of different cell types and stimulation of a gene of interest overexpression as the CAMP gene, with important antimicrobial and angiogenic effects on cutaneous wound healing.

Biography

Maria P is a Microbiologist and Bioanalist from the University of Antioquia. Her experience has been focused on scientific research, and, currently, she is a member of the Tissue Engineering and Cell Therapy Group. As a PhD student, with a student loan from COLCIECIAS (scholarship Program No.727 of 2015), she has been working on the development of a non-viral transfection system of human fibroblasts and keratinocytes, incorporated in an 3D skin model in order to over-express the antimicrobial peptide hCAP 18-LL 37 as a strategy for the treatment of skin wounds.

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Notes:

Ji Sook Han et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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2,7"- Phloroglucinol-6,6'-bieckol protects INS-1 pancreatic β cells against high glucose-induced apoptosis

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Background: Impaired function and decreasing numbers of pancreatic β cells are key factors in development of type 2 diabetes.

Aim: The aim of this study is to investigate whether 2,7"-phloroglucinol-6,6'-bieckol protects INS-1 pancreatic β cells against high glucose-induced glucotoxicity and apoptosis.

Results: High-glucose (30 mM) treatment led to glucotoxicity and induced apoptosis in INS-1 pancreatic β cells. But treatment with 10~50 μM of 2,7"-phloroglucinol-6,6'-bieckol significantly alleviated the glucotoxicity and increased the cell viability. The treatment with 2,7"-phloroglucinol-6,6'-bieckol decreased dose dependently intracellular reactive oxygen species, lipid peroxidation, and nitric oxide levels increased by high glucose treatment. Furthermore, 2,7"-phloroglucinol-6,6'-bieckol significantly reduced pro-apoptotic Bax, caspase 9, and caspase 3 expressions, whereas it increased anti-apoptotic Bcl-2 and PARP expressions. When the type of cell death was identified using annexin V/propidium iodide staining, 2,7"-phloroglucinol-6,6'-bieckol significantly decreased the numbers of early apoptotic and late apoptotic cells induced by high glucose.

Conclusion: These results suggest that 2,7"-phloroglucinol-6,6'-bieckol might be useful as a potential pharmaceutical agent to protect the pancreatic β cells against high glucose-induced apoptosis.

Biography

Ji Sook Han is a Professor and is doing research on developing a bioactive compound from natural plants, especially seaweeds, and investigating its effect for the prevention and treatment of obesity and type 2 diabetes. The active compound containing in seaweeds may be a good anti-diabetic source by improving insulin secretary defect or insulin resistance. It may also be a potential anti-obesity source owing to its inhibitory effect on adipogenesis. She evaluates the effect and mechanism of a bioactive compound isolated from natural plant through *in vitro* and *in vivo* study.

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Notes:

Abdulaziz Alhedethe, Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Substandard *Amoxicillin* in Sierra Leone

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Bacterial resistance to antibiotic is posing a global health threat as many antibiotics no longer work against urinary and skin infections. Prevalence of substandard medicine in the developing countries can lead to further development of new strain with antibiotic resistance. Sierra Leone is one of such countries where multidrug resistant Shigella dysenteries serotype and tet (x)- containing clinical isolates are already detected. A mystery shopper has visited a local market in Sierra Leone and purchased 6 different brands of Amoxicillin capsules, which has been analysed using spectroscopic methods. The sample of Amoxicillin capsules has been purchased using convenience sampling approach at an undisclosed location in Sierra Leone. The 100 mg of sample was dissolved in D2O and 100 mg of sample was dissolved in CD3OD. The dissolved sample was vortexed for 30 seconds, followed by centrifugation. The supernatants were filtered when transferred in to NMR tubes. The 1D 1H and 1H2D COSY NMR spectra were acquired using JEOL ECA 600 MHZ at 298 K and were processed JEOL Delta software. The weighing of the content of the capsules has provided initial indication that some of the purchased medicine is substandard. Furthermore, preliminary NIR measurement has suggested that there is significant variation in the sample composition between manufactures. The pilot study of the quality of medicine in developing countries has indicated that substandard medicine is freely available on the market despite efforts by governments to improve their healthcare system. The poor quality medicine can harm patients directly via lack of effort or toxicity of additional components, but it can also contribute to the spread of bacterial resistance to antibiotics.

Biography

Abdulaziz Alhedethe is a fully qualified Pharmacist committed professional with a genuine interest in improving patient's services and customer awareness focused on compliance. He is self-motivated and able to take the initiative, able to give specialized services to help patients' manage conditions. He is able to guide customers on the selection of medicines brands, medical equipments and health care supplies.

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Dina S. El-Kafrawy et al, Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Validated stability-indicating HPLC-DAD method for simultaneous determination of sertaconazole nitrate, Sorbic acid and Methylparaben in cream dosage form

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This study deals with the development and validation of a comprehensive stability-indicating high performance liquid chromatography with diode array detection (HPLC-DAD) method for simultaneous determination of sertaconazole nitrate (SN), sorbic acid (SA) and methylparaben (MP). To the best of our knowledge, no published methods could be found in the scientific literature for analysis of this ternary mixture. Effective chromatographic separation was achieved using Venusil XBP CN column (4.6 × 250 mm) with gradient elution of the mobile phase composed of mixed phosphate buffer pH 2.5 and acetonitrile. The quantification of SN was based on measuring its peak areas at 225 nm, while the quantification of MP and SA was based on measuring their peak areas at 259 nm. SA, MP and SN peaks eluted at retention times of 4.76, 6.77 and 11.28 min, respectively. Analytical performance of the proposed HPLC procedure was thoroughly validated with respect to system suitability, linearity, ranges, precision, accuracy, specificity, robustness, detection and quantification limits. The linearity ranges for SN, MP and SA were 1–200, 1–250 and 0.5–100 μg mL−1, respectively, with correlation coefficients >0.9999. The analytes were subjected to forced-degradation conditions of neutral, acidic and alkaline hydrolysis, oxidation, photo and thermal degradation. The proposed method proved to be stability-indicating by resolution of the analytes from their forced-degradation products. Moreover, specificity of the method was verified by resolution of the analytes from more than 15 pharmaceutical compounds of various medicinal categories. The validated HPLC method was successfully applied to the analysis of the cited compounds in their combined cream dosage form. The proposed method made use of DAD as a tool for peak identity and purity confirmation.

Biography

Dina S. El-Kafrawy is graduated 2003 from faculty of pharmacy, Alexandria university. She has her expertise in development and validation of new analytical methods for the determination of various drugs in their pure form and different dosage forms, also development of stability indicating analytical methods for many drugs and their simultaneous determination with their degradation products and related substances. She has got her master in pharmaceutical sciences 2007 and her PhD 2012.

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Notes:

S Hernandez Castro et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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A PET study with [11-C] Raclopride in Hemiparkinsonism model: Preliminary results on the effect of a TiO_2DA matrix implanted in the caudate nucleus

S Hernandez Castro[1], **P Vergara-Aragon**[1], **G Valverde-Aguilar**[2], **David Diaz-Diaz**[1], **Aurora Sanchez-Garcia**[3], **Ketzalzin Meza-Aupart**[1], **Aratxa Cabrera-Laguna**[1], **Paul Jiménez-Prado**[1], **Jose Mendoza-Escalona**[1], **Fernanda Gutierrez-Rivas**[1] and **Gerardo Luna-Leon**[1]

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It is now widely accepted that compensatory mechanisms are involved during the early phase of Parkinson's disease (PD) to delay the expression of motor symptoms. Our objective was to determine the effects on motor behavior in a TiO2DA implant inserted in the caudate in a hemiparkinsonism rat model and its correlation with the *in vivo* binding of [11-C] raclopride to D2 dopamine receptors in its basal ganglia. Each rat underwent a PET study, before and after treatment with microimplant. Male Wistar rats (250-300 gr) were used and divided into 4 groups: Sham, Lesioned (Lx), Lx+implant and Implant. Post-lesion for 21 days anxiety behavior and locomotor activity of the rats of each group through the open field test was evaluated. The test was made in an acrylic box (with transparent walls and floor), whose floor is divided with painted black lines forming's squares and illuminated with floodlights. The test was recorded for five minutes; the following measurement parameters were assessed: total distance traveled and the number of crossed lines marked on the floor. The tests were recorded. In each group analysis of microPET was done, each rat underwent a PET study, before and after treatment with microimplant. The implant induced an increase in the *in vivo* binding of [11C] raclopride in the striatum of hemiparkinsonian rats. This observation indicates that there is a higher amount of transporters bound to striatal dopamine; higher dopamine levels were found in the Lx+Imp group than in the Lx group as well as a larger number of dopaminergic neurons in striatum in the histological analysis. This observation indicates that the microimplant with dopamine produce an increase in extracellular levels of dopamine sufficiently to inhibit raclopride binding, this effect probably due to dopamine release from TiO2DA matrix implanted in caudate nucleus.

Biography

S Hernandez Castro is a 3rd year Medical student from the Universidad Nacional Autonoma de Mexico. She has been a part of the investigation program from the Faculty of Medicine since 2014 and she was part of the Organization Committee of the International Contest of Medical Knowledge organized in the faculty since the same year. Also, she is a Technician in Histopathology certified by the same university.

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Notes:

P Vergara-Aragón et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Is it possible to reverse the motor alterations with dopamine supply content in an amorphous matrix in a hemiparkinsonian rat model?

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The aim of this study was to evaluate the effect that applies an amorphous matrix with dopamine obtained by sol-gel method produces in the caudate nucleus of induced hemiparkinsonian rats. The estimation of this matrix with dopamine effects was evaluated by behavioral, histological and neurochemical tests. We used 64 male Wistar rats about 250-300 g aleatory divided in 4 groups of 8 each one with free access to water and food. The groups that conformed each experimental block were: Control (C), Lesioned (Lx); Lesion + implant (Lx-IMP) and Implant (Imp). The behavioral evaluation was made on day 1, 21, 90, 180 and 360 of the experimental phase. It was made an evaluation of the exploratory behavior and induced twist. We exanimated the fine motor in the reach test, number of induced twist with APO and we determinate the DA levels by HPLC in the SN and NC. The results showed differences ($p<0.05$) between Lx group compared with control in the test made. Also, we found statistically significant differences between Lx and Lx+Imp groups with reports of improvement in the implant group. These results suggest that the dopamine was released through the nanoporos that has the matrix with dopamine walls resulting in a frank rise in the number of squares walk in the open field test for the Lx+Imp group, less number of induced rotations, better performance in the reaching task and superior dopamine levels compare with Lx group. With these results we can conclude that a matrix with dopamine implanted in the NC of hemiparkinsonian rats causes a beneficial effect that we attributed to the released dopamine in the rats with hemiparkinsonism + implant caudate nucleus.

Acknowledgement: The authors acknowledge the financial supports of SIP 20170002, DGAPA-PAPIIT IT200813 and DGAPA PAPIIT IT202417

Biography

P Vergara-Aragón has done her MD and PhD in Psychological Research and has worked in the Faculty of Medicine UNAM in Mexico for more than 30 years. She is collaborating with the Physics Institute of the National Polytechnique Institute. Her research is focused on the field of Parkinson Disease (PD): Study of the nigrostriatal pathway degeneration, and involved mechanism caused by rotenone and 6-OHDA; stabilization of dopamine and its use as treatment for PD; the study of the effects produced *in vivo* of a TiO2 amorphous matrix as a reservoir for dopamine in a PD model in rats; description of the cognitive implications of PD in patients; toxicity and biological implications of rotenone exposure in animal models.

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Blanca I Ketzalzin Meza-Aupart et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Evaluation of the effects that produce a micro-implant with dopamine stabilized and inserted in the caudate nucleus in hemiparkinsonism rat model induced on motor activity and its relationship to the levels of dopamine

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Aim: The purpose of this project was to determine the effects of an implant TiO2DA inserted in the caudate nucleus in a rat model hemiparkinsonism induced on motor activity and its correlation with dopamine and serotonin levels.

Material & Methods: Male Wistar rats (250-300 g) were used, which were randomly divided into 4 groups: a) control b) injury (Lx); c) Lx+implant (Lx+I); d) Implant (I). For 21 days post-injury motor activity was evaluated and for: 1. The exploration behavior, the test was recorded for five minutes, and were assessed global activity time, and inactivity time; 2. The rotational behavior was recorded for fifty minutes, through count of spins; 3. The swimming forced test evaluated the activity and inactivity in the fishbowl and test was recorded. In each group, test for determination levels of dopamine was performed, by means of HPLC.

Results: The exploratory behavior in the Lx group showed a decrement significative of activity exploratory regarding control group, for the other hand, Lx+I group enhanced the activity exploratory and movements in relationship to Lx group, showing similar behavior to the control group. The group I had not showed significantly difference to control group. In the rotational behavior, the control group rats showed spins to the predominant side, Lx group increased the number of spins toward contralateral injury side with respect to control group, Lx + I group revealed similar activity to control group and showed significant difference to Lx group. In the swimming force test the Lx + I group, increased significantly swimming behavior in relationship to Lx group. Implant group showed hyperactivity in swimming behavior. HPLC showed an increased level of DA in Striatum vs. Lx and Control group. The results obtained in our model suggest that the TiO2DA implant in the caudate nucleus of rats induces a beneficial effect that can be attributed to the dopamine released from the TiO2DA complexes into caudate nucleus.

Biography

Blanca I Ketzalzin Meza-Aupart is a Medical student in the Faculty of Medicine of the National Autonomous University of Mexico (5th semester). She is a part of the program for the Support and Promotion of Student Research (AFINES) at the Faculty of Medicine. Her research project is focused on the field of Parkinson Disease (PD), specifically: Degeneration study of the nigrostriatal pathway caused by the effect of rotenone and 6-OHDA; Toxicity and biological implications to model animals caused by the exposure of Rotenone; Stabilization of Dopamine whit a TiO2 amorphous matrix and its use as treatment for PD; The study of the effects that a TiO2 amorphous matrix produces as a dopamine reservoir in PD model in rats; Description of the cognitive , motor and behavioral implications of PD in rats with induced hemiparkinsonism and; Description of the cognitive , motor and behavioral implications of PD in rats with induced hemiparkinsonism and TiO2 implant treatment.

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Notes:

Guadalupe Valverde Aguilar et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
DOI: 10.4172/2167-7689-C1-025

Release of dopamine encapsulated in a TiO_2 matrix in the striatum improves the motor activity in hemiparkinsonism model of the rat

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[1]CICATA- Instituto Politécnico Nacional, México
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Statement of the Problem: Parkinson´s disease is a neurodegenerative disorder characterized by progressive loss of dopaminergic neurons in the substantia nigra causing dopamine depletion in the striatum. The purpose of this research was to evaluate the temporal stability of dopamine encapsulated in a titanium dioxide (TiO2) matrix synthesized by sol-gel method under atmospheric conditions. The formation of the oxidation products from dopamine were analyzed by color change of the microimplant, optical absorption and infrared spectroscopy. The evaluation *in vivo* on the locomotor activity in the open field test of hemiparkinson rat model was studied.

Material & Methods: a) TiO2 precursor solution. A mixture of Tetrabutyl orthotitanate and diethanolamine which prevent the precipitation of oxides and stabilize the solutions was obtained with deionized water. Tetraethyleneglycol was added to the above solution under stirring. b) TiO2/DA solution. To 20 ml of TiO2 solution prepared in section (a), the Dopamine was added and the sol was stirred at room temperature under darkness. The states of dopamine oxidation were evaluated using infrared spectroscopy. Forty Wistar rats were divided into 4 groups: Sham, Lx (hemiparkinsonian), Lx + TiO2/DA matrix, and TiO2/DA matrix only. Induced rotation test and locomotor activity task were performed on days 0, 1, 21, 90 days after the insertion of the TiO2/DA in the caudate nucleus.

Findings: Results show that the TiO2 matrix can protect the dopamine inhibiting its chemical instability and retarding its oxidation gradually. Less induced rotations and better performance in the locomotor activity during the 90 days of the experimental evaluation suggest that probably dopamine successfully stabilized and it was released from its reservoir in the striatum.

Conclusion: Advantages of this treatment are its easy and fast elaboration, low cost and immediate benefits on the motor disturbances presented by the animals with hemiparkinsonismo.

Biography

Guadalupe Valverde Aguilar obtained her PhD in Physics (2003) at Institute of Physics, UNAM. Her Post-doctoral stay was made in UCLA, USA for two years. Her research is focused on electrical and optical properties from amorphous and nanostructured sol-gel materials. Her field of research includes photoluminescence, drug delivery, photoconductivity and hydrogen production. She has published 58 papers in international journals.

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Notes:

Eman I El Kimary et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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High performance thin layer chromatographic resolution of the enantiomers of some racemic β-blockers using β-cyclodextrin as chiral selector

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Statement of the Problem: Large number of β-blockers' marketed formulations contain racemic mixtures except for levobunolol and betaxolol. As the two enantiomers have different stereoselective mechanisms, they should be considered as different drugs. Taking into consideration the numerous side effects of these drugs and that the only pharmacologically active enantiomer is the levo- one whereas the dextro- enantiomer is inactive or harmful in some cases, there is no doubt that reliable and rapid methods should be developed for monitoring the stereoselective synthesis or checking enantiomeric purity.

Methodology: The present work involves economic novel procedure for separation of the two (+) and (-) enantiomers of the drugs sotalol, carvedilol and betaxolol using β-cyclodextrin as chiral mobile phase additive. Chromatographic separation was performed on Fluka HPTLC silica gel plates 60 F254 (20×10 cm). The mobile phase used consists of acetonitrile-methanol-acetic acid-water (4:3:0.2:1 v/v) and containing 0.3 mM β-cyclodextrin. Detection of the spots was performed using iodine vapor or densitometrically at 245 nm for carvedilol or at 220 nm for both betaxolol and sotalol.

Findings: Using the proposed method, linear calibration graphs were obtained for (-) and (+) enantiomers of betaxolol in the ranges 0.5-6.0 and 0.4-6.0 μg/band, respectively ($r>0.998$, $n=6$) with good accuracy and precision (%Er and %RSD <2.0%). Limits of detection for (-) and (+) enantiomers were 0.15 and 0.13 μg/band, respectively. The sensitivity for the detection of sotalol and carvedilol racemates was 0.3 and 0.2 μg/band, respectively.

Conclusion & Significance: The proposed method is selective and simple for separation of the enantiomers of carvedilol and sotalol and quantitation of both (-) and (+) betaxolol enantiomers in the bulk and in pharmaceutical preparatio.

Biography

Eman I El Kimary is an Associate Professor of Pharmaceutical Analytical Chemistry and Quality Control at the Faculty of Pharmacy, Alexandria University, Egypt. She received BSc in Pharmacy in 2003, Master's degree in Pharmaceutical Analysis in 2007 and PhD in Pharmaceutical Analysis in 2011 from Faculty of Pharmacy, Alexandria University. Currently, she is teaching general and physical chemistry, analytical chemistry, instrumental analysis and pharmaceutical quality control to pharmacy students at Alexandria University. She has the practical experience in working with devices such as: High performance liquid chromatography, polarograph, spectrofluorimeter, spectrophotometer, etc. She attended about 22 scientific and professional workshops and training courses and published about 18 research papers in peer reviewed scientific journals and about 8 abstracts in national and international conferences. She served as a Reviewer for more than 5 journals specialized in analytical chemistry and its applications.

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Formulation and characterization of *Piribedil* buccal tablets

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Piribedil is a piperazin derivative drug used in the treatment of Parkinson's disease. Orally administrated *piribedil* has low bioavailability (10%) accompanied with gastrointestinal and cognitive side effects. Buccal tablets are thin and flat tablets with 5-8 mm diameter which are applied to the oral mucosa in the mouth cavity. This route of administration increases bioavailability of drugs by eliminating the hepatic first pass effect and reduces side effect risks with controlled release by lowering the required dosage. In this study, buccal tablets were prepared by using three different polymers; carbopol (CP), hydroxypropyl methylcellulose (HPMC) and carboxymethyl cellulose (CMC) at three different concentrations to achieve controlled release. Physicochemical properties of powder and tablet formulations were investigated and dissolution studies were conducted. These tablets were also subjected to stability studies for 6 months at 40±2oC and 75±5% relative humidity. Physical characterization results were satisfactory and met compendial limits for all formulations. Slowest drug release was observed with CP followed by HPMC and CMC respectively. Drug release kinetics displayed diffusion-polymer relaxation for CP and HPMC and diffusion-tablet erosion for CMC tablets. Piribedil was found to be compatible with other tablet ingredients and tablets retained physical properties after 6 months of stability studies. Buccal tablets containing piribedil designed for the first time may serve as a new alternative for the Parkinson's disease treatment.

Biography

Burak Çelik has completed his graduation from Faculty of Pharmacy at Yeditepe University and PhD from Istanbul University, Department of Pharmaceutical Technology. He is currently working at Bezmialem Vakıf University, Faculty of Pharmacy as a Research Assistant.

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Notes:

Ji Sook Han et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Pheophorbide a isolated from *Gelidium amansii* inhibits adipogenesis by down-regulating adipogenic transcription factors in 3T3-L1 adipocytes

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[4]Jeju National University, Republic of Korea

Background: Adipocyte lipid accumulation causes adipocyte hypertrophy and adipose tissue increment, leading to obesity. Thus, this study investigated the anti-adipogenic effects of pheophorbide A isolated from *Gelidium amansii* in 3T3-L1 adipocytes.

Methods: Upon differentiation of 3T3-L1 pre-adipocytes into adipocytes, they were treated with pheophorbide A (0–83 μM).

Results: Pheophorbide A inhibited triglyceride accumulation and stimulated glycerol release in a dose-dependent manner in 3T3-L1 adipocytes. In addition, pheophorbide A significantly decreased leptin levels in 3T3-L1 adipocytes. Pheophorbide A inhibited adipogenesis via suppression of the expression of adipogenic transcriptional factors including peroxisome proliferator-activated receptor γ (PPARγ), CCATT/enhancer binding protein α (C/EBPα), sterol regulatory element binding protein 1c (SREBP1c), and fatty acid synthase (FAS). It also induced the expression of phosphorylation of AMP-activated protein kinase (AMPK).

Conclusion: Pheophorbide A isolated from *Gelidium amansii* inhibit adipogenesis by down-regulating adipogenic transcription factors in 3T3-L1 adipocytes. These results suggest that pheophorbide A may be useful for the prevention or treatment of obesity owing to its inhibitory effect on adipogenesis.

Biography

Ji Sook Han is a Professor and is doing research on developing a bioactive compound from natural plants, especially seaweeds, and investigating its effect for the prevention and treatment of obesity and type 2 diabetes. The active compound containing in seaweeds may be a good anti-diabetic source by improving insulin secretary defect or insulin resistance. It may also be a potential anti-obesity source owing to its inhibitory effect on adipogenesis. She evaluates the effect and mechanism of a bioactive compound isolated from natural plant through *in vitro* and *in vivo* study.

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Notes:

Katerina O Filatova et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Nano- and submicro-sized mesoporous silica particles with tunable size and porosity as perspective biopharmaceutically active excipients

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Conventional development in an understanding of the reasons of diseases with a deepening of knowledge in pharmacokinetic mechanisms allows developing modern dosage forms for the effective, safe and reliable application of bioactive compounds at the targeted site of action within a desirable time and duration. Unfortunately, current excipients cannot meet all the requirements to the modern pharmaceutical formulations and mostly play a role of fillers. However, an active ingredient is just one part of the medicine administered to the patient and it is the formulation of the drug and an excipient that translates drug properties into clinical effect. It is shown that dosage forms engineered using the nano- and submicro-scaled excipients have an additional functionality and can control a pharmacological effect of a drug. Nanomaterials as active excipients not only improve pharmacokinetic of cargo molecules but also increase their solubility and permeability, which is of great importance because just nearly 25% of all pharmaceutically active compounds are recognized as highly soluble and permeable, while the rest of them has either/or low solubility and permeability or even both of them simultaneously with other disadvantages (very short or very long shelf-life, poor adsorption through GIT). In the sight of aforementioned a concept of therapeutic treatment is realized in a development of silica-based nanomaterials that maintain drug concentration in GIT at a desired value as long as possible, i.e. they are able to exert a control on the drug release rate and duration, for further pharmaceutical implementation as an active excipient in solid dosage forms. Silica-based submicro- and nanoparticles were prepared using a template sol-gel approach in the presence of cationic and nonionic surfactants. Methotrexate was loaded into silica-based mesoporous materials with different textural properties. An amount of the drug loaded and an *in vitro* release kinetics were revealed as a function of the pore size of the materials. Release of methotrexate from synthesized carriers in comparison with the release from the commercially available pharmaceutical form mimicking an oral administration was investigated. It was turned out that silica-based materials exhibit control release kinetic with the absence of a burst effect, while the later one is considerably worst in an adjustment of controllable *in-vitro* pharmacokinetic of a drug. Mesoporous materials with a wide range of size (25-1000 nm) and variable textural characteristics were obtained that allowed to adapt different synthetic routs for further use as the perspective reservoirs for carrying in pharmaceutical means. Further development of the pharmaceutical forms on the basis of silica-based nano- and submicro-materials will ensure that a drug will be available at the desired site within the required time and duration. Those materials can serve as substituents of current fillers in pharmaceutical formulations.

Biography

Katerina O Filatova has completed her Master's in 2009 from VNMU Pyrogov b.n., Pharmaceutical Faculty. Currently, she is studying Doctoral program at the Technological Faculty at the TBU in Zlin, Czech Republic.

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Docking study of 2-aroyl-[1]benzopyrano[4,3-c]pyrazol-4(1H)-one derivatives and related hydrazide-hydrazones and their antimycobacterial activity

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A series of coumarin-linked hydrazide–hydrazones 4a-e and 2-aroyl-[1]benzopyrano[4,3-c]pyrazol-4(1H)-ones 5b-g were synthesized via an efficient one-pot protocol. All compounds demonstrated significant minimum inhibitory concentrations (MIC) ranging from 0.28 to 1.69 μM against reference M. tuberculosis H37Rv strain. The cytotoxicity against the human embryonic kidney cell line HEK-293 was also evaluated and the selectivity of the antiproliferative effects was thus assessed. All compounds displayed good SI values ranging from 33 to more than 645. In general, 2-aroyl-[1]benzopyrano[4,3-c]pyrazol-4(1H)-one derivatives 5b-g possessed potent antimycobacterial activity combined with low cytotoxicity what resulted into SI values higher than that of their open chain analogues 4a-e. The activity of the tested compounds may be attributed to the significant interactions with the inhibitor binding cavity of M. tuberculosis Enoyl-ACP reductase and\or related to ability of the tested compounds to penetrate mycobacterial cells.The above observations show that the novel hydrazide–hydrazones 4a-e and 2-aroyl-[1]benzopyrano[4,3-c]pyrazol-4(1H)-one derivatives 5b-g have potential as antimycobacterial agents. The results of the study can be utilized to further optimize and improve the potency and selectivity toward ENR enzyme by varying the basic skeleton and the substituents.

Biography

Valentin Karabelyov has completed his secondary education in 2013 from National High School of Maths and Science. Now he is studing in the Medical University of Sofia, Faculty of Pharmacy and he is a fourth year student of Faculty of Pharmacy. He works as an assistant in a pharmacy from 3 years ago. He is interested in the fields of LC-MS, Organic synthesis, Pharmacognosy, Pharmacology and Pharmacotherapy. Last year, Valentin participated in the European Chemistry Congress, where he presented a poster on the theme ,, Anticonvulsant activity of newly synthesized benzoylhydrazones with 2H-chromene and coumarin moieties in ICR mice.

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PVA-composite membranes for biomedical applications: A review of blended polymers

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A series of excellent poly(vinyl alcohol) (PVA)/polymers blend hydrogel membranes were reviewed using different crosslinking types to obtain proper polymeric dressing materials, which have satisfied biocompatibility and sufficient mechanical properties for wound dressing application. The importance of biodegradable–biocompatible synthetic polymers such as; PVA, natural polymers such as; alginate, starch, and chitosan or their derivatives has grown significantly over the last two decades due to their renewable and desirable biological properties. The properties of these polymers for pharmaceutical and biomedical application needs have attracted much attention. Thus, a considered proportion of the population need those polymeric medical applications for drug delivery, wound dressing, artificial cartilage materials, and other medical purposes, where the pressure on alternative polymeric devices in all countries became substantial. The review explores different polymers which have been blended previously in the literature with PVA as wound dressing blended with other polymeric materials, showing the feasibility, property change, and purpose which are behind the blending process with PVA. The wet-retentive dressings have been chosen previously based on the type of wound-shape. Conversely, polymeric hydrogel membrane dressings were found currently a convenient for any wound and burn, regardless the wound-shape. The first generation of membranes dressings is based on natural polymers, which are among the core topics intensively discussed in literatures. Biopolymers (e.g. chitosan, glucan, alginates, and hyaluronan) are more efficient as a wound-healing accelerator than synthetic polymers. Interestingly, the wounds covered with biopolymers, e.g. chitosan-based dressings showed fast healing rate and scarless healing, which are similar to those of normal skin. The second generation of dressings is based on the combination between biopolymers and synthetic ones using favorable physical crosslinking method that is a convenient for healing process. PVA the most frequent and versatile synthetic polymer was blended with either biopolymers or synthetic ones for wound dressing fabrication. PVA-biopolymer composite membranes exhibited better biological and antimicrobial activities than those composite with synthetic polymers, mainly PVA-chitosan and PVA-alginate membranes. Moreover, PVA-biopolymers composite membranes containing healing agents (e.g. Aloe vera, PEG, sterculia /Arabic gums) or antibiotics (e.g. sod. ampicillin or gentamicin) suggested being typical dressings for acute and chronic wounds. Some polymers like hydroxypropyl methylcellulose were added into nanofibers to keep high water retention and the moist environment. The third generation of dressings is based on PVA-nanoparticles and composite membranes were exploited to achieve the features of polymer and nanofillers for improving the performance of dressings for faster healing rate, pain relieving role, and easier removal. It is elaborated that the incorporation low content of ZnO or silver nanoparticles promoted feasibly the biological activity and microbial resistance of PVA-composite membrane. Graphene-based membrane dressings showed a surprised resistance against Gram negative bacteria. Finally, it have decided that natural polymers based dressings have outperformed synthetic polymers, while additives were incorporated to accelerate the healing or improve the mechanical potential, which were lately found advanced therapeutic impact as wound dressings.

Biography

Elbadawy A Kamoun (PhD Assoc. Prof.) received his PhD in Macromolecular Chemistry at the Braunschweig University of Technology (TU-BS) in February 7th, 2011 (Braunschweig, Germany). He obtained four Post-doctoral fellowships in 2012, 2014, 2016 from Institute for Technical Chemistry (TU-BS, Germany) and in 2013 from Dep. of Macromolecular Sciences, Fudan University in Shanghai, P R China, respectively. In April 3rd, 2016, he got promoted as Associate Professor at Polymeric Materials Res. Dep., SRTA-City, Egypt. His main interests are in polymeric membranes, for biomedical applications, wound dressings and for fuel cells, hydrogels, polymeric materials for electronic packaging, and photopolymerization.

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Role of the pharmacist in decreasing discharge medication discrepancies: A prospective observational study

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Medication Reconciliation (Med.Rec) is a major intervention which reduces medication discrepancies and subsequent patient harm at different patients' care transitions. Data on the incidence of the unintended medications discrepancies ranges from 40–50% upon admission to acute care hospitals and 40% at hospitals discharges. Pharmacists' role in Med.Rec is highly recommended due to their distinct knowledge, skills, and abilities to establish and maintain effective Med.Rec process. Pharmacy Med.Rec at admission or discharge is a crucial step for an error free environment. Outpatient pharmacist play a lead role in detecting medication related problems; this urges the need to translate their qualitative values into quantitative measures.

Primary objective: to investigate the impact of outpatient pharmacists' interventions during discharge reconciliation, in reducing medication errors and discrepancies. Secondary objective: to detect the most common medication related problems.

Methods: A prospective observational study, conducted at a 62-bed tertiary care cancer center (National Centre for Cancer Care & Research) in Qatar. All discharged patients were included in the study over duration of 10 months (from 1st April 2014 to 31st January 2015). Patients who were discharged from the chemotherapy infusion unit were excluded. A standardized intervention form was generated to document interventions. Collected data were categorized into medication error or medication discrepancy. A statistical analysis included exploratory analysis and descriptive statistics using STATISTICA 11.0 Version.

Results: Total of 591 discharge prescriptions included, 278 (47%) required pharmacist interventions; with 190 medication discrepancies and 122 medication errors. The most common medication related problems were incomplete orders (34%) and prescribing restricted medication without privilege (29%).

Conclusion: Outpatient pharmacists have a significant role towards detecting and reducing medication errors and discrepancies upon patient discharge. However, despite their effective interventions, most of these medications related problems are preventable. An improved quality process and awareness can create an efficient medication safety environment.

Biography

Dr. Shereen Elazzazy received her bachelor degree in Pharmacy from Egypt in 1997 and her Doctor of Pharmacy degree at Purdue University, USA in 2011. She has extensive international experience working in Egypt, KSA, and Qatar, and recently completed internship in Indiana, USA. Her areas of expertise are mainly oncology, nutrition, palliative care, aseptic pharmaceutical preparations and pharmaceutical registration/ regulations. Currently she is an Asst. Director of Pharmacy - Clinical Services in the National Center for Cancer Care and Research, Qatar, an Adjunct Clinical Faculty in College of Pharmacy, Qatar University, a Clinical Preceptor for Collage of Science, North Atlantic, Qatar, local mentor for Pharmacy School, Queen's University, UK, and a Clinical Sponsor, PharmD program, University of Colorado, USA. She has numerous peer-reviewed publications and active presentations in national, regional and international conferences in the areas of oncology, hematology, infectious diseases, palliative care, clinical pharmacokinetics, and nutrition

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Valery Gmiro et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Comparative study of analgesic effect of N-decyltropine (IEM-1556), adenosine and mecamylamine

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Mecamylamine, nonselective antagonist of cholinergic nicotinic receptors after intramuscular (i.m.) and intragastric (i.g.) administration causes maximal analgesia in the tail-flick test in only 30% of the rats, and also reduces time of paw licking in the formalin test of only 30% compared with the control, suggesting relatively weak analgesic activity of mecamylamine in both tests. Adenosine in a dose of 25-30 mg/kg and IEM-1556 (N-decyltropin chloride) in a dose of 1-3 mg/kg after intramuscular and intragastric administration cause maximal analgesic effect in the tail-flick test and formalin test in 80-100% of the rats. Dipyridamole inhibiting reuptake of adenosine, in 9-12 times reduces ED50 of adenosine and IEM-1556, and antagonist of adenosine receptors of 1,3-dipropyl-8-phenylxanthine (DPX) in 3.8-4.5 times increases ED50 of adenosine and IEM-1556 in both tests. The received results, evidence in favor of participation of endogenous adenosine in the mechanism of the analgesic action IEM-1556. Preliminary anesthesia of the gastric mucosa with 1% lidocaine and subdiaphragmatic gastric vagotomy almost equally in 3.7-4.4-fold increase ED50 IEM-1556 and adenosine in both tests, indicating the involvement of vagal afferents in gastric mucosa in the development of analgesic action both IEM-1556, and adenosine. Coincidence of mechanisms of the vagus-stimulating and analgesic action of exogenous adenosine and IEM-1556 demonstrates that IEM-1556 as a probable liberator of endogenous adenosine after system and oral administration in a low dose of 1-3 mg/kg causes development of analgesia as a result of stimulation of adenosine -sensitive vagal afferents in gastric mucosa. In higher doses the analgesic effect of IEM-1556 (which isn't eliminated by DPX, vagotomy and lidocaine) is presumably explained by additional blockade of cholinergic nicotinic receptors in CNS.

Biography

Valery Gmiro is the leading Researcher of Institute of Experimental Medicine (Russia). He has published more than 150 papers in reputed journals. The main scientific interest concerns the Chemistry and Pharmacology of biologically active compounds. He is the USSR State Prize Winner for the investigations in the field of Physiology of Synaptic Transmission. During the last years, he has been working on the problem of the creation of adaptogenic drugs acting through activation of afferent nerves. These drugs were shown to be effective tools to study the mechanisms of transmission of afferent signals and may be of interest in clinical usage.

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Sahar S Nasser et al., Pharmaceut Reg Affairs 2017, 6:1(Suppl)
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Effect of denosumab versus zoledronic acid on calcium levels in cancer patients with bone metastasis: An observational retrospective cohort study

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Background: Bone-targeting agents (BTA) like zoledronic acid (ZA) and denosumab (DE) are approved for prevention of skeletal-related events (SREs) in patients with bone metastases (BM) including hypercalcemia of malignancy (HCM). Hypocalcemia has been observed with both ZA and DE. However, studies showed a higher incidence of hypocalcemia with denosumab. International guidelines do not favor one BTA over the other. Due to the differences in patients' characteristics and treatment related factors; hypocalcemia incidence might differ in varying cancer settings.

Primary Objective: Primary objective of the study is to identify the incidence of hypercalcemia and hypocalcemia in ZA and DE groups.

Secondary Objective: Secondary objective is to identify the correlation between calcium supplement and calcium level control.

Methods: An observational retrospective cohort study was conducted by reviewing patients' electronic records, laboratory and medication reports from August 1st 2015 till July 31st 2016. Adult cancer patients diagnosed with BM secondary to a solid tumor or multiple myelomas and receiving either ZA or DE were included. Other indications for BTA were excluded. BTA administration visits were collected, evaluated and analyzed.

Results: A total of 271 patients (1367 visits) were included in our study. Over incidence of hypocalcemia in DE group compared to ZA was (4.1% vs. 3%, OR=0.72, CI 95% [0.43–1.19]). Hypercalcemia was reported in both groups (3.5% vs. 5.3% respectively, CI 95% [0.97–2.4]). Breast cancer was the most common malignancy associated with hypocalcemia (70%) followed by (10%) in both prostate cancer and multiple myelomas. Patients received calcium supplement were 23% less likely to develop hypocalcemia (RR=0.77, CI 95% [0.48–1.23]).

Conclusion: Despite hypocalcemia was common in DE group, it was not statistically significant. Adequate calcium intake substantially reduces the risk of hypocalcemia. Our results highlight the importance of preventing hyper and hypocalcemia upon BTAs initiation and during treatment by regular monitoring of calcium levels, and providing calcium supplements accordingly.

Biography

Sahar S Nasser has received her Bachelor's degree in Pharmacy from Qatar University, College of Pharmacy (CCAPP accredited) in 2011. She began her pharmacy career at the National Center of Cancer Care and Research (NCCCR). She is also a Clinical Preceptor for undergraduate pharmacy students and got promoted to Senior Pharmacist in 2015. She has recently completed her Post-graduate year 1 (PGY1) Pharmacy Practice Residency in Hamad Medical Corporation (in candidate status for accreditation by ASHP). Her early-career focus was on patient centered care practice and medication safety. Throughout her career, she participated in various educational activities directed to healthcare providers, students and patients. Her main research interest is in improving cancer patients' outcomes and cancer epidemiology.

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The effect of ranitidine intakes on hemodialysis efficacy among end stage renal disease (ESRD) patients in Saudi Arabia

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Statement of the Problem: Inefficiency of hemodialysis (HD) is a major cause of the increased rate of morbidity and mortality observed in patients with end stage renal disease (ESRD). The recommended techniques to optimize HD achievement are still not fully successful. This may, at least in part, relate to inadequate understanding of the factors affecting the HD process, including drugs taking by these patients. Previously, we demonstrated that hemodialysis efficiency, particularly in patients with less than 50 years of age may be improved by decreasing the serum uric levels. In the current study, we assessed the potential relationship between ranitidine intake and hemodialysis efficiency among ESRD patients in Hail, Saudi Arabia. Methodology: A total of 275 hemodialysis patients (122 males and 153 females) were enrolled in this retrospective study. The range was 25 to 83 years with median age of 51 years. Blood sampling was collected pre- and post-HD to calculate the HD efficiency indices, particularly Kt/V, creatinine reduction ratio, uric acid ratio, and urea reduction ratio. Results: We found that the proportion of female patients with ESRD was significantly higher (60%; $p<0.05$), than the males in the patient group examined. Among hemodialysis patients, the incidence of hypertension was 86 % ($p<0.05$). There was a positive association between ranitidine supplementations and HD efficiency. A significant increase in Kt/V ($p=0.03$) ratio was detected in patient taken ranitidine. Also, significant increase in creatinine ($p=0.008$), uric acid ($p=0.008$), and urea ($p =0.029$) reductions were observed. Conclusions: Taken together, the results of this study indicate that the hemodialysis efficiency in HD subjects may be significantly improved by supplementation with ranitidine.

Biography

Dr Alaraj (Associate Professor) was educated at Warsaw University, Poland and received a MS in Chemistry and Drug Technology in 1987. He obtained his PhD in 1995 from the College of Pharmacy, Medical University of Warsaw, Poland, having worked on the effects of polypeptide on the activity of some antiepileptic drugs. Dr Alaraj moved to "Mossakowski Medical Research Centre", Polish Academy of Sciences where he begun research in calcium signaling and role of glucose on neurodegeneration. Since joining the Medical Faculty-University of Hail (2008), Dr Alaraj has been mainly involved in evaluating the hemodialysis efficiency and implication of uric acid in kidney impairment and other aspects of kidney diseases- among end stage renal disease (ESRD) patients. Recently he has identified that serum uric acid negatively affect the efficacy of HD. He is currently involved in identifying the relationship between drugs used and HD efficacy among ESRD patients.

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Cardioprotective effects of β-sitosterol from *Linum usitatissimum* against isoproterenol-induced myocardial infarction in rats: A biochemical, electrocardiographic and histological features

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Myocardial infarction (heart attack) is the irreversible death (necrosis) of heart muscle secondary to prolonged lack of oxygen supply (ischemia). The present study was designed to evaluate cardioprotective effect of β-sitosterol, the major sterol of flaxseed oil, *Linum usitatissimum*, against isoproterenol induced myocardial infarction in rats. The research started with evaluating the sterol composition of *Linum usitatissimum*. Then, studying cardiovascular protective effect of its major sterol, β-sitosterol is based on cardiac damage markers especially electrocardiographic changes, histopathological modifications, troponin T and total cholesterol serum level. According to chemical analysis, this extract is composed essentially of stigmasterol (10.45%), avenasterol (13.30%), campesterol (25.33%) and β-sitosterol (44.08%). Male rats were randomly divided into four groups namely control (C), isoproterenol (ISO), isoproterenol treated group with clopidogrel (0.1 mg/kg body weight of clopidogrel/day) (CLO+ISO) and group treated with β-sitosterol (40 mg/kg body weight/day) (BS+ISO). Isoproterenol injection showed changes in electrocardiographic patterns, including ST-segment elevation. It caused the increase of the serum levels of troponin T and other cardiac injury biomarkers with anti-hypertensive effect through inhibition of angiotensin converting enzyme serum level. It also leaded to the appearance of edema and necrosis in myocardial tissue. However, β-sitosterol pre-co-treatment prevented almost all the parameters of isoproterenol-induced myocardial infarction in rats. To conclude, β-sitosterol, which is the active sterol of flaxseed oil, has a significant cardioprotective effects against isoproterenol-induced myocardial infarction.

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Genotoxic/anti-genotoxic activities of *Clematis flammula* extracts

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Clematis flammula leaf extracts are widely used in folklore medicine in Algeria to treat anti-inflammatory disorders and anticancer potential. Validation of the use of medicinal plants should also shed the light on their safety, based on the lack of their cytotoxicity and genotoxicity. The aim of our study was to assess the cytotoxicity and genotoxicity/anti-genotoxicity of the plant leaf extracts by the Allium cepa root test. In the same context, we tested their anticancer potential on two ovarian cancer cell lines OVCAR3 and A2780. Morphological observations of Allium cepa root cells after treatment by 100 and 300 µg/kg of *C. flammula* leaf extracts, sodium azide and a mixture of both have revealed that an absence of toxicity was observed for the plant extracts contrary to sodium azide. However, the combination of *C. flammula* extract at 300 µg/ml with sodium azide has induced a shortening of the root bulb (ΔL between – 1.22 mm and 0.02 mm) associated with marked changes in color, form, and consistency. Similarly, the mitotic index (MI) was impacted by sodium azide (100 µg/ml) especially in prophase but not with the extract (100, 300 µg/ml). The results are confirmed by the increase of chromosomal aberrations (C-mitosis, anaphase bridges and micronuclei) following sodium azide treatment. On the other hand, the MTT test indicated that survival of ovarian cancer cells (OVCAR3) was reduced to half at 10 µg/ml after 72 h which was less effective than that against A2780 of which survival was reduced to almost 30% at the same concentration and time scale. Bioactive compounds were identified by HPLC-MS.

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Patient counseling and patient education services to enhance medication safety and to improve patient compliance

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HKU-SZH (The University of Hong Kong-Shenzhen Hospital) has adopted good practices from the West and has implemented an advanced clinical pharmacy system. We use near-patients and near-doctors approach to provide high quality of clinical pharmacy service to patients and the healthcare professionals. We regard medication safety and quality of patient care as our highest priorities. Patient education is one of our quality improvement tools to enhance medication safety, improve patient compliance and optimization of drugs use. Since 2013, a team of clinical pharmacists have prepared over 50 types of patient drug information leaflets, 2 comprehensive booklets for warfarin and diabetic patients, and 9 sets of videos to show patients to use different types of inhalation devices, oral syringe, tablet cutter and tablet crusher. In addition, our clinical pharmacists provide patient counseling service in the smoking cessation clinic, diabetic clinic and pediatric respiratory clinic on weekly basis. The clinical pharmacist also delivers educational talks to patients in the cardiac rehabilitation center bi-monthly, to the antenatal patients on "safety of drugs use in pregnancy" annually and to the diabetic patients on endocrine ward on the use of insulin weekly. Every 2 to 3 months, the pharmacists provide teaching sessions to patients and the public in the out-patient forum on different topics such as effective use of insulin, drugs use in hepatitis B, medication safety in children, use of different inhalation devices, and drugs use for smoking cessation. Furthermore, the clinical pharmacists provide patient counseling on the wards for stroke patients as per stroke clinical pathway, and for patients who are on warfarin using the comprehensive warfarin booklet and the patient leaflet that we prepared. The clinical pharmacists have received good feedback from the healthcare professionals and the patients regarding our patient counseling and patient education services, and we also see the positive impact in the medication incidents occurrence. The clinical pharmacy team endeavors to improve the quality of pharmaceutical care, with an aim to improve the safety and efficacy of drugs use..

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Cytotoxic and anti-inflammatory effects of *Pistacia lentiscus* leaf extracts

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The present study was carried out to evaluate the anticancer and anti-inflammatory properties of *Pistacia lentiscus* leaf extracts, a plant widely used in Algerian traditional medication, using various *in vitro* techniques. The results showed that the crude extracts were not cytotoxic against mammary tumor EMT6 cell lines at all the concentrations tested (25–100 ug/ml). However, a relevant cytotoxic activity was noticed against melanoma tumor B16F10 and ovarian cancer cell lines (A2780 and SKOV3) with IC50 values of 56.40 ug/ml, 10 ug/ml and 18 ug/ml, respectively. Moreover, a significant expression in the apoptotic and pre-apoptotic cells A2780 and SKOV3 has been shown after treatment with 10 ug/ml and 25 ug/ml of the crude extract. In contrast, no cell cycle arrest in A2780 cell but an increase in Phase G1 was observed. On the other hand, P. lentiscus extracts induced a significant reduction of pro-inflammatory cytokines (TNF-α, IL-1β and IL-6) and a stimulation of the release of anti-inflammatory cytokines (IL-10) in activated macrophage. HPLC and NMR analyses of crude extracts and fractions allowed the identification of many compounds which may be responsible for the observed biological properties. These results may well be the premise for new natural products with chemotherapeutic attributes.

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Chemopreventive effect of n-3 PUFAs and Atorvastatin in rats with bladder cancer

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Bladder cancer remains a huge concern for the medical community because of its incidence and prevalence rates, as well as high percentage of recurrence and progression. Omega–3 polyunsatu¬rated fatty acids (n–3 PUFAs) and atorvastatin (ATOR) proved anti-inflammatory effects through PPAR-γ mechanism. However, their chemopreventive effect still remained to be examined and clari¬fied. In the current study, bladder cancer was induced in rats by the chemical carcinogen BBN. n-3 PUFAs (DHA and EPA 2:3 w/w; 1200 mg/kg) and/or ATOR (6 mg/kg) were given orally daily to rats for 8 consecutive weeks concomitantly with BBN, and continued for further 4 weeks after cessa-tion of BBN administration. The histopathological examination of rat bladder revealed presence of tumors and absence of apoptotic bodies in sections from BBN group, while tumors were absent and apoptotic bodies were clearly observed in sections from rat groups treated with n-3 PUFAs, ATOR, or both drugs. The study of the molecular mechanisms illustrated downregulation of COX-2 and P53 (mutant) genes and suppression of TGF–β1 and the lipid peroxidation product malondialdehyde in serum of rats of the three treated groups. This chemopreventive effect was confirmed by and associ¬ated with lower level of bladder tumor antigen (BTA) in urine. However, the combined treatment with both drugs exhibited the major protective effect and nearly corrected the dyslipidemia that has been induced by BBN. Collectively, n-3PUFAs and ATOR, besides having anti-inflammatory proper-ties, proved a chemopreventive effect against bladder cancer, which nominates them to be used as adjuvant therapy with other chemotherapeutics.

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Characterization and wound repair potential of essential oil *Eucalyptus globulus* Labill.

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Eucalyptus species has been used for treating several diseases such as sinusitis, bronchitis, toothache, kidney disorders and rheumatism in worldwide traditional medicine. In Turkey, *E. globulus* leaves are used to treat wounds. The purpose of this study was to evaluate, for the first time, the chemical composition of the essential oil from the fruits of *E. globulus* and its wound healing activity. Since wound repair is related to inflammatory associated conditions, the supposed anti-inflammatory activity of the oil was investigated. Essential oil from E. globulus, isolated by hydrodistillation, was analyzed by gas chromatography–mass spectrometry. Linear incision and circular excision wound models on rats were used for the wound healing activity of the oil, and acetic acid-induced increases in capillary permeability model in mice was used for the anti-inflammatory activity. Analysis of the essential oil showed that the main components were eucalyptol, α-phellandrene, β-phellandrene, cymene, 4-terpineol, α-pinene, α-thujone, α-terpinene and γ-terpinene. The essential oil comprises 53.67 % eucalyptol. It exhibited significant wound healing activity in the models studied, and the oil revealed a significant inhibitory effect on inflammation. These findings add significant information to the wound healing and anti-inflammatory activities of E. globulus, therefore justifying and supporting the use of this plant in traditional folk medicine.

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Insights into research on the anti-inflammatory and antinociceptive activities of *Scandix iberica Bieb.*

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It is thought that bioactive compounds from plant foods may have beneficial health effects and decrease the risk of chronic inflammatory diseases. In Turkish folk medicine, flowers of the *Scandix iberica* Bieb. (*Apiaceae*) have been used to combat rheumatic pain. The aim of this study is to appraise the anti-inflammatory and antinociceptive activities of the different types of extracts prepared from S. iberica carrageenan, Prostaglandin E2 (PGE2) and serotonin-induced hind-paw oedema, acetic acid-induced capillary permeability and 12-O-tetradecanoyl-phorbol-13-acetate (TPA)-induced mouse-ear oedema models were used to appraise anti-inflammatory activity. Antinociceptive activity was tested using a p-benzoquinone induced abdominal constriction method. Among the extracts, only the n-Hexane extract was shown to possess a noticeable anti-inflammatory and antinociceptive activity in mice without inducing any gastric damage at 100 and 200 mg/kg doses, while the rest of the extracts were entirely inactive. The activity of the n-Hexane extract led to a greater appreciation of some phenylpropanoids, mainly estragole (88.90%), through Capillary Gas Chromatography-Mass Spectrometry (GC-MS).

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Design and synthesis of new 2-substituted benzimidazoles as dual inhibitor for c-Met and VEGFR-2

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C-Met (a receptor tyrosine kinase) has been shown to collaborate synergistically with VEGFR-2 (a member of vascular endothelial growth factor receptors belonging also to tyrosine kinase), resulting in promoting development of angiogenesis and progression of various human cancers. In recent years, some c-Met/VEGFR-2 dual inhibitors have been reported or have entered clinical trials. For example Treanda (bendamustine hydrochloride) comprises a benzimidazole ring with a butyric acid substituent and was approved by FDA for the treatment of chronic lymphotic leukemia. The rational design of target molecules was based on its *in silico* molecular docking study and *in silico* ADMET study to provide an insight about the binding mode into binding sites of both c-Met/VEGFR-2 as a dual inhibitor. Thus, the benzimidazole ring of bendamustine was retained, buturic acid was replaced by nitro group and the bis-(chloroethyl) amine group (mechlorethamine) was substituted with several biologically active scaffolds such as oxadiazole, thiadiazole, and triazolo-thiadiazines. Five series (5a-b, 7a–o, 10a-d, 13a–b and 15a–c) of 2- substituted benzimidazole derivatives were synthesized via condensation of 4-nitro-o-phenylenediamine with α-ketoglutaric acid. The cytotoxic activities of some of the designed analogues were carried out at the National Cancer Institute (NCI), USA; at a single dose (10 μM), against full NCI 60 human cell lines. Most of the tested compounds, 5b (793196/1), 7i (793197/1), 13a (793191/1), 13f (793193/1), 13i (793192/1), 15a (793199/1) and 15b (793200/1) exhibited significant anti-proliferative activity. Further, all of the prepared compounds are under enzymatic screening for their inhibitory activity for both c-Met and VEGFR-2 as dual inhibitor.

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In-person assister availability and plan enrollment in the health insurance marketplace under the Affordable Care Act in the US

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Statement of the Problem: The health insurance marketplace under the Affordable Care Act (ACA) has run in-person assistance programs to help consumers' plan decisions. Consumers apply for the coverage through the website (healthcare.gov) except for those who live in states running the state-based insurance marketplace. Consumers seek for in-person assistance because they lack confidence to apply on their own and need help understanding the plan choices. Recent attention has been given to developing the decision support tool in hopes to promote consumers' direct engagement in plan decision¬-making. However, this approach should be taken with caution because of the characteristics of marketplace consumers. They are low¬ and middle¬ income population and are less likely to be literate enough to do the plan decision-¬making on their own. This study aims to describe the county-level assister availability and marketplace enrollment, focusing on the rural-urban differences.

Methodology & Theoretical Orientation: The 2016 marketplace enrollment data released by the Department of Health and Human Services and 2015 Small Area Health Insurance Estimates were used for the analysis. The assister data was constructed using healthcare.gov. Four states in the US were analyzed. Wilcoxon Rank-Sum test was performed for the number of assisters and 2016 plan enrollment.

Findings: About a quarter of Hispanics in poverty was uninsured in all four states. Uninsured rate was higher among the Hispanics in poverty who are eligible for the premium subsidies compared to all income levels. Marketplace enrollment for 2016 and potential marketplace enrollees vastly varied across counties. The number of potential marketplace enrollees was larger in rural counties than in urban counties. However, percent enrolled in potential enrollees in rural counties was only about half of urban counies.

Conclusion & Significance: The results suggest more rigorous outreach efforts on marketplace enrollment in rural areas.

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Anti-diabetic activity of *Nigella sativa* oil through its effect on some enzymes and signaling molecules in Streptozotocin-induced diabetic rats

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The black seeds of Nigella sativa have different biological activities and the anti-diabetic effect is among these activities. Streptozotocin (STZ)-induced diabetic rats were treated daily with NS oil (NSO) in order to study the effect on some enzymes and the expression of some insulin receptor-induced signaling molecules. The administration of NSO to STZ-induced diabetic rats induced significantly the activity of arylsulfatases and enhanced the antioxidant enzymes. Moreover, it significantly induced the gene expression of insulin receptor compared to non-treated rats. This treatment of NSO was combined also with some drugs (metformin and glimepiride) and an insulin receptor inhibitor; also, it upregulated the expression of insulin like growth factor-1 and phosphoinositide-3 kinase; whereas the expression of ADAM-17 was downregulated and TIMP3 was upregulated. The obtained data markedly confirmed anti-diabetic effect of NSO on antioxidant activity and signaling molecules in the absence and presence of some anti-diabetic drugs. In conclusion, diabetes induces significant alterations of the catalytic characters of arylsulfatases and some oils decrease this alteration through an antioxidant-mediated effect. Moreover, NSO has a potential in the management of diabetes through the modification of insulin-induced signaling and the interaction between herbs and drug.

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3-arylglyceric acid-derived plant polyether: Prospective therapeutic agent

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A new series of linear and regular 3-arylglyceric acid-derived polyether, namely poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl) ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA) was isolated and identified in the water-soluble, high-molecular weight fractions obtained from extracts of different species of comfrey and bugloss. According to data of 13C, 1H NMR, APT, 2D 1H/13C HSQC, 1D NOE and 2D DOSY experiments the polyoxyethylene chain is the backbone of the polymer molecule. 3,4-dihydroxyphenyl and carboxyl groups are regular substituents at two carbon atoms in the chain. The repeating unit of this regular polymer is 3-(3,4-dihydroxyphenyl)glyceric acid residue. Then basic monomeric moiety of this polymer, 3-(3,4-dihydroxyphenyl) glyceric acid (DPGA) was synthesized via Sharpless asymmetric dihydroxylation of trans-caffeic acid derivatives using an osmium catalyst. It is well known that epoxides are valuable synthons in organic synthesis and have been introduced into pharmaceutical applications, such as in the synthesis of antitumor drugs. Subsequently, the building block for the production of derivatives of PDPGA, methyl 3-(3,4-dimethoxyphenyl)glycidate was synthesized based on the Darzen reaction or by oxidation with oxone in order to produce in future derivatives of synthetic analogue of natural polymer through ring-opening polymerization of 2,3-disubstituted oxirane. PDPGA is endowed with intriguing pharmacological properties as anticomplementary, antioxidant, anti-inflammatory, burn and wound healing and anticancer properties. PDPGA and DPGA exerted anticancer activity *in vitro* and *in vivo* against human prostate cancer (PCA) cells. However, anticancer efficacy of PDPGA is more effective compared to its synthetic monomer. Overall, this study identifies PDPGA as a potent agent against PCA without any toxicity and supports its clinical application.

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Ciprofloxacin for the treatment of non-resolving pneumonia in a tertiary care pediatric hospital

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Purpose: Data regarding the use of ciprofloxacin in children with no resolving pneumonia are scarce. The present study aims to evaluate the effect of ciprofloxacin therapy in pediatric patients with non-resolving pneumonia.

Methods: Over the past year, all pediatric patients with non-resolving pneumonia who received ciprofloxacin treatment in the pulmonary unit of Al-Rantisy Specialized Pediatric Hospital in Gaza, Palestine, were included in this retrospective study. Ciprofloxacin was given for all patients in a dose of 20 mg/kg/day divided into two doses. Patient demographic data, clinical symptoms recorded, sputum culture findings and ciprofloxacin therapeutic outcome were gathered. Data were analyzed using computer software SPSS version 11.

Results: The study included 57 patients with non-resolving pneumonia, 36 males and 21 females with mean age of 3.4 years, ranged from 2 months to 8 years. Fever (73.7%) and cough (89.5%) were the most common symptoms. Positive culture was obtained in 42 (73.6%) patients while 15 (26.4%) showed negative results. The most common organism isolated in the positive cultures was Pseudomonas aeruginosa 26 (62.0%). Among the study sample, 23 (40.4%) patients received ciprofloxacin as empirical therapy and 34 (59.6%) received this drug depending on culture sensitivity results. There was a significant decrease in body temperature levels ($P<0.001$) at day 1, 2 and 3 of ciprofloxacin treatment. Overall, ciprofloxacin was effective in the treatment of 53 (93.0%) patients of the present study. Only 4 (7%) cases showed resistant to this therapy. The mean length of hospital stay was 7.5 days. No side effects were reported during the course of this study.

Conclusion: Data of the present study suggest that ciprofloxacin is effective and safe, including as initial monotherapy, for the treatment of pediatric patients with no resolving pneumonia.

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Expression of antimicrobial peptide Hcap18/LL-37 following non-viral delivery of plasmid DNA encoded by CAMP gene in human fibroblasts and keratinocytes

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Since the incidence of breast cancer increases dramatically all over the world, the search for effective treatment is an urgent need. Metformin (MET) has demonstrated anti-tumorigenic effect both *in vivo* and *in vitro* in different cancer types. The present work was designed to examine on molecular level the mode of action of MET in mice bearing Solid Ehrlich Carcinoma (SEC) and to evaluate the use of MET in conjunction with doxorubicin (DOX) as a combined therapy against SEC. Ehrlich ascites carcinoma cells were inoculated in 60 female mice as a model of breast cancer. The mice were divided into four equal groups: Control tumor, MET, DOX and co-treatment. MET (15 mg/kg) and DOX (4 mg/kg) were given i.p. for four cycles every five days starting on day 12 of inoculation. The anti-tumorigenic effect of MET was mediated by enhancement of adenosine monophosphate protein kinase (AMPK) activity and elevation of P53 protein as well as the suppression of nuclear factor-kappa B (NF-5B), DNA contents and cyclin D1 gene expression. MET and DOX mono-treatments exhibited opposing action regarding cyclin D1 gene expression, phosphorylated-AMPK (PAMPK) and NF-5B levels. Co-treatment markedly decreased tumor volume, increased survival rate and improved other parameters compared to DOX group. In parallel, the histopathological findings demonstrated enhanced apoptosis and absence of necrosis in tumor tissue of co-treatment group. MET proved chemotherapeutic effect which could be mediated by the activation of AMPK and related pathways. Combining MET and DOX, which exhibited different mechanisms of action, produced greater efficacy as anticancer therapeutic regimen.

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Optimization of the parameters of spherical agglomeration method

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In the industry area, direct compression is one of the most important techniques for the formulation of solid form drugs. For this, the active agent, so as our target product should possess appropriate parameters for example increased flow rate generated by large-size (>100 □m) spherical or nearly spherical (roundness < 1.5) crystals or crystal agglomerates. For improving the morphology, spherical crystallization techniques can be used, like typical and non-typical ones. In case of non-typical methods (like antisolvent crystallization, cooling crystallization or combined method) mainly the physico-chemical parameters are changed. Typical methods (like quasi emulsion solvent diffusion method) use three solvents. From our previous work it became clear that spherical agglomeration is suitable for improving the morphology of ambroxol hydrochloride (AMB-HCl). This work aims at the optimization of the parameters of this method. For this, a factorial design was applied and then the results were evaluated with STATISTICA for Windows program. The critical parameters were as follows: agitation type and time, temperature differences between the solvent (dimethyl sulfoxide) and the antisolvent (ethyl acetate), composition of the solvent system (solvent/antisolvent ratio). The average size, aspect ratio and roundness of the products were analysed by LEICA Q500 MC Image Processing and Analysis System, then the ones with proper morphology were chosen for further experiments. With an additional factorial design, effects of other parameters were examined such as saturation rate and feed rate of AMB-HCL solution. The products were also examined by an individually-developed hardness test. Four products were proved to possess suitable morphology compared to the target product. The application of horizontal shaker with shorter mixing times and lower temperature differences had a positive impact on the morphology of AMB-HCl. The hardness of the products was large enough to keep the spherical particles stable.

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Anti-myocardial ischaemic effect of pseudo-ginsenoside GQ injection against beta1-adrenoceptor (β1-AR) in rat cardiac myocytes (H9c2)

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Statement of the Problem: Myocardial ischemia (MI) is a prevalent complicated heart disorder worldwide. It is a clinically common pathophysiological phenomenon which characterized by reduced blood supply to the heart, resulting in nutrients depletion and causing hypoxia. Although there are many precious researches on MI injury, it is perennial among the leading causes of morbidity and mortality in humans in the industrialized countries. Therefore, research of an efficient agent for MI injury remains an important issue. Pseudo-ginsenoside GQ (PGQ) injection (1.1 class chemicals), firstly developed by our lab., is based on PGQ obtained by modifying 20(S)-ginsenoside Rg3 with the biological degradation and the chiral semi-synthesis method, etc., which was approved by the Chinese State Food and Drug Administration for the treatment of myocardial ischemia and phase I trial was carried on to evaluate the safety of PGQ injection.

Methodology & Theoretical Orientation: The effects of PGQ injection on the cardiovascular physiology of MI injury rats were examined by measuring various electrocardiographic parameters. NBT staining method was utilized to measure the heart infarct size, and the levels of LDH, CK, SOD, AST, MDA and cTnT were measured to further evaluate and validate the protective function of PGQ injection during MI injury. Flow cytometry and western blot analysis were used to detect the β1-AR expression *in vitro*.

Findings: Both data and histopathological examination all demonstrated that PGQ injection could significantly improve the heart function and decrease infarct size. And the levels of CK, LDH, AST, MDA and cTnT were decreased and the activities of SOD were increased. The underlying mechanism was explored by flow cytometry and western blot, and results showed that the expression of β1-AR was decreased by PGQ injection.

Conclusion & Significance: This study provides the substantial evidence for the effect of PGQ injection on myocardial ischemia.

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Ide sequestration, release and ecology of the anticancer drug Taxol from fungal endophytes

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Taxol is produced by Taxus trees and their resident endophytic fungi. A mystery has been why these endophytes synthesize Taxol apparently redundantly. A defining feature of these trees is that they can propagate branches from long-lived buds that lie underneath the bark; branch emergence is accompanied by bark cracks, potential pathogen entry points. Here, we show that Taxol acts as a fungicide against wood decaying fungi (WDF) to which these long-lived trees are susceptible. Reducing endophytes in plants resulted in increased WDF growth. Endophytes sequestered Taxol in intracellular hydrophobic bodies (Hb), which prevented plant cytoxicity. Taxol-producing endophytes with these Hb localized to vascular rays within wood, but hyperaccumulated where the rays intersected branch points and associated air pockets. Chloromethane, a chemical released by WDF, along with chitin or WDF, induced Hb release from endophytes. Hb was released from endophytes by exocytosis; chloromethane induced exocytosis genes. Combined, Taxol-producing endophytes contribute to the survival of their host by protecting their nutrient-rich vascular system and branch points against systemic fungal pathogen invasion.

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Antifungal activity of essential oil from *Artemisia campestris L* on Fungal Species Development

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This work studies the antifungal capacity of the essential oil of spontaneous aromatic plant with vocation medicinal used in the traditional treatments in the South-West of Algeria: Artemisia campestris L. The local plant tested gives a good essential oil yield (0.37%). The physico-chemical analysis of the essential oil of this plant specie has enables to us to even characterize to identify our oil. Antifungal activity of the essential oil was studied witch respect to seven fungal strains with various concentrations. The results of direct contact method show that the oil of Artemisia campestris L. is proven very effective on the mycelial growth of the moulds. All strains were inhibited at concentration as weak as 1/70 (v/v), Fusarium oxysporum f.sp. albedinis and Penicilluim expansum were most sensitive, being inhibited as from 1/800 (v/v) and 1/500 (v/v) respectively. This essential oil has a fungistatic effect. In addition to the growth of the mycelium, the essential oil of plant showed, *in vitro*, a antifungal activity at least important on the two other developmental stages, germination and the sporulation, of all fungi . All strains were inhibited at concentration as weak as 1/100 (v/v). Fusarium oxysporum f.sp. albedinis was most sensitive, being inhibited as from 1/1500 (v/v).

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Riluzole ameliorates learning and memory deficits in Ab25-35- induced rat model of Alzheimer's disease and is independent of cholinoceptor activation

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Statement of the Problem: Alzheimer's disease (AD) is a major global public health concern and social care problem that is associated with learning, memory, and cognitive deficits. Riluzole is a glutamate modulator which has shown to improve memory performance in aged rats and may be of benefit in Alzheimer's disease. Methodology & Theoretical Orientation: In the present study, its beneficial effect on attenuation of learning and memory deficits in Ab25-35-induced rat model of AD was assessed. . Finding: Riluzole administration at a dose of 10 mg/kg/day p.o. improved spatial memory in Morris water maze and retention and recall in passive avoidance task and its protective effect was not neutralized following intracerebroventricular microinjection of muscarinic or nicotinic receptor antagonists. Further biochemical analysis showed that riluzole pretreatment of intrahippocampal microinjected rats is able to attenuate hippocampal AChE activity and lower some oxidative stress markers, i.e. MDA and nitrite, with no significant change of the defensive enzyme catalase. Furthermore, riluzole prevented hippocampal CA1 neuronal loss and reduced 3-nitrotyrosine immunoreactivity. Conclusion & Significance: It is concluded that riluzole could exert a protective effect against memory decline induced by intrahippocampal Ab25-35 through anti-oxidative, anti-cholinesterase, and neuroprotective potential and its beneficial effect is possibly independent of cholinoceptor activation.

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Pharmacological properties of Tulathromycin on mature male albino rats

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In the search for a novel antibiotic offering high efficacy against Bovine Respiratory Disease (BRD) and Swine Respiratory Disease (SRD) from a single administration, scientists screened hundreds of novel analogs based on literature macrolide templates for desired characteristics of spectrum, potency, and an indication of pharmacokinetic behavior that would support fast onset and extended duration of activity *in vivo*. During the course of the research programs, a novel class of macrolide, subsequently termed triamilides, was discovered with strong activity against gram-negative respiratory pathogens and desirable pharmacokinetic behavior, characterized by high and extended tissue levels in host animals. Tulathromycin is a novel macrolide antimicrobial with a triamilide structure found to be effective against bacterial respiratory pathogens in cattle and swine. The present study was carried out to evaluate the adverse effects of tulathromycin at different periods on reproductive system, hematological parameters, biochemical analysis and histological changes in liver, kidney, spleen and heart in male albino rats. Fifty rats were used in the present study for two experiments. In the first experiment, rats were randomly divided into two equal groups each of 15 animals. The first group received single subcutaneous injection of tulathromycin at a dose level of 10 mg/kg B.wt. The second group used as a control and injected subcutaneously with physiological saline solution at a dose of 2 ml/kg B.wt. In the second experiment, rats were randomly divided into two equal groups each of 10 animals. The first group received subcutaneous injection of tulathromycin at a dose level of 10 mg/kg B.wt. repeated once every week for eight successive weeks. The second group used as a control and injected subcutaneously with physiological saline solution at a dose of 2 ml/kg B.wt. by the same manner. The obtained results showed that single and repeated s.c administration of tulathromycin at a dose level 10 mg/kg B.wt. in mature male rats produced significant reduction in reproductive organs' weights in addition to increase in sperm counts, motility and abnormalities throughout periods of experiments. There was a significant decrease in WBCs count throughout periods of the second experiment as compared with control group. Rats treated with single and repeated tulathromycin showed significant increase in serum ALT, AST ALP, urea and creatinine levels allover periods of the experiments. It could be concluded that both single and repeated subcutaneous administration of tulathromycin at a dose level 10 mg/kg B.wt. in male albino rats induced several adverse effects. These effects were represented by certain fertility troubles which were noticed as reduction of some reproductive organs weights, changes in semen characters, biochemical disturbances in addition to some histological alterations in liver, kidneys, spleen and heart. Moreover, repeated subcutaneous administration of tulathromycin produced zinker's necrosis in the heart at 2nd week from last drug administration.

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Isolation of ulceroprotectivec cucurbitane type triterpenoids from *Cucumis melo* seeds

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Medicinal plants are the richest bio-resources of drugs in traditional medicinal systems, modern medicines, folk medicines, intermediate and chemicals entitled for synthetic drugs. Plants provide a source of inspiration for novel drug development as they contain a vast array of substances that treat chronic diseases. *Cucumis melo* seeds have been traditionally used for treating various health ailments. The main aim of our current study is to isolate Cucurbitane-type triterpenoids from *Cucumis melo* seed extract and conduct antiulcerogenic activity of the isolated compound. Phytochemical investigations of methanolic seed extract of *Cucumis melo* was carried out which showed the presence of various important phytoconstituents. The main active constituents of *Cucumis melo* have shown a number of potent pharmacological activities. The isolation of Cucurbitane-type triterpenoids was carried out by column chromatography using methanolic seed extract of *Cucumis melo*. Mobile phase hexane and hexane-ethyl acetate (98:2) was used to run the column. TLC profiling was done simultaneously in an appropriate solvent system (hexane: ethyl acetate, 97:3). Various fractions were collected. The fractions with similar Rf value were pooled together. Fractions giving single spot in the TLC were regarded as pure. The isolated compound showed positive result for Liebermann-buchard test from which we can conclude that the isolated compound might be triterpenoid. The structure of the isolated compound was determined by IR, 1HNMR, 13CNMR techniques. The spectral analysis of the isolated compound showed following results: IR: It showed the peaks at 3383, 2976, 2814, 1721, 1465, 1123 cm-1 indicated the presence of alcoholic group; 1H NMR (400 MHz, CDCl3): δ 0.66-1.29 (m, 24H, -CH3), δ 1.32-1.38 (m, 4H, H7, H8, H9, H10), δ 1.40-1.51 (m, 4H, H10,H19, H20, H21), δ 1.52-1.59 (m, 3H, H11, H6, H22), δ 1.61-2.38 (m, 2H, H4, H3), δ 3.16-3.20 (m, 6H, H1, H2, H12, H13, H15, H17); 13C NMR (400 MHz, CDCl3): δ 15.99, 16.13, 18.01, 18.33, 19.32, 20.94, 25.16, 27.43, 27.46, 28.00, 29.71, 29.86, 34.30, 35.60, 37.18, 38.07, 38.73, 38.87, 40.02, 40.85, 42.84, 43.01, 47.99, 48.32, 50.45, 55.32, 79.00, 109.34, 109.67 (C=C), 150.96 (C=O). From the above result, the isolated compound was elucidated to be tetracyclic triterpenoid. As triterpenoids are mostly responsible for anti-ulcerogenic activity so the isolated compound was further evaluated for antiulcer activity by pyloric ligation induced gastric ulcer, water immersion stress ulcer and indomethacin induced ulcer models in Wistar albino rats. In the pyloric ligation induced gastric ulcer model, the isolated compound at the dose of 300 mg kg-1 showed significant reduction in gastric volume, free acidity and total acidity i.e., 1.79±0.12, 31.58±0.31 and 72.95±0.11 respectively. The percentage inhibition was found to be maximum at the dose of 300 mg kg-1 in all the three animal models. The percentage inhibition was 56.6, 66.3 and 61.2 in pyloric ligation induced gastric ulcer, water immersion stress ulcer and indomethacin induced ulcer models respectively. All the above gathered results the isolated compound i.e., Cucurbitane-type triterpenoids was found to be potent against gastric lesions and therefore can be used as future natural anti-ulcerogenic agent.

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