Pharmaceutical Sciences Abstracts
Third Annual International Conference on Pharmaceutical Sciences
2-5 May 2016, Athens, Greece
Edited by Gregory T. Papanikos
3rd Annual International Conference on Pharmaceutical Sciences, 2-5 May 2016, Athens, Greece: Abstract Book
Pharmaceutical Sciences
Abstracts
3rd Annual International Conference on Pharmaceutical Sciences
2-5 May 2016, Athens, Greece

Edited by Gregory T. Papanikos
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Preface

This abstract book includes all the summaries of the papers presented at the 3rd Annual International Conference on Pharmaceutical Sciences, 2-5 May 2016, organized by the Pharmaceutical Research Unit of the Athens Institute for Education and Research. In total there were 35 papers, coming from 18 different countries (Algeria, Austria, Brazil, China, Colombia, Egypt, France, Germany, India, Indonesia, Iran, Ireland, Italy, Jordan, Malaysia, Poland, Saudi Arabia, and UK). The conference was organized into nine sessions that included areas of Pharmaceutical Sciences and other related fields. As it is the publication policy of the Institute, the papers presented in this conference will be considered for publication in one of the books and/or journals of ATINER.

The Institute was established in 1995 as an independent academic organization with the mission to become a forum where academics and researchers from all over the world could meet in Athens and exchange ideas on their research and consider the future developments of their fields of study. Our mission is to make ATHENS a place where academics and researchers from all over the world meet to discuss the developments of their discipline and present their work. To serve this purpose, conferences are organized along the lines of well established and well defined scientific disciplines. In addition, interdisciplinary conferences are also organized because they serve the mission statement of the Institute. Since 1995, ATINER has organized more than 150 international conferences and has published over 100 books. Academically, the Institute is organized into four research divisions and nineteen research units. Each research unit organizes at least one annual conference and undertakes various small and large research projects.

I would like to thank all the participants, the members of the organizing and academic committee and most importantly the administration staff of ATINER for putting this conference together.

Gregory T. Papanikos
President
CONFERENCE PROGRAM

Monday 2 May 2016

07:30-08:30 Registration and Refreshments

30-09-00 (ROOM B-Mezzanine Floor) Welcome & Opening Remarks

Dr. Gregory T. Papanikos, President, ATINER.
Dr. George Poulos, Vice-President of Research, ATINER & Emeritus Professor, University of South Africa, South Africa.

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09:15-10:30 Session I (ROOM E-10th FLOOR): Advancing and Emerging Trends in Pharmacology and Biochemistry

Chair: Olga Gkounta, Researcher, ATINER.

1. Anna Goraca, Professor and Director, Chair of Experimental and Clinical Physiology, Medical University of Lodz, Poland & Beata Skibska, Professor, Medical University of Lodz, Poland. Oxidative Stress in Skeletal Muscle: Role of Nrf2 and Effect of α-Lipoic Acid.

2. Lincy Joseph, Professor and Head, Pushpagiri College of Pharmacy, India & *Mathew George, Principal and Professor, Pushpagiri College of Pharmacy, India. Anticonvulsant Activity of Certain Novel Isoxazole Derivatives.

3. *Michele Vitolo, Professor, University of São Paulo, Brazil, Juliana Rodrigues Ract, Professor, University of São Paulo, Brazil & Sara Anunciação Braga Silva, Young Fellow, University of São Paulo, Brazil. Feasibility on the Use of Acid Value for Evidencing the Esterification of Glycerol with Caprylic Acid Catalyzed by Lipase.

4. Noujoum Zmouli, Assistant Professor, University Hospital Establishment of Oran (EHUO), Algeria, Lamia Ait Ouali, Assistant, University Hospital Establishment of Oran (EHUO), Algeria, Houari Toumi, Chief of Department Pharmacology, University Hospital Establishment of Oran (EHUO), Algeria & Mohamed Hammadi, Professor, University Hospital Establishment of Oran (EHUO), Algeria. Monitoring Antiplatelet Therapy: Contribution Biological Tests to Screen a Resistance.

10:30-12:00 Session II (ROOM E-10th FLOOR): Trends in Drug Delivery and Formulating Development I

Chair: Lincy Joseph, Professor and Head, Pushpagiri College of Pharmacy, India

1. Kirti Rani, Assistant Professor, Amity University Uttar Pradesh, India. Preparation of Pennisetum Glaucum Amylase Loaded Bovine Serum Albumin Nanoparticles by Desolvation Method.

2. Ahmed Donia, Lecturer, Tanta University, Egypt, Omar Mady, Associate Professor, Tanta University, Egypt & Esmat Zein Eldin, Professor, Tanta University, Egypt. Lipid Based Matrices as Colonic Drug Delivery System for Diflunisal (In-vitro, In-vivo Study).

3. Magdalena Paczkowska, Ph.D. Student, Poznan University of Medical Sciences, Poland & Daria Szymanowska-Powalowska, Assistant Professor, Poznan University of Life Sciences, Poland. Impact Studies of Biopolymers on Solubility of Poorly Water Soluble Drugs: A Case Study of Tebipenem Pivoxil.


5. Hossein Zolfagharian, Associate Professor, Razi Institute, Iran. Preparation and Characterization of Chitosan Nanoparticles Containing Compsothethus Scorpion Venom.

12:00-13:30 Session III (ROOM E-10th FLOOR): Recent Trends in Modern Pharmaceutical Chemistry and Analysis

Chair: *Michele Vitolo, Professor, University of São Paulo, Brazil

1. Vivekanand Chatpalliwar, Professor, and Head, SNJB’s Shriman Sureshdada College of Pharmacy, India, Saurabh C. Khadse, R. C. Patel Institute of Pharmaceutical Education and Research, India & Chandra Shekar D. Upasani, SNJB’s Shriman Sureshdada College of Pharmacy, India. Design, Docking, Synthesis and in vitro Binding Studies of Few Benzamide Derivatives with Glucokinase Enzyme.

2. Aymen Yassin, Associate Professor, Cairo University, Egypt, Norhan Sheraba, Quality Control Specialist, VACSERA, Egypt & Magdy Amin, Professor, Cairo University, Egypt & Hamdallah Zedan, Professor, Cairo University, Egypt. Comparison between Different Endotoxin Removal Methods Applied during Pharmaceutical Quality Control Testing of Antisera Preparation.
3rd Annual International Conference on Pharmaceutical Sciences, 2-5 May 2016, Athens, Greece:
Abstract Book

Beata Morak-Młodawska, Lecturer, Medical University of Silesia, Poland, Krystian Pluta, Professor, Medical University of Silesia, Poland, Małgorzata Jeleń, Lecturer, Medical University of Silesia, Poland, Małgorzata Latocha, Head of Department of Cell Biology, Medical University of Silesia, Poland & Kinga Suwińska, Professor, Institute of Physical Chemistry, Polish Academy of Sciences, Poland. Synthesis and Anticancer Action of Novel Diaziphenothiazine Derivatives.

13:30-14:30 Lunch
14:30-16:30 Urban Walk (Details during registration)

Chair: Vivekanand Chatpalliwar, Professor, and Head, SNJB’s Shriman Sureshdada College of Pharmacy, India

Mehran Tahmisian, Head of Research Unit, University of Normandy, France, Narges Yousefi, Student, University of Normandy, France, Stéphane Guillozet, Engineer, University of Normandy, France & Martine Dhilly, Assistant Engineer, University of Normandy, France. Imaging Lymphoma: 

16:30-18:00 Session IV (ROOM E 10TH FLOOR): Emerging Trends in the Field of Pharmacognosy

Efthymia-Eleni Tsoutsou, Researcher, University of Siena, Italy, Elisabetta Miraldi, Confirmed Researcher, University of Siena, Italy, Paolo Giordani, Senior Researcher, University of Genoa, Italy & Laura Cornara, Associate Professor, University of Genoa, Italy. Skin Wound Healing: From Mediterranean Ethnobotany to Evidence based Phytotherapy.

18:00-20:00 Session V (ROOM E 10TH Floor): An International Symposium on Diabetes

Chair: George Poulos, Vice-President of Research, ATINER & Emeritus Professor, University of South Africa, South Africa.

Laura Maria Doina Popov, Head of Pathophysiology and Pharmacology Department, Institute of Cellular Biology and Pathology “N. Simionescu” of the Romanian Academy, Romania. Cardiomyocyte Mitochondrial Networking in Diabetes.

Fatima Regina Silva, Professor, Federal University of Santa Catarina, Brazil, Camila Pires Mendes, MSc Student, Federal University of Santa Catarina, Brazil, Mayara Brich, Undergraduate Student, Federal University of Santa Catarina, Brazil, Ana Luzia Ludwig Moraes, Undergraduate Student, Federal University of Santa Catarina, Brazil, Allisson Jhonatan Gomes Castro, Ph.D., Pos-Doc Student, Federal University of Santa Catarina, Brazil, Patricia Devantier Nesenfeld, Ph.D., Pos-Doc Student, Federal University of Santa Catarina, Brazil, Ricardo José Nunes, Professor, Federal University of Santa Catarina, Brazil & Marisa Jâdna Silva Frederico, Ph.D., Pos-Doc Student, Federal University of Santa Catarina, Brazil. Mechanism of Action of New Associated Analogues Glimepiride/Pioglitazone on Glucose Homeostasis.

Yasser Bustanji, Professor, University of Jordan, Jordan, Mohammad Hudaib, University of Jordan, Jordan, Hatim Al-Khatib, University of Jordan, Jordan, Mohammad Mohammad, University of Jordan, Jordan & Bhaba Almasri, Al-Azhar University, Gaza Strip. Identification of New Compounds from Ginkgo Biloba Extract as Potential Pancreatic and Hormone Sensitive Lipase Inhibitors for Management of Obesity. (PHA)

Andriana Margariti, Lecturer, Queen’s University Belfast, UK. Restoring the Endothelial Cell Function in Diabetic Patients through the Novel and Powerful Approach of Cell Reprogramming.

21:00-23:00 Greek Night and Dinner (Details during registration)

Tuesday 3 May 2016

09:00-11:00 Session VI (ROOM E 10TH FLOOR): Diabetes, Obesity and Nutrition

Chair: Aymen Yassin, Associate Professor, Cairo University, Egypt
### Mechanisms of Drug Release and Determination the Percent of Each.

**20:30 - 22:00 Dinner (Details during registration)**

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<td><strong>Thursday 5 May 2016</strong></td>
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Lessons from the Past: How the Clinical Pharmacy Practice was Established in Jordanian Governmental Hospitals?

In order to improve the Quality of Health Services it is essential to introduce the Clinical Pharmacy Practice in Governmental Hospitals together with the newly established Job Description. In addition of introducing new Clinical Pharmacy Departments with their divisions in all Hospitals.

Since August 2000 it was observed by the author the absence of Clinical Pharmacists in the Governmental Hospitals, consequently several claims were presented to train and recruit clinical pharmacists in the twenty nine hospitals.

Therefore the main driving force behind this thorough investigational study which commenced on August 2002 is to provide the evidence for this major need of introducing the clinical pharmacists in the Governmental hospitals in order to prevent the patients from the risk of unavoidable drug/drug interactions and to reduce the excess unneeded prescribed medications (prevent irrational drug use).

Method: Simple Questionnaire was designed and distributed to all twenty nine Governmental Hospitals to inquire about the main Criteria that should be in the Organizational Structure of any Hospital (as number of Clinical Departments, and physicians, the number of Pharmacists and Clinical Pharmacists, the presence of the clinical Pharmacy Department and Divisions in the Organizational Structure of each Hospital. The Answers were pooled and the collective data was studied and analyzed.

Results: As a result of studying all the collective data, conclusions with proposals were presented.

It was found that only one clinical pharmacist was employed in each of two hospitals out of the twenty nine governmental hospitals.

It was a striking evidence for the major need to train and recruit many clinical pharmacists in each governmental hospital.

Discussion: This study was a strong tool to convince the highest authority in the Ministry of Health (the Minister of Health) for the urgent need to recruit new clinical pharmacists in the twenty nine governmental hospitals. Consequently on February 2005 the Minister of Health requested officially from the Civil Service Bureau to recruit each year the newly graduated Pharm. D Pharmacists or the MSc degree holders in Clinical Pharmacy in the Ministry of Health (MOH) Hospitals.

In addition of implementing the presented long term plan for training the already existing pharmacists in the Hospitals to study for having their MSc degree in Clinical Pharmacy or for studying Pharm.D by granting them Governmental Scholarships to study in our Universities.

Parallel to that the newly established Job-Description was founded and the establishment of new Departments and Divisions were under discussion for the near future Hospitals Organizational Structure Plans.

By these radical changes the Quality of Patient Care in the Governmental Hospitals would be upgraded by reducing the number of prescribed medications to the inpatients and avoiding health complications resulting from the risk of possible unavoidable drug / drug interactions.
Imaging Lymphoma: [$^{18}$F] Fludarabine PET/CT from Bench to Bedside

[$^{18}$F]-Fludarabine is a novel positron emission tomography (PET) radiopharmaceutical for lymphoid malignancies. The rationale supporting its development was the high selectivity of fludarabine uptake within lymphoid cells irrespective of their cycle activity, and the fluorine atom within the drug, which replaced by a [$^{18}$F] radionuclide confers the positron-emitter property. A preclinical studies, after i.v injection of [$^{18}$F]-fludarabine, were designed as a “proof of concept” on animal models and showed - a marked tumor uptake in lymphoma-bearing mice and - revealed during rituximab therapy that [$^{18}$F]-fludarabine uptake characteristics was not modulated. In addition, a comparison was made with [$^{18}$F]FDG with regard to the sensitivity and the agreement with histologically-derived data and the results were in favour of [$^{18}$F]-fludarabine for PET imaging. Thus, [$^{18}$F]Fludarabine-PET/CT may be a promising method for evaluation of lymphoma, including surveillance during therapy. For this purpose, a clinical trial was undertaken and ten patients with B-cell chronic lymphocytic leukemia (B-CLL) and diffuse large B-cell lymphoma (DLBCL) were enrolled. The preliminary results are encouraging and will be presented.

References:
Dhilly M et al, Mol Imaging Biol 2014;16:118-26
Hovhannisyan N et al, EJNMMI Res 2015;5:23
Identification of New Compounds from *Ginkgo Biloba* Extract as Potential Pancreatic and Hormone Sensitive Lipase Inhibitors for Management of Obesity

Obesity is a worldwide problem that is rapidly affecting both developed and developing countries. According to a recent report from the World Health Organization, it is estimated that worldwide more than 1 billion adults are overweight, at least 300 million of them clinically obese. *Ginkgo biloba* L. (Ginkgoaceae) has been used for medical purposes for centuries in traditional Chinese medicine. The standard extracts of *G. biloba* leaves are now more usually used as dietary supplements or phytomedicines in Western countries.

In this study the methanolic extract of *Ginkgo biloba* L. (Ginkgoaceae) was investigated as an inhibitor of pancreatic lipase (PL) and Hormone sensitive lipase (HSL) in an attempt to explain its hypolipidemic activity. The lipase activity was quantified by a colorimetric assay that measures the release of p-nitrophenol in well controlled studies.

In *vitro* assay of *G. biloba* leaves extract inhibited both PL and HSL in a dose dependent manner with micro molar activities. Further investigations were performed employing theoretical docking simulations and experimental testing to uncover the active constituents responsible for *G. biloba* antilipase activity. Different ginkgolides A, B, C, J, K L, and bilobalide were identified and tested for their potential PL and HSL inhibition.

Using molecular docking, terpene trilactones, including ginkgolides and bilobalide, were found to fit within the binding pocket of PL via several attractive interactions with key amino acids. Experimentally, ginkgolides A, B and bilobalide were found to inhibit PL significantly (IC$_{50}$ = 22.9, 90.0 and 60.1 µg/mL, respectively). Moreover, these terpene trilactones could also inhibit the HSL in the same manner. Our findings demonstrated that the hypolipidemic effects of *G. biloba* extract can be attributed to the inhibition of PL by, at least in part, terpene trilactones. In conclusion, this work can be considered a new step towards the discovery of new natural safe hypolipidemic PL inhibitors.
Vivekanand Chatpalliwar  
Professor, and Head, SNJB’s Shriman Suresh Dada College of Pharmacy, India  
Saurabh C. Khadse  
R. C. Patel Institute of Pharmaceutical Education and Research, India  
&  
Chandrashekar D. Upasani  
SNJB’s Shriman Suresh Dada College of Pharmacy, India

**Design, Docking, Synthesis and *in vitro* Binding Studies of Few Benzamide Derivatives with Glucokinase Enzyme**

Glucokinase enzyme (GK) is involved in glucose utilization in liver and has also been implemented in Glucose-dependant release of insulin in the pancreatic β-cell. Activation of glucokinase enzyme therefore, has emerged as a strategy to increase glucose utilization. The world-wide endeavours to design compounds (GKA: Glucokinase activators) that would activate the glucokinase enzyme so as to develop suitable drugs to treat *Type 2 diabetes*, has culminated in library of numerous compounds; benzamide derivatives have been at mainstay amongst them.

The ligand-protein interaction involves ARG63 and TYR215, which are submerged in a cleft between two domains. Albeit, binding of the ligands with amidine backbone of ARG63 is believed to be involved in activation of the enzyme; the hydrogen-bond interactions of ligands with TYR215 had been noticed to elicit mutagenic effects. Present work describes the design, docking of benzamide derivatives that bind with ARG63, much the way similar to the standard GKA, RO-28-1675, and simultaneously defer from TYR215.

Molecular modeling studies involved, Molecular Design Suite (*VLife MDS 3.5*), simulated protein 1V4S, virtual structures of standard and newly designed benzamide derivatives.

The structures were docked in the catalytic site of 1V4S to obtain respective docking score (in KJ/mol) and the amino acid residue involved in each interaction. Based on the study, few molecules were selected for synthesis and other molecules were outright rejected. The criteria for such selection, scheme of reactions to synthesize selected molecules, results of their *in vitro* binding with glucokinase enzyme are presented.
Bhaswati Choudhury  
Ph.D. Research Scholar, Institute of Advanced Studies in Science and Technology, India

Raghuram Kandimalla  
Ph.D. Research Scholar, Institute of Advanced Studies in Science and Technology, India

&

Jibon Kotoky  
Professor, Institute of Advanced Studies in Science and Technology, India

Antioxidant and Anticancer Activity of *Garcinia Morella* Fruit on T cell Murine Lymphoma

Traditional knowledge (TK) based medicines have gained worldwide attention and recently the scientific community is focussing in proper pharmacological validation and identification of lead compounds for the treatment of various diseases. The North Eastern region of India is the heritage of valuable traditional herbal remedies. *Garcinia morella* Desr. (Guttiferae) is one such medicinal plant endemic to this region and is used by the traditional healers for the treatment of inflammatory disorders. The present study was aimed to evaluate the antioxidant and anticancer activity of *G. morella* (GM) fruit methanol extract in different *in vitro* and *in vivo* experimental conditions. The results of this study showed that GF methanol extract possessed *in vitro* antioxidant and anticancer properties. The anticancer activity was further confirmed by the results of *in vivo* administration of GF (200 mg/kg) for ten days to Dalton's Lymphoma (DLA) induced mice. GF extract significantly increased the mean survival time (MST) of the animals, decreased the tumour volume and restored the haematological and biochemical parameters. The present study for the first time indicates the anticancer property of GF on DLA. Further from the experiments conducted to elucidate the mechanism of action of GF on DLA, it can be concluded that GF exerts its anticancer effect through induction of caspases and DNA fragmentation that ultimately leads to apoptosis. However further experimentation is required to elucidate the active principle and validate this findings in various *in vivo* settings.
Lipid Based Matrices as Colonic Drug Delivery System for Diflunisal (In-vitro, In-vivo Study)

Hydrophobic lipid based materials have been widely used in formulations for obtaining controlled release drug delivery systems. Beeswax as a natural substance, Stearic acid as a saturated fatty acid and Glyceryl mono stearate as a wax like solid were selected to obtain formulations different proportion to optimize the colonic delivery of diflunisal.

Melt granulation technique was used for preparation of different formulations. Drug release study performed in different pH dissolution media using continuous drug release technology at various pH values (1.2, 6.8 &7.4). The obtained results showed that, in all release media with different pH values, the order of drug released from the different matrices with different ratios could be arranged as follow 1:5 > 1:3 > 1:1 drug : wax ratios. This abnormal behavior of the drug release necessitated the study of the physico-chemical characteristics of the solid dispersion of the drug in the different waxy matrices prepared with different ratios.

The instrumental analysis of the pure drug and its solid dispersions in different waxy matrices with different ratios showed that the drug changed from polymorph II to forms either I or III or both. These changes depend on the drug-waxy matrices used ratios. Accordingly it can be concluded that, this unstable highly soluble polymorph is responsible for the unexpected drug release phenomena obtained.

In - vivo study using 12 albino rats, that were scanned under X - ray machine after 2, 4, 6 and 8 hrs of administering the formula of choice. The obtained results showed that the dose reached the colon after 8 hrs. Colon targeting was proved by X - ray scanning and continuous drug release technology.
Solmaz Ghaffari
Department of Medical Nanotechnology, Faculty of Advanced Sciences and Technology, Pharmaceutical Sciences Branch, Islamic Azad University, (IAUPS), Tehran, Iran and Young Researchers and Elite Club, Pharmaceutical Sciences Branch, Islamic Azad University, (IAUPS), Tehran, Iran.

&

Parisa Jourghanian
Islamic Azad University, Iran

Preparation and Evaluation of Sustained Release Curcumin Loaded Solid Lipid Nanoparticles

The aim of this study was preparation of curcumin loaded Solid Lipid Nanoparticles (SLNs) with high loading efficiency, small particle size and prolonged release profile to overcome problems regarding bioavailability of poorly water soluble compounds like curcumin. To reach stable SLNs, freeze-drying was done using mannitol as cryoprotectant in two different percentages. Cholesterol was used as carrier because of good tolerability and biocompatibility. Optimized SLNs had 112 and 163 nm size before and after freeze drying, respectively with 71±2% loading efficiency in which more than 90% of loaded curcumin was released after 48 hours. Figure 1 and Figure 2 show the SEM picture and drug release profile of prepared SLNs. DSC studies were done to demonstrate the reason of prolonged release. Anti microbial studies were done to observe increase of diffusion of curcumin to lipid structures after loading on SLNs. Studies demonstrated that probably some hydrogen bonds between cholesterol and curcumin resulted in prolonged release of curcumin. Also lipid structure of cholesterol could cause to enhanced permeability to studied bacteria to increase antibacterial characters of curcumin. According to particle size, release profile, loading efficiency and enhanced permeation to bacteria, the designed curcumin SLNs could be candidate for formulation of different dosage forms or cosmeceutical products.

Figure 1. SEM picture of curcumin SLNs. Figure 2. Release profile of curcumin through SLNs.
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**Oxidative Stress in Skeletal Muscle: Role of Nrf2 and Effect of α-Lipoic Acid**

**Introduction:** α-Lipoic acid (LA) is a natural antioxidant and possess beneficial effects on oxidative stress parameters in skeletal muscle. It is a disulphide compound which serves as a coenzyme for mitochondrial respiratory enzymes pyruvate dehydrogenase and α-ketoglutarate dehydrogenase. Nrf2 is a regulator of cellular resistance to oxidants. Nrf2 activation can protect muscle against the oxidative stress induced by lipopolysaccharide (LPS) (Escherichia coli 026-B6).

**Objective:** The aim of the study was demonstrate whether antioxidant effect of α-lipoic acid during oxidative stress induced by LPS is mediated through Nrf2 pathway.

**Materials and Methods:** Experiments carried out on rats, which were treated intraperitoneally with saline or α-LA (60 mg/kg) 30 min after LPS administration. After 5 h of observation, the animals were killed and their femoral muscles from thigh were isolated for the measurements lipid peroxidation, hydrogen peroxide (H2O2), free sulfhydryl groups (-SH) concentration and expression of Nrf2 (transcriptional nuclear factor erythroid-2-related factor 2).

**Results:** Injection of LPS alone resulted in the development of shock and oxidative stress, the indicated by a significant increase in skeletal muscle lipid peroxidation and H2O2 concentration and a decrease in skeletal muscle free-SH groups content. Administration of α - LA after the LPS challenge resulted in an increase in total -SH group concentration and increase in Nrf2 expression, and a decrease lipid peroxidation and H2O2 concentration in the skeletal muscle compared with the LPS groups.

**Conclusion:** The results indicate that α -LA treatment effectively protected the skeletal muscles against endotoxin-induced oxidative stress. This effect of LA is mediated through Nrf2 pathways.

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Experimental Validation of Ethnopharmacological Data Obtained via Informant Consensus Factor (ICF) and Use Value (UV) for Some Anti-microbial Jordanian Medicinal Plants and Chemical Evaluation of the Active Volatile Oils

Two Jordanian medicinal plants used traditionally for treatment of diseases, caused mainly by microorganisms, were chosen as the material of our present study based on their high informant consensus factor (ICF) and plant use value (PUV) measures as reported in ethnopharmacological surveys conducted in different Jordanian regions. These plants, namely; Ruta chalepensis (Feijen), and Varthemia iphonoides (Ktaile), were selected in order to evaluate their antimicrobial activity for purpose of validating their traditional uses. The anti-bacterial and anti-fungal activities were evaluated for the crude plant extracts (aqueous and alcoholic) and the volatile oils (VO) obtained from the collected plant materials. Moreover, the chemical composition of the VOs, showing notable anti-microbial activity, was evaluated by means of GC/MS. Results showed that the VO of R. chalepensis and V. iphonoides have moderate to high activity against the tested microorganisms, while, the water and alcoholic extracts of the selected plants didn't show any antimicrobial activity, except for the 40% w/v water extract of R. chalepensis which exhibited a moderate activity against B. subtilis and S. aureus, and 40% w/v water extract of V. iphonoides which exhibited a moderate activity against B. subtilis, S. aureus and E. coli. The oil from V. iphonoides showed a wide range of components including monoterpenoid hydrocarbons (1.6%), sesquiterpene hydrocarbons (2.4%), oxygenated monoterpenes (42.9%), and oxygenated sesquiterpenes (21.6%). Borneol, accounting to 19% of the oil composition represented the principal compound, while, 1,8- Cineole (5.8%), bornyl acetate (2.7%), and α-Terpineol (2.4%) were identified as other major components of the oil. The oil of R. chalepensis was found to be predominated by ketones including 2-undecanone (75.5%), the principal component, 2-nonanone (5.8%), 2-tridecanone (4.5%), and 3-dodecanone (0.9%).
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Anticonvulsant Activity of Certain Novel Isoxazole Derivatives

**Background:** Many literature studies indicate inhibitory action of bicyclic isoxazole gamma-aminobutyric acid (GABA) analogues. In this light hereby prepared many Isoxazole derivatives which screened for anticonvulsant activity by chemically induced method and maximal electroshock seizure (MES) method.

**Aim:** To synthesize novel Isoxazole derivatives, characterize them and subject for screening anticonvulsant activity.

**Method:** Chalcones are prepared by the reaction of aromatic aldehydes with aromatic ketones in aqueous alcoholic alkaline medium. Then these are made to react with hydroxylamine hydrochloride and sodium acetate to prepare title compounds. The prepared isoxazole compounds are subjected to in vivo anticonvulsant screening by chemical induced convulsion method using Pentylene tetrozole and by MES method.

**Results:** None of the tested compounds are superior to Diazepam which was the standard. Two compounds have given protection against convulsion for 25 minutes; In those compounds Phenyl ring at fifth position of hetero ring carried NO₂ group and phenyl attached at third position of hetero ring possessed OH as R₂' substitution. An another compound also showed equal action where first phenyl ring at 5th position had CH₃ substitution and NH₂ in second phenyl ring attached at third position of hetero ring. Moderate protection have been given in another set of compounds where Bromine substituted in Phenyl ring at fifth position and Methyl group in second phenyl ring at third position of hetero ring. Another compound also exhibited similar moderate effect which possess Bromine in phenyl ring attached at fifth position but phenyl ring at third position of hetero ring carries OH functional group.

**Conclusion:** Presence of nitrated (R₁/R₃) aromatic ring at 5-C and hydroxyl substituted phenyl ring at 3-C of Isoxazole exhibited maximum protection against convulsion.

Acknowledgement: This study is funded by SERB of DST-Govt. of India.
Development and Elucidation of Mechanism of Action of Poly Herbal Formulations to Treat Diabetic Neuropathic Pain

According to WHO report, 5% world population is suffering from diabetes. Prolonged or untreated diabetic patients suffer from a chronic condition called neuropathy. Pain is the main manifestation of diabetic neuropathy (DN) which shows classical symptom like loss of sensation and numbness in the feet, hands and legs that can be accompanied by painful tingling or burning sensations. The present study was aimed to evaluate the herbal formulations ADNP45 (Hydro alcoholic extract of Aegle marmelos, Curcuma longa, Desmodium gangeticum, Gmelina arborea, Oroxylum indicum, Stereospermum suaveolens, Tribulus terrestris and Uraria picta) and ADNP21 (Hydro alcoholic extract of Aegle marmelos, Curcuma longa, Desmodium gangeticum, Gmelina arborea, Oroxylum indicum, Stereospermum suaveolens and Tribulus terrestris) against diabetic neuropathy in rats. DN condition was induced in wistar rats by single intraperitoneal injection of streptozotocin (STZ) 40 mg/kg and leaves the rats untreated for four weeks. Further drug treatment was continued for four weeks with both the herbal formulations. Pain was evaluated at different time intervals throughout the study by hot plate, cold plate, tail immersion and formalin tests. At the end of the study, motor nerve conduction velocity (MNCV) was measured. All the animals were sacrificed and sciatic nerve was collected to measure the inflammatory markers like TNF-α, IL-1β, IL-6 and IL-10. Nerve oxidative stress was measured by evaluating the levels of super oxide dismutase (SOD), catalase (CAT) and nitric oxide (NO). Herbal formulations ADNP45 and ADNP21 exhibit significant antinociceptive and antiallodynic property against diabetic neuropathic pain in rats which was confirmed by levels of inflammatory and oxidative stress markers in treatment groups. The present study was concluded that both the herbal formulations showed protective effect against diabetic neuropathy in rats.
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Inhaled Lidocaine Powder for Oropharyngeal Anaesthesia

Clinical procedures such as awake fiberoptic bronchoscopy, laryngoscopy, gastrointestinal endoscopy, and tracheal intubation may cause pain to the patient. Thus topical oropharyngeal anaesthesia is applied to suppress the discomfort. Lidocaine is commonly used for this because its safety is well established.

Currently available dosage forms of this anaesthetic include liquid throat spray, lozenge, viscous gargling solution, and nebuliser solution. The throat spray is efficacious but has poor palatability. The lozenge tastes better but its anaesthetic effect is less satisfactory. Patients dislike the viscous mouth feel of the gargling solution. Nebulisation produces small droplets that may deposit in the peripheral lungs, leading to systemic absorption and adverse effects. Therefore, this study aims to evaluate in vitro the feasibility of inhaled lidocaine powder for oropharyngeal anaesthesia. Advantages of a solid formulation include higher physical chemical stability and more convenient storage than the aforementioned liquid formulations. The median volumetric diameter of lidocaine hydrochloride monohydrate particles (Sigma-Aldrich, USA) measured by laser diffraction (LS 13320; Beckman Coulter, USA) was 67.6 µm. One hundred and thirty five milligrams of the powder was dispersed from an Osmohaler® (RS-01; Plastiape, Italy) into a Next Generation Impactor (Copley Scientific, UK) at 30, 60, and 90 L/min of airflow to examine aerosol performance (n= 3). The dose deposited in the throat increased with air flow. The mean throat dose at 90 L/min was 90.7 mg, i.e. 67% of the loaded dose. This high deposition in the throat was due to inertial impaction of the large particles at that site. The mean fine particle dose < 5 µm rate was very low (0.12 mg, i.e.0.09% of the loaded dose at 90 L/min). This implies that systemic absorption of the drug from the lungs should be minimal in vivo. Thus the lidocaine powder may be potentially used for oropharyngeal anaesthesia.
Novel Potential Excipient for Buccal Delivery

Summary: Biomaterials have gained immense interest in the pharmaceutical research in the last decades. Hyaluronic acid a carbohydrate and mucopolysaccharide was chemically modified in order to achieve and establish a promising platform for buccoal drug delivery.

Aim: Novel biomaterial was tested for its potential for buccal drug delivery.

Background: Polysaccharide hyaluronic acid (HA) was chemically modified with cysteine ethyl ether (CYS). By immobilization of the thiol bearing ligand on the polymeric backbone the thiolated bioconjugate HA-CYS was obtained.

Methodology: Mucoadhesive, permeation enhancing and stability potential as well as mechanical, physicochemical properties further mucoadhesive strength, swelling index and residence time were investigated. The developed thiolated bioconjugate displayed enhanced mucoadhesiveness on buccal mucosa as well as permeation behavior and polymer stability. The near neutral pH and negative cytotoxicity studies indicated their non-irritability and biocompatible nature with biological tissues. Further, the model drug sulforhodamine 101 was incorporated to determine its drug release profiles.

Results: The synthesized thiomer showed no toxicity. The mucoadhesion of thiolated hyaluronic acid on buccal mucosa was significantly improved in comparison to unmodified one. The biomaterial showed 2.5-fold higher stability in polymer structure. The release of sulforhodamine in presence of thiolated
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A New Mathematical Approach for Investigation the Mechanisms of Drug Release and Determination the Percent of Each

Contribution of Fickian diffusion and polymer relaxation on the drug release process could be estimated upon applying Peppas-Sahlin model for the drug release data. The amount of drug released by each mechanism could not be estimated due to the use of fix rate constant value for each mechanism all over the drug release time (k1&k2). On applying another mathematical method (substitution) on the cumulative drug release data from microcapsules in which the drug entrapped in the forms of solid solution, homogenous solid dispersion and reservoir for drug crystal, it could calculate constant rate values for each mechanism at each unit time. Then it could calculate the amount of drug released by each mechanism at each unit time and their summation was completely equal to the practically determined amount of drug released at the same time. These results could be correlated to the image of the determined drug entrapment methods and to another established used models which are normally support each other’s. These models are Zero order, Higuchi model and Korsmeyer-Peppes model. In addition the substitution method was applied to the amount of drug released during each period of time. Then the cumulative amount of drug released by each mechanism could be calculated. Fitting of the three cumulative drug released (practically measured one, calculated amount released by Fickian mechanism and that by polymer relaxation) was found to follow polynomial with grade four. In every case, the polynomial equation of the practically measured cumulative drug release is the exact summation of the polynomial equations of the two mechanisms. Accordingly, it was concluded that, the application of the substitution method will indicate the role of each drug release mechanism at each unit time. Moreover overlap, alternate, predominate and also combination of all drug release mechanisms at each unit time can be clearly observed which bring us to some extend to the reality of the drug release process which is a dynamic complex one.
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**Antidiabetical Effect of Standardized Extract of Indonesian Kanunang Leaves (Cordia Myxa L.)**

Diabetes mellitus (DM) is a metabolic disease that is affected by highly blood sugar (glucose). This occurred because of either insulin secretion or insulin resistance. Prevalence of DM in Indonesia is very high case, and it is predicted about 21.3 millions people in 2030 will be suffer from it disease. DM can be treated by modern drugs and herbal medicine. One of several plants to treat of DM is Kanunang (Cordia myxa L. Boraginaceae Family). In vitro study have been done with inhibiting of α-glucosydase enzyme. This research was conducted that C. myxa leaves extract could be inhibiting of α-glukosidase enzyme activity with IC50 value is 35.89 µg/mL (compare with positive standard 117.20 µg/mL). The conclusion of this research that the C. myxa extract is potential to develop as a antidiabetic medicine.
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Restoring the Endothelial Cell Function in Diabetic Patients through the Novel and Powerful Approach of Cell Reprogramming
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**Synthesis and Anticancer Action of Novel Diazaphenothiazine Derivatives**

Phenothiazines are an important class of heterocyclic compounds with a variety of biological activities such as antipsychotic, antihistaminic, antitussive, antiemetic. Some modifications of the phenothiazine structures were directed into aza- and diazaphenothiazines. Previously synthesized dipyrido[1,4]thiazines (1,6-, 1,8- and 2,7-diazaphenothiazines) were shown to possess interesting antiproliferative, anticancer, antioxidant and immunosuppressive activity correlating to some degree with their lipophilicity. In continuation of our search we obtained new derivatives of dipyrido[1,4]thiazines being 3,6-diazaphenothiazines.

\[
\begin{array}{c}
\text{R} = \text{H, alkyl, aryl, heteroaryl, dialkylaminoalkyl} \\
\end{array}
\]

The parent compound 10H-3,6-diazaphenothiazine was further transformed into N-substituted derivatives with alkyl, heteroaryl and pharmacophoric alkylaminoalkyl groups. Using \(^1\text{H}\) and \(^{13}\text{C}\) NMR two-dimensional spectroscopy (\(^1\text{H}-^1\text{H} \text{COSY, ROESY, HSQC, HMBC}\)), mass spectrometry (EI and FAB MS) and X-ray analysis the right structure of the products were determined. For those compounds, the anticancer action on selected tumor lines (MCF-7, SNB-19, C-32) was investigated. The compounds exhibited differential inhibitory activities but two compounds were more active (\(IC_{50} = 0.4 \mu\text{mol}\)) than cisplatin. For the most active compound the expression of \(H3, TP53, CDKN1A, BCL-2\) and \(BAX\) genes was detected by the RT-QPCR method. The gene expression ratio \(BACL-2/BAX\) could suggest the mitochondrial pathway of apoptosis.
Mitochondrial Dysfunction, Common Final Pathway for Aging and Alzheimer’s Disease: Therapeutic Aspects

Mitochondrial dysfunction has been shown over the last years as common final pathway for brain aging and Alzheimer disease. Might it also represent a promising treatment strategy? Ironically, the evidences available now go back to some rather old drugs. The best clinical data shows EGb761 (Ginkgo extract) which improves impaired mitochondrial function, reduces ROS and apoptosis, elevates ATP, improves respiratory chain function, and improves synaptic plasticity. Another old drug is piracetam, which is still used at in many countries worldwide to treat cognitive impairment in aging, brain injuries as well as dementia. Its acceptance of as an antidementia drug was hampered by the lack of a clear mechanism of action. Our’s and other’s recent data clearly show improvement of mitochondrial dysfunction due to brain aging and other situations of elevated oxidative stress including AD like pathology. Similar properties could recently been shown for levetiracetam, an antiepileptic with promising properties as an antidementia drug. Another example is dimebon, an old antiallergic drug developed in Russia. A phase II trial indicating substantial therapeutic improvement could not be reproduced in a subsequent large-scale phase III trial. Dimebon also specifically improves mitochondrial function in many in vitro and in vivo experiments. While all three drugs seem to have different targets, for each mitochondrial improvement goes parallel with specific alterations of mitochondrial dynamics. None of the three is the magic bullet. However, they definitively are good enough to serve as proof of concept for improving mitochondrial function as a valid treatment strategy for AD and might serve as starting point for future drug development.

Literature
Antidiabetic and Antioxidant Effect of Palmatine in STZ-Induced Diabetic Rat Model

Coscinium fenestratum (CF) is a medicinal plant mostly indigenous to India and Sri Lanka. The plant is used in ayurveda and siddha medicine for treating inflammation, diabetic mellitus among others. We have previously reported the antidiabetic activity of dichloromethane (DCM) stem crude extract and partially purified Fraction E of Coscinium fenestratum. HPLC analysis of fraction E has shown the presences of Palmatine. Palmatine (protoberberine alkaloid) and Fraction E were studied for their antidiabetic and antioxidant effect in streptozotocin (stz)-induced type 2 diabetic rats. Oral administration of Fraction E (20mg/200g) and Palmatine (0.4mg/200g) caused a significant decrease in blood glucose level and increase weight in diabetic animals. There was also a significant increase in antioxidants enzymatic activity such as catalase, superoxide dismutase, reduced glutathione synthetase and a decrease in lipid peroxidation levels. They decreased the levels of triglycerides and high density lipoprotein (HDL) and increased levels of low density lipoprotein (LDL) in lipid profile; reduced Hemoglobin and Red Blood Cell (RBC) levels and increased White blood Count (WBC) levels in the hematology test; decreased urea levels and increased creatinine levels in renal function test. They also reduced the alkaline phosphatase (AP), Aspartate Transaminase (AST) and Alanine Aminotransferase (ALP) levels in the liver function test and histology images showed rejuvenation of the β-cells in pancreas. This investigation demonstrates significant antidiabetic activity of Fraction E and Palmatine.
Impact Studies of Biopolymers on Solubility of Poorly Water Soluble Drugs: A Case Study of Tebipenem Pivoxil

In drug development, enhancing the oral bioavailability of poor water soluble drugs remains most challenging aspects. One of the method of increasing drug solubility is combining with excipients which are polymers. Such polymer are natural derivatives of cellulose derivatives (e.g., hydroxypropylmethylcellulose, HPMC) or starch derivates (e.g., cyclodextrins, CDs).

Tebipenem pivoxil is the first oral carbapenem antibiotic which is a prodrug. The estrification of the carboxylic group at C-2 of β-lactam ring increased its chemical stability permitting oral administration but simultaneously decreased its solubility. As a result of the activity of carboxyesterase, located in the epithelium of the gastrointestinal tract, tebipenem pivoxil converts to tebipenem characterized by a broad, potent antibacterial and bactericidal activity.

The aim of the present study was to study the influence of polymers (hydroxypropylmethylcellulose, β-cyclodextrin, 2-hydroxypropyl-β-cyclodextrin and methyl-β-cyclodextrin) on tebipenem pivoxil solubility.

The systems of tebipenem pivoxil with polymers were prepared by kneading tebipenem pivoxil with suitable polymer at the ratio 1:1 with continuous stirring for 30 min. Then was kept at 308 K at an ambient relative air humidity. Obtained systems were characterized by in vitro dissolution study to compare the effects of polymers on the preparation of solid dispersion and dissolution enhance.

As analytical methods for identification of tebipenem pivoxil-polymer systems differential scanning calorimetry (DSC), infrared (FT-IR) and Raman spectroscopy were applied.

In vitro dissolution studies of tebipenem pivoxil were performed according to European Pharmacopoeia by using an Agilent 708-DS Dissolution Apparatus [1]. As the acceptor solution, artificial gastric juice (pH 1.2) stimulating gastric environmental was used. The changes of dissolved drugs concentrations were measured by using HPLC-DAD method [2].

Results of chromatographic analysis confirmed lack of changes in the profile of impurities of tebipenem pivoxil for its systems with polymers.
during dissolution studies. Significant changes of shapes of dissolution curves were observed in depends on polymers which were used.

The findings of the present study demonstrated that HPMC slowdown the release profile of tebipenem pivoxil. While solubility of tebipenem pivoxil was modified by combining with CDs in regards to content of tebipenem pivoxil (increased about 10%) in acceptor solutions and shapes of curves characterizing its apparent solubility.

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Cardiomyocyte Mitochondrial Networking in Diabete

The transient physical connectivity of intracellular organelles gathers a particular attention nowadays as it generates a dynamically continuous network that allows organelles content exchange and signals transfer according to the cellular metabolic requirements. Evidence for such interactions in diabetic cardiomyocytes (CMs) and identification of molecules involved are now under intensive research anticipating contractile dysfunction alleviation in cardiomyopathy. The aim of this disclosure is to link electron microscopy evidence on organelles networking within diabetic left ventricular CMs to the newly identified molecules/mechanisms beyond it. The issues examined are: (i) the intermitochondrial communication, demonstrated in adjacent mitochondria by the extensive connectivity (“kissing”) of their outer membranes (OMMs) and by cristae organization into coordinated pairs, while distal organelles contact is accomplished by elongated nanotubular protrusions (“nanotunneling”); together, these form the structural basis for transfer of electrochemical signals and exchange of OMMs components or matrix proteins; (ii) the mitochondrion - nucleus interaction encompass a plethora of aspects, such as the close relationship between their genomes, codification of mitochondrial proteins by the nuclear genome, the common intervention in preserving cellular energetics homeostasis, and the control of stress-induced mitochondrial dysfunction by activation of “retrograde signaling” (attribute of mitochondrial “quality control” function) and by stimulated transcription of specific nuclear genes that produce adaptive changes in mitochondrial protein levels; (iii) the OMM is physically tethered to the endoplasmic/sarcoplasmic reticulum, mediating lipid transport between the two membranes, and assisting fragmentation (“fission”) of dysfunctional mitochondria followed by removal of malfunctioning part (by “mitophagy”), and maintenance of a “healthy” mitochondrial population. Together, mitochondrial networking within CMs may encourage the transfer of “healthy” autologous mitochondria into dysfunctional CMs (i.e. the intercellular organelle transfer); such “mitochondrial therapy” portrays a novel regenerative strategy to replenish mitochondrial mass and to preserve myocardial energetics in diabetic cardiomyopathy.
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**Preparation of Pennisetum Glaucum Amylase Loaded Bovine Serum Albumin Nanoparticles by Desolvation Method**

In present work, Pennisetum glaucum amylase was extracted and loaded into bovine serum albumin nanoparticle with butanol through glutaraldehyde by desolvation method. Pennisetum glaucum is very popular for having rich source of amylase and amylase was extracted from its 3-4 days seedlings. Bovine serum albumin was chosen as bio-compatible matrix used for the preparation of amylase loaded nanoparticles. Characterization of prepared nanoparticles was done by Dynamic Light scattering (DLS) and reported size was found to be in the range of 200nm to 500nm. Kinetic parameters were also carried out for free amylase and bound amylase to perform the comparative analysis for their optima e.g. pH, incubation time, substrate concentration, CaCl2 concentration and temperature effect. Thermal stability of bound enzyme was enhanced and it was found at 70°C for 2 hours 25 minutes and reported thermal stability for free enzyme was at 40°C for 50 minutes only. And, storage stability of bound enzyme at 4°C was also increased for 4 months as compared to free enzyme which was reported for one day only. Hence, the enhanced thermal stability and storage stability of bound amylase were also increased the industrial viability of Pennisetum glaucum amylase for its further use in food, pharmaceutical, leather and detergent industries. Biodegradation analysis of prepared nanoparticles was also performed by using 10U units of alkaline protease to study the controlled release of bound amylase from bovine serum albumin nanoparticles in reaction mixture.
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**Petals of Crocus Sativus L. as a Potential Source of the Antioxidants Crocin and Kaempferol**

Crocus sativus L. is an autumn-flowering geophyte extensively cultivated in countries such as Italy, Spain, Greece, Turkey, Iran and India. The only part used of the whole plant is its dried stigmas which have been used as a valuable spice and traditional medicine for centuries; the other parts of the flowers are normally wasted.

Recently, attention was paid to the identification of natural antioxidants from the petals. The antioxidant activities were mainly attributed to carotenoid and flavonoid compounds, kaempferol and crocins. These bioactive compounds have important biological activities including prevention of heart and vascular disease, oocyte prevention and cancer. Crocins are glycosides of the carotenoid crocetin which is known to inhibit nucleic acid synthesis and cell proliferation. Numerous reports have shown that kaempferol and/or its glycosides induce cell death in a variety of cancer cells from different tissues.

The antioxidants were extracted using aqueous alcohol followed by flash column chromatography purification, and analysed using thin layer chromatography (TLC) and high performance liquid chromatography (HPLC) by comparison with authentic standards. Crocin and kaempferol were further characterised by infrared (IR), mass spectroscopy (MS), nuclear magnetic resonance (1H & 13C NMR). Kaempferol was assayed for toxicity towards MCF-7 breast cancer cell lines and multi-drug resistant MDA-MB468 breast cancer cell lines and MCF10A a normal breast cell line. In addition to their antitumor activity, in vitro biological assays have been exerted in order to assess the cardiovascular effects of the compounds. The cardiac activity assays, on guinea-pig left and right atria, as well as their relaxant activity on
guinea-pig vascular (aorta) and nonvascular (ileum) smooth muscle will be studied.

The presence of very high amounts of antioxidants, notably of kaempferol, in saffron petals makes that we should considered them an important resource rather than a waste product. Petals of sativus L. have commercial potential as a source for kaempferol and crocetin glycosides, natural compounds with antioxidant activity that are considered to be the active ingredients in saffron-based herbal medicine. This study is currently in progress.
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Complementary and Alternative Modalities Prevalence as a Weight Control tool in Jordan

Potential association of obesity with life threatening diseases was documented in literature. To date, obesity prevalence is rising up, urging individuals toward complementary and Alternative modalities (CAM). This study investigated the prevalence of CAM as a weight control alternative among adults in Jordan.

Cross sectional survey using an interviewer administered questionnaire was used. Data was collected from 1388 participants. The overall use of CAM within the past year among normal weight (BMI from 18 to <25), overweight (from 25 to <30), mildly obese (from 30 to <35), moderately obese (from 35 to <40) and extremely obese (>40) adults was compared. Association between participants’ BMIs and the use of CAM modalities was also explored.

The response rate was 93.3 %. Forty nine percent of the participants were overweight or obese. Almost half of the participants had tried to control or reduce their weight. Out of which, 72.6 % approved the use of CAM therapy interventions. The pattern of CAM use varied with participant’s weight. Herbal dietary supplements were more convenient for elderly overweight and obese. Green tea exhibited the most commonly used herbal dietary supplement, based on relatives’ advice. Mardaqoosh was a pertinent module for weight reduction in overweight individuals. Sixty eight percent of the obese participants disagreed or didn’t know about possible CAM-drug interaction.

Obese participants are more likely to use CAM in combination with conventional medical intervention, and may therefore be at a greater risk for potential adverse interactions. Therefore, evidence based information about CAM efficacy, effectiveness, adverse effects and possible interactions is of great importance to provide participants with more effective and safe integrative medical services.
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Mechanism of Action of New Associated Analogues  
Glibenclamide/Pioglitazone on Glucose Homeostasis  

The sulfonylurea glibenclamide is one of the most used compounds to control the hyperglycemia in diabetic patients. Pioglitazone a thiazolidinedione excels in controlling diabetes mellitus by increasing insulin sensitivity in insulin-dependent peripheral organs. Objective: To study the secretagogue activity of new analogue JO4, supported by the junction of glibenclamide structure associated with the portion of pioglitazone, on antidiabetic activity. Methods: Male adult Wistar rats fasted for 16 h were treated with JO4 (1 and 10 mg/kg, i.p). After 30 min of treatment rats received a glucose overload (4 g/kg, i.p), blood was collected at zero time, 15, 30, 60 and 180 min for glucose measurements. The serum insulin as well as in vitro insulin secretion was measured with/without JO4. Isolated pancreatic islets were incubated for 60 min in HEPES-KRb with 45Ca2+ at 37 ºC, pH 7.4 with O2:CO2 (95:5 v/v). It was studied the effect and the mechanism of action of JO4 (106, 109 and 10−12 M) on 45Ca2+ influx in islets with/without agonist/antagonists of ionic channels or protein kinases (CEUA PP00479).Results: JO4 improved glucose tolerance and stimulated insulin secretion at 15, 30 and 60 min. In addition, JO4 stimulated in vitro insulin secretion after 30 min of incubation in isolated pancreatic islets. JO4 stimulated calcium influx that was enhanced in the presence of glibenclamide. The diazoxide and nifedipine inhibited the effect of JO4. However, flunarizine did not change the effect of JO4. Thapsigargin and dantrolene did not alter the effect of JO4. On the other hand, H89 and RO310432 blocked the stimulatory effect of JO4 in calcium influx. Conclusion: These results show the potential role of JO4 as an insulin secretagogue by acting through the K+ /ATP channels, CCDV. Beyond, PKA and PKC seem to downstream the signal transduction of JO4 for insulin secretion and glucose homeostasis. Financial support: CNPq, CAPES-PPGBQA/UFSC.
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Design, Synthesis and in Vivo Biological Evaluation of Novel Hypoglycemic Glycosylated Sulfonylureas

Diabetes mellitus (DM) is a major degenerative disease with a serious cause of maladies in the 21st century. DM is commonly treated by the administration of insulin, biguanides and sulfonylureas. This study describes the design, synthesis and in vivo testing of glycosylated aryl sulfonylurea compounds as a novel antihyperglycaemic agents in streptozocine-induced diabetic mice. These novel compounds posses the pharmacophoric features essential for the sulfonylurea antidiabetic agent and the glucosamine moiety which serve as a homing unit toward selective uptake by pancreatic β-cells and thus reduce their cardiotoxic side effects. 2-Deoxy-2-(4-chlorophenylsulfonylurea)-d-glucopyranose was found to be the most potent antihyperglycaemic agents among the synthesized compounds. This investigation indicates the importance of this novel class as potential antihyperglycaemic agents.
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Mucoadhesive and Efflux Pumps Inhibitory Properties of Thiolated Polymers

The aim of this study was to design thiolated polymers generated by substitution of hydroxyl groups with thiol moieties and to evaluate their mucoadhesive and efflux pump inhibitory properties. According to its various biological activities, such as antiviral and antitumor activities, and applications in food and pharmaceutical industry, carrageenan was chosen for modification using thiourea as thiol-bearing ligand. The amount of thiol groups attached to the polymer was quantified by Ellman’s test. The mucoadhesive properties of the resulting thiolated polymers were evaluated on porcine intestinal mucosa using rotating cylinder test. The viscosity of mucus-polymer mixture was measured as a function of time using rheometer. The cytotoxicity of polymers was assessed in Caco-2 cells by resazurin assay and multidrug resistance protein 2 (MRP2) inhibitory effects were investigated in cell monolayer using sulforhodamine 101 as MRP2 substrate. Kappa- and iota-carrageenan exhibited 176.6 and 109.5 ± 18.3 μmol thiol groups/g of polymer, respectively. The residence time on porcine intestinal mucosa of test discs comprising thiolated kappa- and iota-carrageenan was 6.4- and 1.8-fold prolonged compared to those comprising non-thiolated polymers, respectively. The dynamic viscosity of mucus incubated with thiolated polymers was significantly increased over a time period of 4 h suggesting disulfide bridges formation between mucin and polymer backbone. The cytotoxicity studies showed that 0.1% of thiolated polymers were non-toxic within 3 h of incubation. The cellular uptake of MRP2 substrate in Caco-2 cells treated with thiolated kappa- and iota-carrageenan was 1.4- and 1.3-fold enhanced in comparison to non-treated control, respectively. The improvement ratio of permeated sulforhodamine 101 across cell monolayer from apical to basolateral side compared to control was 1.6 and 1.3 in presence of thiolated kappa- and iota-carrageenan, respectively. These findings suggest mucoadhesion and efflux pump inhibition of thiolated carrageenan that might be useful for various drug delivery systems.
Skin Wound Healing: From Mediterranean Ethnobotany to Evidence based Phytotherapy

Phytotherapy plays an important role in wound healing. Medicinal plants have represented for thousands of years the only remedy for wound care, and still maintain an important therapeutic role thanks to peculiar and desirable features of plant phytocomplexes. The use of herbal preparations exploiting synergistic and multitasking activities is distinctive of phytotherapy as a branch of pharmacology and could be alternative, more often complementary, to the use of monomolecular synthetic drugs. The European Medicines Agency (EMA), as well as WHO and ESCOP, confirms that one of the most frequent indications for which many medicinal plants are used in the European Community and in the rest of the world, is the treatment of skin disorders and minor wounds. The study of medicinal plants used in wound healing has its origins in the ethnobotanical knowledge and in folk medicine. Ethnobotany encompasses both wild and domestic species, and is rooted in observation, relationship, needs and traditional ways of knowing.

Various ethnobotanical investigations that took place in Italy and in Greece, have confirmed the use of many species nominated by EMA, ESCOP and WHO, for use in wound healing. The interviewed subjects have also provided important practical details about the use of medicinal plants for the treatment of tissue lesions. They have also described how every single plant, as well as every preparation, is destined to a specific type of wound. This work summarizes the medicinal plants used in Mediterranean countries, particularly Italy and Greece, for wound healing, reporting mechanisms of action, clinical efficacy and peculiar characteristics. These data provide the rationale for using different natural remedies on different types of wounds, showing that local health seeking strategies can help in resolving wound healing problems.
Evaluation of a Novel Mouthwash from Azadirachta Indica and Chlorhexidine on Human Gingival Fibroblast (Hgf) Cell Line

Chemical plaque inhibitors are toxic when used for longer duration. However, herbal preparations are less toxic as compared to chemical mouthwashes and shows excellent results. Owing to these reasons, Neem and Sanguinarine have been used for the inhibition of plaque and gingivitis. The present study attempts to assess the influence of Chlorhexidine (CHX) and Neem Extract (NE) on Cultured Human Gingival Fibroblasts (hGF). Fibroblasts were derived from healthy gingival biopsy specimens harvested aseptically. The effects of CHX and NE were evaluated on cultured hGF through morphological and biochemical assays. Morphological studies with hGF indicate altered morphology beyond 1% CHX. However, NE shows similar results at higher concentrations. Cytotoxicity and Antioxidant analysis of NE displays remarkable safety as compared with CHX with less than 32% cytotoxicity even at 100% conc. CHX beyond 1% concentration exhibits toxic effect on hGF at 1 minute time exposure. However, NE does not adversely affect the fibroblasts even up to 50% concentration showing less toxic effect in comparison with CHX on these cells. The cytoprotective, oral friendly quality of NE emphasize the superiority of NE over CHX.
Feasibility on the Use of Acid Value for Evidencing the Esterification of Glycerol with Caprylic Acid Catalyzed by Lipase

Mono, di and tricaprylin are good emollients and surfactants. Monocaprylin has also antiviral and antimicrobial activities, being used in collutors (mouthwash), in microbial decontaminant solution for textile raw materials, and as preservative against pathogens in foods. Caprylins can be attained either by controlled glycerolysis in presence of Ca(OH)2 at 230oC or glycerol/caprylic acid esterification catalyzed by soluble or insoluble lipase (Lypozyme RM IM®). The advantages of enzyme catalysis are specificity, mild reaction conditions and low formation of environmental unfriendly compounds. Moreover, insoluble lipase presents high stability against pH, temperature, shear-force damaging and denaturing substances, as well as low steric hindrance on the enzyme/substrate interaction at the catalytic site, negligible change on the enzyme conformation structure and low diffusion effect during catalysis. This paper deals with the use of Acid Value (AV), an acid-base titration method, for determining the acidity of the medium resulting from caprylic acid (CA) and glycerol (GLY) enzyme esterification, as well as the blends of these two components (GLY/CA) in different proportions used as substrate for the reactions. Controlling an industrial process by using a reliable, cheap and simple analytical method, whose apparatus could be disposed and handled near the reactor in operation, would be of great interest by the industry. Response surface methodology (RSM) was used to determine the effects of temperature, reaction time, and GLY/CA molar ratio on the caprylin production optimization. The AV of the blends decreased with an increasing molar ratio GLY/CA and a coefficient of variation of 11% for the AV method was obtained. The RSM did not provide a clear statistical correlation between AV and the reaction parameters selected as variables. However, near 77% of AV were in the range between 50 and 100 mg NaOH/g, including the experiment performed under the conditions of 60 oC, 8 h, and GLY/CA molar ratio of 2, in which the highest monocaprylin production yield of about 50% was obtained.
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Comparison between Different Endotoxin Removal Methods Applied during Pharmaceutical Quality Control Testing of Antisera Preparation

Endotoxin contamination is a serious problem that threatens the safety of all parenteral drugs. Snake bites represent a life threatening health hazard in many rural areas especially in developing countries. The only treatment is the administration of snake antivenom which has to be given by injection on a strict schedule after the bite. Snake antivenoms are prepared by injecting animals, usually horses, with a mixture of snake venoms, collecting the animal blood to separate the antibodies produced by the animal. These antibodies are then purified and fractionated and used as the antivenom. Due to the very complicated method of preparing snake antivenom, it is very common that they suffer from endotoxin contamination and they can fail in quality control testing.

In this study, a strict environmental monitoring program was applied to identify the source of endotoxin contamination during the various steps of manufacturing the snake antivenom in a vaccine production facility. Three different endotoxin removal techniques (ultrafiltration, ion-exchange and affinity chromatography) were compared to identify the most appropriate method for removal. The results showed that the fractionation and purification areas of the snake antivenom preparation were heavily loaded with high gram-negative bacterial counts which served as a source of endotoxin contamination. These bacterial counts were more concentrated in the air and on surfaces than personnel operating in these areas. Bacterial contamination was actually observed in different intermediate stages of the preparation itself with the exception of the bulk and final product. Affinity-resin based chromatography proved to be the most effective endotoxin removal method with the optimum protein recovery. Our results indicate that implementation of good manufacturing practice (GMP) in pharmaceutical firms is the key for production of sterile and endotoxin free preparations.
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**Monitoring Antiplatelet Therapy: Contribution Biological Tests to Screen a Resistance**

Antiplatelet therapy aspirin and thienopyridine (clopidogrel, prasugrel or ticlopidine) is the cornerstone of the treatment for patients with coronary artery disease (CAD). Thienopyridines are a class of selective, irreversible ADP receptor/P2Y12 inhibitors used for their anti-platelet activity. Inter-individual variability in the response to thienopyridine is frequent, well established and observed in a fairly large proportion of patients. A rapid advance in the knowledge of this phenomenon has shown that this variability is related mainly to differences in active metabolite production from the prodrug. Patients presenting biological resistance, determined through platelet function tests or genetic tests predicting the existence of low metabolism, have a higher risk of cardiovascular accidents.

Objectives: Our aim to suggesting the most convenient functional method in monitoring the dual antiplatelet treatment (DAPT) in CAD patients. Methods: Different methods can be use to analyze a platelet reactivity: light transmission aggregometry (LTA), measure of the phosphorylation of the vasodilator-stimulated phosphoprotein (VASP) by flow cytometry or enzyme linked immunosorbent assay (ELISA), platelet function analyser (PFA-100® or 200®), VerifyNow P2Y12, Multiple Platelet Function analyzer (Multiplate®, Plateletworks®, thromboelastography (TEG).

Conclusion: This work provides a background to the current controversies surrounding the issue of testing for the effectiveness of antiplatelet therapy and reviews the various phenotype-based laboratory tests to measure aspirin and thienopyridine response and their correlation with clinical outcomes. On the basis of the current evidence and trying to be cost-effective, testing should be considered on a case by-case basis, especially in patients who present with an acute coronary syndrome or stent thrombosis. In the case of stable CAD, we think that testing might be helpful in particular risk groups of patients to avoid ischemic complications.
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Preparation and Characterization of Chitosan Nanoparticles Containing Compsobuthus Scorpion Venom

Chitosan is widely used in pharmaceutical and medical purposes due to its properties such as biodegradability, biocompatibility, low toxicity, haemostatic, bacteriostatic, fungistatic, anticancerogen and anticholesteremic properties. Chitosan also acts as a penetration enhancer by opening the tight epithelial junctions; therefore, it is particularly exploited in protein and vaccine delivery. Chitosan nanoparticles have been widely investigated for the delivery of polypeptides such as insulin, tetanus toxoid, diphtheria toxoid.

Nanoparticles were prepared by ionic gelation of tripolyphosphat (TPP) and chitosan. The optimum encapsulation efficiency 99.9% and loading capacity 80.4% were obtained by chitosan concentration of 2 mg/ml, chitosan - to - TPP mass ratio of 2 and Compsobuthus venom concentration of 500 mg/ml. the nanoparticle size was about 109 nm. (polydispersity index: 0.34) while the zeta potential was positive. Fourier transform infrared (FTIR) spectroscopy confirmed triplyphosphoric groups of TPP linked with ammonium groups of chitosan in the nanoparticles. Transmission electron microscope (TEM) imaging showed a spherical, smooth and almost homogenous structure for nanoparticles.

The in vitro profiles release of nanoparticles exhibited a burst release of approximately 18.4% in the first 8 hours, and followed by a slow and much reduced additional release for about 120 hours.