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TOWARDS A New Pharmacy Era

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ABSTRACT BOOKLET

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Hormonal treatments for prostate adenocarcinoma

Prof. Ahmed Abbady

Future directions in the treatment of overactive bladder syndrome

Prof. Martin C. Michel

The overactive bladder syndrome (OAB) is a prevalent condition that impairs the quality of life of the afflicted patients and their partners. Current first-line medical treatments are muscarinic receptor antagonists and β_3-adrenoceptor agonists. However, none of these is curative and most patients discontinue treatment within the first year, largely driven by unmet efficacy expectations. Specifically, the symptoms of urgency and nocturia are poorly served by existing treatments. The quest for better treatments is limited by the fact that OAB is not a disease entity but a symptom complex, and multiple diseases may lead to these symptoms. These various diseases are unlikely to share a single causative factor, indicating that it is unrealistic to expect markedly improved treatment efficacy from any individual medicine for the overall OAB population. Thus, even a drug that is 100% effective in a subgroup of OAB patients will only have limited efficacy in the overall population. The inability to identify such subgroups has become a major hurdle for commercial drug development in OAB. Therefore, major progress in the OAB field can only be expected when academic research has identified subgroups of patients that share a specific pathophysiology that can be addressed by specific medicines.

Medication Therapy Management (MTM) of Prostate Cancer: A Clinical Pharmacy Perspective

Dr. Noha El Bassiouny

Prostate cancer (PCa) is one of most common cancers affecting male population worldwide, with a long clinical course. Over the past two decades, the pharmacists' value in the health care team, alongside with physicians, nurses, and oncology social workers, continues to increase. Clinical pharmacists can play a vital role in the management of PCa through effectively participating in checking drug interactions, dose verification, assessment of drug stability and administration route. In addition, clinical pharmacists can successfully assist in the prevention and handling of the potential complications and possible side effects of hormone therapy and chemotherapy that might impact patients' quality of life. Development of a trusting patient–pharmacist communication can help patients validate their concerns, and involves, in addition to information exchange, the sharing of thoughts, desires, and fears, that would assist in addressing drug therapy problems, and lead to better health outcomes.

Innovative Medicines in Egypt: Our Own Experience with Cyclocreatine as a Novel FDA-Designated Cardioprotective Drug

Prof. Salwa A. Elgebaly

Heart disease is the leading cause of death worldwide and it is predicted to persist due to the progressive aging of population. Ischemia of the heart such as in the case of a heart attack is a result of diminished blood flow to heart tissue. Pharmacologic therapies to reduce reperfusion injury after clot removal, have not been so successful leading to an increase in the incidence of heart failure (approximately 50% of heart attack patients). Based on our recent pre-clinical efficacy studies, the U.S. Food and Drug Administration (FDA) has awarded the Orphan Drug Designation (ODD) to Nour Heart, Inc. and Prof. Salwa A. Elgebaly for Cyclocreatine Phosphate with the unique designation for: "*Prevention of Ischemic Injury to Enhance Cardiac Graft Recovery and Survival in Heart Transplantation*". Currently, Prof. Elgebaly is preparing the FDA-required Investigational New Drug (IND) application to initiate Phase I Clinical Trials in the U.S.

Innovative Medicines in Egypt

Strength: 1. Highly Skilled Egyptian Scientists
2. Strong FDA-Regulated Phase II and Phase III Clinical Trials

Opportunities: 1. Develop Newly Discovered Molecules to Pharmaceutical Products.
2. Manufacture Active Pharmaceutical Ingredients (APIs).
3. Manufacture *Innovative* Medicines for Local Market and Export Worldwide.

Main Challenges: 1. Preclinical *Animal Facilities* Certified by AAALAC International.
2. *Know-How* of:
a) API *Manufacturing* Meeting Global Standards (U.S. and European).
b) API *Scaling Up* from Grams to Kilograms to Tons.
c) *Facilities* Built to Meet Global Standards.
d) Egyptian *Employees* Applying Global Standards.

Strategies for Success: 1. Implement AAALAC International in Egypt.
2. Establish a Globally Compliant Pharmaceutical City to include:
API Facilities and Finished Product Facilities.
3. Establish 3 Academic API Training Centers.

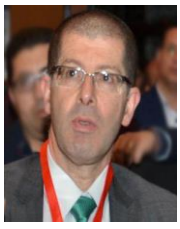
Highlights of hypertensive and vasculotoxic effects of cyclosporine

Prof. Mahmoud M. El-Mas

Hypertension has been recognized as a troublesome adverse effect for cyclosporine (CSA) soon after its introduction for immunosuppression in the late 1970s. Turmoils in peripheral vasodilator as well as vasoconstrictor machineries have been proposed to explain the hypertensive action of CSA. Moreover, despite its limited capacity to diffuse to brain tissues, accumulated evidence suggests an intermediary role for the central nervous system in CSA hypertension through as yet unidentified mechanisms. In this communication, we report on the roles of central sympathoinhibitory pathways of α_2-adrenergic and I_1-imidazoline receptors and their downstream effectors, e.g. nitric oxide synthase (NOS) and heme oxygenase (HO), in the elicitation of CSA hypertension. Integrative and molecular studies were also sought to determine whether vascular endothelin and thromboxane signaling is imperative for the revelation of CSA hypertension. Finally, we studied the hemodynamic interaction of CSA with NSAIDs with differential COX1/COX2 selectivity and the roles of renovascular fibrotic and endothelin receptors in the observed responses. Collectively, the data showed that CSA elicits its hypertensive action via the interruption of central I_1-receptor/eNOS/HO/cGMP signaling and facilitation of vascular fibrotic and constrictor effects of endothelin. Additionally, celecoxib, but not indomethacin, improved the hypertensive, renovascular fibrotic, and endothelin dysregulating effects of CSA. The therapeutic potential of targeting these pathways in the amelioration of the hypertensive and perhaps other detrimental cardiovascular effects of CSA is warranted.

Update in treatment of hypertension

Prof. Amr Zaki



Evolution of medical treatment in diabetic macular edema

Assoc. Prof. Ahmed Souka

Modulating Adipose Inflammation as an Early Target in Diabetic Vascular Dysfunction.

Assoc. Prof. Ahmed F. El-Yazbi

Diabetes remains a major health and economic burden with significant cardiovascular morbidity and mortality. Despite rapid advances in care for diabetic patients, the current standards of practice aimed at optimizing blood glucose levels fall short of reversing or halting the progression of diabetic vascular complications. Moreover, a considerable proportion of patients present with significant cardiovascular involvement at initial diagnosis implicating an alternative mechanism, set in action prior to hyperglycemia, as the root cause of this pathophysiology. Our research focuses on the investigation of the different factors contributing to the early cardiometabolic interaction. For this purpose, we study the vascular and metabolic structural and functional changes in the early prediabetic stage. In the past few years, our laboratory has championed a case for isolated peri-vascular adipose tissue inflammation as the primary culprit contributing to the early onset of cardiovascular deterioration in metabolic dysfunction. Here, we summarize results from our recent work providing novel molecular insight into the mechanisms underlying the incidence of low-grade localized inflammation in the peri-vascular and epicardiac fat tissue initiating vascular impairment at a stage where gross/systemic signs of inflammation are not detectable. Moreover, we highlight potential targets for future therapeutic interventions newly identified in our studies, in addition to the design and screening of innovative tools for this purpose. Further, the audience will be provided with an overview of ongoing clinical efforts to validate novel biomarkers for this early stage of cardiometabolic dysfunction.

Clinical pharmacy in oncology practice..One team

Dr. Hazem El Mansy

As a Pharmacy profession: where are we going to be

Prof. Mostafa Fahmy

The presentation will tackle challenges are related to pharmacy profession (education and practice) and to raise hot points on the stage to be discussed as:
1- As a profession where are we going to be?
2- what are the monsters we are facing in our profession and how we are going to tame them
3- addressing the gaps between education and practice
4- international trends shaping the future of Pharmacy profession
5- with AI what is next?

learning objectives

At the end of the presentation will be able to:

1- Distinguish the underlying trends creating the need of pharmacy to develop a future plan
2- describe the key components for a future strategic plan for the pharmacy profession
3- Specify key elements which need to be in place to drive the vision for the pharmacy profession
4- Plan to tackle the monsters we are facing in our profession
5- Forecast trends in the governance of the profession

Transforming a BPharm into a PharmD: a paradigm shift

Prof. Pierre Moreau

Development of Competency-based Pharmacy Education

Assoc. Prof. Andries S. Koster

Implementation of a competency-based pharmacy curriculum (CBPE) is a time-consuming, complicated process and requires careful planning and monitoring, usually taking several years. This presentation will describe the steps necessary for the design, implementation, and quality improvement of such a curriculum. Practical suggestions will be given, that can help in introducing a competency-based curriculum.

A first requirement is agreement on the tasks of a pharmacist, commitment, institutional stability, and a goal-directed developmental perspective of all stakeholders involved. After the choice for entering into CBPE is made and a competency framework is adopted (step 1), intended learning outcomes are defined (step 2), followed by analyzing the expected developmental trajectory (step 3) and the selection of appropriate assessment methods (step 4). Designing the teaching-learning environment involves the selection of learning activities, student experiences, and instructional methods (step 5). Finally, an iterative process of evaluation and adjustment of individual courses, and the curriculum as a whole, is needed (step 6). Successful implementation of CBPE requires a system of effective quality management and continuous professional development (as a teacher) of the faculty and preceptors involved.

Clinical pharmacy, paradigm that expands the medical profession

Prof. Nermine Sabry

Pharmacovigilance and Medication Safety in the Middle East

Assoc. Prof. Thamir Alshammari

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. Both pharmacovigilance and medication safety are topics with continues changes with respect to all stakeholders, pharmaceutical companies, hospital and health institutions, and drug regulatory agencies especially with the changes in the international regulations. Many challenges are facing people working in the area of medication safety starting from the regulators to HCPs and pharma representatives. These challenges and changes included many areas starting from reporting to risk communications. The focus of pharmacovigilance was on adverse drug reactions (ADRs) reporting, however, these have changes to focus more on active surveillance by accessing clinical data (previous and post approval) and study the safety signals from early stages of animal studies. The new data, tools and techniques are undoubtedly paving the way to a brighter and more insightful future.

In the Middle East and North Africa (MENA), the practice of both driplines varies among the countries as some countries have advance systems and practice while other countries have only the minimum requirements of the safety culture.

The talk will cover the following points:

What is the concept of pharmacovigilance and medication safety)

What are the changes in pharmacovigilance?

The current pharmacovigilance situation in MENA area.

How these changes affecting the current situation in MENA region

HCPs, pharma safety people and regulators and how they should deal with these changes.

How these stakeholders are going to work together to facilitate the transmission period into the new changes.

New excellences in Pharmacovigilance

Dr. Amr Saad, BSc. Pharm, MSc, PhD.

Pharmacovigilance

With the increasing and ever- more stringent regulations in pharmacovigilance, the regulatory authorities face greater demands for patient welfare and safety, which become prominent especially after the Thalidomide disaster. These in turn necessitate standard levels of monitoring and data analysis that ensure safe drug delivery. This can be only attained by well-structured pharmacovigilance centres backed-up with a robust legal framework and clear guidelines.

Moves by the Arab League

In order to cope with these changes and to unify guidelines and performance across the Arab world, Arab ministers of health came to a common decree (number 7) in their 37th regular meeting in March 2012. Under the umbrella of the Arab League 'The Higher Technical Committee for Medicines' was established with representatives from all Arab countries, to create common Arab guidelines in pharmacovigilance, and in bioequivalence. This committee elected Dr. Amr Saad, head of the Egyptian centre, to lead the committee across all its rounds. The committee has finished the final drafts of the two common guidelines which were submitted to the 38th regular ministers meeting, and which has been approved by them.

Guidelines adopted

The new Common Arab guidelines is mainly adapted from the newly-established international Good Pharmacovigilance Practice (GVP), composed of 16 different modules together with some product/population specific considerations, as well as annexes and templates of submission. The Guidelines were published in March 2014 and the effective date will be 1st July 2015. It is expected that these guidelines will significantly influence pharmacovigilance practice in general in the whole Arab world, and will increase such activities including reporting rates and signal detection in that part of the world. It will also help some Arab countries to develop in the area of 'Regulatory Pharmacovigilance'.

Nanoparticle-based strategies in Oncology

Prof. Jean-Pierre Benoit

Nanomedicine, an emerging new field created by the fusion of nanotechnology and medicine, is one of the most promising pathways for the development of effective targeted therapies with Oncology being the earlier and the most notable beneficiary to date. Indeed, drug-loaded nanosystems provide an ideal solution to overcome the low selectivity of the anticancer drugs towards the cancer cells in regards to normal cells and the induced severe side effects. Nanoparticle and liposome-based systems encapsulating drugs are already used in some cancer therapies. Most of them accumulate in tumors according to the enhanced permeability and retention effect (EPR) that affects both the blood and lymphatic vessels.

Unfortunately, many aggressive tumors are poorly vascularized what represents a severe limitation for these nanomedicines. Other avenues must be explored to optimize their action.

In this context, we have developed new bio-inspired nanocarriers, the lipid nanocapsules, that mimic the lipoproteins, with a size range of 20-100 nm.

Their biodistribution reveals interesting features. For instance, they interact with a specific subset of immune cells, the myeloid-derived suppressive cells (MDSCs), that play a significant role in promoting tumor growth. The targeting of these cells could be relevant to change the immune status of a tumor, favoring the action of the cytotoxic immune cells.

Another strategy that allows to bypass the EPR effect in poorly vascularized cancers is the local administration of nanocarriers, directly in the tumor. *In situ* radiotherapy of glioma has been performed with radioactive lipid nanocapsules with promising results in terms of survival.

Intersection of drug repurposing and nanotechnology: Emerging opportunities for new therapies

Prof. Labiba Khalil El-Khordagui

The development of a new drug is a long and complex process, with extremely high investment and a low success rate. Among powerful drug discovery tools that emerged over the past decades to support the research and development process, drug repurposing is currently gaining increasing momentum as a strategy intended to reduce overall development costs and timelines. Drug repurposing can be defined as the process of discovering new therapeutic indications for existing drugs to treat common, neglected and rare diseases. Although, many drugs including sildenafil, thalidomide and ketoconazole have been repurposed serendipitously for different indications, drug repurposing has evolved into an innovative, data-driven, cutting-edge strategy with bioinformatics and cheminformatics methodologies. Growing evidence indicates that the clinical efficacy of repurposed drugs can be greatly enhanced by drug delivery strategies, particularly those based on nanocarrier vectors such as liposomes, nanoparticles and nanocapsules. Accordingly, intersection of drug repurposing and nanotechnology may be anticipated to boost the outcomes of repurposed drugs, by enhancing efficacy and safety via modulating drug release profiles, biodistribution and site-specific retention. In addition, drug delivery systems may provide a platform for multifunctional combination therapies aiming at increasing activity and reducing the dosages of the individual components. The aim of this presentation is to provide a brief overview of different aspects of drug repurposing with emphasis on nanotechnology-based repurposed drug delivery systems. Our research efforts in combining nanotechnology and drug repurposing for the development of new potential nanomedicines for the treatment of a neglected tropical disease and cancer are highlighted.

New insights into the pharmacokinetics of nanoparticles

Prof. Frederic Lagarce

Nanoparticles and rod-like particles for inhalation drug delivery

Prof. Marc Schneider

For the treatment pulmonary diseases such as cystic fibrosis inhalation is an interesting route for local application of drug substances. However, applying e.g. antibiotics needs to address solubility issues as well as protection and reduction of drug efficiency in mucus and biofilms. Those hydrogel-like structures impede the diffusion of drug carriers but also pure drugs depending on their physicochemical properties. To facilitate coughing and to fluidize the viscous mucus patients often inhale mucolytics such as N-acetylcysteine (NAC) via nebulization. To allow nanoparticles to penetrate and diffuse easily to deliver the drug a matrix of two drug used to obtain nanostructured microparticles. Forming a salt bridge between NAC and the antibiotics during spray drying of the sample resulted in an active powder with up to three drugs for local treatment. Arranging these nanostructured particles as rods allowed to influence the uptake kinetics into macrophages. Furthermore, using rod-like nanostructured particles allows to deliver macromolecules such as genetic material. Thus, the genetic modification of macrophage, a hard-to-transfect cell type is possible.

Advances in clinical ophthalmology: triumphs and tribulations for effective and safe drug delivery systems to the eye

Assoc. Prof. Hamdy Abdel Kader

Lipoprotein-mimicking nanocarriers in cancer therapy

Assoc. Prof. Yosra Elnaggar

Development of pharmacy education: non-western prospective

Assoc. Prof. Amira Khalil

Challenges in Psychiatric Pharmacy Practice. The Role of Community and Clinical Pharmacists in Psychoeducation

Dr. Nancy Ali Mahfouz

Applying Psychiatric Pharmacy and reviving the role of Clinical pharmacists in mental health should be on the rise for the following years in pharmacy practice and education.
Removing the social stigma against mental disorders, educating patients about their illness, encouraging them to seek professional psychiatric advice, offering better understanding about psychotropic medications and their side effects are the most crucial roles of pharmacists in this domain.
Our aim as psychiatric pharmacists is to share more practical-based learning experiences with our fellow colleagues in order to provide better services to patients and better collaboration and trust with psychiatrists.

Role of clinical pharmacist in Dual Antiplatlet Therapy (DAPT) choice in Acute Coronary Syndrome (ACS)

Dr. Rasha Wafaie Mahmoud Elsorady

Inpatients with ACS take a number of high-risk drugs such as anti-thrombotic drugs, in addition to other drug types, including diuretics and cardioprotective agents. Pharmacists should support the pharmacological management of these patients by evaluating their clinical condition and laboratory data, due to the frequency of renal failure. Furthermore, it is known that poor adherence to a drug regimen is one of the aggravating factors for ACS .It is necessary to conduct regular patient education to facilitate early hospital discharge and to prevent the recurrence of ACS .In Alexandria University Hospital, a single pharmacist is in charge of both the cardiac care unit (CCU) and the cardiovascular ward. In the course of a patient's hospital stay, from admission to discharge, the pharmacist performs various duties such as evaluating and proposing a medication plan after checking the patient's regular medications, conducting patient education, promoting appropriate prescriptions, overseeing the preparation of injection drugs, and providing drug information to medical staff. There are many cases in which avoidance of drug interactions or overdose, in order to prevent bleeding, is needed. Thus, pharmacists play important roles in the management of patients with ACS by ensuring the efficacy and safety of each patient's drug therapy.

Towards AMR Containment in Africa

Prof. Sabiha Essack

Since their introduction into clinical practice in the 1930s and 1940s, antimicrobial medicines have revolutionized global public health by substantially decreasing the morbidity and mortality associated with infections in humans and animals. Antimicrobial resistance (AMR) is however dramatically eroding our antimicrobial arsenal. If unmitigated, AMR will result in 28 million people falling into poverty, a 7.5% decline in global livestock production and an estimated increase of one trillion US dollars in healthcare costs by 2050[2]. Ten million deaths are expected to be attributable to AMR by 2050 with a disproportionate 4.1 million in low and middle-income countries (LMICs) in Africa[3]. The United Nations General Assembly endorsed the Political Declaration on AMR requiring all member states to develop National Action Plans (NAPs) on AMR. However just 13% of countries in the WHO AFRO region have NAPs on AMR, the vast majority developed with financial and technical assistance from WHO AFRO, the Centre for Disease Dynamics Education and Policy (CDDEP) and ReACT Africa. Where NAPs exist, implementation has been facilitated by the Fleming Fund and there is minimal country commitment. AMR containment requires coordinated multi-pronged, multi-stakeholder, multi-disciplinary partnerships and social compacts at national, regional and global levels, underpinned by unequivocal political leadership, commitment and governance.

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Coagulase-negative staphylococci (CoNS): Hidden champions at the crossroad between humans, animals and the environment

Prof. Wilma Ziebuhr

Staphylococci are both ubiquitous skin colonizers of warm-blooded hosts as well as common human and animal pathogens. While the significance of the coagulase-positive species *Staphylococcus aureus* as infectious agent is undoubted, the role of the large group of coagulase-negative staphylococci (CoNS) is more ambivalent. Apart from their function as commensals, CoNS increasingly occur as opportunistic pathogens endangering mainly hospitalized and immunocompromised patients. Further, CoNS are recognized as significant reservoirs for the evolution and spread of (novel) antibiotic resistance traits, which is reflected by notoriously high (multi)resistance rates detected among both disease-associated and commensal CoNS from humans, animals and even from the environment. The astonishing niche adaptation power of CoNS is best exemplified by *Staphylococcus epidermidis*, the most common CoNS species. Thus, depending on the habitat, *S. epidermidis* strains and lineages may vary concerning antibiotic resistance, mobile genetic element carriage as well as the capacity to form biofilm communities. In addition, *S. epidermidis* is capable of intra-strain variation by generating a high degree of both genetic and phenotypic heterogeneity within a single-cell-derived population. Recent research suggests RNA-mediated riboregulation by small non-coding RNAs to play a significant role in the process by influencing carbon and energy metabolism, apoptosis-like autolysis and biofilm matrix expression. From a population perspective, riboregulator-mediated heterogeneity serves niche adaptation by generating novel variants fit to meet changing external conditions (including antibiotic stress), thereby supporting persistence and survival of the bacterial community as a whole. Tackling riboregulation might therefore represent an interesting future anti-infective strategy to interfere with CoNS infections.

The great escape from “ESKAPE” pathogens: An overview of our five-year vaccine research

Assoc. Prof. Mohammed Bahey-El-Din

Bacteria have utilized sophisticated defenses against antibiotics which changed the clinical situation from susceptibility to multi-drug resistance (MDR), extensive-drug resistance (XDR) and eventually the disastrous Pan-drug resistance (PDR). This situation is one of the most difficult crises that face mankind with the serious threat of untreatable deadly infections. The six major pathogens that are overwhelmingly becoming resistant to antibiotics were given the acronym “ESKAPE”. These include *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter* species. In our research group, we focused on investigating potential vaccine candidates against several members of the ESKAPE pathogens. Recombinant outer membrane proteins, namely OmpK17 and OmpK36, of *K. pneumoniae* showed promising protection in murine infection model. The iron acquisition protein, HitA, and the N-terminal outer membrane porin (OprF) of *P. aeruginosa* elicited strong immunogenicity and enhancement of opsonophagocytosis of the pertinent pathogen. Moreover, several antigens of *A. baumannii* were tested in-vivo but unfortunately without promising outcome. Finally, recombinant Basic Membrane Protein (BMP) ABC transporter protein of *E. faecium* was found to protect against relevant challenge in murine infection model. Interestingly, some of the tested antigens had high similarity with antigens of different pathogens. This implies that these antigens can provide simultaneous protection against different pathogens. Adjuvant selection was an important factor in the vaccine protection outcome. Overall, the road to effective vaccines against the ESKAPE pathogens seems winding and full of unexpected obstacles. Intensive research and bioinformatic analysis should ultimately and hopefully culminate in developing effective vaccines against these monster pathogens.

Imidazo[2´,1´:2,3]thiazolo[4,5-d]pyridazin analogues as new scaffold of DHFR inhibitors

Prof. Hussein I. El-Subbagh

Mining natural libraries for new glycan interactions using native mass spectrometry

Prof. John Klassen

Interactions between complex carbohydrates (glycans) and glycan-binding proteins mediate many physiological and pathophysiological processes. Identifying these interactions is fundamentally important and improves human health by guiding development of new diagnostics and therapeutics. However, uncovering functional interactions is hindered by the diversity of glycan structures (with few available in purified form), their varied presentations (as glycolipids or glycoproteins), and their low affinities. A promising approach to overcome the limited availability of purified glycans is shotgun glycomics, whereby glycans are released from glycoproteins or glycolipids in cells or tissue or extracted from biological fluids and screened against proteins. This strategy has been implemented primarily using arrays: glycans are labeled, fractionated, printed on slides and screened. Glycan arrays, however, have many limitations. They typically contain mixtures of glycans, necessitating follow-up studies to establish ligand identity, exhibit artefacts associated with glycan modification and immobilization, as well as protein labeling, and are prone to false negatives.

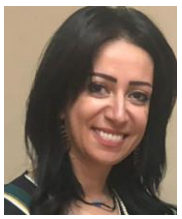
An attractive alternative to arrays is catch-and-release electrospray ionization mass spectrometry (CaR-ESI-MS). This rapid, sensitive, label- and immobilization-free assay allows for the simultaneous screening of hundreds of glycans. The assay is also suited to screening natural libraries. In this presentation, an overview of CaR-ESI-MS screening, with an emphasis on glycan libraries, will be given. This will be followed by recent applications to natural glycan libraries. Specific examples will include the screening of human milk oligosaccharides against human, bacterial and viral proteins and *N*-glycans from serum glycoproteins, immune cells and tissue against anti-ganglioside antibodies and human Siglecs.

Molecular modeling: a tool to tackle selectivity among closely related isozymes

Dr. Amgad Elbohy

Biochemistry era to drive modern drug discovery; implication of the adventurers

Prof. Nadia Hamdy



Biochemistry (Biological chemistry) provide information on the dynamics and energetics of compound–target interactions for the identification and/or development of new drugs; **Pharmaceutical Biochemistry, together with patho-biochemistry and pharmacological biochemistry**.

No matter what the disease(s) are CVD/DM/hepatic disease or oncology, etc. They always are associated with biochemical changes at the cellular and/or molecular levels. Moreover, adverse drug reactions or effects (ADR/ADE) or resistance notably; **pharmacovigilance** and biotransformation of drugs in the human body (PD), involve complicated biochemical processes.

In addition to small molecule-based drugs, new approaches such as bioengineering, regenerative and stem cell research, biologics, gene therapy and gene targeting for disease management has emerged.

New **"OMICS" methodologies**, such as proteomics, transcriptomics, epigenomics, metabolomics, biomarkers, micro-markers, glycomics and pharmacogenomics have been developed and applied in oncology and diabetes treatment research and drug development. Consequently, the **post-genomic era** becomes a golden era for biochemical research, drug target identification and pharmaceutical development; drug discovery.

Finally, the combination of digital processing, internet technology, artificial intelligence (AI), computer algorithms and Internet of Things (IoT) for results of population based clinical trials, paved the way for accelerated drug discovery and the **personalized and/or precision oncology or CVD.**

Quantification of DNA damage induced by different pharmaceutical, nutraceutical products

Assoc. Prof. Amira F. El-Yazbi

Human DNA plays a vital role in numerous biological processes. Exposure of DNA to different chemical insults leads to damage at the molecular level, which consequently leads to carcinogenesis, and cell death. Small molecules, such as drugs, can interact with DNA via covalent or non-covalent interactions. If drug-binding causes DNA damage in normal cells, then it may affect the replication cycle leading to mutations that would ultimately lead to cell over growth, i.e., cancer. Currently available methods for the sensitive detection of damaged DNA consist of multi-step procedures, are time- consuming, require expensive instruments and reagents and destroy the sample. As well, the exposure of DNA to most insults causes sequence-dependent damage, thus most of these methods are limited for the detection of DNA damage in specific DNA sequences and cannot be used for generic damage screening. As such, these methods are neither cost-effective nor suitable for routine everyday analysis applications. The main goal of this study is to develop a simple, inexpensive, high through-put, mix-and–read methods for the sensitive detection of DNA damage induced by different pharmaceutical and nutraceutical products. In addition to quantification of the minimum concentration of each drug that causes DNA damage in order to assesse the potential safety of different pharmaceutical products. In this study, we explored the interaction of several FDA-approved pharmaceutical drugs with DNA. For this purpose, we have used several analytical techniques, including absorption spectroscopy, MALDI-TOF mass spectrometry and fluorimetric analysis. This talk will discuss the application and the results of the proposed techniques.

System biology and genomics of microbial pathogens

Prof. Ramy Aziz

Genomic epidemiology of transmission and antimicrobial resistance of *Campylobacter* from farm to fork

Assoc. Prof. Mohamed Elhadidy

The foodborne bacterial pathogen *Campylobacter* is among the most common causes of human gastroenteritis with consumption and mishandling of retail chicken is considered one of the most important infection sources. The alarming increasing rates in antibiotic resistance of *Campylobacter* isolates raised the concern about studying the molecular mechanisms of resistance. The aims of this study were to: 1- Determine the extent that the dynamics in genomic content of endemic *Campylobacter* contributes to clinical disease severity, transmission routes, and source attribution. 2-Determine the dynamic of antibiotic resistance and investigate the clonal structure and genetic determinants of resistance. The comparative genome analysis identified core and pan genome of *Campylobacter* species and how this is related to population structure, evolution of host/niche adaptation, and maintenance of *Campylobacter* species. The sequence information is uploaded into a central worldwide database, thus providing a community resource enabling researchers to enrich knowledge about the global diversity, transmission, population structure, ecology, and evolution of this important human pathogen. Data from environmental isolates provided novel insights on the importance of different potential sources of transmission of *Campylobacter* species, thus identifying potential intervention strategies and targets. Such findings are critically needed to reduce human disease burden from zoonotic pathogens in Egypt and other developing nations.

Pharmacogenomic biomarkers for personalised liver diseases treatment: current and future prospectives

Assoc. Prof. Ahmed Waheid

Hepatitis C virus (HCV) is a universal health problem. HCV infection may proceed to liver fibrosis, cirrhosis, and eventually hepatocellular carcinoma. SNPs have been proposed as the next generation biomarkers for the identification of gene loci associated with various liver complications following infection with HCV.

The present study examined the role of (-964 A/G) SNP of IL-27p28 rs153109 and (-308 G/A) SNP of TNF-α rs1800629 on the progression of HCV infection in genotype 4a infected patients. We also screened the promoter region of the PKR gene in HCV Egyptian patients. 309 subjects were enrolled in the current study. HCV infected patients were divided into several groups: HCV spontaneous resolvers (SRs), chronic HCV patients, fibrotic, cirrhotic and HCC patients. Genotyping was performed using PCR-RFLP and DNA sequencing.

We found a significant difference between the HCC and fibrosis groups ($p = 0.00$), and also between the cirrhosis and fibrosis groups ($p = 0.031$) in the studied TNF-α SNP. With respect to PKR, two functional SNPs were detected. In rs12992188C>T polymorphism, The TT genotype is significantly different between SVR and NR (OR/95%CI, $P = 0.014$). Furthermore, we discovered two novel SNPs in the PKR promoter region. Our data showed the unique presence of the TT genotype in SRs group in PKR -226 C/T. This means that subjects with the TT genotype were more likely to clear their HCV infection than those with the CC genotype. Therefore, we conclude that PKR rs12992188, -226 C/T, and TNF-α rs1800629 polymorphisms are potential genetic-biomarker for HCV progression.

PROFESSIONAL POSTERS

PHS 101: Tailoring novel lecithin organogels for enhancing targeting potential of Terconazole into the skin: Microbiological and permeation studies

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Skin mycosis has grown up in the last decades affecting almost 20%–25% of the world's population. Recently, cutaneous candidiasis caused by Candida species was considered the most prevalent superficial mycosis. Terconazole (Tr), one of the most active triazoles for vaginal candidiasis, has not so far employed for the treatment of cutaneous candidiasis owing to its poor skin permeation and challenging physicochemical properties. Therefore, our work group was the first to seek for investigating Tr potential in treatment of skin mycosis via integration into different types of Lecithin-based organogels such as Lecithin microemulsion and liquid crystalline organogels.

Ternary phase diagram was constructed to identify the region of formation of both types of nanogels. Microstructure of such nanogels was confirmed by polarized light microscopy and transmission electron microscopy. The study was endeavored to investigate the potential of such novel nanogels in comparison with conventional gels. The optimized organogels possessed promising physicochemical characteristics based on particle size, rheological behavior, pH, loading efficiency, and in vitro antifungal activity. Ex-vivo and in-vivo deposition studies demonstrated significant enhancement of terconazole deposition into the rat skin from both microemulsion and liquid crystalline organogels comparing to conventional gels. In addition, skin sensitivity and histological examinations confirmed their non-irritant potential. Overall, lecithin organogels could be tailored to enhance targeting of drugs into the skin.

Keywords: Organogels; Terconazole; Liquid crystals; Microemulsion; Skin targeting; Skin mycosis.

PHS 102: Polymeric versus lipid nano-vesicles for enhanced bioavailability of the anticancer flutamide

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Liposomes are the most commonly known vesicular system. However, they suffer from a number of stability problems. Polymersomes are promising carrier to solve these stability issues of liposomes. Polymersomes were prepared by solvent switching technique and successfully optimized with narrow particle size, 143 nm, and highly negative zeta potential - 33.4 mV. Colloidal stability, Stability in GIT and circulation were performed. Finally, in- vitro cytotoxicity on prostatic cancer cell line, PC3 was investigated. A significantly higher stability in GIT fluids was observed for polymersomes compared to liposomes with 90% of polymersomes remains intact after 6 hours. Stability in circulation was also higher for polymersomes in comparison with liposomes. In addition, polymersomes showed higher proliferation inhibitory effect on PC3 cell line with 2 folds lower IC_{50} compared to liposomes.

Keywords: Liposomes; Polymersomes; Stability; Cytotoxicity.

PHS 103: Lecithin-based emulsion pre-concentrates for improved oral bioavailability of anticancer soy phytoestrogen

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Daidzein (DAI), one of the major soy phytoestrogens, is a promising innovative agent in prophylaxis and treatment of breast and prostate cancer. However, DAI suffers from poor bioavailability (6.1%) due to its challenging physicochemical characteristics; poor aqueous solubility and low liposolubility, and extensive metabolism. This work aimed to enhance DAI oral bioavailability via lecithin-based emulsion pre-concenntrate (LBEPs). Different LBEPs were formulated using Phosal 53MCT, which is medium chain triglyceride oil with 53% lecithin, alone or with relatively low amount of different surfactant/co-surfactant mixtures. Upon aqueous dilution, LBEPs can easily disperse into homogenous emulsion. Compared to other self-nanoemulsifying systems, LBEPs can address health and pharmaceutical problems associated with high surfactant concentration through using lecithin as the main emulsifier. DAI complexion with lecithin content of LBEPs was performed to enhance DAI solubility in oil content of LBEPs. Assessment of the prepared LBEPs included complete in-vitro characterization and in-vivo bioavailability study. In-vitro appraisal encompassed robustness to dilution, particle size analysis, zeta potential determination, transmission electron microscopy, in-vitro drug release, and stability study. Selected LBEPs (DAI:Phosal® 53MCT complex without any added surfactants/co-surfactants mixture) was monodisperse upon aqueous dilution with nano-range globule size (485±15 nm). The globules had negative charges (-41.7±1.15 mV) and were spherical with typical appearance of oil/water emulsion. The system was robust to dilution in different media using different dilution folds. LBEPs showed enhanced drug release compared to free DAI suspension and DAI:Phosal physical mixture. Moreover, Cmax and AUC_{0-6} after oral administration of DAI-loaded LBEPs (20 mg DAI/Kg) enhanced by 7.46-and 2.38-fold, respectively, compared to DAI suspension. In conclusion: LBEPs can be a promising strategy to improve oral bioavailability of anticancer soy phytoestrogen; DAI.
Keywords: Daidzein; Emulsion pre-concentrate; Lecithin-complex; Oral bioavailability.

PHS 104: Design and evaluation of simvastatin loaded nanosponges for enhanced wound healing activity

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The present study aims to the development and evaluation of controlled release nanosponges containing simvastatin using ethyl cellulose for local delivery of drug and prolonging its action. Materials: Poly vinyl alcohol, Ethyl cellulose, Simvastatin, Dichloromethane. Different ethyl cellulose nanosponges were prepared by emulsion solvent evaporation technique using different organic solvents, different polyvinyl alcohol concentrations, and different drug to polymer ratios. Characterization of nanosponges was performed by particle size measurement, surface area and porosity measurement, morphological examination by SEM, in-vitro release study, FT-IR, DSC analysis and in-vivo wound healing activity. Particle size of the prepared formulas was in the range of 320-800 nm. The optimized formula showed controlled release of simvastatin with 61.95± 3.6 % after 48 hrs, specific surface area was decreased by 2.5-fold after drug loading from 26.5 m2/g to 10.3 m2/g indicating that pores were filled with drug. SEM micrographs illustrated spherical nanosponges with porous surface. FT-IR showed no interaction between the components of nanosponges and simvastatin. DSC revealed partial amorphization of the loaded simvastatin. In-vivo wound healing activity showed a significantly higher closure rate in simvastatin loaded nanosponges treated group compared to all other tested groups. Histological examination of skin samples at the end of experiment showed no scar formation and more skin appendages. Results suggest the feasibility of improving Simvastatin wound healing activity with scar prevention and skin formation with good quality, by the sustained release effect resulting from simvastatin encapsulation into ethyl cellulose nanosponges.

Keywords: Ethyl cellulose; Nanosponges; Simvastatin; Local delivery; Wound healing.

PHS 105: Chitosan-lecithin hybrid nanocarriers for enhanced catechin bioavailability

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Catechin hydrate, a green tea polyphenol, has grown interest in the past few years for its powerful antioxidant activity and its use in preventing and treating numerous diseases including cancer. Unfortunately, it has poor oral bioavailability of less than 5%. This study aimed to elaborate and compare between two kinds of chitosan-lecithin hybrid nanocarriers for enhancing the oral bioavailability of catechin hydrate. Namely, chitosan-coated liposomes and phospholipid-coated chitosan nanoparticles were prepared followed by physicochemical, ex vivo and biological appraisal in male Wistar albino rats. Both nanocarriers exhibited small particle size of 137 nm and 203 nm, narrow PDI of 0.15 and 0.23, and zeta potential of +36.8 mV and -19.9 mV for chitosan-coated liposomes and phospholipid-coated chitosan nanoparticles, respectively. Additionally, both systems showed significant improvement in digestive stability against bile salt compared to conventional liposomes. However, with respect to *ex vivo* permeation and *in vivo* pharmacokinetics study, results demonstrated superiority of chitosan-coated liposomes over phospholipid-coated chitosan nanoparticles in enhancing intestinal permeation and oral absorption of catechin. This was explained by the ability of chitosan-coated liposomes to enhance catechin bioavailability (AUC, C_{max}) and sustain its effect (T_{max}). Hence, elaborated chitosan-coated liposomes proved to be a promising nanoplatform to enhance catechin oral efficacy.

Keywords: Chitosan-coated liposomes; Phospholipid-coated chitosan nanoparticles; Catechin hydrate; Oral; Digestive stability; Ex vivo permeation; In vivo pharmacokinetics.

PHS 106: Novel Rhein-phospholipid complex mediated dermal delivery; Development, in-vitro and in-vivo studies

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Rhein (RH), an anthraquinone derivative has proven to be a promising molecule for treating several skin disorders thanks to its pleiotropic pharmacological activities like antimicrobial, antifungal, antioxidant and anti-inflammatory activities. However, RH low water/oil solubility and poor skin permeability halted its topical delivery. This is the first work to investigate the expediency of tailoring a Rhein–phospholipid complex (RH– PLC) to improve RH challenging physicochemical properties and its skin permeation. The phospholipid complex was prepared employing different methods and different RH:PL molar ratios. The selected RH–PLC was characterized in terms of infrared spectroscopy (IR), differential scanning calorimetry (DSC) and powder X-ray diffraction (PXRD), water/n-octanol solubility, particle size, zeta potential, in-vitro release study and ex-vivo skin permeation study. RH-PLC was also in-vivo evaluated concerning skin penetration and skin irritation. RH–PLC was successfully developed at stoichiometric ratio 1:1 using a co-solvent evaporation method exhibiting the highest complexation efficiency (95%). RH-PLC formation was confirmed with FTIR, DSC and XRPD analysis. RH-PLC showed significant increases in water/n-octanol solubility and permeability through the excised rat's skin in comparison with the control. In-vivo confocal laser scanning microscopy study confirmed the significant improved RH-PLC permeability into deep rat skin layers by 3.3 folds when compared to RH suspension. Besides, an absence of any skin irritation signs upon topical application of RH-PLC on healthy rats. Phospholipid complex approach might be one of the suitable approaches to improve permeability of RH and other promising abandoned poor-permeable drugs.

Keywords: Rhein; Phospholipid complex; Skin penetration; Topical application.

PHS 107: Formulation development and stabilization of Myricetin solid lipid nanoparticles for improved local treatment of lung carcinoma

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Myricetin (MYR) is a flavonoid with great biomedical application due to its antioxidant, anti-tumor and anti-inflammatory properties. However, MYR suffers from many obstacles like poor solubility and stability in either elevated temperatures or physiological pH, which restrained its pharmaceutical development and further clinical application. The major goal of this research encompasses design and characterization of a stable novel nanoscopic pulmonary delivery system for MYR in an attempt to enhance its therapeutic activity and sustain its effect for local treatment of lung carcinoma. To protect MYR against degradation, gelucire-based solid lipid nanoparticles (SLNs) loaded with MYR were prepared using hot homogenization method. The effect of different lipids, stabilizer type and concentration were investigated. Moreover, the influence of preparation temperature, medium pH and antioxidants on stability of MYR in free form or encapsulated was investigated. Results revealed that, adopting hot homogenization method at 55^{o}C allowed successful development of MYR-SLNs with acceptable particle size of 76 nm, zeta potential of -22.5 mV, and encapsulation efficiency of 84.5%. However, for SLN preparation at elevated temperature (80 oC), the presence of fat soluble antioxidant is a must otherwise 60% drug degradation was observed. Interestingly, supplying physiological buffers as well as simulated fluids with stabilizers as Tween 80 and Poloxamer 407, or water-soluble antioxidant like sodium sulfite obviously reduced MYR degradation rate constant up to 300-folds and prolonged the half-life compared to free MYR in these media. The release study revealed that the rate of drug release from nano-system is affected by lipid nature and chain length of the fatty acids. That's why Formula F2-07 which prepared with gelucire 50/13 exhibited slower release profile (53.5%) after 24h compared to F1-02 contains gelucire 39/01(65.5%). In conclusion, this approach provides a promising alternative for manipulation of MYR overcoming its challenging limitations.

Keywords: Phytomedicine; Solid lipid nanoparticles; Gelucire; Myricetin.

PHS 108: Preparation, characterization and in-vivo evaluation of glibenclamide solid solutions using injection molding technique

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This research work aimed to study applicability of using hot melt techniques like injection molding in preparation of glibenclamide (GB) solid solution loaded dosage forms and their ability to enhance GB dissolution rate as well as GB bioavailability. Manufacturing of GB extrudates using different polymers by the injection molding technique was studied. The used polymers were Povidone (K25), Soluplus® (polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft co- polymer), and Kollidon®VA64 (vinylpyrrolidone-vinyl acetate copolymers). Physicochemical properties for GB, polymers, physical mixtures, and extrudates were evaluated using differential scanning calorimetry, and miscibility was estimated by Hansen solubility parameter**.** Extrudates were milled to obtain granules of specific size range and evaluated for bulk, tapped density and flowability. GB loaded granules were formulated as tablets and characterized for hardness, weight variation and disintegration time. Dissolution rates of the different formulations were evaluated in phosphate buffer pH 6.8 compared to unprocessed GB and a reference medication**.** Comparative bioavailability study on conventional reference product and selected solid solution loaded dosage forms was performed on male sprague dawley rats**.** GB solubility was highest in soluplus® followed by PVP®VA64 and PVP K25. Solid solution granules at GB concentration 10% w/w were successfully prepared using PVP K25, PVP®VA64 and Soluplus. PVP®VA64 and Soluplus® extrudates showed much better manufacturability than PVP K25. Granules of GB extrudates as well as formulated tablets showed significantly higher dissolution rate in comparison to GB raw material and reference medication. PVP K25 and PVP®VA64 showed much faster drug release rate than Soluplus®. Injection molding was successful to prepare GB solid solution extruded granules and loaded tablets with improved dissolution rates. Moreover, in vivo performance expressed in area under plasma-concentration plasma curve in first 24 hours was two-fold higher than conventional reference product.

Keywords: Molding; Glibenclamide; Extrudates; Solid solution.

PHS 109: Post- market assessment of the quality of Glibenclamide commercial tablets.

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Glibenclamide is an oral second-generation hypoglycemic sulfonylurea. This class suffers from hydrolysis. Two degradation products (DP) were specified in the British Pharmacopoeia known as impurity (A) and impurity (B). Their limits are 2.4 % and 0.4 % respectively. It should be noted that the BP uses a thin layer chromatographic method for quantitative analysis of these two DP. It is worth mentioning that there was no limit specified for moisture content. Purpose of this study was to evaluate the commercial batches of glibenclamide tablets using the quality control tests. Dissolution test, levels of degradation products and moisture content were carried out at different storage conditions, room temperature and under accelerated conditions (40°C, 75% RH). Dissolution rate profiles were constructed with four time intervals (15, 30, 45 and 60) for comparison between different batches instead of the pharmacopoeial single point test. A reported validated HPLC method was used for quantitative determination of degradation product (A) limit for the studied brands. The moisture level was determined using loss on drying method. The examined tablets showed variable dissolution rate profiles. Dissolution studies revealed that the tablets of one brand did not comply with the pharmacopeial limit neither at room temperature nor under accelerated conditions. Limits of DP (A) varied from (0.65 to 5.14%). Significant differences existed between the stability of brand product (UK) and other generic brands (I, II and III). Glibenclamide tablets of brand product (UK) exhibited lowest percentage of moisture content (0.05%) as well as good chemical stability. The values of moisture content of some brands exceeded 1%. It could be concluded that the limit of moisture could affect the stability of glibenclamide. The high level of DP (A) could affect the safety and effectiveness of Glibenclamide.

Keywords: Glibenclamide; Degradation product; Dissolution; Moisture content; HPLC.

PHS 110: Lyophilized oily core polymeric shell nanocapsules of a class-II BCS antihypertensive drug: Design, formulation and *in-vitro* evaluation

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Polymeric nanocapsules are core and shell nanostructures usually in the size range of 150 -300 nm where the poorly water soluble drug can be encapsulated inside an oily core. Olmesartan Medoximil (OLM) is a class-II BCS antihypertensive drug which has a very low oral bioavailability about 26% mainly due to poor aqueous solubility. Formulation of OLM in the form of a nanosystem is a trend to enhance its oral bioavailability. Eight oily-core polymeric shell nanocapsules formulae were prepared using interfacial deposition of preformed polymer method to study effect of two formulation variables (type and concentration of surfactant) and one processing variable (magnetic stirring rate) on Particle size (PS), Zeta potential (ZP), Polydispersity Index (PDI), Entrapment Efficiency (EE). Span 40 and span 60 were used at two different concentrations 0.35 g% and 0.70 g%. All formulae were prepared using magnetic stirring rates 500 and 800 rpm. *In-vitro* release study was carried out on all formulae using dialysis bag method. Optimum formula was imaged using Transmission Electron Microscope (TEM) to ensure the formation of spherical nanocapsules. The optimum formula was then lyophilized to fit inside a hard gelatin capsule. Lyophilized formula hard gelatin capsule was subjected to *in-vitro* dissolution test versus the pure drug capsule. Optimum formula was the one prepared using Span 60 at concentration of 0.7g% and stirring rate 500 rpm. It showed PS of 196.4±25.6 nm, ZP of -24±7.3 mV and PDI 0.37±0.07. Entrapment Efficiency was 84.33±2.1% and Cumulative % release after 8 h was 94±5.4%. TEM images showed a perfect spherical nanocapsules with a clear polymeric coat. *In-viro* dissolution profile of the lyophilized formula from capsules was higher than that of pure drug by 20%. Thus, OLM oily core polymeric nanocapsules are a very promising system to overcome poor aqueous solubility and improve oral bioavailability.

Keywords: Olmesartan; Polymeric; Nanocapsules; Oily core; Nanoprecipitation.

PHS 111: 3D printing of scaffolds for cell delivery and tissue engineering

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Not surprisingly, there are current challenges to address before 3D Bioprinting becomes clinically relevant. 3D Bioprinting of scaffolds has gained much interest in medical applications as tissue engineering, and tissue repair. It offers control over cell distribution within the scaffold and scaffold geometry which acts as physical support to the new developing tissue. In addition, scaffolds can act as delivery carriers for growth factors necessary to enhance developing tissue growth. This study aimed to illustrate the advantages of using 3D bioprinting of Scaffolds for Cell Delivery as well as Tissue Engineering. The authors performed a computerized systemic literature review of studies related to 3D bioprinting in fabrication of biologically relevant scaffolds from electronic databases Science Direct, PubMed and Google Scholar from 2006 to mid-2019. This study showed that 3D Bioprinting can simply be achieved by modifying conventional commercial 3D printers to print bioinks (polymers, cells and growth factors). The resolution of different 3D bioprinting techniques offers valuable design flexibility which opens more frontiers to their use in the medical field. In 3D bioprinting, the deposition of biomaterials in micrometer scale to form the required scaffolds is achieved using one of the major bioprinting methods. These include extrusion-based, inkjet, stereolithography- based, and laser assisted methods. Each of these methods has its problems related rheological properties of the bioink affecting its printability, selection of suitable processing parameters and curing method which may affect cell viability, the ability of the deposited layers to withstand the pressure exerted by the vertically deposited layers on top to prevent scaffold collapse during printing and mechanical strength of the final prepared scaffold. We now have good reasons to build hope on the future of tissue engineering using 3D printing.

Keywords: 3D bioprinting; Scaffold; Tissue engineering; Bioink.

PHS 112: 3D printing from one dose fits all to a dynamic dose developer

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Traditional pharmaceutical industry is based on large-scale production with multiple steps and expensive facilities making it relatively inflexible and economically not reasonable in terms of compounding and fabricating of personalized medicine and preparing dosage forms with complex geometry. This study aimed to describe the emerging advances of using 3D printing for preparing oral solid dosage forms. The authors performed a computerized systemic literature review of studies associated with 3D printing of oral solid dosage forms (OSDF) from electronic databases Science direct, PubMed and Google Scholar from 2013 to mid-2019.This study showed that 3D printing shows high potential as an alternative manufacturing process in fabricating OSDF and devices. Several 3D printing approaches have been used to produce OSDF including fused filament fabrication (FFF) and pressure assisted microsyringe (PAM). FFF requires preparation of a filament via hot melt extrusion containing the drug and suitable additives/polymers. This filament is then introduced in the 3D printer and used to print the required 3D structure using a suitable computer aided design. It requires high temperatures during production and printing of the filament, thus is not suitable for thermosensitive drugs. Whereas, in case of PAM, the drug dispersed in a suitable formulation is extruded by pressure through a nozzle, using a piston or a screw to directly print the required computerized structure followed by curing or drying the formed structure. The printing process can be carried out at or even below room temperature. Owing to its flexible and precise manufacturing capability, 3D printing approach is expected to set an innovative platform providing a highly adjustable, affordable, minimally sized, more accurate, safer and digitally controlled patient-tailored medicines, in addition to fabrication of a dosage form with complex geometries.

Keywords: 3D printing; OSDF; Patient-tailored medicines; FFF.

PHS 113: Are nanoparticle preparations the best technique for dissolution enhancement of water-insoluble drugs: A comparative study using Candesartan Cilexetil as a model drug

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The objective of this study was to investigate the influence of different traditional methods in improving the solubility and the dissolution rate of Candesartan Cilexetil (CAD) as compared to nanoparticle preparations. The applied techniques were solid dispersions, inclusion complexes and preparation of drug-nanoparticles. Following preparations, all samples were characterized for their dissolution and other physicochemical properties. Results of dissolution studies revealed an increase in the dissolution rate of all samples. The highest dissolution rate was achieved using solid dispersion of the drug with PVP K-90. Physicochemical investigations (XR, DSC and FT-IR) suggested formation of hydrogen bonding, and changing in the crystalline structure of the drug. With regard to inclusion complexes, a more stable complex was formed between hydroxypropyl-β-cyclodextrins (HP-β-CD) and CAD as indicated by phase solubility diagrams. Anti-solvent method resulted in preparation of stable nanoparticles, as indicated by zeta potential (ζ), with average particle size 238.9 ± 19.25 nm using PVP K-90 as a hydrophilic polymer. It was concluded that nanoparticles preparations succeeded in improving the drug dissolution rate, it may have some advantages but it was not superior to other traditional methods.

Keywords: Solid dispersion; Inclusion complex; Nanoparticles; Candesartan; Comparative study.

PHS 114: Gastro-retentive Metronidazole floating raft system for *Helicobacter Pylori* eradication

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Purpose: The study demonstrates the feasibility of prolonging gastric residence time and release rate of metronidazole (Mz) by preparing floating raft system (FRS).
Materials and Methods: The floating raft system (FRS) depends on using ion-sensitive in situ gel forming polymers; sodium alginate (Alg) and gellan gum (G) in 3, 4, 5 and 0.5, 0.75, 1% w/v concentrations respectively. Sodium citrate 0.25% w/v, and calcium carbonate 0,0.5, 1, 2% (C) were incorporated in all formulations. Lipids; Glyceryl mono stearate (GMS), Precirol® and Compritol® were incorporated into G-based formulation ($G_{1\%}C_{1\%}$). Mz: lipid ratio was 1:1, except for Mz: GMS formulations, ratios of 1:1.5 and 1:2 were also investigated. Floating, gelation capacities and viscosity parameters were evaluated. Drug release, and kinetics were carried for selected formulae. The selected lipid containing formula was subjected to accelerated stability testing.
Results: $Alg_{4\%}C_{2\%}$ FRS exhibited short gelation lag time (3sec), long duration (> 24hr), floating lag time 1min and duration > 24hr, and a reliable sustained drug release (MDT 6hr). Gellan gum FRSs achieved successful floating gastro retention, but failed to achieve the required gelation capacity. Incorporation of GMS (Mz:GMS 1:1) enhanced the gelation lag time and duration (6 sec and > 24hr, respectively), keeping sustained drug release and formulation stability. **Conclusion:** The improved characteristics of the selected FRS make them excellent candidates for gastric targeting to eradicate Helicobacter pylori.

Keywords: Gastro-retentivity; Alginate; Gellan; Precirol; Compritol; Glyceryl mono stearate.

PHS 115: Repurposing itraconazole for breast cancer: Efficacy enhancement via a dual nanotechnology / combinational therapy approach

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The antifungal itraconazole (ITC) is currently under active investigation for repurposing as anticancer agent against different cancers. ITC inhibits angiogenesis and the hedgehog pathway, promoting apoptosis and autophagy of breast cancer cells. The objective of this study was to improve the anti-breast cancer activity of ITC utilizing a dual nanotechnology/active targeting or nanotechnology/combinational therapy approach based on lipid nanocapsules (LNCs) as drug delivery system. LNCs were prepared by the phase inversion method. For active targeting, folic acid (FA) was incorporated into neutral or cationic LNCs (Didodecyldimethylammonium bromide, DDAB) while LNCs for combinational therapy were dually loaded with ITC and miltefosine (MFS), a membrane active alkylphosphocholine. LNCs were characterized for colloidal, stability and release properties. The anticancer activity of itraconazole-loaded LNCs was screened using MCF-7 human breast adenocarcinoma cell line. *In-vivo* antitumor efficacy of the most active formulations (cationic FA/ITC-LNCs and ITC/MFS LNCs) was assessed in mice bearing Ehrlich cells-induced mammary tumors using ITC solution, ITC-LNCs and doxorubicin injection (DOXO) for comparison. Results indicated good pharmaceutical attributes of LNCs in terms of size (~50 nm), entrapment efficiency (>98%) and stability at 4^{o}C (at least 3 months). Cell culture data showed dose-dependent cytotoxicity of ITC-LNCs against MCF-7 cells and activity enhancement by FA-targeted cationic LNCs and ITC/MFS dual loading. Preclinical findings denoted mainly: Enhanced ITC anticancer activity by nanoencapsulation; intolerable toxicity of cationic FA/ITC-LNCs after 7 day-treatment; significant tumor regression efficacy of ITC/MFS LNCs combinational therapy (expressed as reduction of tumor size and weight) comparable to that of DOXO. This was verified by immunohistochemical evidence of tumor growth inhibition. Efficacy of ITC/MFS-LNCs was substantiated by maintenance of liver and kidney functions of mice at the end of treatment, indicating potential safety. In conclusion, ITC/MFS nanoencapsulation/combinational therapy offers great promise as an effective dual approach to promote repurposing of ITC for breast cancer.

Keywords: Itraconazole; Miltefosine; Lipid nanocapsules; Repurposing; MCF-7 cells; Mammary tumors.

PHS 116: The pharmacokinetic profile of imipenem/cilastin in critically ill patients with pneumonia in the intensive care units of Alexandria Main University Hospital

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Imipenem, a valuable β-lactam carbapenem antibiotic in the treatment of serious infections, is utilized in intensive care units (ICUs) of Alexandria Main University Hospital (AMUH) particularly among critically ill patients. The drug is administered as imipenem/cilastin 500mg/500mg by i.v. infusion over 0.5h q 6h. As carbapenems show time-dependent effect, the percentage of dosing interval during which the unbound plasma carbapenem concentrations remains above MIC (%fT>MIC) is used as activity index, 40% being the target for imipenem. Thus, continuous infusion is optimal for carbapenems administration, but this is impractical for imipenem because of poor stability in i.v. fluids (maximum 4 h). This led to increasing adoption of prolonged infusion (1-3h). However, scarcity of data on imipenem PKs among critically ill patients hinders assessment of prolonged infusion for this patient population. Our objective was to examine imipenem PKs in critically ill patients in ICU settings of AMUH to assess %*f*T>MIC achieved following short imipenem/cilastin infusions every 6h. Twelve pneumonia patients were administered imipenem as < 1h infusion. Two blood samples (peak and trough) were obtained at steady state. Imipenem concentrations were determined by HPLC and subjected to PK analyses and simulations using Phoenix WinNonlin 8.1. The %*f*T>MIC was estimated based on individual PK parameters for MICs 1, 2 and 4 mg/L representing the susceptibility breakpoints to imipenem across Gram-negative bacteria. An open one-compartmental model was fit to plasma concentrations and mean PK parameters calculated. The %*f*T>MIC for MIC = 1,2, and 4 mg/L were 78.3-100%, 50-100%, and 0-100% respectively. Percentage of patients who reached a 100%*f*T>MIC for MICs 1and 2mg/L were 92% and 75% respectively. More than 50% of patients achieved an 80%*f*T>MIC for MIC 4mg/L. In conclusion, target %fT>MIC could be achieved against susceptible isolates without prolonging infusions. Further studies with larger sample size are warranted to substantiate these findings.

Keywords: Carbapenems; Imipenem; Pharmacokinetics; ICU; Critically ill; Alexandria University Hospital.

PHS 117: Tween 80-coated sildenafil nanoparticles for targeted brain delivery: A preclinical hepatotoxicity study

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Nanoparticle-based drug delivery and surface modification of nanoparticles (NPs) with Tween 80 (T80) are two efficient approaches for enhancing brain targeting. However, both approaches may alter the toxicity profile of the encapsulated drug, an aspect not receiving adequate research attention. Our objective was to assess the effect of T80 coating on the hepatotoxicity of chitosan NPs incorporating sildenafil (SF) used a model drug with repurposing potential for neurodegenerative disorders. Uncoated (SF-NPs) and T80-coated SF NPs (T80-SF-NPs) were prepared by ionic gelation and the adjusted formulations were characterized pharmaceutically and morphologically (TEM). Hepatotoxicity of the two NP formulations compared with SF solution was assessed biochemically and histopathologically in male rats upon intraperitoneal administration of the equivalent of 1.5 mg/kg SF for 21 consecutive days. Biochemical testing included the activity of phase I drug metabolizing enzymes (cytochrome c reductase (CcR), aryl hydrocarbon hydroxylase (AAH) and 7-ethoxycoumarin-O-deethylase (EOD) and the protein expression of different cytochrome P isozymes by Western immunoblotting analysis in addition to the activity of antioxidant enzymes (glutathione S transferase (GST), glutathione reductase (GSR), glutathione peroxidase (GTP), catalase (CAT) and superoxide dismutase (SOD)). SF-NP formulations showed *in vitro* characteristics suitable for brain delivery. Biochemical data indicated heterogeneous effects of NPs relative to SF solution on the protein expression of CYP2E1, CYP34A and CYTb5 and activity of metabolic enzymes. Nanoencapsulation significantly attenuated the SF-induced decrease in GST and GR levels and augmented the increase in GPx and SOD activity. Histopathologically, SF induced necrobiotic changes, fibrosis, hemolysis and inflammation which were reduced by nanoencapsulation. T80 coating further improved liver architecture and cells with prevention of inflammation and hemolysis. This study provides the first evidence for the effect of nanoencapsulation and T80-coating of NPs on drug-induced hepatotoxicity. T80-coating greatly suppressed SF hepatotoxicity and enhanced the protective effect of chitosan nanoencapsulation.

Keywords: Sildenafil; Tween 8; Brain delivery; Nanoparticles; Hepatotoxicity.

PHS 118: Development of verapamil HCl-loaded composite electrospun nanofibers: A novel application as wound dressings

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Researchers are aiming to new heights for manufacture of wound dressings with unique properties and sophistication. Different natural, synthetic, biodegradable and biocompatible polymers especially in the nanoscale are being employed to support and provide a quick deposition of healthy tissue for efficient wound management. Nanofibrous meshes are ultra-fine, non-woven polymeric fibers with diameters ranging from several micrometers down to few nanometers; a size range recognized as a key feature of biological processes and functional interactions between the biological macromolecules inside and outside the cells. The resulting large surface to volume ratio and changes in surface properties give these nanofibers the ability of allowing complete and healthy healing process. The aim of the present study is to prepare and evaluate a novel verapamil HCl-loaded composite electrospun nanofibers suitable for the application as wound dressings.
Composite nanofibers were prepared by electrospinning of a blend of the natural, biocompatible polymer sodium alginate (SA) together with polyvinyl alcohol (PVA). PVA, a good fiber forming synthetic polymer, was included to enhance the electrospinnability of SA by decreasing the repulsive force among polyanionic SA molecules. Verapamil HCl- loaded composite nanofibers were characterized in terms of fibers morphology, diameter, drug entrapment efficiency and release profile.
Results suggested that association of PVA with SA enhanced the electrospinnability of SA and allowed an increase of uniformity and smoothness of the developed nanofibers with an average diameter of 156 nm. Also, Verapamil HCL- loaded composite nanofibers showed good pharmaceutical attributes favorable for wound healing including relatively high entrapment efficiency (~80%) and controlled drug release for 24 hr,. The study demonstrated the possible utility of the developed composite nanofibrous meshes as wound dressings.

Keywords: Verapamil HCl; Wound dressing; Sodium alginate; Polyvinyl alcohol; Nanofiber; Electospinning.

PHS 119: Preparation and in-vitro characterization of methyl-dihydrojasmonate solid lipid nanoparticles; A novel approach for cervical cancer treatment

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Cervical cancer is the second most common cancer among women in the developing world. Recent disclosure by the World Health Organization (WHO) stated that cervical cancer has emerged as the largest killer, surpassing breast cancer. Methyl dihydrojasmonate (MDHJ) is an oily derivative of jasmonates, a class of plant stress hormones isolated from Jasmine plant (*Jasminum officinale*). In plant cells, upon wounding or pathogenic attack, methyl jasmonates (MJ) cause induction and accumulation of proteinase inhibitors which are involved in activation of programmed cell death, thus resembling mammalian apoptosis. Recently, a few *in-vitro* and *in-vivo* studies reported the selective anticancer activities of the methyl dihydrojasmonate. The main objective of the current study is the preparation and characterization of a novel targeted nano-based delivery system of the herbal lipophilic drug methyl dihydrojasmonate for the treatment of cervical cancerous lesions. Solid lipid nanopartciles loaded with methyl dihydrojasmonate were prepared using different lipid carriers such as Gelucire 39/01, Gelucire 50/13, Gelucire 44/14, Compritol 888-ATO together with Poloxamer 407 and/or Miglyol in different ratios to achieve maximum drug entrapment coupled with stability. Colloidal properties and pharmaceutical performance indicators were assessed. Methyl dihydrojasmonate solid lipid nanoparticles showed good quality attributes including; particle size and PDI values (PS ranging from 90-150 nm and PDI values ranging from 0.210-0.390), zeta potential (-13.3 mv to -26.9 mv) relatively high entrapment efficiency (~89%), a biphasic release profile suitable for cancer treatment, and a long-term/good stability at room temperature for 18 months study. In addition, cytotoxicity study using Hela cells indicated the efficiency of the optimum methyl dihydrojasmonate solid lipid nanoparticles against cervical cancer cells, suggesting the potential usefulness of the developed formulations which are currently under in vivo investigations.

Keywords: Methyl-dihydrojasmonate; Nanoparticles; Lipid carrier; Cervical cancer.

PHS 120: Prodigiosin-functionalized bacterial ghosts: A novel bioinspired delivery system against colorectal cancer

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Bacterial ghosts (BGs) are highly stable empty envelopes of Gram-negative bacteria, commonly produced by cloned E-mediated gene lysis. BGs are devoid of cytoplasm and genetic DNA, though they retain intact bio-adhesive surface properties and external configurations necessary for specific cellular interactions and immunomodulation. There is growing interest in using BGs as bioinspired carriers for site-specific delivery of anticancer drugs. Our objective was to develop a novel bacteria-based drug delivery system for colorectal cancer. The system was bioengineered utilizing a new type of ghost derived from the Gram-positive *Lactobacillus acidophilus* (LA), a probiotic with natural tropism to the colon. This was used as vector for prodigiosin (PDG), a bioactive secondary bacterial metabolite having anticancer activity. LA ghosts (LAGs) were prepared employing a modified specific chemical exposure protocol and separated by gradient centrifugation. Variables were controlled for 100% ghost yield. LAGs were visualized by light microscopy using a new low-cost ghost-specific staining method. The ghost content of cytoplasmic DNA and proteins (intracellular and envelope proteins) relative to live LA was assessed using agarose and SDS-PAGE gel electrophoresis respectively. PDG obtained from the bacterium *Serratia marcescens*, was loaded into LAGs under adjusted conditions for maximum loading. LAGs were evaluated for pharmaceutical attributes, in terms of size, zeta potential, loading efficiency and release properties. The anticancer activity of PDG-loaded LAGs was assessed using HCT-116 human colon cancer cell line and 5-fluorouracil (5-FU) as standard. Results indicated PDG anticancer activity ~81% that of 5-FU and relatively low cytotoxicity of blank LAGs. However, a synergistic anticancer effect was exerted by PDG-loaded LAGs. In conclusion, PDG-functionalized LAGs offer great potential as a bacteria-based delivery system for colorectal cancer.

Keywords: Bacterial ghost; Lactobacillus acidophilus; Prodigiosin; Colorectal cancer; Drug delivery; 5-fluorouracil.

PHS 121: Mandible osteomyelitis; evaluation of a novel chemical induction method and local treatment with an antimicrobial biomimetic hydrogel

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Osteomyelitis (OM) of the mandible, a challenging inflammatory bone disease following chronic infection, may lead to progressive bone loss. Current treatment involving extensive surgical debridement along with prolonged systemic antibiotic therapy, has limited success because of low antibiotic levels in bone. A dual localized bone regeneration/antimicrobial therapy approach evaluated using appropriate animal models may contribute to treatment improvement, given that current OM induction involves aggressive surgical procedures and inoculation of bacteria inside the mandible bone marrow. Our objective was to evaluate a novel chemical OM induction technique and a dual local bone regeneration/antibiotic delivery treatment approach in rabbits. A composite hydrogel made of collagen (Col), reinforced with hydroxyapatite nanoparticles (nHA) and functionalized with gentamicin (Gent) was developed. OM was induced by inserting arsenic trioxide paste via an access opening in the root canal of lower right central incisor of anaesthetized rabbits. Cotton wool plugging allowed contamination of the lesion with oral flora. Four weeks post MO induction (verified by clinical, radiological and histological examination), the causative tooth was extracted, and necrotic bone debrided. Rabbits were divided into 3 groups: Control (saline-treated) and treatment groups (single treatment with injectable Gent-Col/nHA compared to Gent-Col hydrogel scaffolds which were secured by watertight-suture). Bone defects were evaluated at four and twelve weeks using computed tomography scanning, histopathologically and histomorphometrically. Results indicated effectiveness of arsenic trioxide in inducing clinically relevant OM and generally good soft tissue healing in the treatment groups. At four weeks, rabbits in the Gent-Col/nHA group showed faster bone regeneration with more condensed trabeculae relative to the Col/nHA group. However, at 12 weeks, both treatments prevented unfavorable longitudinal bone contraction of extraction socket. In conclusion, findings regarding chemical induction of mandible OM and local treatment with injectable bone regeneration/gentamicin delivery scaffolds would contribute to improved OM treatment.

Keywords: Osteomyelitis; Collagen; Hydroxyapatite; Gentamicin; Drug delivery; Injectable scaffold.

PHS 122: Voriconazole-loaded solid lipid nanoparticles and nanostructured lipid carriers for treatment of pulmonary aspergillosis: An in-vitro comparative study

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Pulmonary aspergillosis is a life-threatening fungal infection with high incidence in Egypt due to prevalence of chronic respiratory diseases and malignant tumors. Triazoles are the mainstay of therapy for treatment and prophylaxis. However, increased azole resistance has become a significant challenge in the effective management of aspergillosis. Consequently, second generation triazoles, e.g., voriconazole (VRZ), were proposed to overcome this resistance. Unfortunately, systemic administration of such potent drug (VRZ) comes at the expenses of increased pharmacokinetic variability, adverse effects and systemic toxicity. Hence, local administration of VRZ loaded lipid nano-delivery systems can successfully reduce the dose, decrease the adverse effects, prevent rapid drug clearance and enhance the fungal uptake. From these perspectives, the efficiency of VRZ containing solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) were investigated. A comparative toolset of analysis in terms of particle size, PDI, loading capacity, entrapment efficiency and drug release were used to compare between them. In addition, *in-vitro* assessment of the anti-fungal capabilities of the parent drug in comparison to the nano-formulated systems was conducted. These studies showed that compritol-caproyl 90 (70:30) containing NLCs possess smaller particle size (166.5nm±2.4) compared to compritol SLNs counterparts; (194.4nm±7.5). Moreover, caproyl 90 incorporation increased significantly VRZ affinity towards the nanoformulations resulting in high drug loading (1.5mg/mL) and entrapment efficiency (77% ±2.06) with much lower burst release (less than 40% after 30 minutes compared to 70% for SLNs). Collectively, these results strongly proposed VRZ-NLCs as effective lipi- based systems in management of pulmonary aspergillosis with remarkable fungal uptake.

Keywords: Voriconazole (VRZ); Solid lipid nanoparticles (SLNs); Nanostructured lipid carriers (NLCs); Pulmonary aspergillosis.

PHS 123: Preparation of liquid oral controlled release system of Nimodipine

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Nimodipine, Class II drug, is a calcium channel blocker frequently used in critical care settings. It is mainly absorbed from upper gastrointestinal tract. Accordingly, development of gastro-retentive formulation will be beneficial specially for critical care patients if the developed system was in liquid form to facilitate administration through nasogastric tubing. The study developed gastro-retentive mucoadhesive liquid oral controlled release formulation via *in situ* gelation. Nimodipine solid dispersions (SD) were prepared using Poloxamer 407, employing hot melt technique. Sodium alginate solutions were prepared by dispersion in ultrapure water containing calcium citrate complex according to formulations in. The latter will release free Ca^{+2} in the acidic media to crosslink with anionic alginate chains. Carboxymethylcellulose was added at different concentrations to some alginate solution in order to modulate the release and augment mucoadhesion. Optimized SD microparticles were loaded into all alginate dispersions (3mg/ml). All *in situ* gelling dispersions were characterized regarding gelling capacity and bioadhesion strength. *In vitro* drug release was conducted in simulated gastric fluid for 8 hours. by careful immersion of Petri dish loaded with 10 ml of each formula in the dissolution vessels containing release medium without much disturbance**.** SD microparticles showed considerable improvement in nimodipine dissolution. All alginate systems were pourable. Increasing alginate concentration increased the gelling capacity and reduced drug release rate. Addition of carboxymethylcellulose produced greater mucoadhesion force and control over drug release rate. X-ray radiography showed successful stomach-retention over 8 hours in rabbits, which correlates with the controlled release pattern of the developed systems.

Keywords: Nimodipine; In situ gelling; Mucoadhesion; Gastro-retentive.

PHS 124: The antitumorigenic efficiency of photocatalytic Zinc sulfide nanoparticles.

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Zinc sulfide nanoparticles (ZnS) are one of the inorganic nanocomposites that have gained much attention due to their unique size-dependent luminescent properties. Their quantum size put them amongst the most studied semiconductor nanomaterials. Moreover, the photogenerated electron–hole pair makes them an attractive photocatalytic nanomaterial capable of generating reactive oxygen species; forming the basis behind using ZnS nanoparticles in the photo-degradation of organic dyes. In the biomedical field, ZnS nanoparticles qualifying as member of quantum dots family are frequently used in cell labeling, molecular tagging, drug tracking, and *in vivo* imaging thanks to their superior optical and luminescent properties. However, implicating their unique photocatalytic properties as lethal platforms for targeting and killing cancer cells has not yet been fully explored.

Purpose: Herein, we aimed to investigate the efficiency of photoactivated ZnS nanoparticles in acting as electron donors for cleavage of DNA plasmid, after proofing its ability to photocatalytic degradation of organic dyes. Furthermore, the antitumorigenic efficiency of photocatalytic ZnS nanoparticles on breast cancer (MCF-7) cell line.

Materials and Methods: ZnS nanoporous nanoparticle were synthesized by a solution-phase thermal decomposition method. They were characterized by UV-Visible spectrophotometer and TEM. An Eosin B organic dye was used to assess the photocatalytic properties of ZnS nanoparticles, as well as DNA plasmid. The *in vitro* anticancer effect of ZnS nanocomposites were assessed by flow cytometry and confocal microscopy.

Results and Conclusion: An Eosin B ultra-violet absorption assay displayed a progressive color change in the fluorescent dye. Experimentation using a DNA plasmid demonstrated the cleavage effect of UV-light activated ZnS nanoparticles. Furthermore, the MCF-7 cell line treated with photocatalytic ZnS nanoparticles revealed highest apoptotic index as well as the successful cellular uptake. Therefore, the promising results of ZnS nanoporous encourages their usage dually as anticancer and imaging nano-vehicles.

Keywords: Zinc sulfide nanoparticles, Photocatalytic, DNA plasmid, MCF-7 cell line.

PHS 125: Formulation of lipid nanocapsules with linalool: Investigation into antibacterial properties and uptake by bacterial cells

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The worldwide occurrence of resistance to standard antibiotics and lack of new antibacterial drugs demand new strategies to treat complicated infections. Hence, the components of essential oils such as linalool have been considered as an alternative to conventionally used antibiotics and preservatives. In this work, formulation of linalool-loaded lipid nanocapsules (LNCs), with and without medium chain triglycerides as the part of the oily core, was achieved by the phase inversion method. The obtained nanocapsules showed high entrapment efficiency (above 99%) and very high loading capacity of linalool (>50mg/g total dry weight). The average diameter ranged from 25->200nm depending on surfactant/oil ratio and the total oil concentration. The nanocarriers showed homogenous size distribution (polydispersity index below 0.2) and neutral to slightly negative surface charge. Most of the prepared LNCs were stable for at least one month at room temperature and at 4°C.

Linalool-loaded LNCs displayed activity against several clinically relevant bacteria such as *Acinetobacter baumannii* and *Escherichia coli*, including strains resistant to conventional antibiotics. The antibacterial potency was positively correlated with the percentage of linalool loaded in the nanocapsules. Other factors such as the surfactant/oil ratio, and consequently the size of the LNCs, had only a minor effect on antibacterial properties.

Linalool-loaded LNCs could thus be a promising delivery system for antibacterial application (nanoantibiotic).

Keywords: Lipid nanocapsules; Linalool; Antibacterial; Nanoantibiotic.

PHS 126: Cyclosporine A-loaded lipid nanocapsules for treatment of dry eye syndrome

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Purpose: Cyclosporine A (Cyc-A) is used in severe cases of dry eye syndrome (DES). Due to its low aqueous solubility, it is administered as castor oil eye drops resulting in poor patient compliance. In the present study, an aqueous dispersion of Cyc-A loaded lipid nanocapsules (LNCs) was prepared with its potential *in-situ* gel formation to increase residence time.
Methods: LNCs were prepared using phase inversion and temperature cycling technique. Mean particle size and zeta potential were determined by Malvern Zeta Sizer. Cyc-A-LNC's loading capacity, entrapment efficiency and in-vitro release (in 0.2% tween 80 in phosphate buffer pH 7.4) using dialysis membrane diffusion technique were determined. Cyc-A was quantified using HPLC–UV system. The in-situ gel was prepared by the cold method by adding Poloxamer-407 (17.5 – 25 w/w%) to the formula. Furthermore, chitosan was added to increase the mechanical strength and muco-adhesion of the gel. Viscosity, gelling temperature, as well as effect on colloidal properties of the LNCs were determined.
Results: Cyc-A LNCs had good characteristics; particle size (41.5 ± 3.1 nm), PdI <0.2, and zeta potential (-4 ± 1.5 mV), Cyc-A Loading capacity (0.25g/ml) and entrapment efficiency of 99.8 %. A sustained release of Cyc-A from the LNC formulation was evident when compared to drug suspension. Based on determined gelling temperature, poloxamer concentration (20 %w/w) was selected forming a gel only at physiological temperature. As *in-situ* gel, the average LNC particle size increased to 64.5 ± 2.4 nm with a slight decrease in entrapment efficiency to 98%.
Conclusion: LNCs provide a potentially suitable system for the sustained delivery of Cyc-A in treatment of DES to overcome issues caused by its poor aqueous solubility. The *in-situ* gel should prolong ocular residence time. Possible role of LNCs in further improving Cyc-A efficacy in DES will be investigated clinically.

Keywords: Cyclosporine A; Lipid nano-capsules; In-situ gel; Dry eye syndrome.

PHS 127: Targeting liver cancer stem cell markers and signaling pathways using miltefosine lipid nanocapsules

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Cancer stem cells (CSCs), a small fraction of cells inside a heterogeneous tumor cell population, are major contributors to tumor formation, recurrence, metastasis and failure of chemo/radiotherapy. Targeting CSCs via their surface markers and signaling pathways might revolutionize cancer treatment. Such a novel approach can be greatly enhanced by nanomaterial-based drug delivery. The aim of this study was to evaluate miltefosine-lipid nanocapsules (MFS-LNCs) as a potential nanomedicine to target liver CSCs (LCSCs) for hepatocellular carcinoma (HCC) treatment. LNCs, biomimetic drug carrier modified with oleic acid as membrane permeabilizer, were prepared by a phase inversion method and characterized for pharmaceutical attributes. $CD133^{+}/CD90^{+}$ sub-population of LCSCs lineages from human tumor specimens were isolated and analyzed by fluorescent-activated cell sorting (FACS). The isolated CD133+/ CD90+ LCSCs were treated with MFS-LNCs with different MFS concentrations for 48 h using free MFS and blank LNCs as controls. The cells were then assessed for morphology, viability using cell proliferation WST-1 assay, apoptotic induction and modulation of stemness characteristics signaling pathways that play a role in HCC progression. Compared to controls, MFS-LNCs induced morphological changes and significantly inhibited CD133+/CD90+ LCSCs viability in a concentration-dependent manner. MFS-LNCs also activated caspase 3 activity, induced apoptosis and inhibited the protein expression levels of ALDH, Notch1, Stat 3 and β- catenin, main stemness characteristics signals of LCSCs, in a concentration-dependent manner. In conclusion, LNCs proved to enhance the anticancer effects of MFS against LCSCs probably by inhibiting the p-glycoprotein efflux system and enhancing intracellular delivery. Merging nanomaterial-based drug delivery and CSC biology offers an emerging platform to overcome LCSCs resistance for more effective HCC treatment.

Keywords: Cancer stem cells; Hepatocellular carcinoma; Lipid nanocapsules; Miltefosine nanomaterials.

PHS 128: Formulation and evaluation of triamcinolone acetonide microemulsions as an ocular drug delivery system

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Uveitis is a major cause of vision loss. Triamcinolone acetonide has been widely employed to treat uveitis in the form of ocular injection. The purpose of this study is to investigate the potential of triamcinolone acetonide-loaded microemulsion as an ocular delivery system for treatment of uveitis. The pseudo-ternary phase diagrams were developed by aqueous titration method and various microemulsions were prepared using oleic acid as oil, Cremophor EL as surfactant and propylene glycol as co-surfactant. Among all prepared microemulsions, six formulations were found to be stable thus, they were selected for further characterization according to physicochemical parameters (droplet size, zeta potential, pH, viscosity and conductivity) and *in-vitro* release. The developed microemulsions exhibited acceptable physicochemical behaviour and sustained drug release. However, formulation F3, which is composed of oil: s_{mix}: water (15:35:50) in ratio (1:1) surfactant to co-surfactant, showed the optimal physicochemical characteristics (*i.e.* droplet size 211nm, PDI 0.2 and zeta potential -25mv). Hence, the superior biopharmaceutical behaviour of F3 was evaluated *in-vivo* in white New Zealand rabbits. The *in-vivo* performance of the selected formulation was compared to that of triamcinolone acetonide suspension in experimentally induced uveitis in rabbit model. Intra-ocular inflammation was evaluated by clinical examination for 7 days post-disease induction and was confirmed by histopathological examination at the end of study. White blood cells and protein content were measured in the aqueous humour. The results revealed that, uveitis is successfully induced in rabbit model. The selected microemulsion formulation showed a superior *in-vivo* performance in treatment of uveitis as compared to triamcinolone acetonide suspension. Thus, the developed sustained release triamcinolone acetonide microemulsion could be considered as a potential new topical treatment option that can provide better patient compliance in treatment of uveitis.

Keywords: Triamcinolone acetonide; Microemulsions; Ocular; Drug delivery.

PHS 129: Formulation and evaluation of doxycycline hydrochloride dental drug delivery systems for periodontal diseases

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Periodontal disease is one of the world's most prevalent chronic diseases. It is an inflammatory disease of the supporting tissue of teeth initiated by aerobic and anaerobic bacteria that results in destruction of the periodontal ligament with pocket formation as well as loss of alveolar bone and, ultimately, the tooth. The formed pocket provides an ideal environment for anaerobic pathogenic bacteria. Doxycycline is a broad spectrum tetracycline antibiotic effective against both gram positive and gram negative bacteria including periodontal pathogens. Moreover, it inhibits the activity of the destructive enzyme matrix metalloproteinase thus, enhancing bone regeneration after periodontal disease. So, Intra-pocket administration of doxycycline might eliminate bacteria present deep inside the pocket, maintaining effective drug concentration while minimizing the systemic adverse effects. The aim of this work was to prepare doxycycline-loaded chitosan microparticles (CS-MPs) as intra-pocket sustained release drug delivery system (DDS). CS-MPs were prepared using ionotropic gelation method with tripolyphosphate as a crosslinking agent. The optimum formulation showed entrapment efficiency and drug loading of about 63.57±2.85 % and 31.79± 1.41% w/w, respectively, with mean particle size of 58.19± 11.75 μm. *In vitro* release studies provided sustained release of doxycycline with about 70% released over 24 h. Scanning electron microscopy (SEM) confirmed the spherical nature and smooth surfaces of the microparticles produced. CS-MPs showed higher mucoadhesion with a binding efficiency of about 90% within few minutes. CS-MPs enhance the antibacterial activity of doxycycline as indicated by larger inhibition zone than doxycycline solution against *Escherichia coli* (ATCC 8739), *Staphylococcus aureus* (ATCC 6538p) and *Pseudomonas aeruginosa* (ATCC 9027). The microparticles were stable upon storage for 6 months with non-significant difference between refrigeration and room temperature. These results demonstrated that the CS-MPs can be a promising sustained-release local drug delivery system for periodontal diseases.

Keywords: Doxycycline; Dental; Periodontal; Drug delivery.

PHS 130: Tannic acid as a pH-responsive carrier for cationic antibiotics

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Tannic acid (TA) is plant-derived polyphenolic compound with a unique chemical structure. TA's 10 gallic acid units of 25 hydroxy groups (pK_a~6-8.5) impart a strong negative charge and enables TA to interact with a number of materials via hydrogen bonding and electrostatic interactions. Hence, TA has been successfully used as a carrier/excipient for preparations of nanoparticles, hydrogels and layer-by-layer films with different pharmaceutical applications. In our study, we investigated the efficiency of TA as a pH-responsive carrier for different cationic antimicrobials. Colistin sulfate (COL), gentamicin sulfate (GEN) and gatifloxacin (GAT) were chosen as three cationic antibiotics with variable chemical structures and molecular weights. TA/antibiotic complexes were formed via self-assembly in a pH-dependent manner; association pH, indicated via solution's transmittance at 500 nm, ranged from 4.3 to 5.65; a range where the antibiotics are charged, and TA forms electrostatic interactions and hydrogen bonds. Complexes' size ranged from several hundred nanometers to microns depending on antibiotic type and TA/antibiotic ratio, while the loading efficiency reached 36%. TA/antibiotic interaction was investigated vis spectroscopic tools and molecular docking, revealing a correlation between nature of interaction and complex stability. Optimal complexation requires a balance between drug's molecular weight and charge density to allow stable complex formation. TA/COL and TA/GEN complexes were of superior stability to TA/GAT, due to the latter's unfavorable charge density and distribution. Nevertheless, all complexes showed the intended pH-triggered drug release; at acidic pH, TA is protonated leading to complex dissociation. All loaded drug was recovered at pH of 4.5 similar to that of bacterial infections and corresponded to expected antibacterial effect. In summary, TA proved to be an optimal carrier for cationic antibiotics, resulting in complexes that can be rationally designed to achieve physical stability while delivering the drug in a favorable pH-dependent manner.

Keywords: Tannic acid; pH; Cationic; Antibody; Carrier; Antimicrobial.

PHS 131: Sulfobutylether-β-cyclodextrin/chitosan nanoparticles for enhancement of oral bioavailability of griseofulvin

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Purpose: Limited oral absorption of the antifungal griseofulvin (GF) is due to poor water solubility and high crystallinity. Consequently, failure to reach optimum plasma profile with increased hepatotoxicity on conventional oral administration. The main objective of this research is to formulate chitosan (CS) nanoparticles using Sulfobultylether-β-cyclodextrin (SBE-β-CD) as a polyanionic crosslinker. CS mucoadhesive properties and SBE-β-CD characteristics are predicted to enhance GF oral absorption.
Methods: GF and different molar concentrations of SBE-β-CD were dissolved separately in 90% methanol. SBE-β-CD was added to GF solution to obtain (1:0.5, 1:1, and 1:2) drug/ SBE-β-CD molar ratios and stirred at room temperature to dryness. Complex formation was monitored spectrophotometrically at λ_{max} 292 nm. Phase solubility analysis, differential scanning calorimetry (DSC) and x-ray diffraction were used to confirm complex stoichiometry. Different complex/CS weight ratios were used to fabricate drug-loaded nanoparticles and %Transmittance at 500 nm was measured. Encapsulation efficiency (%EE) was determined indirectly by quantifying the un-entrapped drug. Particle size and zeta potential were also determined.
Results: Phase solubility and absorbance spectra revealed the enhanced aqueous solubility of GF indicating 1:1 GF/SBE-β-CD stoichiometry to be the most favorable one. DSC and x-ray confirmed these results. %Transmittance significantly decreased from 90% to less than 20% at complex/CS weigh ratio of 1:3 and 2:1, respectively. Complex/CS of 2:1 had the smallest particle size of 327 ± 130 nm and +3.6 ± 1.42 mV zeta which is orally accepted. The EE of GF in CS nanoparticles reached 51% ± 2.7.
Conclusions: GF/SBE-β-CD complexation appears a promising strategy to significantly increase the encapsulation of this lipophilic drug in CS nanoparticles with improvement of oral absorption and hepatotoxicity reduction. Future studies will focus on comparing the oral bioavailability of drug-loaded nanoparticles to commercial formulations to explore clinical viability of this novel system for the treatment of tinea infections.

Keywords: β-cyclodextrin; Chitosan; Nanoparticles; Oral; Bioavailability; Griseofulvin.

PHS 132: High encapsulation efficiency of water-soluble metformin into alginate beads via hydrophobic ion-pairing approach

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Hydrophobic ion pairing (HIP) is a known approach for decreasing the solubility of different water-soluble drugs via complexation with charged molecules of opposite charge. Metformin hydrochloride (MET) is an oral antidiabetic drug of BCS class III (high water solubility/ low permeability) resulting in poor encapsulation efficiency into polymeric drug carriers. The significant positive charge of MET amine group (pK_a= 2.8 and 11.6) render it an optimal candidate for HIP formation with anionic ligands. In this study, ion pairs of MET with two different anionic polymers; sodium dodecyl sulphate (SDS; pK_a<2) and Carbopol 940 (CB; pK_a=6±0.5), were studied. By observing maximum solution transmittance (at 520 nm) per pH change, optimum complexation pH of 2.7 and 8 were chosen for formation of MET complexes with SDS (SDS/MET) and CB (CB/MET), respectively. Formed ion-pairs were found to be relatively stable with stability constants of 22 mM for SDS/MET and 30 mM for CB/MET. Additionally, HIP increased the lipophilicity of MET by 460 folds for SDS/MET and 10 folds for CB/MET as determined by partition coefficient measurements. Highest complexation efficiencies, 61.89% and 55.5%, were achieved at polymer/MET charge ratio of 1:1 and 2:1 for SDS/MET and CB/MET, respectively. Transmission electron microscopy and particle size analysis showed that complexes were nanosized assemblies. When loaded into calcium alginate beads, MET encapsulation efficiency reached 49% for SDS/MET and 99% for CB/MET, compared to just 14% for free MET. Importantly, incorporating free SDS or CB with MET (without prior complexation) for alginate beads formation resulted in a much lower encapsulation efficiency of 24 and 20%, respectively, indicating that HIP is essential for achieving high encapsulation efficiency of MET in calcium alginate beads.

Keywords: Encapsulation; Metformin; Alginate; Hydrophobic; Ion-pairing; Solubility.

PHS 133: Preparation of micellar curcumin-spray dried powder formulated in sublingual tablet for oral delivery

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Major challenge for clinical use of curcumin is related to its poor aqueous solubility which massively affects its bioavailability over oral use. The present study was carried out to overcome this problem. An amorphous micellar curcumin (MC)-spray dried powder (SDP) with self-assembled casein was prepared by addition of sucrose as protectant. The dry powder of curcumin loaded micelles were obtained by spray drying technique in the presence of sucrose as protectant. The MC-SDP in form of dry powder were further developed into sublingual tablets. The physical properties of preformed powder were characterized by differential thermal analysis (DTA), X-ray diffraction (XRD), and scanning electron microscope (SEM). Quantitative analysis in form of solutions were analyzed by reverse phase HPLC, UV–visible spectroscopy. The physical properties demonstrated that MC-SD were a bit shrinkage in terms of the particles morphology, regardless the presence of sucrose. Furthermore, melting transitions of curcumin in form of MC-SDP were broaden in all the sample mixtures, as observed in DTA thermogram. The XRD spectra showed that the sharp and very intense peaks of single curcumin crystals were no longer exist in all samples of MC-SDP, indicating that the mixtures were amorphous. Interestingly, further dissolution study of MC-SDP in form of sublingual tablets showed that the presence of sucrose enhanced the dissolution rate where > 80% of curcumin in form of MC-SDP were dissolved within 30 minutes. Therefore, MC-SDP formulated in sublingual tablets provide a more effective formulation for curcumin oral delivery.

Keywords: Curcumin; Casein; Micelles; Sucrose; Spray dry; Sublingual tablet.

PHS 134: Biodegradable multifunctional platform for potential treatment of vaginal candidiasis: In-vitro preparation, in-vivo assessment of antifungal efficacy in rats.

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Vaginal candidiasis is one of the most common gynecological condition affecting more than 130 million women worldwide. The main goal of this research was exploring an innovative approach for the preparation of mucoadhesive, biodegradable system that could be well tolerated by the patients for the vaginal delivery of CLT. Improving the solubility of CLT was first examined using different solubilzers namely; Cremophore® RH40, Inutec® SP1, HPMC, Solutol® HS15, Gelucire® 13, and Gelucire® 14, and revealed that Solutol® HS15 was found to be most effective in enhancing the solubility of CLT, about 200-fold increase in solubility compared to CLT aqueous solubility. Following this, CLT was further incorporated into lyophilized chitosan mucoadhesive vaginal wafers, and characterized regarding their weight variation, drug content, surface pH, swelling index, in-vitro drug release, solid sate characterization and porosity. Results revealed that vaginal wafer; CLT-CH-L1, composed of 1% low molecular weight chitosan showed the highest swelling index and suitable release profile, in addition to having spongy shaped highly porous structure, thus was selected for further studies. The DSC and XRD studies confirmed the amorphous nature of CLT in the prepared lyophilized vaginal wafer. The in-vivo antifungal activity of the vaginal wafer was compared to the market product showing superior antifungal effect in eradicating Candida infection in rats. The present study revealed the feasibility to produce an easily handled effective vaginal dosage form providing greater convenience and better patient compliance serving as a potential delivery system for management of vaginal candidiasis.

PHS 201: Application of logistic versus logarithmic functions for modeling non-linear evaporative light scattering detector responses in the HPLC quantitation of two non-chromophoric compounds of pharmaceutical interest

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Two accurate, sensitive and direct Isocratic Reversed Phase-HPLC methods, using Evaporative Light Scattering Detector, (ELSD), have been developed and fully validated for the detection and quantification of two non-chromophoric drugs; Thioctic acid (TA) and Sucralose (SUC). Chromatographic separation was achieved using C18 Agilant, 5 μm, 15 cm column for both compounds. Mobile phase composed of Acetonitrile: 0.1 M acetic acid (60: 40 v/v), adjusted at pH 2.5, with 0.6 mL/min flow rate and Acetonitrile: Water (70: 30 v/v) with 1 mL/min flow rate were used for TA and SUC respectively. Temperatures of drift tube, column, and spray chamber were set to be 40°C and 30°C respectively during the assay of both drugs. All varying chromatographic parameters were studied carefully. TA and SUC eluted at 4.81±0.02 min and 1.70±0.01 min, respectively. The obtained exponential responses were modeled using logarithmic and logistic transformations. Good Linearity ($r^2>0.99$) was achieved over the concentration ranges of 60-750 ppm and 8-750 ppm for TA and SUC respectively. The developed methods showed excellent precision and accuracy levels. All validation parameters were fulfilled according to the USP and ICH guidelines. Satisfactory percentages of recovery (>95%) resulted upon methods application for the assay of each of the two drugs in their pharmaceutical formulations. Comparative statistical study of applied log- versus logit- functions was performed, where both resulted in satisfactory linear calibration models. However, logistic regression acted more robust towards the higher deviating curvilinear ELSD responses.

Keywords: Weakly or non-absorbing compounds; Linear transformations; Thioctic acid; Sucralose; Logistic Regression.

PHS 202: Design and synthesis of estrone analogs for the treatment of hepatocellular carcinoma

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Purpose: Estrone analogs have begun to interest scientists due to their ability to affect a wide range of biological processes with fewer side effects of estrogen. Estrone is considered as bioisosters to cucurbitacin that have been isolated from family Cucurbitaceae. Cucurbitacins are known for a wide range of pharmacological purposes, especially for their anti-inflammatory and anti-cancer abilities. In the frame of this context, we thought to design and synthesize estrone analogs as EGFR inhibitors for treatment of hepatocellular carcinoma. The designed compounds having the cucurbitacin side chain at C17 separated by rigid moiety like alkynes or heterocycls as triazoles could represent closer analogs to cucurbitacin skeleton.
Materials and Methods: A virtual library of 110 suggested estrone analogues was assembled using OpenEye® molecular docking software and utilizing Omega and Fred applications. Estrone analogs which showed higher affinity to EGFR were synthesized. This study started by insertion of acetylene part to the ketonic C-17 to produce the corresponding proprgyl alcohol in stereoselective manner. The alkyne derivative underwent to different functional transformation as formation of triazole ring through Click chemistry applications.
Results and Conclusion: This approach was adopted in order to produce the design compounds (**1** and **2**). A series of novel analogs and their anti-proliferation activities against HCC will be presented.

Keywords: Hepatocellular Carcinoma; Estrone, EGFR; Docking.

PHS 203: Weighted repeated median as robust non-parametric regression method for simultaneous HPTLC determination of ternary mixture Saxagliptin hydrochloride, Dapagliflozin and Metformin hydrochloride in their pharmaceutical dosage form

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A simple HPTLC method has been developed and validated for the simultaneous determination of the ternary mixture Saxagliptin Hydrochloride (SAX), Dapagliflozin (DAP) and Metformin Hydrochloride (MET) in synthetic mixtures and tablets in a challenging ratio of 1: 2: 200 (SAX: DAP: MET). The drugs were separated followed by densitometric measurements of their spots at 210 nm. The separation was carried out on Merck HPTLC aluminium sheets of silica gel 60 F254 using Chloroform: methanol: acetic acid (8: 2: 0.5 v/v/v) as the mobile phase. Linear calibration graphs of peak area values were obtained versus concentrations in the range of 0.2-1.2, 0.1-1.1 and 15-90 µg/band for SAX, DAP and MET, respectively. Weighted Repeated Median, WRM, as robust non-parametric regression method as well as Ordinary Least Squares, OLS, were both applied to the obtained calibration data of the three drugs. By comparison, the WRM smoother has significantly improved all regression parameters; correlation coefficients, intercept and slope. WRM adapts to linear trends, unaffected by outliers promoting the simultaneous determination of SAX/DAP/MET in the high concentration ratio 1: 2: 200 and even extending to further higher ratios. According to ICH guidelines, different validation parameters were verified for the proposed method and presented.

Keywords: HPTLC; Saxagliptin Hydrochloride; Dapagliflozin; Metformin Hydrochloride; Weighted Repeated Median.

PHS 204: A newly-developed LC-MS method to study possible pharmacokinetic interaction between Linaglptin and Tadalafil upon co-administration in healthy male volunteers

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Objective: This work aims to assess the potential pharmacokinetic interaction between linagliptin (LNG) and tadalafil (TDL) in healthy Egyptian males using a newly developed LC-MS method.
Methodology: Chromatographic separation was achieved on a C18 column. Liquid-liquid extraction from human plasma followed by gradient elution was performed over 8 minutes at flow rate 1 mL/min. Mass spectrometric detection was set at positive ESI and APCI for the determination of LNG, TDL and IS. The assay was validated according to FDA guidelines with CV% and % error of the mean ≤ 20% over a concentration range of 1-1000 ng/mL and 2-1000 ng/mL for LNG and TDL, respectively. A Phase IV, open-label, cross-over drug interaction study enrolled 10 healthy volunteers. Fasting volunteers were administered 20 mg TDL. Serial blood samples were collected up to 96 h. A wash out period of 2 weeks was allowed, multiple oral dosing of 5 mg/day LNG for 13 days. On day 13, fasting volunteers were co-administered 20 mg TDL along their daily 5 mg LNG. Serial blood samples were collected for 12 h post first LNG dose, the morning of each new LNG dose and up to 96 h post co-administration. Pharmacodynamic parameters were measured along the study.
Results: LNG and TDL pharmacokinetics in Egyptian population were similar to reported ones. LNG and TDL single doses did not affect QTc interval. Smoking did not alter the PK or PD of LNG and TDL when administered separately or upon co-administration. Co-administration of LNG with TDL resulted in longer Tmax, ~2-fold decreased CL/F, ~3-fold decreased Vd/F accompanied by ~2.5-fold increased Cmax and AUC of TDL and increased muscle pain and a trend of prolonged QTc interval.
Conclusion: Co-administration of LNG and TDL altered the later PK and increased its side effects which warrant proper monitoring and/or TDL dose adjustment.

Keywords: Diabetes; Hyperglycemia; Gliptins; Liquid Chromatography; Mass spectrometry; Pharmacokinetics; Human plasma.

PHS 205: The combination of derivative technique with emission and synchronous scanning spectrofluorimetry for the spectral resolution of codeine in its mixtures with ibuprofen and phenylephrine

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Purpose: The work presents three simple spectrofluorimetric methods by coupling the derivative technique with emission spectrofluorimetry, constant energy synchronous spectrofluorimetry and constant-wavelength synchronous spectrofluorimetry. These methods were applied for the spectral resolution of overlapped emission spectra of narcotic drug in its mixtures.
Materials: The proposed methods enable the selective and the sensitive analysis of narcotic drug, Codeine (COD), in its binary mixtures with NSAID, Ibuprofen (IBU), as mixture 1 and decongestant drug, Phenylephrine (PHE), as mixture 2 without separation step. Acetate buffer, pH 5, was used as the diluting solvent.
Results: Low values of limit of quantitation (LOQ) were achieved for COD, IBU and PE (64, 512 and 87 ng/mL, respectively). The derivative emission spectrofluorimetry was applied using λex= 236 nm and 275 nm for mixtures 1 and 2, respectively. The constant-energy synchronous spectrofluorimetry was applied using wave number interval of −7000 cm^{-1} analyzing the two mixtures while constant wavelength synchronous spectrofluorimetry was done using $\Delta\lambda$ = 100 nm and 60 nm for mixtures 1 and 2, respectively.
Conclusions: The proposed spectrofluorimetric methods are superior to the previously reported chromatographic methods in being eco-friendly, fast, simple, less time and solvent consumption. ICH guidelines for analytical method validation were followed. The one-way ANOVA test showed no significant statistical difference among the proposed methods.

Keywords: Synchronous scanning spectrofluorimetry; Derivative technique with emission spectrofluorimetry; Codeine binary mixtures; Spectral resolution.

PHS 206: Structure-based design and synthesis of novel hydroxamates as dual targeting inhibitors

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The concept of designing drugs capable of inhibiting multiple targets, or what is known as polypharmacology, emerged as an alternative to the conventional one-drug/one-target approach [1-2]. In the field of epigenetics, this principle can be very beneficial against cancer to overcome the resistance problem. Several attempts to design dual acting inhibitors against multiple epigenetic targets [3-7] or epigenetic and metabolic targets [8-9] were previously reported.
In the present study we designed histone deacetylase (HDAC) inhibitors coupled to different bromodomain-inhibiting scaffolds. Although this approach was previously reported [3-5], we are the first to target selective HDAC isoforms in addition to a non-BET bromodomain. General idea of the developed dual inhibitors is illustrated in the following figure.

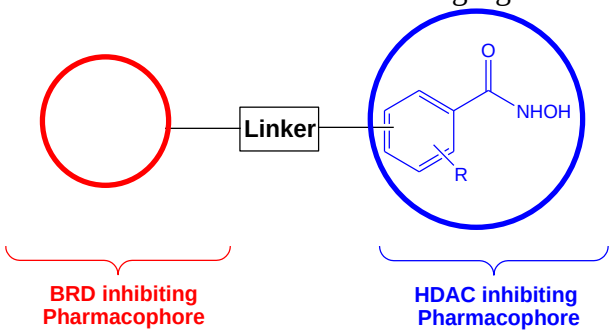

Figure 1. Design of the dual inhibitors

Among the synthesized dual inhibitors, two compounds showed nanomolar activity against both targets. Additionally, we are currently testing the compounds against selected cancer cell lines.

Keywords: Polypharmacology; Bromodomains; Histone deacetylase; Hydroxamates.
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PHS 207: HPLC-DAD method for simultaneous determination of nine penicillin antibiotics: Application to cross contamination studies in non-penicillin facility and cleaning validation of pharmaceutical equipment and its surrounding environment

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Penicillins may cause potentially life-threatening allergic reactions. Thus, possible cross contamination of Penicillins in food or drugs can put people at risk. Therefore, it is important to obtain safe medicine and prevent occupational exposure to penicillin via inhalation by testing non-penicillin drug products for penicillin cross contamination and monitoring facility surface cleaning and air pollution in penicillin facility. This work describes a new sensitive and rapid HPLC-DAD method for simultaneous determination of multiple Penicillin antibiotics namely amoxicillin (AMOX), ampicillin (AMP), clavulanic acid (CLV), floxacillin (FLU), penicillin G (PEN G), piperacillin (PIPER), sultamicillin (SULT), sulbactam (SULB) and tazobactam (TAZO) and its application in studying cross contamination drug products in of non-Penicillin facility and in cleaning validation of pharmaceutical equipment and its surrounding environment. The developed method used reversed phase C18 column with UV detection at 220 nm and a mobile phase composed of methanol: 0.05M phosphate buffer operating at pH 4.0 delivered in a gradient elution mode at a flow rate of 1.5 mL min^{-1}. The proposed HPLC method was statistically validated with respect to linearity, ranges, precision, accuracy, selectivity and robustness to satisfy International Conference on Harmonization regulatory requirements. The proposed method was successfully applied to the analysis of trace amounts of Penicillin antibiotics in different non-penicillin products in their final pharmaceutical forms including tablets, syrup, capsules, cream, respiratory solution and capsule inhaler. In addition, the developed method has been applied in cleaning validation of equipment's surface, walls and floors of penicillin facility and in pharmaceutical dust and waste water. The proposed method can be recommended for the routine quality control of the studied drugs either in cross contamination with non-penicillin facility or in monitoring facility surface cleaning and air pollution in penicillin facility with high accuracy and precision.

Keywords: Penicillin; Cross contamination; Cleaning validation; Air pollution.

PHS 208: Development and validation of UPLC-MS/MS method for the simultaneous quantification of dasabuvir, tamoxifen and its active metabolite 4-hydroxytamoxifen in Wistar rat plasma: Application to pharmacokinetic interaction study

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Hepatitis C virus (HCV) is considered as the main cause of chronic hepatitis and probably liver cirrhosis. Dasabuvir (DSV) is an example of direct-acting antiviral agents (DAAs) that have proven efficiency in the management of HCV. The association of estrogen receptors (ER) and HCV replication suggested the anti-viral activity of the anti-estrogen drug tamoxifen (TAM) suggesting the possible use of the synergistic effect when combining DSV and TAM for blocking the replication of HCV. However, being substrates and inhibitors of efflux transporters (TAM inhibits P-gp, DSV inhibits P-gp and BCRP), there is a possibility for a pharmacokinetic (PK) drug-drug interaction (DDIs). In this work, a new UPLC-MS/MS method was developed and validated for the simultaneous determination of TAM, its active metabolite 4-hydroxy tamoxifen (TOH), and DSV in rat plasma. The method was successfully applied to investigate the PK interaction between DSV and TAM/TOH following the co-administration of DSV and TAM to Wistar rats. Sample preparation was performed using protein precipitation followed by a solid-phase extraction. Chromatographic analysis was performed on Waters BEH^{TM} C18 column using a mobile phase consisting of a mixture of acetonitrile/water containing 0.1% formic acid (80: 20, v/v). The method allowed the determination of concentration ranges 20-1000, 0.1-500, 0.5-500 ng/mL for DSV, TAM, and TOH, respectively. Unexpectedly, results revealed the absence of PK interactions between DSV and TAM/TOH, compared with their single administration, suggesting the safety of co-administering DSV/TAM as an anti-viral combination without the need of dosage adjustment.

Keywords: Hepatitis C virus; Dasabuvir; Tamoxifen; 4-hydroxy tamoxifen; Pharmacokinetic interaction; UPLC-MS/MS.

PHS 209: HPTLC analysis of eye drops formula containing Ketorolac ternary mixture used after Eye Surgeries

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Validated and selective high-performance thin-layer chromatography (HPTLC) method was developed for the determination of ketorolac tromethamine (KTC), phenylephrine hydrochloride (PHE), and chlorpheniramine maleate (CPM) in bulk drug and in combined dosage form. The proposed method depends on using HPTLC for separation of the drugs followed by densitometric measurements of their spots at 261 nm. The separation was carried out on Merck HPTLC aluminum sheets of silica gel 60 F254 using chloroform–methanol–ammonia (7.75:2.25:0.1, v/v) as mobile phase. Linear regression lines were obtained over the concentration ranges 0.12–0.50, 0.075–0.27, and 0.09–0.27 μg band^{-1} for KTC, PHE, and CPM, respectively, with correlation coefficients higher than 0.999. The method was successfully applied to the analysis of the three drugs in their synthetic mixtures and in their dosage form. The mean percentage recoveries were in the range of 98–102% with percentage relative standard deviation values less than 2%. The method was validated according to ICH guidelines and showed good performances in terms of linearity, precision, accuracy, sensitivity, and stability.
Keywords: HPTLC; Eye Drops, Ketorolac; Phenylephrine; Chlorpheniramine.

PHS 210: High throughput HPLC monitoring of ciprofloxacin and tinidazole levels in human plasma: Application to pharmacokinetics

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This work describes an in-vivo assay of Ciprofloxacin (CIP) and Tinidazole (TIN) binary mixture in human plasma and its pharmacokinetic application using a validated HPLC-DAD method with Ornidazole (ORI) as an internal standard. The method was validated according to FDA regulations for analysis in biological fluids. The chromatographic separation was performed using an Agilent C18 (250 x 4.6 mm) column with an isocratic elution using mobile phase composed of 2 % acetic acid solution and acetonitrile (85: 15, v/v). The drugs were resolved with retention times of 6.55, 7.91 and 11.07 min for CIP, TIN and ORI, respectively upon detection at 318 nm. The method was sensitive and selective to analyze simultaneously the two drugs with the internal standard in presence of plasma interferences and drug metabolites, at a single wavelength (318 nm). No extraction procedure was involved and only protein precipitation was required for analysis of the two drugs in human plasma. The proposed method was applied to obtain the pharmacokinetic data of the two drugs following oral administration of single oral dose of 500 mg CIP and 600 mg TIN to six healthy male volunteers. The concentrations of the drugs in plasma were calculated up to 12 or 72 h post dosing for CIP and TIN, respectively, and were in good accordance with the reported values following their individual administration confirming that their co-administration did not affect their individual pharmacokinetics.

Keywords: HPLC; High throughput; Ciprofloxacin; Tinidazole; Pharmacokinetics.

PHS 211: Development and validation of HPLC-DAD method for simultaneous determination of six antimicrobial drugs and three proton pump inhibitors commonly used in management of *Helicobacter pylori* infection. Application to spiked simulated intestinal fluid samples

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This part deals with the development, validation and application of an HPLC-DAD method for the determination of nine antimicrobials and proton pump inhibitors, namely, amoxicillin (AMX), doxycycline (DOX), furazolidone (FRZ), lansoprazole (LNS), levofloxacin (LVF), metronidazole (MTZ), omeprazole (OMZ), pantoprazole (PNZ) and tinidazole (TNZ). The nine drugs are used for treatment of Helicobacter Pylori infection. Effective chromatographic separation between the nine drugs was achieved using Agilent Zorbax Eclipse plus-C18 analytical column (250 x 4.6 mm, 5 µm particle size) and a mobile phase composed phosphate buffer pH 5 and acetonitrile in gradient elution program. The gradient elution started with buffer and acetonitrile ratio 90:10 then it was changed in 15 min to reach 40:60 by volume. The mobile phase was pumped at a flow rate of 1 mL/min. Quantification of the analytes was based on measuring peak areas of AMX at 230 nm, LVF, LNS and PNZ at 290 nm, OMZ at 300 nm, MTZ and TNZ at 320 nm, and DOX and FRZ at 360 nm. The separated compounds eluted at retention times 5.68, 6.43, 7.82, 8.84, 9.42, 10.75, 12.82, 13.74 and 14.90 min for AMX, MTZ, LVF, TNZ, DOX, FRZ, OMZ, PNZ and LNS respectively. Analytical performance of the proposed HPLC procedure was statistically validated with respect to linearity, ranges, precision, accuracy, robustness, detection and quantification limits. The linear dynamic ranges were 5-100, 5-50, 2-40, 10-100, 10-100, 5-50, 2.5-30, 3-30 and 2-30 µg/mL for AMX, MTZ, LVF, TNZ, DOX, FRZ, OMZ, PNZ and LNS, respectively with correlation coefficients > 0.9993. The validated method was successfully applied to the analysis of several laboratory-prepared binary dosage forms as well as analysis of several ternary mixtures in spiked simulated intestinal fluid.

Keywords: HPLC; DAD; Antimicrobial; Helicobacter pylori; Intestinal.

PHS 212: Novel spirooxindoles as apoptotic anti-proliferative agents: One-pot three-component synthesis and *in vitro* biological evaluation

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In our endeavor towards the development of novel anticancer agents[1,2], herein we report a one-pot three-component synthesis of novel spirooxindoles series 4a-s. The newly synthesized spirooxindoles were evaluated of their potential anti-proliferative activity towards hepatocellular carcinoma HepG2 cell line. Spirooxindoles 6a, 6e and 6i emerged as the most potent analogues towards HepG2 cells with IC_{50} = 6.90, 8.40 and 6.30 µM, respectively. Moreover, compounds 4q-s were selected by USA National Cancer Institute (NCI) Developmental Therapeutic Program to be tested *in vitro* for their anticancer activity. Single crystal X-ray crystallographic study revealed that the chiral center of compound 4r has *S* configuration.

Keywords: Spirooxindoles; Apoptotic; Anti-proliferative; X-ray; Hepatocellular carcinoma.

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PHS 213: Development and validation of stability indicating chromatographic methods for determination of the anticoagulant rivaroxaban: application to degradation, kinetics study, assay of dosage form and analysis of spiked urine

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Two, simple and reproducible stability-indicating assay methods were developed for determination of rivaroxaban (RIV) using micellar electrokinetic capillary chromatography (MEKC-DAD) and ultra-performance liquid chromatography (UPLC-DAD). Both methods are versatile as they could be used in several applications; forced degradation studies, kinetics studies, analysis of urine samples and assay of dosage forms. Method I involved the use of micellar electrokinetic capillary chromatography (MEKC). Separation was performed in a deactivated fused silica capillary (50 cm effective length × 50 μm internal diameter). The background electrolyte was 50 mM borate buffer (pH 9.2) containing 50 mM sodium dodecyl sulphate. Injections were performed using hydrodynamic mode under pressure of 50 mbar for 17 sec. The applied voltage was 30 kV. Xipamide (XIP) was used as an internal standard (IS). The diode array detector (DAD) was set at 248 nm for measurement of RIV and 232 nm for XIP (IS). The proposed method allowed separation of the drug and IS at the migration times of 3.57 and 6.93 min for XIP and RIV, respectively. The described method was linear over the range of 2 –100 μg/mL with correlation coefficient 0.9995. Method II was reversed phase UPLC with diode array detector method, which was developed using Zorbax SB-C8 column (2.1 × 100 mm, 1.8 μm particle size) with gradient elution of mobile phase composed of 0.1% phosphoric acid and acetonitrile at a flow rate 0.4 mL/min. The diode array detector (DAD) was set at 248 nm for measurement of RIV. RIV peak eluted at 2.45 min. The resulted linearity ranges were 0.25 – 50 μg/mL for RIV standard and 0.25 – 3 μg/mL in spiked urine using linezolid (LIN) as an internal standard with correlation coefficients were not less than 0.9995. Both MEKC and UPLC-DAD methods proved to be stability indicating by resolving RIV form its forced degradation products after subjecting RIV to stress conditions of hydrolysis, oxidation, photolysis and thermal degradation. Furthermore, the proposed UPLC method was applied to monitor RIV acidic and basic degradation kinetics. Analytical performance of both methods was validated according to International Conference on Harmonization (ICH) guidelines with respect to system suitability, linearity, ranges, precision, accuracy, specificity, robustness, detection and quantification limits. The proposed MEKC and UPLC methods were successfully applied for estimation of RIV in tablet dosage form and in spiked urine samples.

Keywords: Stability; Anticoagulant; Rivaroxaban; Kinetics; Spiked urine.

PHS 214: Design and synthesis of some new benzofuran derivatives as potential anticancer agents: Apoptosis inducers and dual inhibitors of cyclooxygenase-2 and 15-lipoxygenase

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Cancer is a life-threatening, multifactorial and multi-mechanistic disease. Particularly, colorectal cancer (CRC) is the third most common cancer worldwide. Inflammation and oxidative stress comprise highly interrelated biochemical processes directly implicated in cancer development, progression and systemic spread. Therefore, we present herein the design and synthesis of some new hybrid molecules comprising benzofuran scaffold and the bioactive various substituted pyridine-3-carbonitriles, thienopyridines and pyridothienopyrimidines as potential multi-target anticancer agents against colorectal cancer. Furthermore, anti-inflammatory and antioxidant potentials were also evaluated, being key players in carcinogenesis.

Generally, results showed that twelve compounds were more active than the standard 5-FU against colon cancer cell lines (Caco-2 and HCT-116). Flow cytometric analysis of cell death for the most active two compounds using annexin V/propidium iodide revealed that they induced apoptosis via caspase 3/7 activation in treated Caco-2 and HCT-116 cell lines. In addition, they were more potent inhibitors of COX-2 and 15-LOX enzymes than celecoxib, zileuton and quercetin, respectively. They showed significant anti-colitis activity, being more potent than sulfasalazine. They inhibited NO and TNF-α production in DSS-stimulated rat colonic leukocytes. Collectively, they elicited higher antioxidant activity than the reference in DPPH, hydroxyl radical, superoxide anion and ferrous reducing power assays. Docking experiments on COX-2 and 15-LOX enzymes underlined favorable binding patterns. Overall, this series of compounds represents promising leads and/or hits that could supplement the current anticancer drug development pipeline.

Keywords: Benzofuran; Cyclooxygenase-2; 15-Lipoxygenase; Apoptosis.

PHS 215: Multi-target inhibition of cyclooxygenase-2, 15-lipoxygenase and carbonic anhydrase by 1,2,3-triazoles prepared via azide-enolate cycloaddition

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Diverse inflammatory mediators and pathways have been targeted over the years in search for potent anti-inflammatories with minimal side effects. Nonetheless, safe and effective management of inflammatory conditions still poses a challenge to clinical practice. Hence, we present herein the design and synthesis of a new series of 1,4,5-trisubstituted 1,2,3-triazoles and evaluation of their inhibitory activities against COX-2, 15-LOX and carbonic anhydrases (CA) I, II, IX and XII isoforms. Interestingly, literature survey revealed that simultaneous targeting of the three targets (COX-2, 15-LOX and CA) by a single molecule for management of inflammation is still untapped. *In vitro* assay results revealed that ten compounds showed significant COX-2 inhibitory potential with two-digit nanomolar IC_{50} values (42-91 nM, compared to 45 nM for celecoxib). They also displayed relatively weak COX-1 inhibitory activities (8.4-13.6 µM). Their selectivity indices (COX-1/2) were in the range of 92.3-323.8, compared to 326.7 for celecoxib. Moreover, eleven compounds displayed potent 15-LOX inhibitory activities with one-digit micromolar IC_{50} values (1.23-2.87 µM, compared to 3.34 µM for quercetin). The carbonic anhydrase inhibition assay showed that four sulfonamide-bearing triazole derivatives inhibited three hCA isoforms; hCA I, hCA II and hCA XII. The K_I ranges were 5.7–73 nM for hCA I, 6.2–32.9 nM for hCA II, and 6.3–85.9 nM for hCA XII, in comparison to 250, 12.1 and 5.7, respectively for acetazolamide. The *in vivo* anti-inflammatory activity together with the ulcerogenic profile of the most active compounds is currently underway. Docking of the most active compounds into COX-2, 15-LOX and CAs active sites showed similar binding pattern to those of the co-crystallized ligands. Taken together, these results suggest that this series could serve as promising platforms for the development of multi-target anti-inflammatory agents.

Keywords: 1,2,3-Triazoles; Cyclooxygenase-2; 15-Lipoxygenase; Carbonic Anhydrase.

PHS 216: Design, synthesis and biological evaluation of some heterocyclic compounds as β-lactamase inhibitors

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β-lactam antibiotics are valuable therapeutic agents for the treatment of various bacterial infections. However, the emergence of clinical isolates exhibiting resistance to these antibiotics is of great concern. One approach we have investigated was to use small molecules to inhibit Metallo-β-lactamases (MBLs) and re-sensitize resistant strains to the effect of β-lactams. Another approach was to use liposomal formulation which promotes effective interaction between bacteria and drug and increases the lifetime of the entrapped antibiotic. A series of sulfonyl hydrazones of pyrazole and quinoline nuclei have been designed, synthesized and examined for their inhibitory activity toward IMP-1, NDM-1 and AIM-1 MBLs. In addition, the liposomal formulation of meropenem and the most active inhibitor 4q have been developed. The synthesized compounds displayed broad-spectrum inhibitory activity producing more than 95% improvement of meropenem and cephalexin activities.

Keywords: Metallo-β-lactamase; Bacterial resistance; Sulfonyl hydrazones; Liposomal formulation.

PHS 217: Eco-friendly spectrophotometric estimation of the binary mixture Etoricoxib and Thiocolchicoside in their combined pharmaceutical dosage forms

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Two Green, economic and specific spectrophotometric methods have been developed for the simultaneous determination of the binary mixture of Etoricoxib (ETO) and Thiocolchicoside (THI). The first method is based on a first-order derivative ratio spectrophotometry (1DD, Dλ= 2 nm) where ETO and THI were quantified at 243-267 nm (peak-to-peak) and 247 nm for ETO and THI, respectively. The second method depends on calculating the difference in absorbance ratio (RD spectrophotometry) between 270 and 252 nm or 258 and 233 nm for ETO and THI, respectively. Employing distilled water as solvent classifies both methods as potentially environment-friendly ones. The proposed methods were successfully validated as per ICH guidelines. The calibration plots were linear between 5–40 and 2.5–30 μg/mL for ETO and THI, respectively, allowing reliable estimation of both drugs within their tablet ratio. The simplicity, rapidity and accuracy of the proposed methods suggest their application in quality control analysis of ETO and THI raw materials, synthetic mixtures and combined tablets.

Keywords: Etoricoxib; Thiocolchicoside; Derivative ratio spectrophotometry; Ratio difference spectrophotometry.

PHS 218: Assessment and validation of novel stability-indicating chromatographic methods for the estimation of metformin and ertugliflozin without interference with the coformer pidolic acid

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Two novel, sensitive, selective and precise stability indicating chromatographic methods were adopted, optimized, and validated for the simultaneous quantitative determination of ertugliflozin (ERT) and metformin hydrochloride (MET) in their pure and tablet forms as well as in the presence of their forced degradation products. The first method is reversed phase high performance liquid chromatography (HPLC) using a C18 column and a mixture of phosphate buffer and acetonitrile as mobile phase eluted in a gradient mode and chromatograms were monitored by diode array detector at 210 nm. The second method is high performance thin layer chromatography (HPTLC) using silica gel 60 F254 HPTLC plates together with a developing system consisting of a mixture of chloroform, methanol, water and acetic acid then spots were scanned densitometrically at 240 nm. The studied drugs were subjected to stress alkaline, acidic, oxidative, thermal, and photo-degradation and were well separated from the degradation products upon applying the two methods. Different parameters affecting the suggested methods were optimized for maximum separation of the cited drugs from each other, from the co-crystallized pidolic acid as well as from their forced degradation products. The proposed methods were validated in compliance with the ICH guidelines in terms of linearity, ranges, precision, accuracy and selectivity. Good linearity of the methods is expressed by the values of regression coefficients (r) not less than 0.9995. The proposed methods were successfully applied for the quantification of ERT and MET in their commercial tablets.

Keywords: Ertugliflozin; Metformin; HPLC; HPTLC; Stability-indicating; pidolic acid.

PHS 219: Colorimetric determination of maduramicin ammonium using three charge transfer complexation reactions

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Direct spectrophotometric determination of Maduramicin ammonium (MAD) represents an analytical challenge since it is a weak UV-absorbing and lacking a strong chromophore. The present study illustrates the development of three simple, rapid and sensitive colorimetric methods for the routine quality control analysis of MAD based on the formation of colored charge transfer complexes with three electron acceptors namely p-chloranilic acid (p-CA), 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) and picric acid (PA). This work represents the first spectrophotometric determination of MAD since no direct spectrophotometric or colorimetric determination of MAD is available in the literature. The proposed methods were validated in terms of linearity, precision, accuracy and robustness and were effectively applied for the assay of MAD in its pure form and powder dosage form. MAD was effectively determined over concentration ranges of 100 – 1000, 25 – 250 and 30 – 150 µg/mL using P-CA, DDQ and PA, respectively with excellent linearity as showed by the values of correlation coefficients not less than 0.9992.

Keywords: Maduramicin ammonium; Colorimetric determination; Charge transfer complexation; Powder dosage form

PHS 220: Synthesis and *in vitro* biological evaluation of novel 2-indolinone-based derivatives as apoptotic anti-proliferative agents

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In continuation of our endeavor with respect to the development of potent and effective 2-indolinone-based anticancer agents, herein we report the synthesis of two novel series of 2-indolinones **4a-o** and **5a-e**. The *in vitro* anti-proliferative potential of the synthesized compounds **4a-o** and **5a-e** was examined against HT-29 (colon), ZR-75 (breast) and A-549 (lung) human cancer cell lines. Compounds **5b**, **5d** and **5e** are the most active congeners against the tested cancer cell lines with average IC_{50} values of 4.77, 3.39 and 2.37 µM, respectively, as compared with the reference isatin-based drug, sunitinib, which exhibited an average IC_{50} value of 8.11 µM. Compound **5e** was selected for further pharmacological evaluation in order to get insight into its possible mechanism of action. It increased caspase 3/7 activity 2.4- and 1.85-fold between 4 and 8 h of treatment, respectively, at 10 µM concentration and it caused a decrease in the percentage of cells in the G1 phase of the cell cycle with corresponding increase in the S-phase. In addition, compound **5e** increased phosphorylated tyrosine (P-Tyr) levels nearly twofold with an apparent IC_{50} value of 3.8 µM.

Keywords: 2-indolinone; Apoptotic; Antiproliferative; Caspase; Synthesis.

PHS 221: Development and validation of stability indicating HPLC and HPTLC methods for the determination of Lubiprostone

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In the present study two accurate, sensitive and selective stability-indicating methods have been established and validated for analysis of lubiprostone (LUB) in pure and tablet forms as well as in presence of its acidic and alkaline degradation products. The first (I) is a reverse high-performance liquid chromatographic method employing Agilent C18 column (4.6 x 250 mm) with gradient elution of mobile phase composed of acetonitrile and disodium hydrogen orthophosphate buffer (0.05 M, pH adjusted to 2.5 with orthophosphoric acid) at a flow rate of 2mL/min with diode array detector at 256 nm. The second (II) is High-Performance Thin-Layer Chromatographic method using Merck HPTLC plates precoated with 60F254 silica gel on aluminium sheet as the stationary phase developed with chloroform: methanol: ammonia (9.6:0.4:0.03, v/v) as mobile phase. The separated bands were scanned at 257nm. LUB was estimated over concentration ranges of 0.55-16 µg/mL and 0.15-3 µg/mL for methods I and II respectively with excellent linearity as demonstrated by the values of correlation coefficient not less than 0.9998. The proposed methods afforded clear separation of LUB from its degradation products as well as precise and accurate determination of the drug in pure and tablet forms without interference from any of the existing excipients. The proposed analytical procedures were validated as per the International Conference on Harmonization (ICH) guidelines in terms of linearity, limits of detection and quantitation, accuracy, precision, specificity and robustness.

Keywords: Stability-indicating; Lubiprostone; High-performance liquid chromatography; HPTLC.

PHS 222: Synthesis of some novel heterocyclic compounds linked to or fused with phenolic or quinonoid moieties for potential biological activities

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It has been established that quinones and hydroquinones constitute an important scaffold existing in many biologically active compounds. Encouraged by the above-mentioned facts and as a continuation of the research program made in this lab, a number of compounds containing quinone and hydroquinone functions was synthesized. The structures of new compounds were verified by elemental microanalyses, I.R., ^{1}H-NMR as well as studying the ^{13}C-NMR spectra and M.S. for some representative examples. Twenty-nine of the newly prepared derivatives were selected by the NCI and were initially tested at a single high dose (10 μM) in the full NCI 60 cell panel. Four of the screened compounds satisfied the threshold inhibition criteria and passed forwards for evaluation in the full panel five-dose in vitro antitumor screen.

Moreover, Twenty-seven compounds were subjected to in vitro COX-1 and COX-2 isoenzymes inhibition assay. In general, all the tested compounds showed relatively higher selectivity towards COX-2 than COX-1. It was found that four compounds XII, XIV, XLIV and XLVI displayed high selectivity indices and showed potency comparable to the anti-inflammatory drug celecoxib. The tested compounds that exhibited in vitro selectivity indices higher or nearly equivalent to reference drugs towards COX-2 enzyme were further evaluated for their ability to inhibit 15-LOX. The results revealed that all the compounds subjected to lipoxygenase (LOX) inhibition assay inhibited LOX when compared to the reference drug quercetin.

Keywords: Heterocyclic; Phenolic; Quinonoid; COX-1; COX-2; Lipoxygenase.

PHS 223: New hybrid molecules tethering pyridine to quinoline as anticancer PIM-1\2 Kinase inhibitors: Design, synthesis, biological evaluation and docking study

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New molecular hybrids combining pyridine with quinoline were designed and synthesized as anticancer PIM-1/2 kinase inhibitors. The target compounds were evaluated for their in vitro anticancer activity against myeloid leukemia (NFS-60), liver cancer (HepG-2), prostate cancer (PC-3) and Colon cancer (Caco-2) cell lines. Three compounds showed potent anticancer activity against all cell lines with low toxicity against normal human lung fibroblast Wi-38 cell line. Furthermore, these compounds showed potent PIM-1 kinase inhibitory activity and moderate PIM-2 kinase inhibitory activity. In addition, molecular docking study was conducted to reveal the probable interaction with the active site of both PIM-1 and PIM-2 kinases.

Keywords: Pyridine; Anticancer; PIM-1 kinase; PIM-2 kinase.

PHS 224: Pharmacokinetics study of sofosbuvir and ledipasvir in presence of some complementary and alternative medications in healthy rats using LC-MS

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Hepatitis C virus (HCV) is endemic in Egypt with the highest prevalence rate in the world. Sofosbuvir (SOFO), Ledipasvir (LED) Mixture has shown high efficacy against different HCV genotypes.

Many people use complementary and alternative medications (CAM) beside their antiviral regimens. Unfortunately, some CAM have been shown to have the potential to interact with antiviral drugs and cause several adverse events.

Therefore, the aim of this work is to evaluate the effect of some selected CAM on the pharmacokinetic parameters of the mentioned antiviral drugs (AVD), through monitoring their levels in rats' plasma when co-administered with different CAM. Due to the senitivity, selectivity and higher throughput of LC MS, it was used as the analytical tool in this study. Determination of SOFO, GS331007 (SOFO metabolite) and LED in SIM mode was done at m/z $[M+H]^+$ 530, 261 and 890, respectively. Sildenafil was used as internal standard at m/z $[M+H]^+$ 475.

The chromatographic separation was performed using C18 ACE Excel 2 C100 column (100 × 3 mm, 2 μm). Gradient elution was optimized using mobile phase consisted of 0.1% formic acid in water: acetonitrile: methanol pumped at a flow rate of 0.4 mL min^{-1} and injection volume was 10 μL. LC-MS detection was done by SIM mode at positive ionization of both analytes and IS. Bioanalytical method validation as per FDA guidelines was carried out where the proposed method revealed linearity over the concentration range of 5-500, 20-2000, 20-2000 ng mL^{-1} for LED, SOFO and GS331007, respectively.

The CAM could affect antiviral drugs at absorption, distribution, metabolism or excretion. Therefore, this study compares the pharmacokinetic parameters of a healthy rats group receiving AVD alone with one receiving AVD and CAM.

Keywords: Complementary and iternative medications; Sofosbuvir; Ledipasvir; GS331007; LC MS; Rat plasma; Pharmacokinetic parameters.

PHS 225: SAR of pyrazolylpyrazoline analogues targeting *Toxoplasma gondii* calcium-dependent protein kinase *1 (Tg*CDPK1)

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Calcium-dependent protein kinase-1 (CDPK1) from *Toxoplasma gondii* (TgCDPK1) has become captivating target for discovering selective inhibitors to combat toxoplasmosis. Toxoplasmosis infects nearly one third of the world's human population and considered to be one of the leading causes of mortality among adults especially in immunocompromised patients [1,2].

Purpose: It has been found that the initial treatment of toxoplasmosis was failed in around 10% of patients because of drug resistance in *T. gondii* or due to variable *in vivo* drug behavior [3]. *Tg* CDPK1 has been shown to be essential in transduction of the calcium signals, so as it helps in regulating gliding motility, invasion and egress [4], beside its role in parasite reproduction. Its unique active site gatekeeper makes this kinase the target of choice for research practitioners [5].

Methods: The new pyrazolylpyrazoline derivatives were designed and evaluated for their *in vitro* inhibition of *T. gondii* invasion and also for their non-specific cytotoxicity on human foreskin fibroblasts (HFF) host cells.

Results: Results of the assay revealed that aminopyrazolone **6a** and 3-methylpyrazoline thioamide **4a** were found to possess remarkable antitachyzoite activity (EC_{50} = 0.016 and 0.018 μM, respectively) with high safety margin on HFF cells (CC_{50} >30 μM), in comparison to pyrimethamine as reference drug (EC_{50} = 0.37 μM). In addition, they were well tolerated by the experimental animals orally and parentrally up to 200 mg/kg and 100 mg/kg, respectively. Molecular modeling studies into *Tg*CDPK1 active domain showed excellent binding affinities for these promising compounds. Moreover, optimization measures revealed that **6a** and **4a** maintained the improved potency along with low lipophilicity (LE > 0.3 and LLE > 3).

Conclusion: These compounds are considered to be drug-like promising candidates in anti-toxoplasma drug discovery

Keywords: Toxoplasmosis; Protein kinase; Toxoplasma gondii; Pyrazolylpyrazoline; Cytotoxicity; Molecular modeling.

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PHS 226: Design, synthesis and evaluation of some pyrazolo[3,4-d]pyrimidine derivatives bearing thiazolidinone moiety as anti-inflammatory agents

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Two new series of pyrazolo[3,4-**d**] pyrimidine bearing thiazolidinone moiety were designed and synthesized. The newly synthesized compounds were evaluated for their ***in vitro*** (COX-1 and COX-2) inhibitory assay**.** Compounds that showed promising COX-2 selectivity were further subjected to ***in vivo*** anti-in*fl*ammatory screening applying formalin induced paw edema (acute model) and cotton-pellet induced granuloma (chronic model) assays using celecoxib and diclofenac sodium as reference drugs**.** The histopathological and ulcerogenic potential were also determined. ***In vivo*** anti-in*fl*ammatory data showed that compounds **2, 6, 7d** displayed anti-in*fl*ammatory activity higher than both references in the formalin induced paw edema model. On the other hand, compounds **2, 3d, 3e, 7b** and **7d** displayed anti-in*fl*ammatory activity greater than or nearly equivalent to diclofenac sodium in the cotton pellet-induced granuloma assay. Moreover, most of the tested compounds revealed good gastrointestinal safety profile. Collectively, compounds **2** and **7d** were considered as promising candidates in managing both acute and chronic inflammation with safe gastrointestinal margin.

*Keywords: Pyrazolo[3,4-d]pyrimidines; Thiazolidinones; Anti-in**fl**ammatory activity; Ulcerogenic potential; Cyclooxygenase inhibition.*

PHS 301: Prediction of potential cancer-related molecular targets of North African plants constituents using network pharmacology-based analysis

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Nowadays, cancer is considered one of the leading causes of death in developing countries. Due to mediocre socioeconomic status of many North African countries, people resort to traditional medicines for cancer therapy which are of great chemical complexity, interacting with several protein targets leading to synergistic effects. This study aims at the implementation of a holistic network pharmacology approach for identification of the main active constituents of North African plants against cancer molecular targets and to explore their therapeutic mechanism in the different cancer-related pathways. 6844 constituents of North African plants were retrieved from public database and were subjected to ADME filtration resulting in 3194 constituent which were forwarded to target prediction. STITCH database was used for predicting the plant constituents target proteins/genes, while TDD DB and Uniprot databases were used for identifying genes related to cancer. Constituent-target gene (C-T), constituent-pathway (C-P) and plant-constituent-target gene (P-C-T) networks were constructed and KEGG pathway and GO enrichment analysis were performed to decipher the molecular mechanisms and pathways related to cancer. 53 constituents and 36 targets were linked through 329 edges which constituted the main pathways related to cancer. Luteolin, alternariol, apigenin, aloe-emodin and myricetin had the highest combined score in the C-T network, while the genes CASP3, CYP1A1, CYP1B1, PTGS2, MAPK8, AKT1 and EGFR were the most enriched by the constituents in this network. *Euphorbia spp.*, *Hyphaene thebaica*, *Artemisia herba-alba*, bee propolis and *Marrubium vulgare* possessed the largest number of P-C-T interactions. The identified targets were mainly associated with cell cycle arrest and apoptosis in addition to inhibition of cellular proliferation revealing a striking functional association with various signal and cancer related pathways. The obtained results allowed for the prediction and interpretation of the multi-constituent, multi-target, and multi-pathway mechanisms of North African plants as potential source for supportive treatment of cancer.

Keywords: North African plants; Chemical constituents; Network pharmacology; Cancer targets; GO enrichment analysis.

PHS 302: Discrimination and quality assessment of *Nigella sativa* oil from different geographical origin using HPTLC-fingerprint activity relationship and multivariate analysis

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Fingerprint activity relationship modeling is proposed for precise discrimination of chemical and effective consistency of *Nigella sativa* oils from different geographical origins. Efficacy directed-fingerprint analysis was performed by high-performance thin layer chromatography technique, subsequently the data had been utilized for the discrimination of the samples geographical origin. Twenty-seven samples of *N. sativa* oils from three geographical areas (Egypt, Ethiopia and Syria) were collected and their antimicrobial, cytotoxic, anti-inflammatory and analgesic activities were measured. It was found that there was a significant difference in the biological activities of the oils collected. Chemometric analysis of the data helps to discover the crucial marker ingredients for classification through the loading plots of HPTLC-Principal Component Analysis (PCA). Discriminant analyses were calculated depending on HPTLC-targeted chemical fingerprints of five common characteristic peaks. Furthermore, the chosen markers were quantified by validated HPTLC methods, and then the quantitative data as well as the oils bioactive properties were subjected to partial least squares regression (PLSR) analyses. Thymoquinone and free fatty acids (FFA) were revealed as potential markers to distinguish the chemical consistency and efficacy of the oils from the three different geographical origins. Finally, this strategy exploiting HPTLC fingerprint activity relationship modeling enables to screen for efficacy-associated markers for discrimination of *N. sativa* oils from distinctive geographical origins.

Keywords: Nigella sativa oil; Geographical origin; Chemometric analysis; HPTLC; Targeted and untargeted analysis.

PHS 303: Phytochemical and biological investigations of *Crocus sativus* cultivated in the University botanical garden

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This study aimed at phytochemical and biological investigations of *Crocus sativus* cultivated in the University botanical-garden long-term effects exploring its most bioactive-compounds and their main-mechanisms of action. Phytochemical analysis and bio-guided isolation-procedures including RP-HPLC and ^{1}H and ^{13}C NMR utilizing biological models of diabetes, inflammation, and diabetic-neuropathy were used. S-RCED and Spanish-saffron sample (S-SP) alone or in combination with *Camellia sinus* (CS) were investigated. The RP-HPLC analyses showed the presence of Picrocrocin, Crocin I, Crocin II, Crocin I', Crocin II', and Safranal (SAF) in both SSP and S-RCED extracts with higher-concentrations in S-SP. SAF has shown to be the most bioactive-compound in *Crocus sativus*. Both S-SP and S-RCED possessed significant ($P < 0.05$) acute (6h), subchronic (8 days) and chronic (8 weeks) anti-diabetic activities. S-RCED has proven more hypoglycemic potentials when compared to S-SP and SAF. S-SP, S-RCED, and SAF produced significant anti-inflammatory and anti-nociceptive activities against carrageenan induced inflammatory, hyperalgesic and tactile diabetic-neuropathy models, respectively. S-SP, S-RCED, and SAF elevated serum catalase, reduced glutathione, and insulin serum levels ameliorated lipid peroxidation and HbA1c levels, and histopathologically regenerated the pancreatic beta-cells. Combinations with CS showed more significant efficacy than the single components. The oxidative stress reduction, insulin secretagogue, and pancreatic beta-cells regeneration potentials might be responsible for the mechanism underlying the anti-diabetic, anti-inflammatory and anti-diabetic neuropathy activities. The combination with CS showed superiority in efficiency and lowered the overall price of *Crocus sativus* treatment. Therefore, the cultivated *Crocus sativus* might be clinically useful for protecting against many serious disorders.

Keywords: Phytochemical investigation; Crocus sativus; University botanical garden; Pancreatic histopathology; Neuropathy.

PHS 304: Determination of 10-hydroxy-2-decenoic acid content in Royal Jelly products by high performance thin layer chromatography

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A new, simple, stability-indicating HPTLC method was developed for the quantification of 10-hydroxy-2-decenoic acid (10-HDA) in some royal jelly products marketed in Egypt (Royal jelly® 1000 capsules, GR six® capsules & Biostrong® capsules). First and second derivative treatment of the data was performed. The present study shows a comparison between three statistical regression methods for handling data; parametric, non-parametric and weighted regression methods. To validate the stability-indicating power of the developed analytical method, the royal jelly standard was subjected to forced degradation studies including the effect of hydrolysis (acidic, alkaline and neutral), oxidation, photolysis and dry heat. It was found that derivative treatment of the chromatographic response data gives improved quantitation and sensitivity of the chromatographic signals. Weighted regression of the response data is found to be advantageous over the use of both parametric and non-parametric regression models. This was shown by a great enhancement in the accuracy and precision in the analysis of 10-HDA in royal jelly products. Non-parametric regression of the response data is highly advantageous over the usual least squares method. So, this work combines the advantages of the derivative techniques with their elimination of interferences, together with the reliability and efficacy of the non-parametric and weighted analysis of data.

Keywords: Royal jelly; 10-Hydroxy-2-decenoic acid; High Performance thin layer chromatography; Derivative techniques; Weighted regression.

PHS 305: Comparative study of antiprotozoal (antileishmanial) activity and chromatographic screening of *Lotus corniculatus* L. and *Lotus halophilus* species growing in Egypt

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For many years, infectious diseases have been a worldwide problem and have affected quality of life and caused economic hindrance for millions of people. The purpose of this study is to investigate the antiprotozoal activity of the genus *Lotus*. The antileishmanial activity against *Trypanosoma brucei* was determined by Alamar Blue™ assay. It is worth mentioning that this is the first study of the antiprotozoal activity of genus *Lotus*. The ethanolic extracts of the aerial parts of *Lotus corniculatus* L. and *Lotus halophilus* exhibited significant antileishmanial activity against *T. brucei* with % inhibition values of 99 % and 98 %, respectively at sample concentration of 20 µg/ml in a primary antileishmanial assay. Furthermore, in a secondary antileishmanial assay, the total ethanolic extract of *L. corniculatus* L. showed higher activity than that of *L. halophilus*. In addition to that, the chromatographic screening of *L. corniculatus* and *L. halophilus* using HPTLC technique showed that the spots present in the different fractions of *L. corniculatus* were greater in number and more intense, therefore *L. corniculatus* was chosen for further phytochemical investigation. Chromatographic purification of the aerial parts of *L. corniculatus* led to the isolation of ten compounds **(1-10)**. The structure elucidation of the isolated compounds was achieved using spectroscopic techniques, including 1D and 2D NMR. Their chemical structures were identified as 7, 2'-dihydroxy-4'-methoxyisoflavan (vestitol) **(1)**, kaempferol **(2)**, kaempferol 3-*O*-rhamnoside (afzelin) **(3)**, kaempferol 3,7-*O*-dirhamnoside (kaempferitin) **(4)**, kaempferol 3-*O*-(2"-xylopyranosyl) galactopyranoside **(5)**, ethyl-*O*-*β*-D-glucopyranoside **(6)**, soyasapogenol B-3-*O*-glucouronic acid **(7)**, kaempferol-3-*O*-[*β*-D-xylopyranosyl(1"'→2")-*β*-D-galactopyranoside]-7-*O*-*α*-L-rhamnopyranoside (**8**), methyl *O*-*β*-D-glucopyranoside **(9)** and 3-*O*-[α-L- rhamnopyranosyl (1"'- 2")- *β*-D-galactopyranosyl-(1"- 2')- *β*-D- glucuronopyranosyl] soyasapogenol B (soyasaponin I) **(10)**. It is worth mentioning that this is the first time of isolation of compounds **(5)**, **(7)** and **(9)** from genus *Lotus*.

Keywords: Lotus corniculatus L.; Lotus halophilus; Antiprotozoal activity; Antileishmanial activity; Trypanosoma brucei; Soyasaponin I.

PHS 306: Identification of peroxidase inhibitors in plant extracts through validated HPTLC-direct bioautography assays and NMR spectroscopy

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Thin-layer chromatography hyphenated to bioassays is a new tool used for discovery of drugs with diverse biological activities from plant extracts, as it has many advantages; high-throughput, low-cost and reliability which justifies the continuous need for developing such methods. A new HPTLC-bioautography assay for detecting peroxidase enzyme inhibitors was developed and validated in this study. Peroxidases are related to pathogenesis of many diseases such as; atherosclerosis, neurodegenerative disorders, rheumatoid arthritis and are considered as inflammatory markers. The developed new HPTLC-bioautography method was based on reaction of peroxidase with hydrogen peroxide and the subsequent formation of blue color by the reaction between the released oxygen and benzidine. Compounds with peroxidase inhibition activity are observed as yellowish spots against a blue background. Quantitative estimation of peroxidase inhibitors was achieved by applying image analyses techniques, showing good accuracy intra-day and inter-day precisions as well as low LOD and LOQ. The developed method was applied to different *Juniperus* species extracts as a demonstrative illustration. Bioprofiling through HPTLC hyphenated to effect-directed analysis was used for screening of different *Juniperus* species extracts for components exhibiting peroxidase enzyme inhibitory and/or antioxidant effects using DPPH free radical scavenging and *β*-carotene/ linoleic acid bleaching assays. NMR spectroscopy, after bioactive compounds separation using preparative thin layer chromatography, was utilized for the identification of three flavonoids; isoscutellarein-7-*O*-*β*-xyloside, 8-methoxy isoscutellarein, and quercetrin, and three biflavones; hinokiflavone, sotetsuflavone and cupressuflavon.Overall, the developed method proved to be efficient, simple and rapid for identification of peroxidase inhibitors in complex matrices.

Keywords: Bioprofiling; HPTLC-bioautography; HPTLC-NMR; Antiperoxidase; Antioxidant; Juniperus.

PHS 307: A validated UPLC-PDA method for simultaneous determination of three biologically active isoflavans in *Trigonella stellata* extract

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In this study, an ultra-performance liquid chromatography (UPLC–UV/PDA) method was developed for the simultaneous determination of trigonellan glucoside (**1**), isotrigonellan (**2**) and methoxy-isotrigonellan (**3**) in *Trigonella stellata* extract using an external standard method. The extract was prepared using a standardized method by maceration of the dried plant material in ethanol. The three isoflavans (**1-3**) were separated on an Acquity UPLC^{TM} C18 column using gradient elution with a mobile phase consisting of 0.1% (v/v) formic acid aqueous solution and 0.1% (v/v) formic acid in acetonitrile, and UV detection. The method provides linear correlation for all analytes over the investigated ranges with all correlation coefficients greater than 0.998. The validated lower limits of quantitation were 53, 127 and 5 μg/ml for isoflavans **1**, **2** and **3**, respectively. Intra- and inter-day precisions (RSD%) were less than 8.3% and accuracy (RE%) ranged from 90 to 100%. The method's capability to remain unaffected by small, but deliberate variations in method parameters (method's reliability during normal usage) described by the robustness showed RSD% less than 4.6% measured by varying 3 different parameters. The validated method was successfully applied to simultaneously determine the concentration of the three new isoflavans having anti-inflammatory and antidiabetic activities. The results revealed that the validated method can be used for quality control of herbal preparations containing these or similar isoflavans that are marketed for the prevention of inflammation and as antidiabetics.

Keywords: UPLC; Isoflavans; Plant extract; Method validation; Quantitative determination.

PHS 308: Quantitative determination of cupressuflavone as a biomarker in genus *Cupressus* using validated qNMR and HPTLC methods

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Traditionally genus *Cupressus* has been used in treatment of various ailments. The main chemical components of *Cupressus* plants are bioflavonoids. Cupressuflavone is a major biflavonoid in many Cupressaceae plants and considered the main chemotaxonomic marker for *Cupressus* plants. Despite the abundance of cupressuflavone, it has not been intensively investigated as compared to other biflavonoids. Thus, this study represents development and validation of new and time-saving High-performance thin-layer chromatography (HPTLC) and quantitative nuclear magnetic resonance (qNMR) methods for the quantitative determination of cupressuflavone. The cupressuflavone content of hydroalcoholic extracts of five *Cupressus* plants (Leaves and cones of *C. sempervirens var. horizontalis* and *C. sempervirens var. pyramidalis* as well as *C. macrocarpa* leaves) was determined by HPTLC and qNMR. The chromatographic estimation was performed by spotting standard (cupressuflavone) and sample solutions on pre-coated silica gel aluminum plate. Plates were developed using a mobile phase consisting of chloroform: methanol: acetic acid (90:10:10, v/v/drops). Densitometric scanning was performed on Camag TLC scanner III in the reflectance-absorbance mode at λ 289 nm and operated by WINCATS software (V. 3.1). The developed methods were validated according to the International Conference on Harmonization (ICH) guidelines and were found to be precise, specific, sensitive, economical, and reproducible. NMR-based quantification using single internal standard enables the estimation of cupressuflavone without using costly reference standards. There were no significant differences between the assay results obtained by HPTLC and qNMR, with the former possessing slightly lower limit of detection (LOD) and limit of quantitation (LOQ). Quantitation results showed that cupressuflavone is generally more enriched in leaves than cones. Among the studied *Cupressus* leaves, *C. sempervirens var. horizontalis* was found to contain the highest content of cupressuflavone followed by *C. sempervirens var. pyramidalis*, while *C. macrocarpa* contained the least amount. The performed study demonstrates that both HPTLC and ^{1}HNMR can be successfully applied to the quantitative and qualitative analysis of cupressuflavone in complex plant matrix.

Keywords: Cupressus; Cupressuflavone; HPTLC; qNMR.

PHS 309: Bacterial exopolysaccharide as an innovative source for effective human anti-cancer agents

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Carbohydrates represent a very promising class for biologically active molecules. The wide applications of carbohydrate-based drugs in the pharmaceutical and medical fields motivate the continuous exploration for novel naturally occurring biologically active carbohydrates. Bacterial exopolysaccharides, discovered mid-19th century, are diverse group of complex polysaccharides. The implementation of exopolysaccharides in medicine and pharmaceutical industry has grown widely especially in the field of drug discovery for efficient probiotics, antitumor, antiulcer, immunomodulatory, antiviral and cholesterol lowering and anti-reflux therapies. In the current study, the colon cancer suppressive effects of a newly identified Lactobacillus acidophilus cell-free exopolysaccharide against colon cancer cells are explored. The chemical structure of the purified pentasaccharide was investigated by MALDI-TOF mass spectrum, 1D and 2D Nuclear Magnetic Resonance (NMR). The obtained data of the spectroscopic analysis with the aid of 'Determine Structure' module of the CASPER program, confirmed the structure of the newly extracted pentasaccharide; to be: α-D-Glc (1→2)][α-L-Fuc(1→4)] α-D-GlcA(1→2) α-D-GlcA(1→2) α-D-GlcA. The anticancer potentiality of the purified pentasaccharide against both Human colon cancer (CaCo-2) and Human breast cancer (MCF7) cell lines were evaluated. In addition, the immunomodulatory effects of the new oligosaccharide were quantified. The newly identified pentasaccharide, recorded safe dose on normal mammalian cells ranged from 2 to 5 mg/ml with cancer cells selectivity index, ranged of 1.96–51.3. The inhibition percentage in CaCo-2 cellular viability, reached 80.65 with an increase in the ratio of the apoptotic cells in sub-G0/G1 cell cycle phase. The findings of the current study showed that the anticancer potentialities of the Lactobacillus acidophilus cell-free exopolysaccharide are represented through its regulatory effects on both apoptotic and NF-κB inflammatory pathways.
Keywords: Exopolysaccharides; NMR; Mass spectrometry; Human colon cancer.

PHS 310: *Lepidium sativum* phyto-synthesized silver nanoparticles with potential antifungal and cytotoxic activities

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Bio-inspired synthesis of nanoparticles has received immense attention recently due to their diverse and potential applications in the biomedical field. Herein, an environment friendly method was developed to synthesize silver nanoparticles (AgNPs) using aqueous extracts of the aerial parts and seeds of Lepidium sativum, Family Brassicaceae. The phytosynthesized AgNPs were characterized using UV-visible spectral analysis, Scanning electron microscopy (SEM) and Zeta potentiometry. Relying on the UV-Vis absorption spectroscopy, the formation of nanosilver particles was monitored and characteristic surface plasmon absorption peaks were recorded at 420 and 440 nm respectively. SEM confirmed the spherical and polydispersed nature of the formed nanoparticles and Zeta potentiometry demonstrated an average diameter of 150 and 111 nm with a zeta potential of -15.2 and -20mv, for AgNPs phytosynthesized by seeds and aerial parts aqueous extracts, respectively. The phytosynthesized nanosilver exhibited a significant antifungal effect against Candida albicans (ATCC 18804). Implementing the MTT assay, the phytofabricated nanosilver showed promising cytotoxic effect against MCF-7 breast cancer cell line. Intriguingly, neither of the aerial parts or seeds of Lepidium sativum aqueous extracts exhibited any antifungal or cytotoxic effects implying that the detected bioactivities are ascribed to the green synthesized nanosilver. Further investigations are needed to unravel the underlying mechanisms for the observed activities.

Keywords: Photosynthesis; Silver nanoparticles; Lepidium sativum; Antifungal activity; Anticancer activity.

PHS 311: Simultaneous determination of oleuropein biomarker by validated RP-HPTLC method in nine varieties of olive leaves cultivated in Egypt

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Olive (*Olea europaea* L.) is native to the Mediterranean region. The main active constituents of olive oil include oleic acid, phenolic constituents, and squalene. The main phenolic compounds; hydroxytyrosol and oleuropein, give extra-virgin olive oil its bitter, pungent taste. Recent studies reveal the relationship between the major phenolic compound oleuropein and its pharmacological activities including anti-inflammatory, anti-atherogenic, anti-cancer, antimicrobial, antiviral activities, cardioprotective, neuroprotective hypolipidemic and it reduces serum triglycerides. It showed hypoglycemic and antioxidant effect. OLE (oleuropein) possesses a potential protective role against diabetes-induced reproductive disorders, which may be due to its antioxidant activity and its ability to normalize testicular steroidogenesis. Oleuropein is classically quantified by HPLC, which is time and chemical consuming, laborious and expensive. A new easy, quick, simple, economical, and environment-friendly reversed-phase high-performance thin-layer chromatography (RP-HPTLC) method has been established for the simultaneous determination of nine different varieties of *Olea europaea* L cultivated in Egypt. Separation was achieved on RP-HPTLC plates using acetonitrile/methanol mixture as the mobile phase. Detection and quantification of the spots were done using densitometer and UV detection at 240nm. The results showed that densitometry enable the quantitation of Oleuropein at low concentration. The method was validated, in accordance with the International Conference on Harmonization (ICH) guidelines for precision, accuracy, and robustness.

Keywords: RP-HPTLC; Olea europaea; Oleuropein; Densitometry.

PHS 312: Hepatoprotective activity of selected plants belonging to the order Santalales

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The Santalales, an order of flowering plants, is heavily concentrated in tropical and subtropical regions. Two plants belonging to this order and well known of antioxidant and anti-inflammatory activities were selected to study their hepatoprotective effect on paracetamol-induced hepatotoxicity in rats. Administration of paracetamol induced disturbances in hepatospecific serum markers. Additionally, it caused development of oxidative stress. Liver dysfunction was evaluated by measuring serum levels of SGOT, SGPT, ALP, total bilirubin and total protein. These deleterious effects caused by administration of paracetamol were greatly ameliorated by pre-treatment with methanol extracts of the studied plants. The results were compared with the paracetamol control group and another group pre-treated with silymarin. It was found that no significant difference between the silymarin treated group and the two extracts treated groups. Additionally, our results were confirmed by histo-pathological studies for the score of necrosis and inflammatory infiltration. No symptoms associated with toxicity were detected after administration of both extracts orally as a single dose for seven days at different concentrations ranging from 100 to 500 mg/ kg, giving a preliminary indication about the safety of the extracts. The median lethal dose (LD50) was determined to be higher than highest dose tested in both samples. Our results proved that both extracts exert significant hepato-protection against paracetamol-induced toxicity by their ability to ameliorate the lipid peroxidation through the free radicals scavenging activity, which enhanced the levels of antioxidant *org*defense system.

Keywords: Hepatoprotective; Santalales; Paracetamol; Lipid peroxidation; Antioxidant.

PHS 313: Metabolite profiling of different-aged alfalfa sprouts using HPTLC image analysis fingerprint-efficacy relationship coupled with chemometrics

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Sprouting is a commonly applied food processing practice specially in Western countries. Tracking the impact of sprouting of *Medicago sativa* L. (alfalfa) seeds on their phytochemical composition and curative efficacy was implemented in the current study. Sprouting of alfalfa seeds under controlled conditions for eleven days was performed in a biochemical incubator and three samples were randomly taken each day. A total of thirty-six samples (three ungerminated seeds and thirty-three sprouts samples) were collected, extracted and their cytotoxic, antioxidant and antimicrobial activities against five pathogenic microbial strains were measured. Samples were subjected to High performance thin layer chromatography (HPTLC) as a pattern-oriented strategy for metabolite fingerprinting to discover the fluctuations occurring during the sprouting process accompanied by multivariate chemometric analysis. Unsupervised pattern recognition was carried out using Principal Component Analysis (PCA) after extracting the chromatographic fingerprints from HPTLC chromatograms using ImageJ® software. PCA- loading plots demonstrated that luteolin-7-*O*-glucoside, ferulic acid and *P*-coumaric acid were the metabolically significant markers. Thus, simultaneous quantification of these crucial three markers in different aged alfalfa seeds/ sprouts extracts was performed using a newly developed and validated HPTLC-image analysis method. The results of the biological activities together with the quantitative data were further subjected to a Partial Least Squares Regression (PLSR) model for implementing HPTLC fingerprint-efficacy relationship analysis. The results obtained from metabolic pool profiling revealed that sprouting can cause remarkable changes in the phytochemical, nutritional and efficacy characteristics of alfalfa seeds.

Keywords: Medicago sativa L.; Sprouting; HPTLC metabolite profiling; Chemometric analysis; Partial least squares regression.

PHS 314: Antidiabetic activity test of dry extract combination of *Ortosiphon stamineus* leaves and pericarp of *Garcinia mangostana* on mice induced by Alloxan

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The contents of high antioxidant shows the potential from pericarp of mangosteen extract as fungtional source to give some contributions preventing cardiovascular disease through hypoglycemia activity. Java Tea or cat whiskers is the original plant from Indonesia, which have been studied have properties lowering blood sugar levels. The combination of both is expected to become the preferred means of therapy in patients with DM. The purpose of this study was to analyze the influence of dry extract combination of Orthosiphon's leaves and pericarp of mangosteen on blood glucose of alloxan induced-mice (i.p.). The respective doses were given for 7 days and were evaluated in 7 days. Acquired data were analyzed by using One Way ANOVA test and for further analysis was used Pos Hoc Test with LSD method Research shows that the combination of a dry extract with a ratio of 1: 1 and 1:2 (dose of 23.3 mg/kg body weight of mice) have antidiabetic activity with the percent decrease respectively by 32.02% and 37.07%. The dose with ratio 1:1 is the effective dose to decrease glucose level.

Keywords: Antidiabetic; Ortosiphon stamineus; Garcinia mangostana; Glucose level; Dry extract.

PHS 401: Early renal manifestations of metabolic challenge: Renovascular dysfunction preceding hyperglycemia

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Purpose: Metabolic syndrome is strongly related to the development of cardiovascular diseases, diabetes and mortality. Recent studies from our laboratory have shown that in non-obese prediabetic metabolically challenged rats, perivascular adipose tissue (PVAT) inflammation was associated with several cardiovascular anomalies. Interestingly these manifestations occurred prior to the development of hyperglycemia and were linked to the PVAT inflammation. Here, we examined the impact of prediabetic metabolic disturbance on renal function.
Methods: Kidneys from control and mild hypercaloric (HC) fed male Sprague-Dawley rats were isolated, perfused with physiological solution and preconstricted with phenylephrine. Renal endothelial dysfunction was assessed and shown as a loss of the concentration-dependent dilatory effect of carbachol that is mediated with prostaglandins and nitric oxide.
Results: Although our rat model receiving a mild HC diet for 12 weeks did not show changes in body weight, blood pressure nor blood glucose levels, an increase in insulin levels indicating insulin resistance was observed. The kidneys from prediabetic rats showed a non-concentration dependent dilation that appeared to be primarily mediated by the arachidonic acid derivatives, epoxyeicosatrienoic acid. Several molecular and structural abnormalities accompanied the vascular dysfunction including increases in glomerular reactive oxygen species (superoxide generation), glomerular mesangial index and fibrosis, expression of inflammatory cytokines (IL-1), and expression of α-smooth muscle actin in proximal tubular cells indicating a possible epithelial to mesenchymal transformation. Interference with adipose inflammation with non-hypoglycemic doses of metformin (100 mg/Kg/day) or pioglitazone (2.5 mg/Kg/day) not only improved the renovascular function, but also the signs of molecular and structural nephrotoxicity.
Conclusion: While most of the literature focuses on the detrimental effect of hyperglycemia, the results of the present study highlight the damaging effect of the early metabolic dysfunction in absence of increased blood glucose levels. Several possible pathways are implicated, which will be further examined in the future.
Keywords: Metabolic syndrome; Renovascular function; Epoxyeicosatrienoic acid; Adipose tissue inflammation.

PHS 402: The anti-inflammatory effect of allosteric α7-nAChR modulator with/without physical exercise in experimental autoimmune encephalomyelitis in rats

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Purpose: Multiple sclerosis (MS) is a systemic autoimmune disease characterized by chronic neurological inflammation of the CNS. The fact that α7nAChRs are highly expressed in the hippocampus and their essential role in improving neuronal function and spastic plasticity, open up a new perspective suggesting that allosteric nAChR modulators with high anti-inflammatory potential, may be a valuable add on therapy in the treatment of MS. Our study evaluated the possible anti-inflammatory effect of galantamine with/without exercise on the muscle function and disease management during an acute relapse in experimental autoimmune encephalomyelitis (EAE).

Materials and Methods: After one week of adaptation, adult male Sprague Dawley rats were divided into sedentary and exercised groups. EAE was induced with a single subcutaneous injection of spinal cord homogenate and complete Freund's adjuvant in the hind paws and base of the tail. Hereafter, exercised rats were trained on rotarod for 13 consecutive days. At the onset of clinical symptoms, the EAE group was subdivided into positive control,as well as galantamine (5mg/kg/day)and mitoxantrone (2.5mg/kg/day) treated groups for 5days. The progression of EAE was assessed by clinical score and rotarod. At the end of the experimental period, rats were sacrificed and CSF samples were collected for measurement of TNF-α,IL-6, BDNF, BCL-2 and Bax. Brain was dissected out and used for histopathological and immunohistochemical analysis.

Results and Conclusion: Galantamine with regular exercise increased significantly the rotarod score, neuroprotection against EAE and reduced apoptosis, as well as the EAE score. Besides, all inflammatory biomarkers and scores of demyelination were decreased, while regulatory T-cell activity was normalized.

Keywords: Experimental autoimmune encephalomyelitis; Multiple sclerosis; Galantamine; Exercise.

PHS 403: Empagliflozin attenuates cyclophosphamide-induced hepatotoxicity via modulation of Nrf2/HO-1 signaling, oxidative stress, and inflammation

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Purpose: Empagliflozin (EMP); a potent and selective SGLT2 inhibitor; possesses anti-inflammatory, anti-fibrotic, and antioxidant effects. Hence, the current work highlights the potential hepatoprotective activity of EMP against CYP-induced hepatotoxicity in rats.

Methods: Rats is pre-treated with EMP (10 mg/kg/day, orally) for 2 weeks. Then, a single dose of CYP (200 mg/kg, IP) was injected on the 8th day.

Results: CYP induced significant hepatotoxicity that is manifested by functional, biochemical, and histopathological alterations. The obtained results showed that EMP significantly mitigated CYP-induced hepatotoxicity as evidenced with significant attenuation of Oxidative/nitrosative stress along with a marked histopathological restoration of hepatocyte architecture. In addition, EMP significantly decreased hepatic contents of Nuclear factor erythroid 2-related factor 2 (Nrf2) and heme oxygenase-1 (HO-1), which seems to be the key mechanism underlying the hepatoprotective effect of EMP. EMP also significantly attenuated CYP-induced expression of inflammatory mediators; tumor necrosis factor-α (TNF-α) and nuclear factor kappa B (NF-κB) compared to CYP-intoxicated group.

Conclusion: EMP attenuated CYP-induced hepatotoxicity by modulation of Nrf2/HO-1 signaling pathway and consequent inhibition of oxidative stress and inflammation.

Keywords: Empagliflozin; Cyclophosphamide; Hepatotoxicity; Nrf2/HO-1; Oxidative stress; Inflammation.

PHS 404: Molecular mechanism of Tadalafil antinociceptive effect in an inflammatory pain model

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Nitric oxide (NO) plays an important role in acute and chronic pain, at both central and peripheral levels, explaining the fact that agents which promote NO such as phosphodiesterase inhibitors were investigated for their analgesic action. In fact, tadalafil, used in the treatment of erectile dysfunction, has been proven to possess antinociceptive effect. Yet, the exact mechanism behind its analgesic effect is still unclear. Accordingly, the aim of the current study was to elucidate this mechanism in an inflammatory pain model.

Male mice were segregated into four groups which received either the vehicle (polyethylene glycol 400) or tadalafil (1.5mg/kg) or morphine (5mg/kg), or indomethacin (10mg/kg). The analgesic efficacy of tadalafil was assessed using the Von Frey filament test after formalin mice paw injection. The plantar paw of the mice was then dissected to quantify the cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), neuronal nitric oxide synthase (nNOS), tumor necrosis factor-alpha (TNFα), interleukin-1 (IL1) and interleukin-10 (IL10) gene expression using real-time polymerase chain reaction.

The results obtained showed that tadalafil was able to significantly increase the withdrawal force in Von Frey filament test compared to the control that was similar to the effect of indomethacin and morphine administration. Moreover, tadalafil induced a statistically significant reduction in iNOS, COX-2, and TNF-α gene expression. However, nNOS, IL 1, and IL10 were not influenced by tadalafil administration.

As a conclusion, tadalafil exerted its analgesic effect through the simultaneous inhibition of iNOS, COX-2 and TNF-α, inflammatory mediators, which is not the case with the other drugs. Consequently, tadalafil may constitute a novel treatment approach to inflammatory pain management.

Keywords: Tadalafil; Phosphodiesterase 5 inhibitor; Mechanism of action; Antinociception; Inflammatory mediators.

PHS 405: *In vitro* evaluation of *Terfezia claveryi* and *Terfezia boudieri* species for their anti-inflammatory effect

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Desert truffles are edible foods that grow naturally following the rainy season in arid and semi-arid areas of the Mediterranean region, the Arabian Peninsula, and North-Africa, in addition to some parts of South Africa and China. Traditionally, they are used in folk medicine for prophylactic and treatment of different eye ailments, infections, inflammations, and allergies. Truffles are very rich in fibers, carbohydrates, proteins, vitamins and minerals, and their protein content is higher than that of most vegetables. Accordingly, *Terfezia claveryi* and *Terfezia boudieri* species were selected for in vitro anti-inflammatory analysis.

Truffles of both species were homogenized with water, filtered to remove the major debris, and then centrifuged for 15 seconds. The supernatants "aqueous extracts" of both species were concentrated using a rotary vapor, then the concentrates were stored in the refrigerator at 4^{o}C. Hundred grams of each residue was extracted with acetone and butanol prior to use. The test extracts at different concentrations were incubated with egg albumin under controlled experimental conditions and subjected to determination of absorbance at 660nm by using distilled water as a blank. Diclofenac sodium was used as a positive control.

The results showed a concentration dependent inhibition of protein denaturation by both species with a higher curve to diclofenac comparative doses.

As a conclusion, *Terfezia claveryi* and *Terfezia boudieri* possessed marked anti-inflammatory effect against the denaturation of protein in vitro. Consequently, in vivo studies are requisite to prove their anti-inflammatory efficacy.

Keywords: Anti-inflammatory; Truffles; Species; Protein denaturation.

PHS 406: Efficacy of Rosuvastatin and Pitavastatin in a sample of Lebanese dyslipidemic patients

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Pitavastatin and rosuvastatin, HMG-CoA reductase inhibitors, were widely used to treat hypercholesterolemia and reduce the risk of cardiovascular events. Ethnic differences and environmental factors played a crucial role in the control of several conditions that directly contribute to cardiovascular disease (CVD); therefore, it is important to assess the efficacy of statin treatment for different ethnic groups or populations. Such study concerning these two potent synthetic statins, rosuvastatin and pitavastatin, in the Lebanese population has not been reported yet. The goal of the current study was to compare the efficacy of pitavastatin versus rosuvastatin in Lebanese patients with hypercholesterolemia.

This study was a prospective, parallel, clinical trial conducted at a clinical center. Male and female Lebanese patients between the ages of 20 and 75 years were enrolled and divided into 2 groups in a 1:1 ratio. Patients randomly received pitavastatin 2 mg or rosuvastatin 10 mg once daily throughout 12 weeks. Fasting blood samples were collected for determination of total cholesterol (TC), triglycerides (TG), Low-density lipoprotein (LDL-C) and High-density lipoprotein HDL-C at baseline and at the end of the treatment.

The results highlighted that rosuvastatin and Pitavastatin reduced the level of TC by 29.97 % and 28.26 %, respectively with a significant p-value (<0.05). No significant results were found between the two treatments in LDL-C, TG, and HDL-C levels after 12 weeks. Furthermore, pitavastatin has shown a significant decrease in the value of HbA1c by 0.24 ± 0.44 over rosuvastatin which increased it by 0.06 ± 0.27 ($p<0.05$).

As a conclusion, although pitavastatin did not show beneficial effect over rosuvastatin in decreasing the level of LDL, TG, and HDL-C, it decreased HbA1c significantly. This could be an added value to Pitavastatin especially that statins recently have been shown to increase the glucose level.

Keywords: Dyslipidemia; Rosuvastatin; Pitavastatin; Cholesterol; HbA1c.

PHS 407: Anti-arthritic activity of systemic bee venom through multiple mechanisms

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Bee venom is widely used in oriental medicine to alleviate conditions such as rheumatoid arthritis (RA). The current study aimed to evaluate the effect of systemic bee venom (60mg/kg) as an anti-arthritic natural product and to track the possible underlying mechanisms of action in complete Freund's adjuvant-induced arthritic rats.

The development of rheumatoid arthritis signs (knee joint diameters, arthritis scoring index) was detected. Erythrocyte sedimentation rate, serum tumor necrosis factor-α (TNF-α) and serum interleukin-1β (IL-1β) were measured at the end of the study (21 days). A histo-pathological examination followed by immunostaining of NF-κB (P65) was performed on the affected knee joints. In addition, In-vitro COX inhibition activity, carrageenan paw edema test and acetic acid writhing test were performed to evaluate the anti-inflammatory and analgesic effects of the designed dose regimen compared to diclofenac sodium.

The outcomes of this study supported the impact of systemic bee venom on inhibiting the development of RA signs. Bee venom also displayed significant reduction of serum TNF-α, IL-1β and NF-κB in the affected joints which was even superior to standard methotrexate. Moreover, bee venom exhibited good inhibitory activity of COX pathway, in addition to, the anti-inflammatory and analgesic effects that were investigated through rat paw edema and writhing tests.

Therefore, systemic bee venom displayed promising anti-arthritic, anti-inflammatory and analgesic activities through multiple mechanisms implicated in the pathogenesis of rheumatoid arthritis.

Keywords: Rheumatoid arthritis; Bee venom; TNF-α; NF-κB; COX; Analgesic.

PHS 408: Beyond PI3K-mTOR inhibition: Autophagy a novel pathway for synergistic effect of diosmin on the anti-cancer effect of BEZ-235 (Dactolisib) in colorectal carcinoma

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Aims: Colorectal cancer (CRC) is considered as one of the most common types of cancer and leading causes of cancer death over the world. Many evidence support the involvement of various signaling pathways in CRC including; Wnt**,** EGFR, VEGF and NFκ-B. Thus, development of inhibitors targeting these pathways has become an attractive therapeutic strategy. Since combination therapies exploit the chances for better efficacy and decreased toxicity, we aimed to investigate the potential anti-carcinogenic pathways of Dactolisib (BEZ-235) and/or Diosmin (DIO) in the CRC cell line (HCT-116) and whether combination of the proposed two drugs will add beneficial antitumor effects.

Main methods: Determination of IC_{50} (The median inhibitory concentrations) and the combination (CI)/dose reduction (DRI) indices for CRC cell line (HCT-116) treated with different concentrations of BEZ-235 and/or DIO. Caspase-3 activity was assessed colorimetrically, p-Akt, NFκ-B, CD1, VEGF and LC3B were assessed by ELISA technique. Also, LC3-II gene expression was assessed using qRT-PCR technique.

Key findings: Both CI/ DRI indices confirmed the synergistic effect of DIO and BEZ-235. The two drugs abated the PI3K/Akt/mTOR/ NFκ-B axis leading to apoptosis induction (active caspase-3), inhibition of proliferation marker (CD1), angiogenesis marker (VEGF), autophagy protein (LC3B) and LC3-II gene expression. The best effect was mediated by the combination regimen that surpassed the effect of either drug alone.

Significance: The obtained results revealed the potential chemotherapeutic effects of co-administration of BEZ-235 and DIO on CRC cell line model, HCT-116, which encourage future preclinical and clinical researches.

Keywords: Colorectal cancer; BEZ-235; Diosmin; PI3K; NF-κB.

PHS 409: Pioglitazone ameliorates sensory and motor behavioral deficits in a rat ischemic stroke model

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Purpose: Stroke induced neuronal damage and accompanied motor and sensory deficits are one of the most common causes of disabilities in adults. Pioglitazone, a selective PPARγ agonist widely used clinically in type II diabetes, has been reported to have neuroprotective effects in different neurodegenerative and neuroinflammatory diseases including stroke, however, its effect on stoke induced behavioral deficits is not clear. Thus, our study aimed to demonstrate the recovery of motor deficits and sensorimotor impairments mediated by pioglitazone in a global cerebral ischemia model in rats.

Methods: Adult male Wistar rats were either pretreated with pioglitazone (10mg/kg/day p.o) or vehicle for 14 days prior to the induction of cerebral ischemia by bilateral common carotid artery occlusion (BCCAO). Twenty-four hours after reperfusion, the behaviors of rats were assessed using tests of motor and sensory functions. Rats were then sacrificed and infarct volume as well as histopathological changes of brain tissue was evaluated in addition to measurement of oxidative stress and inflammatory markers in the brain homogenate.

Results: Pioglitazone produced a significant improvement of motor coordination and sensorimotor dysfunctions induced by BCCAO along with an obvious reduction in cerebral infarct volume. Furthermore, pioglitazone ameliorated stroke induced oxidative stress by increasing catalase activity and reducing lipid peroxidation. It also improved the inflammations and histopathological alterations induced by BCCAO.

Conclusion: The study confirms the neuroprotective effects of pioglitazone and shows its ability to improve the functional outcome following stroke.

Keywords: Pioglitazone; Stroke; Brain homogenate; Lipid peroxidation.

PHS 410: Metformin and Omega-3 ameliorate NLRP3 inflammasome in Freund's adjuvant induced arthritis via Autophagy/Notch-1 pathway

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Rheumatoid arthritis is a destructive autoimmune disease characterized by infiltration of immune cells into the affected joints, release of inflammatory and degradative mediators, as well as deregulated autophagy process. This study highlights the role of Notch-1 among the network formed between inflammation and autophagy during arthritic progression. Additionally, we investigated the anti-inflammatory effects of metformine and/or omega-3 compared to the conventional methotrexate treatment. ***Materials and methods:*** 42 Sprague-Dawley male rats were allocated into six groups: control, untreated AA, MTX (0.1 mg/kg/day, i.p), Met (200 mg/kg/day, p.o), Omega-3 (200 mg/kg/day, p.o), and Met+Omega-3. Results: metformine and/ or omega-3 improved hind paw swelling and arthrogram scores. Moreover, all treatments, especially the combination regimen, abated tissue content/ mRNA expression of inflammatory markers (CRP, Syk, NLRP3, p(Ser536) NF-κB p65, TNF-α, IL-6) and apoptotic markers (p53, caspase-3 activity). Furthermore, treatments enhanced the mRNA expression autophagy-related markers (LC3BII, Beclin-1), besides the tissue content of the anti-apoptotic Bcl-2. However, the gene expression of Notch-1 and p62 were downregulated by various treatments. These results entailed an improvement in histological scores. In conclusion: the immunosuppressive effects of Met and/or omega-3 against adjuvant induced arthritis are mediated, partially, by modulation of inflammation, and apoptosis possibly via the involvement of Syk/NLRP3/NF-κβ and Beclin-1/Notch-1 signaling pathways.

Keywords: Rheumatoid; Metformin; Omega-3; NLRP3; Autophagy; Notch-1.

PHS 411: Generation of functional neural precursor cells from bone marrow stromal cells using Thyroid hormone

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Transplantation of Neural precursor cells (NPCs) is a promising potential therapeutic strategy for neurodegenerative diseases. However, the derivation of engraftable NPCs from different cell lines has proven difficulty and primary NPCs are not readily available. Here we report the generation of induced NPCs (iNPCs) by direct lineage conversion. Forced expression of the two transcription factors PAX6 and DLX2 along with downregulation of SOX2 was sufficient to reprogram human bone marrow stromal cells into iNPCs. Induction of iNPCs generation was achieved with Thyroid hormone (TH). TH is an uprising drug tool for tissue repair generally, in addition to neural cells induction and maturation. More importantly, iNPCs could give rise to mature neural cells that could replace multiple host injured cells when transplanted and entangled with host cells. We propose direct lineage reprogramming as a viable alternative approach for the generation of iNPCs for use in disease modeling and regenerative medicine.

PHS 501: Developing country-specific preventable drug-related morbidity indicators for primary healthcare

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Purpose
It is the responsibility of pharmacists to manage drug-related problems to ensure the greatest benefit to the patient. In order to prevent drug-related morbidity, pharmacists should be aware of medicines that may contribute to drug-related problems, due to their pharmacological action, and how to appropriately manage this. The aim of this study was to develop preventable drug-related morbidity (PDRM) indicators for the primary healthcare sector in South Africa.

Materials and methods
A literature study was conducted to compile a comprehensive list of PDRM indicators, as developed internationally, using the search engines Google Scholar and PubMed. MESH terms used to retrieve suitable articles was "preventable drug-related morbidity indicators". The list of indicators was evaluated for face- and content-validity. Face validity was done in duplicate by 2 sets of independent researchers to ensure 1) no duplication of indicators when compiling a single list, 2) inclusion of only medication available in primary healthcare, and 3) inclusion of only medication currently available in South Africa. Content validity was done by 10 healthcare practitioners to ensure pharmacological correctness and application.

Results
A comprehensive list of PDRM indicators from the USA, UK, Portugal, Australia, India and Canada were compiled containing 324 PDRM. 184 indicators were found to be duplicates and were omitted, leaving a final list of 140. The 140 PDRM indicators were evaluated for face-validity, and 94 were accepted as relevant to primary health care in South Africa. 46 indicators did not comply with the criteria and were omitted. After face validity 79 indicators met the predefined consensus and 15 were removed.

Conclusion
This study is a first step in compiling a list of PDRM indicators for South Africa. It is important to take cognizance to the fact the health systems differ vastly internationally, and it is therefore important to develop country-specific indicators.

Keywords: Drug-related problems; Preventable; Morbidity; Primary healthcare.

PHS 502: Knowledge, attitude and practice regarding performance-enhancing drugs use among undergraduate students

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In a competitive setting, particularly in sports, individuals tend to achieve superiority and win against their opponents. Consequently, several substances are commonly used by young adults to enhance their performance, relieve stressors, and change their appearance. The most popular performance enhancing drugs (PEDs) used are androgenic anabolic steroids (AAS), human growth hormone (hGH), insulin, erythropoietin, beta hydroxyl-beta-methylbutyrate, and stimulants. Nevertheless, PEDs carries several side effects that affect negatively the whole body and are in almost all cases neglected by their consumers.
The current study aimed to assess the knowledge, attitude and practice of university students regarding the uses of PED.
A cross-sectional, descriptive study was conducted by administering a self, anonymous questionnaire to university students. The participants were selected by convenience after obtaining their informed consent. Data collected was analyzed using SPSS. Means with standard deviations, frequencies, and percentages were calculated to describe the characteristics of the respondents. Chi-square test and t-test were used when appropriate to evaluate the statistical differences between medical and non-medical students. A *P*-value of <0.05 was considered significant.
Participants were divided between medical (44.6%) and non-medical (55.4%) faculties, where medical students obtained a significantly higher knowledge score of 9.78 ± 1.84 compared to non-medical students who scored 6.12 ± 1.40. This was relevant specially in term of side effects knowledge. Of the studied sample, 4% used PEDs and all of them were males. Twenty-five percent of the users where from medical faculties while 75% from non-medical ones. Of the PED users, 93.8% were offered PEDs specifically by coaches. A significant association was revealed between higher income status and PED use.
Although PED use was not found to be prevalent, non-medical students showed insufficient level of knowledge leading to the necessity for educational programs on PED in order not only to decrease its use but also to prevent their harmful adverse effects.

Keywords: Attitude; Knowledge; Practice; Performance-enhancing drugs; Undergraduate students.

PHS 503: Economic evaluation of the clinical pharmacist role in rationalizing antibiotic prescriptions in outpatient clinics

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The extensive consumption of antibiotics in the outpatient clinics has become one of the most pivotal factors in the spreading of antimicrobial resistance, surprisingly; the majority of patients receiving antibiotic prescriptions have no explicitly confirmed infection. Hence, justifying the use of antibiotics has become a necessity not an option, for decreasing the risk of adverse drug events, and diminishing the financial burden of the huge cost of antibiotics. As most studies focused on the inpatients antibiotics prescriptions, the aim of this study was to evaluate the role of clinical pharmacist in rationalizing the outpatient antibiotics prescriptions.

A non-randomized clinical trial has been held in Ras Elteen General Hospital, Alexandria, Egypt, on two consecutive periods; February to April 2018 before intervention, and 2019 after intervention. The clinical pharmacists evaluated the outpatient prescriptions manually for appropriate antibiotics selection and their indications according to the Infectious Diseases Society of America guidelines (IDSA), over three months before and after the clinical pharmacists' intervention with the physicians; and Cost-benefit analysis was performed to estimate the economic benefit of the clinical pharmacist intervention.

The clinical pharmacist team found that the difference before and after the intervention was statistically significant 1294 (68-11047) and 1121 (65-7761) respectively (Z= -2.023, P= 0.043), and clinical pharmacist intervention decreased the total antibiotic prescriptions all over the three months by 2.06% with a Benefit-Cost Ratio (BCR) of 1.04, and a net benefit of + 2106 L.E.

The significance of this study in the evaluation of the clinical pharmacists' interventions and expanding their activities to outpatient clinics revealed positive economic benefits and is worth dissemination to large hospitals.

Keywords: Antibiotics; Rationalization; Cost-benefit; Clinical pharmacist.

PHS 504: Counseling pregnant patients in the community pharmacy: Time to meet the ugly truth

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Purpose: Self-medication, which is defined as the purchasing and use of medicines by individuals to treat self-recognized illnesses or symptoms, is a common practice in developing countries. Such practice is associated with increased risk of drug interactions and adverse drug reactions. Self-medication in pregnant women carries additional risks of developing harmful effects to the fetus. The quality of community pharmacy services is among multiple factors that contribute to the prevalence of this phenomenon and associated problems. Therefore, we sought to evaluate knowledge and counseling skills of pharmacy staff for self-medicating patients asking for doxycycline (an antibiotic with potentially teratogenic effects) to treat acne symptoms.
Methods: Using stratified random sampling, about 150 community pharmacies were chosen to be visited by a simulated patient (SP) in Minia, Egypt. SP was trained to purchase doxycycline on behalf of his pregnant sister to relieve her acne symptoms. SP was refrained from telling pharmacy staff members about his sister's pregnancy status unless asked. As doxycycline was not available in 41 pharmacies, only 109 encounters were included in the final analysis.
Results: Except for one pharmacist, all pharmacy staff members dispensed doxycycline without acquiring any piece of information from the SP. About 25% of staff members did not abstain from dispensing even after SP had told them about his sister's pregnancy; assuring him of doxycycline safety during pregnancy.
Conclusion: Our findings showed that inappropriate management of self-medication cases in community pharmacies has reached almost epidemic proportions in Upper Egypt; rendering high rates of adverse drug reactions highly anticipated.

Keywords: Self-medication; Simulated patient; Patient counseling; Pharmacy practice.

PHS 505: Dietary supplements: Knowledge, perception, and attitudes use among pharmacy students

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Purpose: There has been a marked expanding use of herbal products and dietary supplements in many advanced and developing countries. However, data about consumption patterns and knowledge about these products is limited among Lebanese pharmacy students. The present study aimed to assess the knowledge and attitudes of pharmacy students towards herbal dietary supplements.

Method: A cross-sectional observational descriptive study was conducted. A face-to-face, 23-item survey was administered to pharmacy students by convenience in a university. Statistical analysis was conducted using SPSS.

Results: Forty-seven point three percent out of 355 pharmacy students assessed had used at least one dietary supplement in their lifetime. Fish oil, fibers, and cranberry were the highest herbal dietary supplements used among pharmacy students. To treat or cure a specific disease or health problem was the highest reason why pharmacy students take dietary herbal supplements. Ginkgo Biloba was the highest ineffective dietary supplement according to the students' opinion for treating a specific condition. Internet was the highest source of information used by all pharmacy students to determine the use of herbal dietary supplements. Health benefits knowledge of Ginkgo Biloba, St. John's Wort, Ephedra, Ginseng, Fish oil, Ginger, Saw palmetto, and Glucosamine by percentages of 62.8%, 55.8%, 53.5%, 53.5%, 53.2%, 53%, 50.7%, and 12.1%, were known, respectively. Students answered correctly the questions related to the side effects of Ginkgo Biloba, Ephedra, Echinacea, and St. John's Wort by percentages of 62%, 53.5%, 39.2%, and 1.7%, respectively.

Conclusion: Although some dietary supplements were weakly known by pharmacy students, the overall knowledge was considered sufficient. Nevertheless, the use of some commonly used dietary supplements such as glucosamine as well as the side effects of others such as St. John's Wort should be covered in greater depth in the curriculum.

Keywords: Knowledge; Dietary supplements; Attitude; Pharmacy; Students.

PHS 506: Role of pharmacovigilance in patient safety and public health

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Pharmacovigilance is concerned with monitoring of the safe use of drugs and medicinal products, in order to minimize their risks. The aims of pharmacovigilance are to enhance patient care and patient safety related to the use of medicinal products. It is considered an essential tool to support public health programmes in relation to the use of medicines, by providing reliable information to assess the benefit- risk profile of medicines. This is for both newly released products and those that are already established in the market.

The WHO has established a Programme for the International Drug Monitoring, in collaboration with Uppsala Monitoring Centre (Sweden), grouping more than 150 countries that share the vision of safer and more effective use of medicines. The objective of this programme is to monitor and detect the harm caused by medicinal products, in order to reduce the risks to patients and to establish worldwide standards and systems for pharmacovigilance.

The aims of pharmacovigilance are highly correlated with the third WHO Global Patient Safety Challenge: "Medication without harm", which goal is to reduce severe, avoidable medication-related harm by 50%, in five years.

Pharmacovigilance role is performed through the spontaneous reporting of adverse drug reactions (ADRs), which are an important cause of morbidity and mortality worldwide, in addition to their economic burden and healthcare costs. Its lifecycle include data collection of the individual case safety reports (ICSRs), MedDRA coding, analysis and causality assessment, benefit-risk evaluation, signal detection and risk management by the application of certain measures and specifications to prevent or minimize risks. Finally an effective and open communication of the information and the actions taken should be transmitted to the public and healthcare professionals.

Keywords: Pharmacovigilance; Patient safety; Benefit/ risk evaluation; Risk management.

PHS 507: Risk factors for acquisition of ventilator-associated pneumonia in the critical care units of Alexandria Main University Hospital, Alexandria.

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Ventilator-associated pneumonia (VAP), a life-threatening hospital acquired lung infection, may be inevitable to some ventilated patients in intensive care units (ICUs). Carbapenems are the antibiotics of choice for broad spectrum activity and safety. However, their overuse may lead to VAP caused by carbapenem-resistant bacteria. This has raised concerns of health professionals about risk factors for VAP in ICUs. Our aim was to investigate the clinical and epidemiological risk factors involved in VAP acquisition and those leading to VAP caused by carbapenem-resistant Gram-negative bacteria in ICUs of Alexandria Main University Hospital (AMUH). A retrospective case control study based on WHOnet database for VAP patients diagnosed according to CDC criteria was conducted in 2014-2017. Patients who did not meet CDC criteria for VAP were included in the control group. Patient profiles were surveyed for potential risk factors and prevalence of Gram-negative bacteria among VAP cases. During the study, 42 patients were diagnosed with VAP and 58 VAP episodes took place. Gram-negative prevalence was 58.6% for *Acinetobacter baumannii* (of which only 2 isolates were carbapenem susceptible), 37.9% for *Klebsiella pneumoniae*, 31% for *Pseudomonas aeruginosa*(PA), 13.8% for *Proteus* spp and 12% for *E. coli*. Polymicrobial cultures characterized 44.8% of the VAP episodes. Univariate analysis indicated that ICU, ventilator, and nasogastric tube days, in addition to previous surgery and metronidazole therapy were the main risk factors for VAP. Multivariate analysis verified significance of ICU and nasogastric tube days independently as risk factors. Steroid therapy days were the main risk factor for VAP due to carbapenem resistant PA. Prolonged ICU stay and enteral feeding proved highly associated with VAP in AMUH. In conclusion, hospital VAP preventive measures and implementation of antibiotics stewardships are highly warranted. Moreover, clinical studies evaluating possible use of carbapenems or other antibiotics in combinational therapies are needed.

Keywords: Carbapenems; VAP; Pneumonia; WHOnet; ICU; AMUH.

PHS 508: Dosing accuracy of measuring devices provided with antibiotic oral suspensions and used by the Lebanese mothers

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Oral "For-reconstitution" antibiotics are widely available in Lebanese market and from different manufacturers. Most of these preparations are used for a wide range of differently aged pediatric groups. Antibiotics prescribed for infants and young children are usually dispensed as oral suspensions because of children's inability to swallow tablets or capsules, unavailability of certain antibiotics in a chewable tablet form and the discomfort, expense, and associated risk of antibiotic injections. Appropriate use of antibiotic suspensions includes the correct reconstitution, concentration, dose administration, duration of treatment, and storage conditions. To improve accurate dose measurements, oral liquid medications usually come with a dose delivery device such as medication cups, droppers, calibrated spoons, and syringes. Syringes have many advantages; they are accurate even for small volumes, they are easy to use and to be cleaned. Regarding dosing cups, dosing error are common with them, so as a general rule they should not be used for doses less than 5 ml even if the cup has calibration less than 5 ml.
Being aware that exact dosing is essential, the present study investigated the dosing accuracy of measuring devices provided with antibiotic oral formulations (generics/brand) and used by Lebanese mothers.
After constituting the oral suspension as labelled, the drugs were given to mothers working at the Lebanese International University to withdraw a pre-specified dose to simulate the dispensing behavior in everyday life. To obtain informative results, dosing uniformity was evaluated by determining the content of individual doses using HPLC according to USP monographs.
Results showed that measuring devices provided with the product exhibited a significant variability in dosing accuracy. Provided syringes showed better results for dose uniformity with no significant deviation from the labelled content in comparison to spoons which may result in less accurate dose administration.

Keywords: Dosing accuracy; Antibiotic; Oral suspension; Measuring devices; Lebanese; Mothers.

PHS 601: Evaluation of citric acid and clove oil as edible anti-virulence and resistance-modifying agents against problematic Klebsiella clinical isolates in Egypt

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Purpose. *Klebsiella* spp. are regarded as terrifying pathogens that threaten different healthcare systems. These pathogens possess a variety of virulence factors which markedly account for their pathogenicity.
Materials and Methods. Three virulence factors (capsule formation, hypermucoviscosity and biofilm formation) were screened, phenotypically and genotypically, among selected Egyptian Klebsiella clinical isolates. Two safe edible agents, clove oil and citric acid, were evaluated for their effect on bacterial capsule formation using the Anthony capsular staining method and the transmission electron microscopy. The antibiotic-resistance modifying activity of both agents was tested against selected troublesome isolates showing resistance to amikacin, meropenem and cefotaxime. Molecular docking of citric acid and eugenol with NDM-1, as well as the docking of citric acid with AAC(6′)-Ib and CTX-M-15 were carried out to explain the resistance modifying activity of the tested agents.
Results. Capsule formation was the most significant virulence factor that was detected in all isolates. Both citric acid and clove oil resulted in a significant reduction in the size of the bacterial capsules. Citric acid showed promising synergistic effects when combined with the studied antibiotics against all the tested isolates. However, clove oil showed a synergistic effect only against 50% of the tested isolates when combined with meropenem. Relying on their binding efficiency mode obtained from molecular docking studies, the tested agents were recognized as promising inhibitors of the studied enzymes.
Conclusion. Both citric acid and clove oil are auspicious anti-virulence and resistance-modifying agents that can be combined with conventional antibiotics to combat virulent and multidrug resistant Klebsiella isolates. As no inhibitor for medical treatment has yet been approved for NDM-1 or other classes of metallo-β-lactamases, we hereby, present citric acid and eugenol as potential inhibitors and we recommend further *in vitro*, as well as structural modifications studies.

Keywords: Klebsiella; Virulence factors; Bacterial capsule; Clove oil; Citric acid; Polymerase chain reaction; Transmission electron microscopy; Molecular docking.

PHS 602: Evaluation of ciclopirox as a virulence-modifying agent against multidrug resistant *Pseudomonas aeruginosa* clinical isolates from Egypt

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The continuous rise in reported resistance to antimicrobial agents and the shortage in provision of new antibiotics has encouraged the repurposing of older drugs to combat infections caused by problematic pathogens as *Pseudomonas aeruginosa*. Since, targeting pathogen's viability has the disadvantage of induction of selective pressure with resistance development, the use of agents that hinder bacterial virulence is nowadays intensively discussed. Ciclopirox, a forgotten antifungal agent with iron chelation potential, was evaluated in this study for its ability to inhibit virulence factors expressed by 26 clinical MDR *P. aeruginosa* isolates collected from Alexandria Main University Hospital, a tertiary hospital in Egypt. Treatment with 9 µg/ml of ciclopirox, nullified the hemolytic activity of 70% of tested isolates, reduced pyocyanin production by 4-12 fold, subsided protease secretion in 46% of isolates, lowered twitching and swarming motility by 37.5% and 85%, respectively, and decreased biofilm formation by a range of 1.5- 4.5fold. Quantitative real-time PCR conducted to examine gene expression profiles of cells treated with ciclopirox showed that genes encoding alkaline protease production (aprA) and pyocyanin biosynthesis (phzA1) were downregulated. Due to current interest in ciclopirox in hematological malignancies treatment, its systemic administration is investigated with a resultant satisfactory drug safety profile and adequate oral absorption. Calculation of appropriate clinical dose and assessment of therapeutic index is a necessary step to permit the repositioning of ciclopirox from its role as merely a topical antifungal agent to a promising virulence-modifying agent against one of the most problematic Gram-negative pathogens, *P. aeruginosa*.

Keywords: Ciclopirox; Virulence; Pseudomonas aeruginosa; Protease; Pyocyanin.

PHS 603: *In-vivo* evaluation of *Klebsiella pneumoniae* outer membrane proteins OmpK36 and OmpK17 as potential vaccine candidates

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Klebsiella pneumoniae is a Gram-negative bacterium that is reported as a serious nosocomial and community-acquired pathogen globally. In the current study, two outer membrane proteins of *K. pneumoniae*, namely OmpK36 and OmpK17, as well as their fusion protein cognate F36/17 were investigated as potential vaccine candidates in a mouse infection model. Three immunoadjuvants, namely synthetic hemozoin (Hz) adjuvant, the Gram-positive Enhancer Matrix (GEM) adjuvant and incomplete Freund's adjuvant (IFA) were examined. Heterologous recombinant expression of OmpK17 and OmpK36 antigens as well as their fusion protein was successful in *Escherichia coli*. Mice were immunized three times with the individual recombinant purified antigens adjuvanted with one of the three adjuvants. Two weeks after the last booster, mice were challenged with a lethal dose of *K. pneumoniae* and immune protection was assessed. Animals immunized with subcutaneous IFA-adjuvanted antigens showed the best results with survival percentages of 60, 50 and 50% for groups immunized with OmpK36, OmpK17 and F36/17 respectively. Animals immunized with GEM- or Hz-adjuvanted *K. pneumoniae* antigens did not reveal any significant protection following bacterial challenge. Serum IgG1, rather than IgG2a, antibodies were dominant following vaccination indicating shift towards T helper type 2 (Th2) immune response. Opsonophagocytic assays demonstrated significant percentage killing in animals immunized with IFA-adjuvanted antigens. In conclusion, OmpK36 and OmpK17 are promising vaccine antigens as evidenced from the current murine infection model. Further optimization of the immunization conditions is warranted, particularly the employed immunoadjuvants, to fulfill complete protection against *K. pneumoniae.*

Keywords: Klebsiella pneumoniae; Vaccine; Outer membrane proteins; OmpK17; OmpK36; Hemozoin; GEM adjuvant.

PHS 604: Do we need to raise the bar to properly identify methicillin resistant *Staphylococcus aureus*?

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Background: Methicillin resistant *Staphylococcus aureus* (MRSA) is a notorious pathogen causing hard to treat infections in hospital and community settings. This highlights the need for rapid, accurate and cost-effective identification tools to guide the appropriate treatment. In this study, we are evaluating the effectiveness of different phenotypic and molecular techniques to correctly identify the isolate to the species level as well as determining methicillin resistance.
Methods: A total of 107 staphylococcal isolates were collected from Alexandria Main University Hospital over four months in 2015. Isolates identity was checked using conventional phenotypic methods such as growth on mannitol salt agar (MSA) and DNase agar, coagulase testing using Dryspot Staphytect Plus™ test and polymerase chain reaction (PCR) detection of *16S rRNA* and *nuc* genes in addition to using Matrix- assisted laser desorption/ionization (MALDI-TOF) as a gold standard for identification. Cefoxitin disc diffusion and PCR detection of *mecA* were used to assess methicillin susceptibility.
Results: Relative to MALDI-TOF, all methods were highly sensitive (100%) in detecting *S. aureus*. However, Dryspot Staphytect Plus™ test was the most specific (93.33%), followed by growth on DNase agar (86.67%), PCR (50%) and finally growth on MSA (6.67%). The tests also showed positive predictive values in the same decreasing order. On the other hand, methicillin resistance detection using both disc diffusion and PCR showed the same results.
Conclusions: Dryspot Staphytect Plus™ test is a fairly accurate method for *S. aureus* identification with high sensitivity and predictive power. It has the advantages of low cost, speed and ease of use without the need for special training and sophisticated machinery. Regarding methicillin resistance detection, cefoxitin disc diffusion remains a favored method in low resource settings because of its low cost.

Keywords: MRSA; Staphytect; PCR; MALDI-TOF; Cefoxitin.

PHS 605: Prevalence and mechanisms of Linezolid resistance among Egyptian Staphylococcal clinical isolates

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Background: Antibiotic discovery changed the face of medicine in the first half of the 20th century. Following the introduction of most antibiotic classes in clinical practice, bacteria developed resistance to their action making many effective antibiotics practically useless. The discovery of new antibiotic classes became a must, and one such example is the oxazolidinones with linezolid as the lead agent. This study investigated the current prevalence and mechanisms of linezolid resistance among staphylococcal isolates obtained from Alexandria Main University Hospital between 2011 and 2015.

Methods: Linezolid resistance was determined using disc diffusion and confirmed by minimum inhibitory concentration determination. Linezolid resistant mutants were selected through serial passages in linezolid sub-inhibitory concentrations. To study the mechanisms of resistance, polymerase chain reaction (PCR) was used to detect *cfr* gene, and PCR and sequencing were carried out to investigate the mutations in the different alleles of 23S rRNA gene. In addition, combinations of linezolid with other antimicrobial agents and anti-inflammatory agents were investigated using time kill and modified checkerboard assays.

Results: This study comprised 232 clinical staphylococcal isolates, linezolid resistance was found to be 3% (n=3) and only among the isolates collected in 2015. However, successive exposure to linezolid sub-inhibitory concentrations selected for three resistant mutants out of nine susceptible isolates. These mutants became more resistant towards the other antibiotics more than their susceptible parents. One of the resistant isolates was shown to carry *cfr* gene which was plasmid borne. Sequencing of the different alleles of 23S rRNA gene revealed a G2603T point mutation in two isolates. In addition, combinations of linezolid with doxycycline, imipenem, ibuprofen or aspirin were synergistic against the tested isolates.

Conclusions: The resistance to linezolid remains fairly low against the Egyptian isolates. However, strict antimicrobial stewardship guidelines need to be observed in Egyptian hospitals to guard against the development of resistant mutants.

Keywords: Linezolid; Staphylococcal; PCR; Antimicrobial stewardship; Resistance.

PHS 606: Yes, we can. A local antibiotic policy changing prescription pattern in outpatient clinics

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The alarming trends of antibiotic resistance are challenging healthcare professionals worldwide. Antibiotic resistance is mainly caused by antibiotic abuse which points optimizing antibiotic use as a way out. This study focused on the establishment of a local antibiotic policy and measurement of its effects in six outpatient clinics of Borg Al-Arab general hospital in Alexandria and consisted of three phases. The pre-protocol survey ran for three months and determined the differential frequency of prescribed antibiotics/month. The second phase was the design and implementation of an antibiotic use protocol based on international guidelines. The post-protocol survey ran for one month to determine and compare the frequency of prescription of the different antibiotics. Implementation of the antibiotic use protocol decreased the overall unnecessary antibiotic prescription. In case of otitis media, antibiotic prescription decreased 77% with amoxicillin/clavulanic acid being the most prescribed antibiotic. For respiratory tract infections, antibiotic use decreased in most of the cases, including sinusitis (49%), bronchitis (61%) and common cold (51%), the latter two being mostly viral in origin. Symptomatic treatment increased 0% to 15% and 32% to 61% in case of pharyngitis and sinusitis, respectively. Ciprofloxacin remained the most prescribed agent (58%) for urinary tract infections. Antibiotic prescription rates decreased in uncomplicated skin infections (cellulitis (88%), impetigo (80%) and diabetic foot infection (63%)). In case of gastroenteritis, cefotaxime prescription dropped from 21% to 1%. The cost benefit analysis showed a twofold reduction in the cost of antibiotics following protocol implementation. Antibiotics weren't misused for the treatment of most infections monitored, yet they were overused. The new protocols decreased unwarranted antibiotic prescription and encouraged symptomatic measures. It is recommended to use the current model of antimicrobial stewardship in the different clinics of Borg Al-Arab Hospital and to apply it to other hospitals to decrease the emergence of antibiotic resistance.

PHS 701: Oxidative stress mediated by NMDA2B expression by flavoring agents containing monosodium glutamate in rat hippocampus: Neuroprotective effect of curcumin

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Monosodium glutamate (MSG) is a popular flavor enhancer used in food industries. Oxidative stress is well documented in MSG induced neurotoxicity. The compounds having antioxidant properties like curcumin reportedly possess beneficial effects against various neurotoxic insults. Hence, the present study has been designed to evaluate the neuroprotective effect of Curcumin on MSG-induced neurotoxicity in rats. Rats were divided into four groups: Control untreated, MSG treated group, curcumin treated group and MSG + curcumin treated group. Curcumin (300 mg/kg body weight orally) day after day was given for 4 weeks along with MSG (6 mg/g body weight orally). After month, rats were scarified, serum samples were collected and brain hippocampi were isolated, and homogenized. Serum acetylcholine esterase enzyme activity determined. Hippocampi for NMDA2B gene were assessed by RT-PCR. Treatment with curcumin significantly attenuated acetylcholine esterase activity in MSG-treated animals. MSG elevated the NMDA2B gene expression with a significant decrease after CUR addition. Hence, this study demonstrates that glutamate exposure may induce over-activation of NMDA-type glutamate receptors that may increase Ca^{2+} influx into neurons. This Ca^{2+} can be taken up by mitochondria, where it may stimulate the generation of oxidative species that damage the cell. curcumin as flavor enhancer protects against MSG-induced neurotoxicity in rats. Recently, an Inter-individual variability study of antioxidant enzyme activity in healthy young adults from Delta University is designed. The relation between three known antioxidant enzymes and genetic polymorphisms will be examined. A substantial component of this variability may be attributable to excessive exposure to diet containing MSG.

Keywords: Curcumin; Monosodium Glutamate; NMDA2B; Oxidative Stress.

PHS 702: 3D Cell Culture in Cancer Targeted Therapy Discovery

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Unquestionably, the use of 2D cell cultures does not accurately represent the functions of 3D tissue cultures that mimic the tumor microenvironment a crucial thing for tumor growth and cell metabolism. Until the year 2009 all in vitro cytotoxicity testing has been performed using 2D cell cultures, and it will be very important to demonstrate a suitable 3D cell model and compare the results with 2D cell cultures. Purpose. This study aimed to explain the importance of using 3D cell cultures in cancer targeted therapy discovery. Materials and Methods. The author performed a computerized systemic literature review of studies related to the application of 3D cell culture from electronic databases PubMed, Web of Knowledge and Google Scholar from 1980 to 2019. Results. This study showed the critical role of 3D cell cultures in studying heterotypic crosstalk and the microenvironment of tumor cells, which proved to be key determinants of the multistep process of tumor development. They are proved to be responsible, to a significant extent, for the poor response and resistance of cancer cells to molecular-targeted therapies. When cancer drug responses have been directly compared in 2D and 3D tumor cell culture models, differential drug sensitivity between the two models can be manifested as either greater resistance or enhanced sensitivity in the 3D culture. In consequence, a broad consensus has emerged that in vitro 3D tumor cell cultures provide more appropriate preclinical models to evaluate the potencies of cancer drug leads for solid tumors, and that the application of these models have the potential to improve the success rate of drug candidates that advance into mouse tumor models and clinical trials. Conclusion. In conclusion, the author also anticipate that it can potentially be applied to in vitro toxicity testing of new drug candidate compounds.

Keywords: 3D cell culture; Cytotoxicity; Targeted therapy.

PHS 703: Exploiting the epigenetic regulation: Estrogen receptor beta-1 as a promising therapeutic candidate in prostate cancer

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Purpose: Estrogens represent key factors in prostate biology, cellular proliferation and differentiation as well as cancer development and progression. Estrogens exert their actions through two distinct estrogen receptors (ER), namely ER-α and ER-β. ER-β role remains as a matter of debate. However, the expression of estrogen receptor (ER)-β appears to be lost during prostate cancer progression through hypermethylation mechanism. Studies pointed to the success of epigenetic drugs such as 5-aza-2′-deoxycytidine (5-AZAC) and Trichostatin A (TSA) in re-expressing ERβ in prostate cancer cells. The current study aimed to explore the potential anti-carcinogenic effects resulting from re-expressing ERβ1 using 5-AZAC and/or TSA, followed by stimulation with its selective agonist, Diarylpropionitrile (DPN), in prostate cancer cell line PC-3. Materials and Methods: Cells were treated with 5-AZAC, TSA, DPN and combinations thereof. Afterwards, they were subjected to proliferation assays, determinations of ERβ1 expression, protein levels of active caspase-3, cyclin D1, β-catenin and VEGF. Results: Treatment with these drugs exhibited an increase in ERβ1 expression to different extents as well as active caspase-3 levels. Meanwhile, a significant reduction in cyclin D1, VEGF and β-catenin levels was achieved as compared to vehicle control group. Interestingly, the triple combination demonstrated the most prominent anti-tumor responses in terms of increased apoptosis, reduced proliferation as well as angiogenesis. Conclusion: The results corroborates the notion that ERβ1 is a tumor suppressor protein and suggest that sequential ERβ1 expression and activation can offer potential anti-tumor responses. The study highlights that merging epigenetic and hormonal therapies may be beneficial in treating advanced prostate cancer.

Keywords: ERβ1; Prostate cancer; Epigenetics; 5-Aza-2'-deoxycytidine; Trichostatin A.

PHS 704: Isolated compounds from *Cuscuta pedicellata* ameliorate oxidative stress and upregulate expression of some energy regulatory genes in high fat diet induced obesity in rats

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Background: Cuscuta pedicellata and some of its isolated compounds were suggested previously to have an anti-obesity effect in rats. This study aimed to investigate the effect of ten isolated compounds from C. pedicellata on insulin resistance, some oxidative stress markers and expression of the mitochondrial uncoupling protein-1 (UCP-1) and Carnitine palmitoyltransferase-I (CPT-1) genes in brown adipose tissue of high fat diet (HFD) rats.
Methods: One hundred and four male albino rats were divided into 13 groups. Group (1) was considered as normal untreated rats. Obesity was induced in all other groups by HFD. Group (2) served as obese control group and groups (3-11) were treated for four weeks with C. pedicellata extract or one of its isolated compounds (naringenin, kaempferol, aromadenderin, quercetin, 3,5,7,30,50-pentahydroxy flavanone, naringenin-7-O-b-d-glucoside, aromadenderin-7-O-b-d-glucoside, taxifolin 7-O-b-d-glucoside, kaempferol-3-O-b-d-glucoside [astragalin], and quercitin-3-O-b-d-glucoside [isoquercitrin]). At the end of the experiment, rats were then sacrificed under anesthesia and their brown adipose tissues were dissected out for determination of UCP-1 and CPT-1 genes using quantitative PCR. Blood samples were collected for determination of blood glucose, insulin, thiobarbituric acid reactive substances (TBARS), superoxide dismutase (SOD) and catalase.
Results: A significant reduction in homeostasis model assessment-insulin resistance (HOMA-IR) and TBARS levels was observed in rats treated with C. pedicellata crude extract and some of its isolated compounds, with a significant increase in SOD and catalase levels and upregulation of UCP-1 and CPT-1 genes expression compared to the obese control group.
Conclusions: This study suggests a beneficiary role of C. pedicellata in reducing insulin resistance, oxidative stress and enhancing energy expenditure.

Keywords: Cuscuta pedicellata; Oxidative stress; High fat; Obesity; Energy regulatory genes.

PHS 705: Serum MIF level as a clinically biomarker at the early pre-symptomatic stages of Alzheimer's disease in diabetic patients

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Pre-symptomatic stages of dementia could be more frequent at early onset of other diseases as diabetes mellitus (DM). A non-enzymatic glycation reaction could be represented through Alzheimer's disease (AD) pathology and is associated with hyperglycemia. Macrophage migration inhibitory factor (MIF) is a cytokine in which early glycation and oxidation of it in AD brain was previously identified. This modification inhibits MIF enzyme activity and ability to stimulate glial cells. MIF is involved in immune response and insulin regulation, hyper-glycaemia, oxidative stress and glycation are all implicated in AD. Therefore, the current study aimed to investigate that serum MIF could predict brain neurodegeneration at the early pre-symptomatic stages of Alzheimer's disease in diabetic patients. **Patients & Methods:** Subjects were divided into: **Group 1** (n=10): Normal control Non-diabetic subjects. **Group 2** (n=10): Diabetes mellitus patients with non-symptomatic AD (DMNAD). **Group (3)** (n=20): Diabetes mellitus patients with Pre-symptomatic AD (DMPAD). Blood samples were collected from all groups. In this study, participants were assessed using a short form of the IQCODE to evaluate for dementia. Additionally, all the participants had a physical examination, including assessment of glycated haemoglobin, fasting blood glucose and lipid profile. MIF level was measured. **Results:** A total of 24 diabetic patients (80%) had pre-symptomatic dementia, 19 of whom were women. Pre-symptomatic dementia in the diabetic patients was significantly associated with advancing age, female gender, duration of diabetes and hypertension. MIF level in serum is negatively correlated with symptoms of dementia that it diminished at the pre-symptomatic stages of Alzheimer's disease. **Conclusion:** Diagnosis processes could not be used as routine examinations for still pre-symptomatic AD. So, serum MIF level could predict brain neurodegeneration at the early pre-symptomatic stages of Alzheimer's disease in diabetic patients which may support its potential utility as a clinically useful biomarker.

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Keywords: MIF; Biomarker; Alzheimer; Diabetes; Glial cells.

STUDENT POSTERS

PHS 801: Nanotechnology-based drug delivery systems for enhanced anticancer activity of resveratrol against brain tumor

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Resveratrol (RES), one of the chief phytoestrogens, has well-proven anti-cancer effect against many types of cancer especially brain cancer. However, its clinical application as anti-cancer agent is hindered by poor bioavailability, low aqueous solubility, chemical instability and extensive metabolism. In literature, various resveratrol loaded-nanocarriers have been fabricated to enhance RES anticancer effect against brain tumor; such as: lipid core Nanocapsule (LNCs), liposomes, solid lipid nanoparticles (SLNs), polyethylene glycol-poly lactic acid nanoparticles (PEG-PLA NPs), and methoxypolyethylene glycol-poly(caprolactone) nano fibers (NFs). Some nanocarriers passively accumulate at brain tumor tissue due to enhanced permeability and retention effect; such as: RES-loaded SLNs and LNCs. Others; such as: liposomes and PEG-PLA NPs were modified with transferrin as targeting ligand to brain tumor cells. On the other hand, RES-loaded nanofibers were prepared for local implantation at tumor site. All these nanocarriers were less than 250 nm and showed high RES encapsulation efficiency (above 80%). These nanocarriers showed sustained drug release compared to free RES. Moreover, they showed enhanced in vitro cytotoxicity and lower IC50 against glioma cell line (either U87 MG cells or c6 glioma cell lines). RES-loaded SLN showed higher systemic circulation and brain accumulation compared to RES alone. Other nanocarriers (LNCs, liposomes, NFs, PEG-PLA) showed enhanced in vivo anticancer effect and improved survival in animal models of brain tumor. In conclusion, nanocarriers seem to be a promising approach to enhance anticancer effect of RES against brain tumor.

Keywords: Resveratrol; Brain tumor; In vitro cytotoxicity; In vivo antitumor effect.

PHS 802: Worsening Cardiac Autonomic Neuropathy on Progression to Type 2 Diabetes: Systemic Inflammation, Central Inflammation, and Autophagy

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Cardiac autonomic neuropathy (CAN) commonly occurs early in the course of diabetes with significant cardiovascular risks. CAN development is linked to hyperglycemia; however, current understanding extends it to pre-diabetes. The instigating cause of CAN, its temporal progression, and responsiveness to therapy remain ill-defined. To address these questions, we developed a rat model of mild hypercaloric intake (4.035 versus 3 KCal/g) developing only hyperinsulinemia after 12 weeks of feeding. Type 2 diabetes was induced by low-dose streptozotocin (40 mg/kg). Progression to diabetes was associated with worsened baroreceptor sensitivity on invasive hemodynamic recording. Pre-diabetes was characterized by an exaggerated pressor response to phenylephrine (PE) and only a blunted parasympathetic reflex, related to perivascular adipose inflammation and responsive to treatment with non-hypoglycemic, anti-inflammatory doses of metformin (100 mg/Kg) and pioglitazone (2.5 mg/Kg). However, hyperglycemia brought about blunted vasoconstriction and a decrease in sympathetic outflow related to systemic inflammation. Persistent parasympathetic insult was only reversed by combination treatments, with Insulin and Metformin/Pioglitazone (at non-hypoglycemic doses), producing the greatest decrease in sera IL-1b. Signs of focal cardiac ischemia were associated with a drop in maximal rate of rise of ventricular pressure (dP/dt). Brainstem examination revealed persistent oxidative stress and emerging inflammation with concomitant microglial activation manifested by elevated IL-1b and Iba1, respectively. This was accompanied by suppressed autophagy reflected by an increase in p62 and a decrease in Beclin-1. Treatment of differentiated pheochromocytoma (PC12) cells with high free fatty acids (FFA, 1.6 mM) and insulin (40 mIU/ml), high glucose (HG, 100 mM), or a combination of HG and FFA did not suppress autophagy. Only treatment with sera from diabetic rats did, providing a link between systemic and central inflammation. Our results outline a series of successive involvement of different disease components in the pathology of CAN and highlight the importance of stringent therapies targeting them.

Keywords: Type 2 Diabetes; Cautonomic neuropathy; Inflammation; Autophagy.

PHS 803: Assessment of microbiological quality of household drinking water in Alexandria, Egypt

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Background: Sewage contamination of household drinking water poses a serious health hazard. Absence of indicator organisms linked to fecal contamination must be confirmed to ensure microbial safety of drinking water (1). The aim of the present study is to assess the microbiological quality of tap chlorinated drinking water in different districts in Alexandria, Egypt.
Methods: We collected 15 household tap water samples from 14 different districts in Alexandria using aseptic sampling techniques (2). Presumptive, Eijkmann's and indole tests were employed to detect total coliforms, thermotolerant coliforms and Escherichia coli, respectively using proper controls.
Results: Only one (sample 15) out of the 15 samples showed positive lactose fermentation in the presumptive test with an estimated count of 2 coliform cells per 100 ml of water sample as deducted from probability tables. Another sample (sample 8) showed a faint color change but no gas production. Eijkmann's and indole tests were performed to confirm the results seen with samples 8 and 15 and both were negative. This indicates the presence of environmental but not fecal coliforms in samples 8 and 15.
Conclusions: All drinking water samples were found to be microbiologically safe. However, the chemical quality of drinking water, including measurement of the concentrations of chlorine, arsenic, lead, fluoride and total dissolved salts, must also be assessed to ensure the complete safety of drinking water in Alexandria (3).

Keywords: Water analysis; Tap drinking water; Coliforms; Presumptive test; MPN; Eijkmann's test; Indole test.

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PHS 804: Knowledge is power! Raising public awareness to fight antimicrobial resistance.

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Background: Infectious diseases are among the leading causes of death worldwide. This is worrisome because of the increasing capacity of the pathogens to develop resistance to most antibiotics. Antibiotic overuse and misuse are the main drivers of resistance development. Centres for diseases control and treatment launches an annual campaign to raise awareness of antibiotic misuse hazards and to promote their judicial use. Similar efforts are lacking in Egypt, this study aimed to assess the knowledge of the general public in Alexandria of antibiotic misuse risks and their habits towards antibiotic use, in addition to mounting a campaign to increase awareness.
Methods: A questionnaire was used to collect responses from study participants who were members of different sports clubs in Alexandria. The survey gathered data about past antibiotic use, knowledge and attitudes towards antibiotics. Consequently, the same groups of people were later targeted in a campaign to raise awareness toward antibiotics and bacterial resistance. A post awareness questionnaire assessed the effectiveness of the awareness sessions.
Results: In total, 294 persons participated in this survey. Eighty percent of the participants took antibiotics last year, of these, 85% used antibiotics for common cold. Besides, 32% of the participants stopped the antibiotics when they felt better despite the finding that 68% of the participants have heard about antibiotic resistance. The awareness campaign succeeded in decreasing the percentage of those believing they need antibiotics for any infection to 5%, and 100% of the participants stated that they won't prompt their doctors to prescribe antibiotics. Moreover, 95% of participants opted to finish the antibiotic regimen.
Conclusion: Although awareness of antibiotic resistance is rising, some wrong perceptions hold fast, highlighting the need for continued awareness as part of a structured and national public health program for a wider outreach for the Egyptian population.

Keywords: Knowledge; Public awareness; Antimicrobial resistance.

PHS 805: Staphylococcal nasal carriage among pharmacy students in Alexandria

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Background: *Staphylococcus aureus* nasal carriage occurs even in healthy individuals who may infect others. *S.aureus* can also colonize the immunodeficient or vulnerable patients and cause symptoms varying from boils to life-threatening nosocomial staphylococcal infections. Aim of work: Assessment of the staphylococcal nasal carriage and resistance rates among healthy Alexandria University Pharmacy students. Materials and Methods: One hundred ninety-six nasal swab specimens were obtained and grown on nutrient broth. Identification of *S. aureus* in the samples was accomplished by growth on Mannitol salt agar (MSA) and DNase agar plates. Antibiotic sensitivity was assessed by disc diffusion method using cefoxitin discs to test for methicillin resistance. Results: Out of the 196 samples,30 were contaminated and thus excluded. The remaining 166 swab specimens yielded a total of 315 isolates, of which 111 were presumed *S. aureus* and 164 coagulase negative staphylococci as shown from growth on MSA. Growth on DNase confirmed the identity of 49 isolates (from 28 samples) as *S.aureus*, of these 61. 22% (30/49) were methicillin resistant (MRSA). The MRSA isolates were also resistant to fucidic acid (76.67%), erythromycin (40%), tetracycline (26.67%), co-trimoxazole(10%), chloramphenicol (10%), gentamicin (6.67%), teicoplanin(6.67%), vancomycin (3.3%), clindamycin (3.3%), rifampicin (3.3%), linezolid (3.3%), yet totally susceptible to mupirocin and moxifloxacin. Conclusion: One in six students was a *S. aureus* carrier, and the commensal was MRSA in more than half of the tested pharmacy students' population which is considered a high carriage rate and warrants special consideration of personal hygiene habits.

Keywords: Methicillin resistant Staphylococcus aureus; Antimicrobial resistance; Egypt; Personal hygiene.

PHS 806: Antibiotic consumption in the community: Is it veering from the straight and narrow?

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Background: The rapid spread of antibiotic resistance is a global nightmare. Antibiotic resistance occurs when bacteria stop being killed or inhibited by once-effective antimicrobial agents. Resistant infections are harder to treat resulting in lengthier hospital stays and more expensive healthcare. The main drivers of antimicrobial resistance are antibiotic overuse and misuse, especially in cases of viral infections such as common cold. Aim of work: To assessthe levels of antibiotic consumption among outpatients in different districts of Alexandria. Methodology: We conducted a survey in 13 different community pharmacies over the course of four hours to collect data about the classes and volumes of antibiotics sold by prescription or otherwise, relative to antihistaminics and analgesics. In addition, we collected data from the pharmacists in the participating pharmacies about their own perception of antibiotic consumption rates. Result: Average demand for antibiotics/hour was (2.57/47%), lower than that for analgesics and antihistaminics (3.1 /53%). The average demand for antibiotics with a prescription was (1.48 / 57.5%), without a prescription (0.54 /21%) and based on the pharmacist's recommendation (0.5/19.45%). B-lactams were in highest demand (61.9%), followed by macrolides (29.1%), flouroquinolones (28.35%), tetracycline (2.98%), aminoglycosides (2.98%), glycopeptides (2.98%) and theoxazolidinones(2.98%). Polymyxins were never purchased during the study. The pharmacists' assessment of the rates of antibiotic consumption concurred with these findings, albeit they reported polymyxins use in 1.79% of the cases Conclusions: Prescribed antibiotic use occurred more often than non-prescribed use. Yet, antibiotic self-medication was more frequent than antibiotic consumption following a pharmacist's recommendation. This stresses the need for targeted awareness campaigns to reduce unwarranted antibiotic use and highlights the role of pharmacists in delivering such campaigns.

Keywords: Antimicrobial resistance; Antimicrobial stewardship; Outpatients; Self-medication; Awareness.

PHS 807: Electrophoretic analysis of some *para* amino benzoic acids, benzophenones and parabens in cosmetic preparations

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Capillary electrophoresis is described as a green and environment friendly analytical method. It offers many advantages including the use of small amounts of reagents and materials in order to decrease the environmental pollution and the harmful effects of currently used chemicals on human health. Moreover, it offers fast and highly efficient separation with performing high voltage electrophoresis in capillary tubes and enhanced heat dissipation that permits the use of high potentials for separation. In addition to its low operating cost and need for minimum sample cleanup. Therefore, it is highly recommended for capillary electrophoresis to be one of the most used methods for quality control purposes of pharmaceuticals and cosmetic products in the market. Sunscreens are one of the most commonly used cosmetic products. Here, we provide a brief review of the analysis of different sunscreen active ingredients using capillary electrophoresis. Numerous compounds are now used as active ingredients in sunscreens to absorb ultraviolet radiation and protect skin from sunburns. Para amino benzoic acids (PABA), benzophenones, cinnamic acid and its derivatives and parabens are considered the most commonly used active ingredients in sunscreen formulations. In this work, we will present a brief review on their analysis using capillary electrophoresis. This work will demonstrate the different optimization conditions used, such as pH, buffer composition and concentration and electrophoretic parameters. In addition to the effect of organic modifiers, surface active agents and graphene quantum dots on various electrophoretic separation will be presented. Also, various validation parameters and all analytical figures of merits will be discussed. Finally, a comparison of the discussed methods will be presented including run times, linearity between the peak-area ratios and concentration, reproducibility, selectivity, sensitivity, accuracy and precision.

Keywords: Electrophoresis; Benzoic acids; Benzophenones; Parabens.

PHS 808: Adherence to and effectiveness of local antimicrobial treatment guidelines in pneumonia patients

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Background: Pneumonia can be caused by several bacterial species, viruses and fungi. It occurs as a result of nosocomial as well as community acquired infections and remains an important cause of death, especially in developing countries. In the era of multi-resistant pathogens, it is crucial to establish proper treatment guidelines to improve cure rates and reduce resistance development. The present study is concerned with assessing the effectiveness of local antimicrobial treatment guidelines in improving clinical outcomes in pneumonia patients. Methods: A questionnaire was used to follow up pneumonia patients admitted to the emergency units at Alexandria Main University Hospital (AMUH). Limited epidemiological data were collected, in addition to the antibiotics prescribed as part of the treatment regimen, co-morbidities and clinical outcomes. Results: Ten adult patients were included in the study. They were 60% males with median age of 60 years. Two patients (20%) had a history of smoking and three (30%) were diabetic, with one patient (10%) suffering from asthma and another (10%) reporting respiratory problems. The majority of the patients (70%) were diagnosed with community acquired pneumonia, with sepsis in 57.1% of the cases. The remaining three patients (30%) suffered from hospital acquired pneumonia, with sepsis in two cases (66.67%). Of the total ten patients, 70% improved over the study. The most commonly prescribed antibiotics were levofloxacin (60%), cefoperazone/sulbactam (50%) and cefepime (40%), in agreement with the local guidelines in 70% of the cases. Conclusion: Although rates of hospital acquired pneumonia detected in the study are moderate, we recommend stricter infection control to prevent the spread of such infections. The findings also suggested above average compliance with pneumonia treatment local guidelines in AMUH. We recommend more vigilance in applying the local guidelines towards a better clinical outcome.

Keywords: AMUH; Antibiotics; Hospital acquired infections; Community acquired infections.

PHS 809: Intra-abdominal sepsis management: Are we doing it right?

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Background: Sepsis is a devastating response of the body to an infection, following the release of inflammatory mediators into the bloodstream. It can lead to multiple organ dysfunction and is life threatening. Intra-abdominal sepsis (IAS), or peritonitis, is the second most common type of sepsis. If unchecked, it can lead to septic shock with a 1% mortality rate. In this study, we are monitoring the appropriateness of the antibiotic regimens prescribed patients suffering from IAS at the Emergency Units at Alexandria Main University Hospital (AMUH). Methods: Nine patients admitted to the Emergency Units at AMUH and suffering from IAS were included in the study. Data about the antibiotic regimen the patients were prescribed were collected from medical records and the patients were followed up for one week to monitor their response to treatment. The treatment regimens were then checked against the International Diseases Society of America (IDSA) guidelines for treating IAS. Results: Only three patients (33.3%) were given the right regimen in accordance with IDSA guidelines. Two of these patients improved while the third deteriorated. Of the six patients not receiving proper antibiotic treatment, three (50%) deteriorated, two (33.33%) remained stable, and one (16.67%) improved. Regarding the regimen, only two patients (22.22%) were on a single antibiotic while the rest were taking a combination of antibiotics due to the severity of their conditions and the underlying co-morbidities. Moreover, imipenem/cilastatin, teicoplanin, levofloxacin, metronidazole, and fluconazole were most commonly prescribed. Imipenem/cilastatin was prescribed in combination with other antibiotics to (44.44%) of the patients while teicoplanin, levofloxacin, metronidazole, and fluconazole were used in combination with other antibiotics by (33.33%) of the patients. Nevertheless, only one out of five patients (20%) receiving one or more of the previous drugs was on the right prescribed drugs as in the guidelines. Conclusion: Treatment regimens in our setting didn't follow the IDSA guidelines for managing patients with IAS in most of the cases. The results at hand sound an alarm for the need to reassess IAS treatment guidelines to provide patients with the right remedy while reducing the risk for antimicrobial resistance development.
Keywords: AMUH; Peritonitis; IDSA; Treatment outcome.

PHS 810: Computer-assisted discovery of novel natural product inhibitors of Brk tyrosine kinase for triple negative breast cancer control

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Breast cancer (BC) is the most commonly diagnosed cancer in women and the second most common cancer overall. Triple-negative breast cancer (TNBC) is an aggressive subtype constituting 15-20% of all cases and lacks estrogen (ERα)/progesterone (PR) receptors expression and HER2 amplification. Compared to other BC subtypes, TNBC is diagnosed at a younger age, higher grade, larger tumor size, leading to higher mortality rates. Clinically, patients with TNBCs have poor prognosis with few available therapeutic options, particularly in its late invasive and metastatic stages. Due to its heterogeneity, TNBC lacks effective targeted therapies; although TNBC patients initially respond to chemotherapies, they often relapse with drug resistant metastatic deadly diseases, suggesting the urgent need for an expanded repertoire of targeted therapeutics to satisfy such clinical oncology unmet need. Among possible potential drivers of TNBC proliferation, metastasis and survival, the oncogene protein tyrosine kinase 6; PTK6 (hereafter Brk) has gained considerable attention as an attractive molecular target for therapeutic blockade with small molecule (SM) inhibitors. Brk which is expressed in approximately 70% of TNBCs, where it acts to promote survival and metastatic lung colonization. In this study, a small but chemically diverse library of natural products a virtual screening approach was adopted for screening a small in-house library of 450 NPs to discover hits that most likely bind the Brk ATP binding site and stabilize its inactive conformation. The five in silico hits with highest docking scores and optimal fitting were subjected to further biological validation using biochemical assay that assesses the ability of compounds to inhibit Brk phosphorylation in a cell-free setting. Among the tested compounds, compound I was able to inhibit Brk phosphorylation in a dose-dependent manner with an IC_{50} value of 0.56 µM. Importantly, compound I significantly inhibited the proliferation and migration of the triple-negative MDA-MB-231 breast cancer cells, with IC_{50} values of 13.3 and 0.98 µM, respectively, which validated the results of the virtual study. Despite the small size of the used library, the hit rate (1.1%) of the applied in silico approach was comparable to the high-throughput physical screening, but with modest efforts and expenses involved in hit identification. In conclusion, the results support the hypothesis that natural products could provide novel unprecedented pharmacophores for the design of future Brk inhibitors with great potential to selectively control TNBC.
Keywords: Breast cancer; Triple-negative; Brk; Proliferation; Migration; Natural products.

PHS 811: Probing metformin-induced DNA damage

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Metformin, an anti-diabetic agent, was found to also have an anti-cancer effect. It has a protective role, enhances cancer therapy, inhibits migration and invasion of tumor cells. It's mechanism against cancer is via interaction with several metabolic pathways. Growth factors as insulin and insulin-like growth factor can promote tumorigenesis by stimulating the proliferation of epithelial cells, so metformin prevents it by reducing hyperinsulinemia and lowering levels of these signaling. In addition, metformin plays a role in immune response to cancer cells that metformin protects tumor-infiltrating lymphocytes from apoptosis and functional exhaustion. Metformin is also improving the efficacy of an experimental anti-cancer vaccine by promoting the survival of memory T-cells. Metformin inhibits complex I and disrupt oxidative phosphorylation which is important requirement for tumorigenesis inhibition. Furthermore, metformin inhibits migration and invasion of tumor cells, partly by downregulating H19 genes (one of the highest expressed genes during embryogenesis and placental development) via DNA methylation, as H19 promotes tumor cell migration and invasion by inhibiting the micro-RNA let-7 and H19 overexpression enhances the motility and invasiveness; this affects let-7-mediated regulation of metastasis-promoting genes. Lastly, metformin enhances oxidative DNA damage under oxidative condition via enhancing generation of 8-oxo-7,8-dihydro-2'-deoxyguanosine in isolated DNA reacted with hydrogen peroxide and Cu(II) by formation of nitrogen-centered radicals. These nitrogen-centered radicals enhance oxidative damage at guanine residue, which is the most easily oxidized nucleotide in DNA. Such radicals of biguanides may change various DNA damage into specific oxidation of guanine because of the weak reactivity. They have more opportunities for damaging DNA than the hydroxyl radical. Thus, nitrogen-centered radicals of metformin play important role on the increment of oxidative DNA damage by reactive oxygen species. This work will present a breif comparison on the different mechanisms undertaken by metformin for DNA damage and possible methods to probe this damage.

PHS 812: Study of the DNA modifications induced by 2-Phenylbenzimidazole-5-sulfonic acid

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Sunscreen products consist of several ingredients combined to help prevent the ultraviolet radiation (UVR) from reaching the skin. UVR has several clinical effects on the human skin, including erythema, pigmentation, suppression of acquired immunity and possibly photo carcinogenesis on long term exposure. The role of sunscreens in the prevention of actinic keratoses, squamous cell carcinomas, and melanomas have been demonstrated in recent studies. Sunscreens also prevent photo immunosuppression and signs of photoaging. UVR is directly absorbed by DNA in the skin molecules leading to the formation of cyclobutane pyrimidine dimers (CPDs) and pyrimidine (6 -4) pyrimidine photoproducts (6 -4 PPs). This occurs due to the presence of endogenous skin chromophores as DNA and melanin, as well as exogenous as fluoroquinolones and azathioprine; They absorb photon energy becoming unstable “excited” generating reactive oxygen species which subsequently cause damage to the DNA. Therefore, the regular use of a broad-spectrum sunscreen is effective in preventing UVR-induced DNA damage, but that irregular and inadequate use of sunscreen during exposure to UVR results in CPD formation, which may lead to mutation and subsequent cancer development. 2-Phenylbenzimidazole-5-sulfonic acid (PBSA) or (ensulizole), a molecule approved by the U.S. Food and Drug Administration (FDA), is often found in cosmetic sunscreen formulations because of its intense absorption at UV-B wavelengths. The maximal PBSA concentration approved by FDA is 148 mM. Recent reports have proven that PBSA could possibly damage DNA, as well as proteins and lipids, through a photosensitizing mechanism at 4 mM, which is a very low concentration as compared with the 1478 mM authorized by the FDA. This work will present a brief review on the possible molecular DNA modifications that are induced by PBSA and the mechanism of DNA damage involved.

PHS 813: Quantifications of different modifications in DNA upon UV-irradiation

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Absorption of UV light by nucleic acids can result in the formation of molecular lesions leading to mutagenesis, carcinogenesis, and cell death. Thus, understanding DNA damage is important for elucidating molecular mechanisms of diseases. Fluorescent hybridization assays using molecular beacons (MBs) are widely used for detecting DNA damage. The goal of this work is to present a brief review of different probes that are superior to conventional MBs in detecting DNA damage. The first approach was to design MBs with modified DNA backbones such as, locked nucleic acid (LNA) MBs and the chimeric RNA-DNA MB (chMB). Results show that chMBs are more sensitive and selective for DNA damage than LNA MBs that have comparable selectivity to conventional MBs. However, these probes all show a signal that is inversely proportional to the amount of damage. Also, probes with 2-aminopurine (2AP) as a fluorescent base will be discussed where they show no fluorescence for undamaged DNA and fluorescence for damaged DNA. Thus, the more DNA damage, the more 2AP probes are in the hairpin structure and the higher the fluorescence. 2AP probes offer high sensitivity and selectivity comparable to MBs, but are expensive. Thus, the hypochromism probe was introduced. The hypochromic effect arises from the formation of a double-stranded target-hairpin hybrid. With accumulated UV exposure, the target-hairpin hybrid concentration decreases and the absorbance increases. This probe is more selective and is more than ten times cheaper than MBs but is less sensitive. The need for a sensitive, selective and inexpensive probe was the motivation to design the Tb^{3+}/hairpin probe which is the most sensitive and selective probe for the quantification of DNA damage of all probes presented here. In this work, a comparison of these probes will be presented together with some of the possible applications of such probes.