EuroSciCon

DAY 1

Scientific Tracks & Abstracts

European Congress on

Pharma

August 13-14, 2018 Paris, France

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Sessions

Pharmacognosy and Phytochemistry | Pharmacological Sciences | Pharmaceutical Sciences | Drug Targeting and Design | Bio-Pharmaceutics | Novel Drug Delivery Systems | Industrial Pharmacy | Nanotechnology in Drug Delivery

Session Chair	Session Co-Chair
Liming Ye Sichuan University, China	**Isabel Desgagne-Penix** Universite du Quebec, Canada

Session Introduction

Title: Identification and characterization of in vitro and reactive metabolites of vandetanib in RLMs with method quantification using LC-MS/MS: Application to metabolic stability
Sawsan M.Amer, Cairo University, Egypt

Title: Targeting the insulin receptor substrate signaling for prevention of type 2 diabetes mellitus and heart failure
Shaodong Guo, Texas A&M University, USA

Title: Real-time potentiometric sensor; an innovative tool for monitoring hydrolysis of chemo/bio-degradable drugs in pharmaceutical sciences.
Ahmed Ma'mun, Cairo University, Egypt.

Title: Formulation and Characterization of antimicrobial chewing gum delivery of some herbal extracts for treatment of periodontal diseases
Reenu Yadav, Bhabha Pharmacy Research Institute, India

Title: Aspects development of formulation and technology of solutions for peritoneal dialysis in onechamber conteiners
Nataliia Hudz, University of Opole, Poland

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Sawsan M Amer et al., Am J Pharmacol Pharmacother 2018, Volume 5
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IDENTIFICATION AND CHARACTERIZATION OF IN VITRO AND REACTIVE METABOLITES OF VANDETANIB IN RLMS WITH METHOD QUANTIFICATION USING LC-MS/MS: APPLICATION TO METABOLIC STABILITY

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Vandetanib (VNT) is an oral inhibitor of vascular endothelial growth factor receptor. The current work reports the identification and characterization of *in vitro* and reactive metabolites of VNT. *In vitro* metabolites of VNT were generated by incubation with rat liver microsomes (RLMs). Extraction of vandetanib and its *in vitro* metabolites from the incubation mixtures were done by protein precipitation method. N-methyl piperidine ring of vandetanib, a cyclic tertiary amine, undergoes metabolism to form iminium intermediates that are reactive toward nucleophilic macromolecules. Incubation with RLMs in the presence of 1.0 mM KCN to check reactive metabolites as it is often responsible for observed idiosyncratic toxicities including phototoxicity and prolongation of QT interval. Six *in vitro* phase I metabolites, and four cyano conjugates of vandetanib were detected by LC-MS/MS. *In vitro* phase I metabolic pathways were N-demethylation, N-oxide formation, α-carbonyl formation and α-hydroxylation. All metabolic reactions occurred in N-methyl piperidine of vandetanib which causes its instability and toxicity. Validated LC–MS/MS was established for the determination of VNT in rat liver microsomes (RLMs) . This method was applied in metabolic stability investigation of VNT. Resolution of two analytes was performed using C18 column and isocratic mobile phase composed of binary system of 10 mM ammonium formate (pH 4.1) and acetonitrile in a ratio of 1:1. The flow rate was set at 0.25 mL/min and total run time was 4 min with injection volume of 5 µL. Ions were generated by ESI source and analyzed by multiple reaction monitoring mode (basis for quantification) in the Agilent 6410 QqQ analyzer. The linearity of the established method ranged from 5 to 500 ng/mL (r2 ≥ 0.9996) in RLMs. LOQ and LOD was 7.52 ng/mL, and 6.49 in RLMs matrices. The intra-day and inter-day precision and accuracy in RLMs matrix, ranged from 0.97 to 3.08% and 95.8 to 100.09% . *In vitro* half-life was 39.85 min and intrinsic clearance was 3.92±0.28 mL/min/kg.

Biography

Sawsan M Amer, starting higher school in 1972, obtained her Bachelors' in Pharmaceutical chemistry, 1977. She worked as Pharmaceutical Researcher in National Research Centre from 1977-1980 and obtained her MSc in 1980 from Cairo University, faculty of pharmacy, Egypt. She has joined as Assistant Lecturer 1980, became Lecturer in 1985 and Assistant Professor in Analytical Chemistry Department, Faculty of Pharmacy Cairo University in 1995. She has completed her PhD in 1985 from Cairo University. She is Full Professor from 2003-present and Head of Analytical Chemistry Department, Faculty of pharmacy, Cairo University from 2010- 2015. She has worked as a Lecturer in Faculty of Science in 1993 and as a Professor in College of Pharmacy, King Saud University, Saudi Arabia. She has published more than 65 papers in reputed journals and has been serving as an Editorial Board Member of Bulletin, Faculty of pharmacy, Cairo University and Reviewer in *journal of Talanta, Analytical Chemica Acta, Spectrochemica Acta, Saudi Pharmaceutical Journal* & many others. She is a Member of the Syndicate of Pharmacists, the Professional Society of Pharmacists, Egypt, the Society of Analytical Chemistry, Egypt , and in the Society of Saudi Chemists. She has supervised about 30 Master and PhD theses. Also she was involved in judging committee for more than 25 theses.

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TARGETING THE INSULIN RECEPTOR SUBSTRATE SIGNALING FOR PREVENTION OF TYPE 2 DIABETES MELLITUS AND HEART FAILURE

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The heart is an insulin-dependent and energy consuming organ in which insulin and nutritional signaling integrates to the regulation of cardiac metabolism, growth, and survival. Heart failure is highly associated with insulin resistance and heart failure patients suffer from the cardiac energy deficiency, structural and functional dysfunction. Recent studies demonstrated that insulin receptor substrate-1, -2 (IRS-1, -2) are major mediators of both insulin and insulin-like growth factor-1 (IGF-1) signaling responsible for myocardial energetics, structure, function, and organism survival. Importantly, the insulin receptor substrates (IRS) play an important role in activation of the phosphatidylinositide-3 dependent kinase (PI-3K) that controls Akt and Foxo1 signaling cascade, regulating the mitochondrial function, cardiac energy metabolism, and the renin-angiotensin system. Dysregulation of this branch in signaling cascades by insulin resistance in the heart through the endocrine system promotes heart failure, providing a novel mechanism for diabetic cardiomyopathy.

Biography

Dr. Shaodong Guo is Associate Professor with tenure the Department of Nutrition and Food Science at Texas A&M University College. Dr. Guo received his Ph.D in Physiology in the Department of Biology at Peking University, China in 1995. Then he completed his postdoctoral research training in Genetics, Biochemistry, and Medicine in the Institute of Genetics and Developmental Biology of Chinese Academy of Sciences, the University of Illinois at Chicago, and Harvard University, respectively. Dr. Guo was an Instructor in Medicine at Children's Hospital Boston and Harvard Medical School for two years prior to joining the faculty at Texas A&M Health Science Center. Dr. Guo serves as senior editor for the Journal of Endocrinology (IF 4.7) and Journal of Molecular Endocrinology (IF 3.6), and he is the textbook chapter writer for Metabolic Syndrome edited by Ahima published by Springer. Dr. Guo's research interests include the mechanisms of diabetes, diabetic cardiomyopathy, and the action of fuel hormones, focusing on insulin signal transduction, insulin resistance, gene transcriptional control of nutrient homeostasis, and cardiac dysfunction in diabetes. Dr. Guo has been working on the gene transcriptional regulation of metabolic homeostasis by insulin receptor substrate proteins (IRS) and Forkhead FoxO transcription factors with the hope of understanding how the signaling from insulin via IRS to FoxO proteins plays a key role in many fundamental cellular processes, including cellular growth and metabolism. His work has been published in a number of journals including the JBC, Endocrinology, Hypertension, Diabetes, Circulation Research, AJP, MCB, and Nature Medicine, receiving 4,800 citations with an h-factor of 30 based on Google Scholar Citation. Dr. Guo's research has been funded by American Diabetes Association (ADA), American Heart Association, and the National Institute of Health. He is a recipient of ADA junior faculty award, career development award, and Research Excellence Richard R. Lee Award.

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REAL-TIME POTENTIOMETRIC SENSOR; AN INNOVATIVE TOOL FOR MONITORING HYDROLYSIS OF CHEMO/BIO-DEGRADABLE DRUGS IN PHARMACEUTICAL SCIENCES

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In recent years, the whole field of ion-selective electrodes (ISEs) in pharmaceutical sciences has expanded far beyond its original roots. The diverse range of opportunities offered by ISEs was broadly used in a number of pharmaceutical applications, with topics presented ranging from bioanalysis of drugs and metabolites, to protein binding studies, green analytical chemistry, impurity profiling, and drug dissolution in biorelevant media. Inspired from these advances and with the aim of extending the functional capabilities of ISEs, the primary focus of the present paper is the utilization of ISE as a tool in personalized medicine. Given the opportunity to explore biological events in real-time (such as drug metabolism) could be central to personalized medicine. (ATR) is a chemo-degradable and bio-degradable pharmaceutically active drug. Laudanosine (LDS) is the major degradation product and metabolite of ATR and is potentially toxic and reported to possess epileptogenic activity which increases the risk of convulsive effects. In this work, ATR have been subjected to both chemical and biological hydrolysis, and the course of the reactions is monitored by means of a ISE. In this study, we have designed an efficient real-time tracking strategy which substantially resolve the challenges of the ATR chemical and biological degradation kinetics. By utilizing a potentiometric sensor, tracking of ATR chemical and biological degradation kinetics can be performed in a very short time with excellent accuracy. The LOD was calculated to be 0.23 molL^{-1}, the potential drift was investigated over a period of 60 min and the value was 0.25 mVh^{-1}. Real serum samples for measuring the rate of *in vitro* metabolism of ATR were performed. Furthermore, a full description of the fabricated screen-printed sensor was presented.

Biography

Ahmed Ma'mun has his career in Pharmaceutical Industry for almost 11 years in the field of analytical chemistry, methodology and validation. Since 5 years, he is a Quality Control Supervisor in Orchidia Pharmaceuticals for ophthalmic. He has been a Researcher in Analytical Chemistry of Faculty of Pharmacy, Cairo University since 2012. His [Master's Degree] is in hold for the final discussion. His recent publication Real-time potentiometric sensor; an innovative tool for monitoring hydrolysis of chemo/bio-degradable drugs in pharmaceutical sciences" is published in *Journal of biomedical and pharmaceutical analysis*. He is an Editorial Board Member in *Asian journal of Lifesciences*. He is an Invited Speaker and Plenary Speaker in many international conferences worldwide.

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FORMULATION AND CHARACTERIZATION OF ANTIMICROBIAL CHEWING GUM DELIVERY OF SOME HERBAL EXTRACTS FOR TREATMENT OF PERIODONTAL DISEASE

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Chewing gums are mobile novel drug delivery systems, with a potential for administering drugs either for local action or for systemic absorption via buccal route. An antimicrobial chewing gum delivery system of the methanolic extracts of *Beatea monosperma* (barks and twigs), *Cordia obliqua* (leaves and seeds) and *Cuminun cyminum* (seeds) against periodontal diseases caused by some oral pathogens, was designed and characterized on various parameters.

INTRODUCTION: Oral diseases are major health problems with dental caries and periodontal diseases among the most important preventable global infectious diseases. The association between oral diseases and the oral micro biota is well established. Several agents are commercially available these chemicals can alter oral micro biota and have undesirable side-effects such as vomiting, diarrhea and tooth staining. Development of bacterial resistance to presently available antimicrobial agents and their side effects has necessitated the search for new antimicrobial agent. Hence, the search for alternative products over synthetic continues and natural, plant extracts and Phyto- chemicals isolated from plants used as traditional medicines are considered as good alternatives. It was considered worldwide to explore Indian traditional medicinal plants for development of herbal anti microbial chewing gum (as a novel drug delivery system) The aim of the present work was to develop a chewing gum with antimicrobial activity which will cure/protect from various periodontal diseases such as periodontitis, gingivitis, and pyorrhea.

EXPERIMENTAL METHODS: Plant materials procured from local suppliers, and authenticated by taxonomist Dr. Manjusa Saxena. Extraction of plant materials was done by methanol followed by preliminary investigations (Physical characteristics and qualitative chemical tests) and standardization of extracts. Screening of antimicrobial activity was carried out with the help of disk diffusion method against some gram positive (Streptococcus mutans, S.mitis and S.sanguis), gram negative (*A. actinomycetemcomitans, P. gingivalis and B. forsythus)* and fungal strain (*Candida albicans*). Minimum inhibitory concentration assay was performed by agar dilution method recommended by the National Committee for Clinical Laboratory Standards. Dried Extracts of *Beautea monosperma, and Cordia obliqua,* sucrose, glycerol, dried extract of *Cuminum cyminum* as flavoring and coloring agent, magnesium corbonate, and citric acid were added to melted wax and gum base at appropriate temperature. Antimicrobial chewing gums were cut in to the pieces of suitable size and coated by acacia solution (2%w/w) sugar dusting followed by acacia-sugar-calcium carbonate until a smooth surface was produced. Organoleptic characterization was performed at every stage of the development of the formulation. Gum's weight variation, thickness, hardness, friability, drug content uniformity were determined. Standardization of the formulation was performed by taking nicco gum as standard marketed formulation. Release of drugs was studied in pH 6.8 using a mastication device.Total phenolic and flavonoid contents were estimated by folin-Ciocalteu and aluminium chloride method, and stability studies were performed (40oC and RH 75% ± 5% for 90 days) to assess the effect of temperature and humidity on the concentration of phenolic and flavonoid contents. The results of accelerated stability conditions were compared with that of samples kept at controlled conditions (RT). The control samples were kept at room temperature. (25oC, 35% RH for 180 days.)

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RESULTS AND DISCUSSION: Results are encouraging, as all other antibiotics were inactive against these strains. Methanolic extract from *Cordia obliqua, Beautea monosperma and Cuminum cyminum possess* significant antimicrobial activity at very low concentration (15µg/disc, 20µg/disc and 15µg/disc) on oral pathogenic bacteria. Qualitative chemical tests shown presence of flavonoids, phenolics in the extracts, might be responsible for the activity. Formulated chewing gum has optimal hardness, thickness and weight variation (in limit ±5%) as well as has pleasant appearance, fragrance, texture and taste is highly acceptable by the volunteers, as compared to marketed formulation. The drug loading efficiency of the drug in chewing was found to be in range of 98.2 ± 1.80% to 99.2 ± 0.35%. In all the cases, the R values of korsmayer papas model were close to 1. The diffusion coefficient values ranged from 0.6655 to 0.9164. Since the R values of korsmayer papas were close to 1, Drug release from formulation follows matrix diffusion kinetics. Hence, diffusion was the mechanism of the drug release from the medicated chewing gums. Further, observed diffusion coefficient values are indicative of the fact that the drug release from the formulation follows non-Fickian transport mechanism. Most Formulations released 50% of their contents within 25-30 minutes. Results obtained from the accelerated stability studies are indicative of a slight reduction in flavonoids and phenolic contents with time on long time storage. Initial on 0 days the concentration of flavonoid and phenolic contents was 72.98 mg/gm and 18.56 mg/gm on 54th day it was observed 69.56 mg/gm and 16.50 mg/gm and on 90th day it was observed 67.78 mg/gm and 16.00 mg/gm from the results it can be concluded that flavonoid and phenolic contents are reducing with time by the effect of the temperature and moisture. When measured degradation under ambient conditions, degradation was significantly lower than in accelerated stability study.

CONCLUSION: The results of the study support the traditional application of the plants and suggest, plant extracts possess compounds with antimicrobial properties that can be used as potential antimicrobial agents and gums can be a good carrier of herbal extracts. Developed formulation will cure/protect from various periodontal diseases. Further development and evaluations chewing gums including the isolated compounds on commercial scale and their clinical and toxicological studies are the future challenges.

Biography

Dr. Reenu Yadav has completed her PhD at the age of 32 years from NIMS University and postgraduate studies from VNS Institute of Pharmacy, RGPV University. She is professor in Bhabha Pharmacy Research Institute, Bhopal, a premier organization. He has authored 3 books, published more than 30 papers in reputed journals and has been serving as an editorial board member of repute. She has lectured worldwide; she is member of many national and international bodies and awarded with many grants from government.

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