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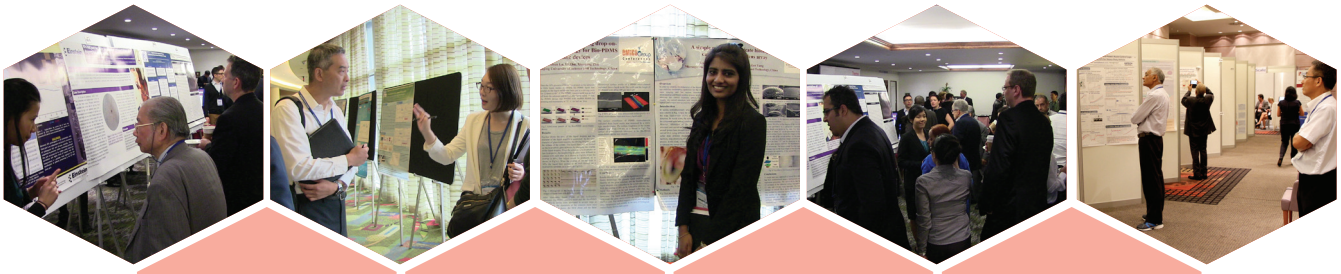
## Posters

## (Day 3)



Dong-Hwan Lee, Clin Pharmacol Biopharm 2016, 5:4(Suppl)
http://dx.doi.org/10.4172/2167-065X.C1.023



# Overcoming multidrug drug resistance in P-glycoprotein/MDR1 over-expressing cell lines by marine derived compound, CSS

**Dong-Hwan Lee**
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This study was performed to investigate the effect of CSS on the p-glycoprotein (p-gp)/MDR1 over-expression which is likely to bring about multi-drug resistance. The CSS is a marine derivative extracted from a oceanophyte under the East Sea of Korea. It was chosen from among 178 marine derivatives after preliminary cytotoxicity tests using human glioblastoma cell line to exclude compounds with severe reactivity and effectiveness screening tests with colon cancer cell line (LS174T). The viability of LST174T and breast cancer cells (MCF-7) treated with CSS was measured using CellTiter-Glo Luminescent Cell Viability Assay (G7571, promega) for 120 hours with or without paclitaxel 10 μM. The concentrations of CSS were 0, 0.001, 0.01, 0.03, 0.1, 0.3, 1, 3, 10, 30 μM. To investigate the mechanism, the expression level of p-gp/MDR1 and PXR were assessed by western blot and RT-PCR with rifampin which induces MDR1 over-expression The CSS 30 μM inhibited the cancer cell proliferation without killing the cells while cancer cells increased without CSS in the 96-well plates. The numbers of LS174T treated with paclitaxel 10 μM decreased by 40% without CSS versus with CSS 10 μM. In case of MCF-7, the rates were 0% without CSS versus 50% with CSS 10 μM. The CSS inhibited the overexpression MDR1 and PXR in the presence of rifampin. The CSS seems to be a potent chemo-sensitizer overcoming multi drug resistance.

## Biography

Dong-Hwan Lee has completed his PhD from Yonsei University College of Medicine. He is an Assistant Professor of Clinical Pharmacology in the Department of Clinical Pharmacology and the Manager of the Clinical Pharmacology division of the clinical trial center in Pusan National University Hospital. He has published 13 papers in reputed journals.

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Adesanwo K Julius et al., Clin Pharmacol Biopharm 2016, 5:4(Suppl)
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# Antimicrobial and antioxidant activities of extracts and isolated compound from *Cola nitida* (Vent) *Schott et Endl* seed

**Adesanwo K Julius, Ogundele S Bayonle and Akinpelu D A**
Obafemi Awolowo University, Nigeria

This study was designed to investigate the seed nut of *Cola nitida* for its phyto-constituents, antioxidant and antimicrobial properties. Dried ground seed nut (2 Kg) was extracted by soaking (trice) in methanol at room temperature for 24 hrs. Combined filtrate was concentrated with rotary evaporator at 45°C. The methanol extract was partitioned with n-hexane, ethylacetate (ETOAc) and n-butanol. Accelerated Gradient Chromatography (AGC) fractionation of ethylacetate extract and subsequent purification of fractions afforded the identification of phytochemicals. Structural elucidation of isolated compound I was done with $^{1}H$ and $^{13}C$ NMR spectroscopic techniques while compound II was identified with GCMS. The crude extract, fractions and isolated compound were evaluated for their antimicrobial and antioxidant activities by agar well diffusion and DPPH radical scavenging methods respectively. Compound I was identified to be caffeine (by its $^{1}H$ and $^{13}C$ NMR spectroscopic data and literature) and compound II as n-Hexadecanoic acid (by GCMS analysis). Compound 1 demonstrated antimicrobial activity against *B. cereus, E. coli* and *P. vulgaris* but low antioxidant activity. However, the methanol and EtOAc etracts showed good antimicrobial and antioxidant activities. The antioxidant activity of the extracts is attributed to the presence of phenolics. These findings established the antimicrobial and antioxidant activities of the extract from the seed nut of *Cola nitida* and also establish the presence of caffeine and n-hexadecanoic acid in the extract.

## Biography

Adesanwo K Julius completed his PhD from University of Ibadan, Ibadan, Nigeria and Post-doctoral studies from KwaZuluNatal University (KZNU) Duban West-Ville South Africa. He is a senior lecturer at Chemistry Department, Obafemi Awolowo University, Ile-Ife, Nigeria. He has to his credit, over 16 publications in reputed journals.

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**Notes:**

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## Dexmedetomidine population pharmacokinetics, adverse reactions and their relationship with blood levels in pediatric patients

**Maria-Gabriela Perez-Guille**
National Institute of Pediatrics, Mexico

**Introduction:** Dexmedetomidine (DXM) is α2-adrenergic drug used for sedation, analgesia and as a co-adjuvant in anesthesia, in surgical procedures, radiology, and instrumentation in pediatrics. Bradycardia and hypotension have been described as the main adverse reactions. This drug is advantageous to have little effect on the respiratory system. Studies concerning DXM pharmacokinetics in pediatric patients and their correlation with blood levels and adverse effects are still needed. In the present work, population pharmacokinetics was used to analyze a sample of pediatric patients treated with DXM.

**Objective:** To describe DXM population pharmacokinetics in pediatric patients, to establish any possible correlation between drug blood concentration and adverse effects.

**Materials & Methods:** The study included 32 pediatric patients (ASA I y II), 2.0 to 18 years-old, who underwent minor surgical procedures and received DXM as per the inductor of anesthesia or as sedative, at a doses of 0.7 μg/kg of body weight in 20 minutes infusion, four blood samples were taken from each patient at different time intervals designated randomly and their pharmacokinetic profile were constructed. Vitals were monitored throughout the entire procedure.

**Results:** No adverse effect was found. Concerning the level of sedation, all patients during surgery reached the Ramsay scale 6 and emerged to level 2. As per the pharmacokinetic parameter obtained in the study are consistent with those previously reported in the literature.

**Discussion:** In this study, no adverse effect was found so we can conclude that the use of DXM is efficient and safe in children and adolescents at a dose of 0.7 mg/kg of body weight.

### Biography

Maria-Gabriela Perez-Guille has studied Medicine from the Universidad Nacional Autonoma de Mexico. She has 30 years of experience in conducting research in the field of Clinical Pharmacology. She has been working at the National Institute of Pediatrics, Mexico as a Researcher in Medical Sciences, Level-D. She is a Member of the Mexican National System of Researchers; Level-I. She has published 41 papers in the field of pharmacology. She is the Director of Medicine students and residents and also a Pharmacology Professor for BSc and MSc students.

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Mei Zhan, Clin Pharmacol Biopharm 2016, 5:4(Suppl)
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# Cost-effectiveness analysis of additional Bevacizumab to chemotherapy for malignant pleural mesothelioma from a Chinese perspective

**Mei Zhan**
West China Hospital, China

**Objective:** To evaluate the cost-effectiveness of addition of bevacizumab to pemetrexed plus cisplatin (PC) for malignant pleural mesothelioma (MPM) following a phase III trial that show an overall survival (OS) benefit with the addition of bevacizumab.

**Methods:** A Markov decision tree based on the mesothelioma avastin cisplatin pemetrexed study (MAPS) was created, comparing bevacizumab+PC to PC alone. Three health states (progression-free survival, progressive disease and death) were analyzed in a Markov model. The costs were calculated from the Chinese societal perspective. Results were reported in quality-adjusted life year (QALY) and incremental cost-effectiveness ratios (ICERs).

**Results:** Bevacizumab+PC came at an ICER of $323343.46 per QALY, which are much more than the accepted willingness-to-pay (WTP) threshold of $23970.00 per QALY in China.

**Conclusions:** Addition of bevacizumab to PC is not a cost-effective first-line treatment for MPM when compared with PC in China.

## Biography

Mei Zhan has graduated from Sichuan University and currently working as a Clinical Pharmacist in West China Hospital of Sichuan University. She has published more than 17 papers in journals of repute.

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**Notes:**

Monika I Konaklieva et al., Clin Pharmacol Biopharm 2016, 5:4(Suppl)
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## Non-transpeptidase binding aryl-thioether β-lactams active against *Mycobacterium tuberculosis*

**Monika I Konaklieva[1], Rostislav Kuskovsky[1] and Kriti Arora[2]**
[1]American University, USA
[2]National Institute of Allergy and Infectious Diseases, USA

We have designed, synthesized and tested a novel class of non-transpeptidase, β-lactamase resistant monocyclic β-lactams that carry an aryl-thio group at C4. These thio-ethers exhibit inhibitory and cidal activity against serine β-lactamase producing *Mycobacterium tuberculosis* wild type strain (Mtb). Some of the compounds have demonstrated minimal inhibitory concentration (MIC) as low as 6.25 μg/ml in 7H9 and 1.5 μg/ml in GAST. Our investigations indicate that these compounds are cidal to both replicating and non-replicating persistent Mtb. These compounds have also shown activity against multi-drug resistant strains of *M. tuberculosis*. Therefore, they are promising candidates for lead discovery. Mechanism of action and target identification studies which are currently underway.

### Biography

Monika I Konaklieva has completed her PhD in Chemistry from SUNY Buffalo in the year 1997. She was a Visiting Professor in Medicinal Chemistry at Midwestern University, Chicago, Illinois. She is currently an Associate Professor at American University. She has published more than 40 papers in reputed journals and has been serving as an Editorial Board Member of several Chemistry journals publishing in the areas of Organic and Medicinal Chemistry.

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**Notes:**

Wan-O Chu et al., Clin Pharmacol Biopharm 2016, 5:4(Suppl)
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## Efficiency of computerized warning system reduces polypharmacy in the elderly

**Wan-O Chu, Chia-Li Lee, Lih-Chi Chen, Li-Ying Huang and Sun-Wen Jung**
Taipei City Hospital, Taiwan

**Objective:** Polypharmacy in the elderly complicates therapy, increases cost and is a challenge for healthcare agencies. Computerized warning system to reduce polypharmacy is a drug optimization process.

**Methods:** We used a prospective before-and-after design among patients aged 80 years or older admitted to Taipei City Hospital from November 1, 2012, through January 31, 2013 before the addition of the warning system and from April 1, 2014 through June 30, 2014 after the warning system was added. We enrolled 189 elderly adults (aged ≥80 years) who had been prescribed 10 or more chronic medications (drugs prescribed for ≥28 days), visited three or more different physician visits during 3 month screening period before warning system setting. Data were analyzed using Pair t test and significance (α) was set at $P<0.05$ by the JMP5.12.

**Results:** We enrolled 189 patients in our study, excluded 30 patients without physician visits after warning system setting, where the ratio of males: females were 89:70. The mean (SD) age of our patients was 85.8 (10.2) years. After the warning system was deployed, there was an immediate and sustained decrease in the rate of orders for the medications. The mean rate of prescribing medications dropped from 14.1 to 11.4 orders per day (SD 2.7; $P<0.001$) and physician visits number decreased from 3.5 to 3.1 per month (SD 0.5; $P<0.001$). There was no evidence that this effect waned over time.

**Conclusions:** Computerized warning system embedded into the healthcare information system (HIS), used in patients, can decrease the medication number quickly and specifically. The financial cost of polypharmacy involves both the direct expenditures for prescription medications as well as significant indirect costs related to hospitalization and treatment of severe adverse drug reactions. Computerized warning system may have a positive impact on prescribers and patients. The mainstay for preventing and managing polypharmacy remains heightened awareness of patients at risk. Pharmacovigilance is required by the patient, physician and pharmacist in thoroughly reviewing and reconciling the patient's medication regimen at every opportunity.

### Biography

Wan-O Chu has graduated from the Department of Pharmacy Taipei Medical University (TMU) and Institute of Biomedical Engineering National Yang Ming University. He is an Adjunct Instructor at TMU and a Pharmacist in Taipei City Hospital, Department of Pharmacy. He has published more than 10 papers in a local journal and 2 posters in International Pharmaceutical Federation (FIP).

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**Notes:**

Wshar Ali Ismael et al., Clin Pharmacol Biopharm 2016, 5:4(Suppl)
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# Determination of some nitroaromatic compounds and some related pharmaceutical compounds using flow injection-chemiluminescence method

**Wshar Ali Ismael and Faizullah A Tofiq**
Salahaddin University, Iraq

A rapid flow injection-chemiluminescence (FI-CL) method was used for determination of 4-nitrophenol and some nitroaromatic compounds. These compounds, which have electron-donating group on the ortho and para positions, undergo on-line reduction using a minicolumn of zinc redactor in acidic medium to their corresponding aminophenols. The produced aminophenols were reacted with permanganate ion and polyphosphpric acid in the presence of dimethyl sulfoxide as enhancer for the produced CL. The method extended to include some related nitroaromatic compounds of pharmacological interest with similar structural formations representative such as metronidazole, furazolidone, nitrofurantoin and nitrazepam. Under the optimum conditions, calibration graphs were obtained in the concentration ranges (0.020-1.50 and 2.00-8.00) μg/ml for 4-nitrophenol, 0.50-14.0 μg/ml for metrnidazol, 0.50-100.0 μg/ml for furazolidone, 0.50-60.0 μg/ml for nitrazepam and 3.0-35.0 & 50.0-120.0 μg/ml for nirofurantoin. The method was successfully applied for the determination of these compounds in dosage.The aim of this work was to develop a simple and rapid method for the determination of 4-nitrophenol and related nitro-drug compounds, not requiring sophisticated instruments but giving results comparable with those obtained by the standard methods in British pharmacopeia.

## Biography

Wshar Ali Ismael has his expertise in analytical chemistry and determination of pharmaceutical formulations. He has used flow injection analysis technique in his researches and has concluded chemiluminescence reactions in his research for detection and analysis of pharmaceutical compounds. He worked as a Lecturer in Chemistry Department, Education College, Salahaddin University, Erbil, Iraq since 1992 until now. He taught instrumental analysis in the Chemistry Department.

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**Notes:**

Cristina Helena Dos Reis Serra et al., Clin Pharmacol Biopharm 2016, 5:4(Suppl)
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# Solubility characterization of didanosine using shake flask and intrinsic dissolution methods: Application for biopharmaceutical classification

**Cristina Helena Dos Reis Serra, Andre Bersani Dezani, Julie Caroline Ferrari Ferreira and Thaisa Marinho Dezani**
University of Sao Paulo, Brazil

The solubilization of a drug orally administered is a mandatory step for its permeation. Two methods have been described in the literature for solubility characterization: shake flask and intrinsic dissolution. Although some values of solubility can be found in the literature, this characterization is not clear for didanosine (ddI). Thus, the solubility of ddI was evaluated using the shake flask and intrinsic dissolution methods. Buffer solutions were prepared at pH 1.2, pH 4.5, pH 6.8, pH 7.5 and purified water. In the shake flask method, ddI was added in each media (150 rpm at 37°C for 72h). For intrinsic dissolution method, the compound was compacted into the wood's apparatus matrix and subjected to dissolution in each media (50 rpm at 37°C up to 150 min). The results obtained in shake flask method showed that 139.37 mL (pH 1.2), 87.72 mL (pH 4.5), 12.54 mL (pH 6.8), 4.09 mL (pH 7.5) and 7.65 mL (purified water) were necessary for drug solubilization. In addition, a very fast intrinsic dissolution rate was obtained for each media: 0.1 mg/min/cm² (pH 1.2), 0.2 mg/min/cm² (pH 4.5), 0.2 mg/min/cm² (pH 6.8), 0.1 mg/min/cm² (pH 7.5) and 0.1 mg/min/cm² (purified water). Results from both methods are in accordance, but some differences in dose strength can explain divergences in the solubility. For intrinsic dissolution, the dose strength is not considered and does not interfere on the dissolution profile. Based on these results, ddI is highly soluble, considering dose:solubility ratio <250 mL and dose number (D0) ≤1 for shake flask method and intrinsic dissolution rate greater than 0.1 mg/min/cm$^2$. Furthermore, the intrinsic dissolution method can be used for early drug development regarding solubility characterization.

## Biography

Cristina Helena Dos Reis Serra is an expert in Pharmacy with emphasis on bio-pharmaceutics considering the following topics: "Gastrointestinal drug absorption, drug solubility and permeability, bioequivalence and oral bioavailability, *in vitro-in vivo* correlation (IVIVC) and pharmaceutical development". Currently, she is a Professor at Faculty of Pharmaceutical Sciences, University of Sao Paulo, Brazil.

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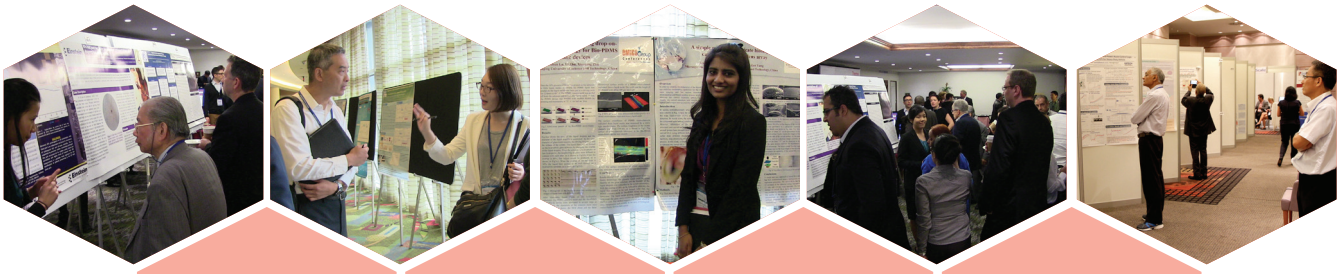

Oztekin Algul, Clin Pharmacol Biopharm 2016, 5:4(Suppl)
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## Investigations on structure-activity relationships and anti-proliferative activities of some bis-benzimidazole derivatives

**Oztekin Algul**
Mersin University, Turkey

As cancer chemotherapy has not yet reached the desired level, intensive studies are continue to develop more potent, more selective and less toxic novel anticancer drugs. In anticancer drug development studies, the effect of novel compounds on apoptotic and anti-apoptotic gene expressions is very important. In our preliminary studies, a series of 2-substituted benzimidazole derivatives were synthesized and tested for their cytotoxic effect against leukemic cell lines. These compounds were particularly found to be quite selective against the hepatocellular carcinoma cell line. Then, the effect of bis-benzimidazol derivative compounds on apoptosis and their mechanism of action were investigated in hepatocellular carcinoma in rats. In this study, anti-proliferative activities of twelve bis-benzimidazole derivatives was evaluated. The synthesized bis-benzimidazole derivatives was to determine the potency and specificity against five different cancer cells [Human Lung Adenocarcinoma Epithelial Cells (A549), Human Renal Cancer Cells (A498), Human Cervical Cancer cells (HeLa), Human Skin Malignant Melanoma Cells (A375), Human Hepatocellular Carcinoma Cells (HepG2) lines] compared to methotrexate (MTX). In conclusion, bis-benzimidazole derivatives exhibited higher anti-proliferative than 2-substituted benzimidazoles.

### Biography

Oztekin Algul has completed his PhD from Gazi University/Turkey in 2000 and Post-doctoral studies from Saarland Universitey/Germany and Connecticut University/USA School of Pharmacy. He has been the Head of Deparment of Pharmaceutical Chemistry in Mersin University/Turkey since 2002.

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# Impact of fungal infection on outcome of critically ill patients: An observational study in critically ill liver patients

**Shubhnita Singh**
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**Background:** Fungal infections represent a significant and serious load in the critical care setting with rising morbidity and mortality. Candidiasis is the main reason of fungal infections in Intensive Care Unit (ICU) patients out of which majority are being caused by *C. albicans* proceeded by Aspergillosis and Mucormycosis. The identification of these infections is complicated and complex and require constant clinical surveillance and exhaustive laboratory testing, radiological testing, culture and biopsy.

**Aim:** The aim of this study was to investigate the impact that Invasive Fungal Infection (IFI) has on the outcomes of critically ill ICU patients.

**Method:** Records of all admissions to Intensive care units were reviewed. IFI was identified using established criteria based on microbiology, histology and radiological testing.

**Result:** Over a period of 6 months a total of 106 patients were identified as having IFL. Out of which 41 cases had miniBAL positive, HRCT evidence was seen in 39 cases, both were positive in 14 cases. *Candida* or budding yeast cells were seen in 35 cases and *Aspergillus* in 6 cases. Both culture and radiological evidence was positive in 9 cases.

**Conclusion:** IFI is frequent in patients admitted in ICU and is associated with excess risk for hospital mortality, longer ICU and hospital stay and greater consumption of medical resources. The newer antifungal agents are potent and have low resistance. But appropriate and judicial use is required.

## Biography

Shubhnita Singh has completed her MBBS from SSR Medical College, University of Mauritius. She has worked with prestigious hospitals like Sir Ganga Ram Hospital, Delhi, India. She has been working on several research projects in Hamdard Institute of Medical Science and Research since February 2014 as Tutor in Department of Pharmacology.

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## Accepted Abstracts

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## Effect of some psychoactive agents on memory in rats with regard to aluminum-induced dementia

**Abdel-Moez Assi, Raafat Abdel-Badeaa Abdel-Aal and Botros Beniamin Kostandy**
Assiut University, Egypt

Alzheimer's disease (AD) is a chronic, progressive, neurodegenerative disorder of the brain. AD is the most common type of dementia. The major histopathological features of AD are neuritic (or 'senile') plaques, neurofibrillary tangles, and a loss of neurons and synapses. The degeneration of cholinergic neuronal systems, in particular those projecting from the basal forebrain to the hippocampus and cerebral cortex, is a consistent feature in the neuropathology of AD. These systems play an intrinsic role in learning and memory processes and the degree of cholinergic degeneration has been shown to correlate with the loss of cognitive function. Memory deficit is not a unitary phenomenon in AD. Up to 90% of patients with dementia develop significant behavioral problems during the course of their illness. Behavioral and psychiatric symptoms as delusions, hallucinations or agitation develop in as many as 60% of community-dwelling dementia patients. The term "behavioral and psychological symptoms of dementia" (BPSD) has been proposed to describe the spectrum of non-cognitive manifestations of dementia. Antipsychotics are frequently added to anti-Alzheimer's therapy to control BPSD, Haloperidol and risperidone are typical and atypical antipsychotics, respectively. Here we are interested in studying the behavioral effects of these antipsychotic agents in rats with AD disease, and their influence during treatment of these rats with memantine, a NMDA receptor blocker used in management of AD.

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## Design, formulation and *in vitro* characterization of Irbesartan solid self-nanoemulsifying drug delivery system (S-SNEDDS) prepared using spray drying technique

**A R Gardouh**
Suez Canal University, Egypt

In this study, a novel liquid SNEDDS containing Irbesartan was formulated and further developed into a solid form by spray drying technique using Aerosil 200 as solid carrier. Results showed that the mean droplet size of all reconstituted SNEDDS was found to be in the nanometric range with optimum PDI values. All formulae also showed rapid emulsification time, good optical clarity and high drug content; and were found to be highly stable. Transmission electron microscopic images showed the formation of spherical and homogeneous droplets with a size smaller than 50 nm, which satisfies the criteria of nanometric size range required for nanoemulsifying formulae. *In vitro* release of IRB from SNEDDS formulae showed more than 99% of IRB release in approximately 90 minutes. Optimized SNEDDS formulae with the smallest particle size, rapid emulsification time, best optical clarity and maximum drug content and rapid *in vitro* release were selected to be developed into solid self-nanoemulsifying drug delivery system (S-SNEDDS) using spray drying technique. The prepared S-SNEDDS formulae were evaluated for flow properties, differential scanning calorimetry (DSC), scanning electron microscopy (SEM), reconstitution properties, drug content and *in vitro* dissolution study. Reconstitution properties of S-SNEDDS showed spontaneous self-nanoemulsification and no sign of phase separation. DSC thermograms revealed that IRB was in solubilized form and FTIR supported these findings. SEM photographs showed smooth uniform surface of S-SNEDDS with less aggregation. Results of the *in vitro* drug release showed that there was great enhancement in dissolution rate of IRB.

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## Effects of hypobranchial glands and squid ink protein extracts from three Mediterranean molluscs on human glioblastoma U87 and HeLa cell line epithelia cervix carcinoma

**Chabchoub Ellouze Soufia, Ben Mabrouk Hazem, Sayari Nejia and Marrakchi Naziha**
Higher Institute of Medical Technologies of Tunis, Tunisia

**Background & Aim:** The aim of this study is to evaluate the effects of tree Mediterranean molluscs co-product protein extracts on human glioblastoma U87 and HeLa cell line epithelia cervix carcinoma. Hypobranchial gland proteins (HGPE) are extracted from the gastropods *Hexaplex trunculus* (HT) and *Bolinus brandaris* (BB). The squid ink proteins are extracted from the cephalopod *Sepia officinalis*.

**Methods:** Proteins are extracted by acetone precipitation. Cell viability is measured using MTT assay. Cell adhesion and migration are established using fibrinogen as matrix.

**Results:** Both HGPE HT and BB are non-cytotoxic substances until 20 mg/ML. They decrease by more than 50% at 25 mg/mL. All HGPE significantly impair migration of U87 cells towards fibrinogen in a concentration dependent manner. Concentrations for 50% inhibition ($IC_{50}$) of male and female HGPE HT are of 3.7 and 4 mg/mL, respectively. They are of 4.2 and 5.8 mg/ml for male and female HGPE BB, respectively. Squid ink proteins block the migration of U87 to fibrinogen in a dose dependent manner. The $IC_{50}$ is about 9.2 µg/mL. This supernatant also inhibits cell adhesion U87 on various types of matrices. Inhibitions are 60% fibrinogen and 25% fibronectin. Similarly, HGPE of both HT and BB inhibits HeLa cell adhesion to fibrinogen at 50 mg/mL. Male and female inhibitions significantly impair at 10 mg/mL and continue until 20 mg/mL. Squid ink proteins inhibit also HeLa cell adhesion. Inhibition significantly impairs at 10 mg/ML and continues until 30mg/mL.

**Conclusion:** HGPE HT, HGPE BB and squid ink proteins may have the potential to serve as a model for future anticancer-drugs development.

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## Design and synthesis of variety of molecules with specific bioactivity

**Mingliang Liu**
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Our research group has been engaged in the design and synthesis of variety of molecules with specific bioactivity for 30 years. Numbers of series of novel compounds were designed, synthesized and evaluated for their antibacterial, anti-TB or antitumor activity. In the antibacterial drug development area, we are focused on new quinolones targeting on topoisomerase II, and two candidate IMB-031124 (Chinfloxacin) and IMB-070593 have been completed for Phase I clinical trials and preclinical trials in China, respectively. In the anti-TB area, many compounds with totally new structural scaffolds were discovered in our lab to have nanomolar activity again drug-sensitive and -resistant MTB strains. And in the antitumor area, we are mainly working on the NO/H2S-releasing non-steroidal anti-inflammatory drugs (NSAIDs) and receptor tyrosine kinase (RTK) inhibitors. Currently, hundreds of compounds synthesized in our lab are evaluated for their antitumor activity.

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## Molecular mechanism investigation of a novel Ruthenium (II) complex inhibits proliferation of human esophageal squamous cell carcinoma

**Jianguo Lin, Liubin Guo, Gaochao Lv and Ling Qiu**
Jiangsu Institute of Nuclear Medicine, China

High toxicity acquired resistance and serious side effects, prompting the search for novel compounds for cancer treatment. Recently, a Ruthenium (II) complex [Ru (p-cymene)(L)Cl2] (L = 1,3-bis(4-(tert-butyl)benzyl)-1H-imidazol-3-ium chloride) , which named L-4, has been synthesized and characterized. The purpose of this study was to investigate the effects of L-4 against human esophageal squamous carcinoma (ESCC) cell line EC109. Different methods to determine the apoptotic pathways triggered by L-4 in EC109 cells were investigated by using flow cytometry, Hoechst 33258 staining, Caspases activation, mitochondria functioning, generation of reactive oxygen species (ROS) and western-blotting techniques. Results showed that a dose- and time-dependent reduction occurred in cell viability after exposure to L-4 in EC109 cells. The flow cytometry analysis showed that L-4 induced cell cycle arrest at G2/M phase in EC109 cells, concomitant to p53 and p21 up-regulation and Cyclin D1 down-regulation. L-4 also induced ROS-dependent and mitochondria-mediated apoptosis in EC109 cells by targeting the glutathione reductase, leading to generation of ROS, Ca2+ overloading, increase of Bax/Bcl-2 ratio, loss of MMP, release of cytochrome c into the cytosol, and then activation of Caspase-3/-9. Whereas, ROS scavengers, N-acetyl-L-cysteine, significantly attenuated the effects of L-4 on reduction of cell viabilities, activity of GR, generation of ROS, loss of MMP, the dysfunction of mitochondria and induction of apoptosis. The preliminary results suggest that the Ruthenium (II) complex, L-4, inhibits EC109 cells proliferation via blocking cell cycle progression and inducing ROS-dependent and mitochondria-mediated apoptosis, and deserves further investigation as a new chemotherapeutic strategy for patients with esophageal cancer.

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## Formulation of hand sanitizer gel using the semi-purified flavonoids from the outer coverings of the red creole variety of *Allium cepa* Linn of family Alliaceae

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This research focuses on the formulation of hand sanitizer gel using the semi-purified flavonoids from the outer coverings of the Red creole variety of *Allium cepa* L. fam. Alliaceae. This study utilizes the experimental method of research. The agar cup diffusion method was used in determining the antibacterial activity of formulation with 40% semi-purified extract as compared to the two (2) locally available leading hand sanitizer brands. *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Micrococcus luteus, Enterobacter aerogenes, Proteus vulgaris, Salmonella typimurium, Klebsiella pneumoniae, Bacillus subtilis* and *Bacillus cereus* were utilized as test organisms. The formulation exhibited antibacterial activity against 8 of 10 bacteria used in the experiment, while Brand A exhibited antibacterial activity against 1 of 10 bacteria and brand B manifested an antibacterial activity against 4 out 10 of bacteria utilized in the microbial assay. Moreover, based on the result of the primary skin irritation test, the formulation is perceptibly not capable of causing irritation to the skin when applied topically. The researchers recommends that thorough investigation of the semi-purified flavonoid extract using instrumental method of analysis and isolation of the pure flavonoid should be conducted in order to determine the specific flavonoid that exhibits the antibacterial activity.

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## Novel approach for the formulation of excipient-less fixed dose combination (FDC) tablets by Hot Melt Extrusion (HME) technology using quality by design approach

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The objectives of the present study were to investigate the properties of HME based tablets containing plain ibuprofen-paracetamol FDC, without a single excipient and to compare it with marketed formulation by applying QbD approach. Paracetamol and ibuprofen were taken at drug/drug mass ratios (5:2). The prepared physical mixtures were extruded using a corotating twin-screw hot melt extrusion. Among the three tested independent variables in DOE, temperature and feeding rate most significantly affected the tensile strength and drug release from the tablet. The melt extruded granules were passed through a 250µm sieve. The maximum optimized ratio (85:5.5:100) determined by DOE was chosen for further analysis. DSC, XRD, SEM were carried out to determine physicochemical changes after melt granulation. The granules were characterized for particle size analysis, flow properties, granule strength. Tablets containing 500 mg paracetamol and 200 mg ibuprofen were compressed at 10.0kN compaction force. The tablets were characterized for tablet hardness, friability, disintegration time and dissolution study. All results were found to be within acceptable USP limits. The optimized extruded batch was stable at 400C, 75%RH for a period of 6 months without changing any dissolution rate and remained into amorphous state.

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## An analysis of medication utilization among the Filipino elderly

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The elderly encounter health care challenges, thus increasing their likelihood of using potentially inappropriate medications (PIM) and experiencing medication-related problems. This study aims to determine the prevalence of the use of PIM, level of medication knowledge and adherence among the nursing home residents and community-dwelling Filipino elderly. An observational cross-sectional study was performed to identify the present medications of the elderly, and the levels of medication knowledge and adherence were determined with the self-reported medication knowledge tool by Burge et al. and the Morisky medication adherence scale. A total of 163 nursing home residents (46.01%) and community-dwelling (53.99%) elderly were interviewed through a purposive technique. Polypharmacy was observed in 25.15% (n=163) respondents, majority of which are community-dwelling (63.41%, n=88). Thirty-six percent of the elderly (n=163) were moderately knowledgeable about their medications. The community-dwelling elderly (n=88) had a significantly greater mean medication knowledge than that of the nursing home residents ($p<0.001$). Seventy-two (44.17%, n=163) elderly had medium adherence, and no significant difference ($p=0.277$) on adherence between the 2 groups were found. Moreover, medication knowledge and adherence are associated with one another ($p<0.001$). The prevalence of PIM use (n=597) based on the 2012 Beers criteria and the PIM-Taiwan criteria are 10.05% and 8.71%, respectively. According to the 2012 Beers criteria, 18 PIM were taken by 32.51% (n=163) of the elderly and the most common were aspirin, diclofenac and mefenamic acid. Based on the PIM-Taiwan criteria, 15 PIM were identified and taken by 25.77% (n=163) of the respondents. The medication utilization of Filipino elderly is average and the use of PIM is present among them.

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## Design, synthesis and biological evaluation of novel 2-phenyl-1-benzopyran-4-one derivatives as potential poly-functional anti-Alzheimer's agents

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Development of Multi-Target Directed Ligands (MTDLs) has emerged as a promising approach for targeting complex etiology of Alzheimer's disease (AD). Following this approach, a new series of 2-phenyl-1-benzopyran-4-one derivatives were designed, synthesized and biologically evaluated as inhibitors of acetylcholinesterases (AChEs), advanced glycation end products formation (AGEs) and also for their radical scavenging activity. The *in vitro* studies showed that the majority of synthesized derivatives inhibited acetylcholinesterase (AChE) with $IC_{50}$ values in the low-micromolar range. Among them, inhibitors 7h, 7k and 7a, strongly inhibited AChE, with $IC_{50}$ value of 6.33, 7.56 and 11.0 nM, respectively, and were more potent than the reference compound donepezil. Moreover, the molecular docking study displayed that most potent compounds simultaneously bind to catalytic active site and peripheral anionic site of AChE. Besides, these compounds also exhibited greater ability to inhibit advanced glycation end products formation with additional radical scavenging property. Thus, 2-phenyl-1-benzopyran-4-one derivatives might be the promising lead compound as potential poly-functional anti-Alzheimer's agents.

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## Assessment of adhesion response to 3D printed materials for ophthalmic device development

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**Introduction & Aim:** Glaucoma is the leading cause of irreversible visual impairment worldwide. Glaucoma surgical devices fail due to a scarring response that resulted in fibrous encapsulation surrounding the device preventing aqueous humor drainage. 3D printing technology has the potential to develop personalized ophthalmic devices or organs with improved cost effectiveness and productivity. Limited experimental data exists as to the biocompatibility response of 3D printed photopolymers. We performed cell adhesion and protein adsorption studies of 3D printed photopolymers compared to materials used in current ophthalmic devices (silicone, polytetrafluoroethylene (PTFE) and poly (methyl methacrylate) (PMMA)) to assess 3D printed materials as a potential route for ophthalmic device development.

**Methods:** 3D printed materials (n=6) were developed using a high-resolution, desktop stereo-lithography (SLA) 3D printer and compared to materials used in current ophthalmic devices. Protein adsorption was quantified using a micro bicinchoninic acid (micro BCA) assay and fluorescein-conjugated bovine serum albumin (FITC-BSA) adsorption. Cell adhesion (monocytes, fibroblasts) was assessed using alamarBlue, CyQUANT and Live/Dead assays. Data were compared using a two-tailed unpaired t-test.

**Results:** 3D printed materials demonstrated low cell adhesion and protein adsorption. Results were similar to those found with materials used in current ophthalmic devices ($P>0.05$). However, it was noted that 3D printed materials demonstrated increased cytotoxicity ($P<0.05$).

**Conclusion:** 3D printed photopolymer materials demonstrated a similar biocompatibility response to currently used materials and may allow for the development of customizable ophthalmic devices or organs. Subsequent testing will determine the adhesion response to 3D printed materials containing anti-scarring agents.

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## Formulation and evaluation of orodispersible film of levocetrizine dihydrochloride

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The aim of present investigation was to develop orodispersible film of levocetrizine for increasing bioavailability and patient acceptance. It was prepared by solvent casting method by different polymer and plasticizer. The taste masking was carried out by Drug Resin complex using Kyron T 134 with 1: 3 ratio with drug. A 32 factorial design was applied for optimization. Prepared film were evaluated for their drug content uniformity, Thickness, Folding endurance, Tensile strength, Percentage elongation, Disintegration time, *In vitro* drug release and Stability study. The drug resin complex with Kyron T 134 show good taste masking with ratio 3:1. The formulation F5 shows higher drug content 96.54±1.59%, less disintegration time 32±1 sec, Tensile strength and folding endurance respectively 0.237±0.067 N/nm$^2$ and 120±3. Film of batch F5 was release 94.3% within 20 min during the *in vitro* dissolution test. These studies indicate that development of orodispersible film with view to patient compliance and to obtain faster onset of action. According to 32 full factorial designs, F5 proved as an optimized batch. Batch F5 remain stable after 1 month accelerated stability study. Drug excipients are compatible to each other was confirmed by FTIR study.

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## Pre-exposure prophylaxis (PrEP) accessibility research and evaluation 2 (PrEPARE 2): HIV risk perception among men who have sex with men (MSM)

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**Background:** Despite greater access to PrEP, a barrier to HIV prevention is inaccurate risk perception by MSM. PrEPARE2 is a randomized controlled trial to determine if providing at-risk HIV-uninfected MSM with a calculated risk score affects PrEP uptake.

**Objective:** Our objective is to compare self-perceived risk (SPR) to an objective HIV risk score (UCSD score).

**Methods:** HIV-uninfected, at-risk MSM were recruited from San Diego testing sites. At-risk for HIV can be defined as having one or more episodes of insertive or receptive condomless anal intercourse (CAI) with a HIV-infected partner or partner of unknown status within 6 months. Enrolled subjects received an iPad survey to assess baseline characteristics including demographics and risk behaviors. SPR score was the subject's perceived likelihood of becoming HIV-infected. The survey also generates the UCSD score, which calculates an individual's risk of becoming infected over one year and places individuals into risk categories, calculated from event frequencies of UAI, history of sexually transmitted infections and shared needle events. SPR and UCSD score categories include low, medium, high and very high. Cohen's kappa coefficient evaluated the agreement between the two measures.

**Results:** Of 78 participants enrolled, median age was 32, 31% identified as Latino, 67% as white, 13% as black. Most subjects had heard of PrEP (78%), and 53% thought they were good candidates for it. Overall, the group had a median of 5 sexual partners in the last 6 months (IQR: 3-10) and 72% had at least one receptive CAI within the past 6 months. The SPR had poor agreement with the objective score (kappa=0.009). Most subjects (55%) underestimated their HIV risk, 36% had concordant predictions, and 9% overestimated their risk. 15 of 16 subjects with a high UCSD score underestimated their risk. Underestimation of risk was not associated with any demographic or risk factors, including number of sex partners and drug use.

**Conclusions:** In this sample of HIV-negative MSM, there was high discordance between self-perceived and actual HIV risk and a tendency to underestimate risk, particularly in high-risk individuals. Greater emphasis on objective HIV risk may be an important component of successful PrEP uptake.

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## Platinum-zoledronate complex blocks gastric cancer cell proliferation by inducing cell cycle arrest and apoptosis

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New platinum complexes with different carrier ligands are developing to overcome the intrinsic or acquired resistance of the tumors during the therapy. A series of novel dinuclear platinum complexes based on the bisphosphonate ligands have been synthesized and characterized. For the purpose of discovering the pharmacology and action mechanism of this kind of compounds, the most potent compound $[Pt(en)]_2ZL$ was selected for systematic investigation of the underlying mechanisms accounting for their anticancer activity. In this study, the human gastric cancer cell lines SGC7901 were selected to investigate the anticancer effects of $[Pt(en)]_2ZL$ on this type of cancer cells. The MTT assay and colony formation assay were used to test the effect of $[Pt(en)]_2ZL$ on the cell viability and proliferation, respectively. The senescence-associated β-galactosidase staining and immunofluorescence staining were also performed to assess the cell senescence and microtubule polymerization. Fluorescence staining and flow cytometry (FCM) were used to monitor the cell cycle distribution and apoptosis, and the expressions of related proteins were further detected with Western blot. $[Pt(en)]_2ZL$ exerted profound cytotoxic and antiproliferative effects on SGC7901 cells, and it also induced cell senescence and abnormal microtubule assembly, indicating the progress of mitotic catastrophe. Cell cycle arrest and apoptosis induced by $[Pt(en)]_2ZL$ were observed with FCM and fluorescence staining. The expressions of cell cycle regulators (p53, p21, cyclin D1, cyclin E and CDK2) and apoptosis-related proteins (Bcl-2, Bax, caspase 3, PARP and survivin) were mediated by $[Pt(en)]_2ZL$, resulting in the cell cycle arrest and apoptosis. Therefore, $[Pt(en)]_2ZL$ exerted antitumor effect via the cell cycle arrest in the G1/S phase and the induction of apoptosis.

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## Community pharmacy and the extended community pharmacist practice roles: The UAE experiences

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The pharmaceutical care and 'extended' roles are still not practiced optimally by community pharmacists. Several studies have discussed the practice of community pharmacy in the UAE and have shown that most community pharmacists only counsel patients. However, UAE, have taken initiatives to allow and prepare community pharmacists to practice 'extended' roles. The aim was to review the current roles of community pharmacists in Abu Dhabi Emirate, United Arab Emirates (UAE). The objective was to encourage community pharmacists towards extending their practice roles. In 2010, Health Authority Abu Dhabi (HAAD) surveyed community pharmacists, using an online questionnaire, on their preferences towards extending their counseling roles and their opinion of the greatest challenge facing the extension of their counseling roles. Following this survey, several programs have been developed to prepare community pharmacists to undertake these extended counseling roles. In addition to that, HAAD redefined the scope of pharmacist roles to include some extended/enhanced roles. Abu Dhabi Health Services (SEHA) mission is to ensure reliable excellence in healthcare. It has put clear plans to achieve this; these include increasing focus on public health matters, developing and monitoring evidence-based clinical policies, training health professionals to comply with international standards to deliver world-class quality care, amongst others. Prior to making further plans to extend community pharmacists' roles, and to ensure the success of these plans, it is imperative to establish the views of community pharmacists in Abu Dhabi on practicing extended roles and to gain understanding and information on what pharmacists see as preferred change strategies or facilitators to change. In an attempt to adapt to the changes occurring and to the growing needs of patients and to maximize the utilization of community pharmacists' unique structured strategies are needed to be introduced to the community pharmacy profession.

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