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# PHS 2022

EGYPT VISION FOR
**HEALTHCARE 2030**

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# ABSTRACT BOOKLET

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*Vice President of the Egyptian Drug Authority*

## Branding Pharmacy Via Education: An Outlook

**Prof. Ayman Noreddin**

*Dean and Vice President for Research and International Relations, Ahram Canadian University*
*Academic Leader, FIP-EMROPHARM*

Pharmacy is going through an evolution process that is changing the scope of practice and offering more opportunities for future pharmacists to participate in patient care and offer new treatment modalities for patients through medicine discovery and development. Multiple practice models are proposed for pharmaceutical care in the community and pharmaceutical industry that responds to the community's needs for advanced health care and novel treatment modalities. A parallel development in pharmacy education is needed to prepare a well-educated and trained pharmacist who can carry the future community responsibilities with confidence and the ability to lead the efforts to provide advanced pharmaceutical care and offer advanced treatment modalities for better health care. Global efforts are underway through WHO/FIP collaboration to build a road map for advanced pharmacy profession development. Several practice models proposed for advanced professional pharmacy services would be discussed. Several drug discovery and development opportunities would be presented with an emphasis on natural product development and phytotherapy. Advanced pharmacy education directions and curricular development would be discussed with defined competence and measurable educational outcomes would be presented.

## Regulatory Governance of Clinical Trials: Pharmacovigilance and Safety Perspective

**Dr. Ashraf El-Fiky**

*Consultant, Clinical Research and Vaccine Safety, WHO*

The Middle East, Mediterranean, Africa (MEMA) region, composes 20% of the world's population. It contributes little to the international effort of health knowledge production, hosting only 6% of the worldwide registered trials. Among the many weaknesses of clinical research in MEMA region is the lack of recognition for the need of developing a sustainable clinical research infrastructure. Lack of a robust, international standards, regulatory framework is the second major hurdle. In addition, there is uncertain public confidence and poor awareness of the importance and the objectives of clinical research. However, the region has a number of attractive features, such as population's size and large pool of eligible patients, least trial saturated of all regions, diversity in genetic profile, and large medication-naive patient populations. An multi-stakeholder effort should act synergistically towards harmonizing the regulatory framework and designing a roadmap for sustainable capacity building in the region, enabling it to produce its own health knowledge and to efficiently join the global knowledge production enterprise. This presentation will discuss clinical trial governance evaluated against the International Conference on Harmonization--Good Clinical Practice (ICH-GCP) guidelines.

## EDA Reference Laboratories: Modernization of National Pharmaceutical Industry

**Prof. Medhat Al-Ghobashy**

*Chairman Advisor for Regulatory & Reference Labs, Egyptian Drug Authority*
*Department of Analytical Chemistry, Faculty of Pharmacy, Cairo University, Egypt*

# EDA Session:

## Fingerprinting, Mathematical Modeling for Certification of Reference Materials

**Dr. Heba Mostafa fayed**

*Egyptian Drug Authority*

Certified reference materials play a pivotal role for pharmaceutical industry. Certification of reference materials is considering modern fingerprint approach for analysis and certification of reference materials in ISO 17025 and ISO 17034 accredited laboratory. Certified reference materials are characterized by a metrological valid procedure for one or more specified properties, accompanied by a reference material certificate that provides the value of the specified property and its associated uncertainty. Certified reference materials are used in multiple disciplines of the measurement processes including for method validation, check the quality and metrological traceability of the product, calibration of measurement systems and for assessing laboratory proficiency. Certified reference materials unit provides a lot of certified reference materials for many strategic products (e.g. Molnupiravir) where the access for such material with the required amounts was very challenging.

## Biosimilars: Prospective Towards Industry Localisation

**Dr. May Ahmed Abd El Aal**

*Egyptian Drug Authority*

Biosimilars are biological medicines that are highly similar to an already-approved reference product. Biosimilars expand the biotherapeutic market and allow better patient access. Biological therapies have introduced a glimmer of hope for many patients with previously untreatable diseases. However, the financial strain of getting such expensive therapies hampered getting advantages from these novel treatments. As patency of these products expires, the development of cost-effective biosimilars allows improved patient healthcare. The establishment of local manufacturing industry targeting the biosimilar products will greatly reduce healthcare expenses and improve overall healthcare serves. In this study; Enoxaparin was received from claiming customer requesting complete biosimilar development study. Enoxaparin is vital product that is used to prevent deep venous thrombosis in patients at risk like pregnant women and after surgical operations. Critical quality attributes of Enoxaparin sodium were evaluated in comparison to the reference product; bioassay and weight average molecular weight. In addition, different stress conditions were applied to assess the degradation kinetics of the biosimilar in comparison to the reference product. The results of the implemented tests elicit minor difference between the two products. However, other essential techniques are currently implemented to complete investigation about the comparability of the products under investigation.

# Pharmaceutical Product Development: Case Studies for Regulatory-Grade Research Services

**Dr. Shaymaa Aly Ibraheem**

*Egyptian Drug Authority*

Driven by competition to finding the most effective way of conducting product development while also adhering to regulatory requirements, both design of experiment and regulatory database are harnessed. This serves collaboration with different pharmaceutical companies in a unique dynamic partnership. In this presentation, it is demonstrated how experimental models can enhance the product development process. One of these models is explored in an example that presented its value and effectiveness, which ultimately resulted in better experience for investigators.

A comparative dissolution test was conducted for two anti-diabetic tablets, reference product and the test product. After comparing the results in the target medium, it seemed that the two products were not similar. By searching the composition of both tablets, it becomes evident that major differences between the two tablets are the cause of failure of test product. The collected data reflected that three basic excipients emerged as potential parameters that may affect release behavior.

For this study, a custom design was implemented. The unique features associated with this design, including user specified runs and disallowable combinations script, allow defining model constrains according to the affordable number of trials. This was specifically advantageous due to the shortage of the mentioned excipients. The prediction profiler of the model suggested a combination of the three critical factors that maximized target desirability. The actual release % of the suggested combination was in consistent with the predicted one with percent bias of 0.85 which reflected the validity of the model.

Such a modernized approach for drug product optimization was evident to be time and cost effective. The result was also aligned to practices of regularity authorities.

# Novel Aspects in Pharmacotherapy:

## Pharmacovigilance in Oncology

**Prof. Ashraf El-Ghandour**

*Vice President of Alexandria University for Graduate Studies and Research*
*Department of Hematology, Faculty of Medicine, Alexandria University, Egypt*

## Advances in Pharmacotherapies: A Personalized Medicine Approach

**Prof. Mahmoud El-Zalabany**

*Department of Pediatrics, Faculty of Medicine, Alexandria University and AAST-MT, Egypt*

Marked advances in targeted drug therapy via researching new pharmacogenomics markers have made it possible to understand the reasons behind the different response of a drug. Targeting disease biomarkers and discovery of polymorphisms of drug metabolizing enzymes, transporters and receptors contribute to variable drug response and provide the basis for optimizing therapy for individual patient. Even though, pharmacogenomics has made few incremental inroads into clinical practice to date, still the genetic makeup-based prescription, design, and implementation of therapy not only improved efficacy of treatments but also minimized toxicity and other adverse effects paving the way towards personalized medical care rather than "one size fits all" approach.

## Recent Advances in Antimicrobial Therapy

**Prof. Ayman Noreddin**

*Dean and Vice President for Research and International Relations, Ahram Canadian University*
*Academic Leader, FIP-EMROPHARM*

Streptococcal pneumonia is a major cause of morbidity and mortality worldwide. Fluoroquinolones are one of the mainstay drugs for treatment of these infections. However emerging resistance poses a threat to the class's future utility. Using Monte Carlo simulation, we evaluated the probable efficacy of ciprofloxacin, levofloxacin, gemifloxacin, garenoxacin, and moxifloxacin in eradicating infections and preventing continued growth of resistance. Methods: Using patient data from strep pneumonia patients in hospitals and MIC data from the CROSS study, drug regimens were compared to see the likelihood of attaining $fAUC_{0\text{-}24}$/ $MIC_{all}$ ratios depicting goal clinical outcomes. Conclusions: Very few regimens are able to prevent further growth of resistant organisms when ParC mutations have occurred. Only garenoxacin and moxifloxacin were able to eradicate extremely resistant isolates in serum and ELF respectively.

## Dapagliflozin Use Beyond Glycemic Control: When Pharmacists Role Becomes More Important than Ever

**Prof. Mohamed Sobhy**

*President and CEO of Interventional Cardiology Center (ICC)*
*Professor of Cardiology, Alexandria University, Alexandria, Egypt.*

## Screening Diabetic Patients Using New Ultra Wide Field Imaging: A Paradigm Shift in Ophthalmology

**Prof. Ahmed Souka**

*Department of Ophthalmology, Faculty of Medicine, Alexandria University, Alexandria, Egypt.*

# Pharmacogenomics and Precision Medicine:

## Pharmacogenetics of Depressive Disorders

**Prof. Ingolf Cascorbi**

*Institute of Experimental and Clinical Pharmacology, University Hospital Schleswig-Holstein, Kiel, Germany*

Major depression is a major global health burden. Although the development of antidepressants helped tremendously to overcome or at least mitigate the diseases, a substantial proportion of patients still suffer from non-response or side-effects. The wide variation in the pharmacokinetics of various drugs can be explained partly by genetic variation contributing to interindividual differences of the activity of metabolic enzymes i.e. cytochrome P450s. Further, drug-drug interactions may contribute to varying plasma concentrations. In contrast, the genetic variation in pharmacodynamics is less understood but recent findings indicate the role of epigenetics in treatment response. Although guidelines have been developed for dose-adaptation and selection of antidepressants, there is still a need to launch large trials to gain further evidence of the clinical benefit. This talk will give an overview on major genetic factors contributing to interindividual variation of response to antidepressants and set-up of clinical trials.

## Pharmacogenotyping: A Proposed Gene Panel

**Prof. Ann Daly**

*Translational & Clinical Research Institute, Newcastle University, UK*

Despite a large number of studies and important advances during the last 30 years approximately, routine genotyping for pharmacogenetic polymorphisms to inform drug prescribing is still performed rarely worldwide. There are some important exceptions to this but these relate mainly to genotyping performed to satisfy regulatory requirements, especially for the HLA alleles B*57:01 and B*15:02, together with TPMT and DPYD variants. More specialised guidelines such as those from the USA-based CPIC and the Dutch Pharmacogenetics Working Group cover a wider range of genes and drugs but adoption in most countries and centres has been more limited. Results from a recent UK-based project which aims to identify a strategy for panel-based preemptive pharmacogenotyping to cover a broader range of genes and drugs will be described. The panel includes several cytochrome P450 genes as well as transporter, phase II metabolism and HLA genes.

## Implementing Pharmacogenetic Testing in Fluoropyrimidine-treated Cancer Patients to Prevent Toxicity

**Prof. Vangelis Manolopoulos**

*Laboratory of Pharmacology, Medical School, Democritus University of Thrace, Greece*

Fluoropyrimidines are widely used for the treatment of solid tumors. Approximately 10-30% of fluoropyrimidine-treated patients develop early-onset severe or life-threatening toxicity. Dihydropyrimidine dehydrogenase (DPD), encoded by DPYD gene, is the rate-limiting enzyme responsible for fluoropyrimidine catabolism. DPYD gene variants seriously affect DPD activity and are well validated predictors of fluoropyrimidine-associated toxicity. DPYD variants rs3918290, rs55886062, rs67376798 and rs75017182 are currently included in genetic-based dosing recommendations for fluoropyrimidines developed by the Clinical Pharmacogenetics Implementation Consortium. On March 2020, European Medicines Agency has recommended that patients receiving fluoropyrimidine therapy should be tested at least for these four DPYD variants before treatment initiation. Furthermore, polymorphisms in several other genes have been suggested to play a role in this effect but evidence is still not conclusive. I will present data from a clinical study in Greek cancer patients confirming the clinical validity of DPYD variations as predictive risk factors for development of fluoropyrimidine-associated toxicities. I will also discuss the current state-of-affairs on fluoropyrimidine pharmacogenomics testing all over Europe.

## Pharmacogenomics of Childhood Leukemia: From Research to Clinical Practice

**Prof. Nathalie Khoueiry Zgheib**

*Department of Pharmacology and Toxicology, Faculty of Medicine, American University of Beirut, Lebanon*

Acute lymphoblastic leukemia (ALL) is the most common cancer in children, accounting for about 30% of childhood cancers worldwide. There is significant inter-individual variability in drug toxicities and disease outcomes, hence the role of pharmacogenomics (PGx) in elucidating genetic polymorphisms in candidate genes for the optimization of disease management. In this talk, I will present current PGx data in association with disease outcome and main toxicities seen in children treated for ALL, with a focus on the most plausible germline PGx variants associated with the highest evidence. I will then follow with a description of ongoing initiatives and data generated from a Lebanese cohort of children with ALL, with suggestions to move forward in implementing preemptive PGx for the individualization of treatment regimens for children with ALL.

## Clinical Pharmacy Practice and Patient Care:

### Herbal Medicine Safe Practice: How to Implement?

**Prof. Ahmed Fathi ELkeraie**

*Department of Internal Medicine & Nephrology, Faculty of Medicine, Alexandria University, Egypt*

Herbal products are widely used worldwide. Although usually advertised and sold under the claim of being natural and safe, they have the potential for both benefit and harm. The standardization of herbal product can be challenging, as the concentration of active ingredients varies by the plant species, part of the plant harvested, maturity, season of harvesting, geographical location, soil composition, weather conditions, storage conditions, processing and extraction, and contaminants. Herbal products can be sold as crude plant materials in 'Attarah' shops and as licensed or unlicensed nutriceuticals. Moreover, unlicensed products could be available through unauthorized sources, and sold illegally through social media or in some 'Attarah' shops, clinics, gyms, and beauty centers. Several studies showed that some of the products sold as nutriceuticals were adulterated. For example, the US Food and Drug Administration (FDA) identified 776 adulterated dietary supplements, from 2007 through 2016. Most of these products were marketed for sexual enhancement (353 [45.5%]), weight loss (317 [40.9%]), or muscle building (92 [11.9%]), with 157 adulterated products (20.2%) containing more than 1 unapproved ingredient. The most common adulterants were sildenafil for sexual enhancement supplements (166 of 353 [47.0%]), sibutramine for weight loss supplements (269 of 317 [84.9%]), and synthetic steroids or steroid-like ingredients for muscle building supplements (82 of 92 [89.1%]). Sibutramine is associated with hepatotoxicity and cardiovascular toxicity and was removed from the markets by the FDA and European Medicines Agency (EMA).

In the Arab world, several studies reported adulteration and unsatisfactory pharmaceutical and microbial quality of herbal products. In Egypt, a study on 6 unlicensed weight-loss marketed products found that products were adulterated with unreported active pharmaceutical ingredients, such as sibutramine, sildenafil, phenolphthalein, and orlistat. Toxicity related to herbal products may occur due to several factors, including direct toxicity; adulteration with drugs or other herbal products; contamination with pesticides, heavy metals, toxins, aflatoxin, and microbes. Sometimes, assuming that herbal products are natural and safe can lead to the misbelief that 'more is better', which can cause significant toxicities from ingesting large quantities. For example, hypertensive emergency due to overuse have been reported with licorice. Another example is ginseng abuse, which was reported to cause cardiovascular, renal, hepatic, and reproductive toxicities, and interactions with anticoagulants. Some herbal products may impact surgery through altered coagulation, (e.g., ginkgo, ginseng, saw palmetto, and garlic), cardiovascular stability (e.g., ephedra), glucose control (ginseng), potentiation of the sedative effect of anesthesia (e.g., valerian and kava), and increased metabolism of perioperative medication (e.g., St. John's wort). Even some of the commonly used herbal products could have undiscovered toxicities.

An example is Aloe vera, as studies showed that ingestion of it would result in metabolism of aloin, its main active compound, the by human gut microflora, resulting in the formation of aloe-emodin anthraquinone, later being associated with several harmful effects such as carcinogenicity, genotoxicity, nephrotoxicity, and purgative.

Adequately powered, double-blinded, placebo-controlled trials on efficacy of herbal products showed that many of them may not be as effective as small trials previously suggested. For example, although widely used as an immune stimulant, a systematic review included 15 randomized trials comparing various echinacea preparations with placebo, showed that there was no benefit of echinacea for the prevention and treatment of common cold. Other herbal products may have therapeutic benefits. For example, soy products have beneficial effects on lipids and cardiovascular health because they are low in saturated fats, high in unsaturated fats, and often rich in fiber. A meta-analysis of the data selected by the FDA indicates continued significance of total cholesterol and low-density lipoprotein cholesterol reduction after soy consumption. Another example is the use of ginger in the management of nausea. In meta-analyses of randomized trials (including over 1000 participants), ginger improved nausea compared with placebo but did not significantly reduce vomiting. Concurrent administration of herbal products may interact with the effect of drugs. Clinical implications of herbal medicine-drug interactions depend on a variety of factors, such as the co-administered drugs, the patient characteristics, the origin of the herbal medicines, the composition of their constituents and the applied dosage regimens. The most reported interactions involve warfarin as the most frequent drug implicated and St. John's wort as the most drug-herb interactions. Despite widespread use, there is paucity of evidence to support safety and efficacy of common herbal teas use during pregnancy. Ginger could be an exception as studies proved safety and efficacy. Due to lack of safety data, pregnant and nursing patients should be advised to avoid herbal supplements as possible. Some studies showed evidence of potential harm. In a systematic review, the use of almond oil and heavy use of licorice were associated with high risk of preterm birth. In a retrospective observational trial, the regular chamomile consumption resulted in a higher risk of pre-term delivery. To ensure safety and efficacy of herbal products, the Egyptian Drug Authority issued The Egyptian Guidelines for Registration of Herbal Medicines and The Herbal Monograph on Wild Medicinal Plants in Egypt. Patients and clinicians should be aware of the potential risks and benefits of the use of herbal products. Clinicians should review use of herbal products as a part of the medication history, assess need, possible interactions, effects, adverse effects, and provide advice to ensure optimal outcomes.

## Clinical Trials in Egypt: Opportunities and Challenges

**Prof. Nihal El-Habachi**

*Department of Physiology, Executive director of Alexandria clinical research center, Faculty of Medicine, Alexandria University, Egypt*

Egypt's global share from clinical trials is very small in spite of being a strategic country in MENA region with large population. There are lots of opportunities attracting pharmaceutical companies to invest in the field of clinical trials in Egypt as the low expenses represented in the Investigator & site fees, cost for trial-related care and much lower overhead fees, travel costs for monitoring sites and Support services (as printing, translation, and local courier fees).
Also, the high quality investigators and site staff, keen to participate in clinical trials. As well as, Large pool of trial-naive, often treatment-naive patients, High incidence and prevalence of certain diseases and less competition for enrolment of patients. On the other hand, there are lots of challenges facing people working in clinical trials as unexplained disapproval set by the concerned Authorities on the exportation of the biological samples to central labs, prolonged and undefined/unpredictable study approval/start-up timelines. Challenges regarding research subjects, investigators, REC, regulatory authorities, sponsors and local facilities as well as our ways to overcome them will be discussed.

## Updates in Pharmacovigilance Worldwide and in the Middle East

**Assoc. Prof. Thamir Alshammari**

*Medication Safety Research Chair, KSU*

The pharmacovigilance practice is growing rapidly worldwide and in the Middle East. Therefore, several guidelines in different countries were updated and their new guidelines were established. All these updates and changes are considered significant milestone in the pharmacovigilance practice worldwide. The updates and new guidelines are varying in their coverage depend on the countries. However, mainly the update covers important parts of the guidelines including the Qualified Responsible Person for Pharmacovigilance (QPPV), deputy QPPV, pharmacovigilance system master file, signal management, risk minimization measures and many other related tasks.

**The objectives of this talk are to:**

- Provide the current and previous situations of the pharmacovigilance guidelines worldwide.
- Understand the need for the updates.
- Identify the modules that include the new updates.
- Describe the changes and their impact on the company pharmacovigilance practices
- Explain the updates in detail.
- Discuss what is needed to be done by the pharmaceutical industries.

## Job opportunities in Health Economics

**Assist. Prof. Gihan Elsisi**

*Department of Economics, American University in Cairo, Egypt*

Following are questions that we ask with in our health care systems: Can the health system support the additional cost for each life saved if the new drug is both more costly and more effective than previous therapies? Cost-effectiveness analyses have assumed greater importance through the development of more sophisticated analytic techniques because of the increasing prominence of these analyses in worldwide drug registration, formulary decision making, therapeutic guideline determination, and individual patient decisions. Health care reform has required methods to evaluate economic and societal value of goods and services and therefore, pharmacoeconomics is used to evaluate value for money expended on health care technologies.

Effective pharmaceutical pricing and reimbursement systems, based on health technology assessment that encompasses economic evaluations, are essential to an efficient sustainable health care system. Different Authorities in Egypt established HTA units, as a step, for the support of pricing and reimbursement decisions. We anticipate that standardization of reporting would lead to progressive improvement in the quality of submissions over time and provide Egyptian healthcare system with health economic evidence often unavailable in the past. Recommendations for pharmacoeconomic evaluations provide an essential tool for the support of a transparent and uniform process in evaluation of the clinical benefit and costs of drugs that do not rely on the use of low acquisition cost as the primary basis for selection.

## Expanding Pharmacovigilance to New Horizon

**Dr. Amr Saad**

*WHO Pharmacovigilance Consultant*

**Pharmacovigilance implementation within Arab health systems**
Pharmacovigilance (PV) implementation within the Arab regulatory authorities becomes prominent especially after publishing the "common Arab guidelines for pharmacovigilance". However, the maturation level varies widely among different Arab health systems. Few countries are fully implementing while others are at early phases.
**Evolution of the regulation**
Different technologies, biological, vaccines, advanced therapeutic medicinal products (ATMPs), medical devices, cosmetics & herbal products are widely used alongside with pharmaceutical products. These necessitates re-tailored PV implementation, as well as, additional PV activities. On the other hand, PV practices should be enhanced for specific patient populations like: paediatrics, geriatrics, pregnancy & breast feeding females. Bio-vigilance; Vaccinovigilance; ATMP-vigilance; medical device vigilance (MDV); Cosmitovigilance; & Hebavigilance, guidelines have been recently launched worldwide to address this new demand. Also, Paediatric-, Geriatric-, pregnancy- & Breast feeding- vigilances have also come to effect.
**Next move**
The Good Pharmacovigilance Practice (GVP) within the Arab region should be expanded to cover these new domains. This will significantly influence pharmacovigilance practice in general in the whole Arab world and will increase reporting rates and signal detection activities for these specific products/populations which in turn will add to the pool of patient safety.

## Dieting Through the Decades: From Byron to Sugar Sucks Diet

**Dr. Nilly Shams**

*Nutrition & Public Health Consultant, Elite Hospital, Egypt*

For practically as long as there has been food, there have been diets. Many of them have been wacky or downright dangerous. In 1820, Lord Byron popularized the Vinegar and Water Diet as one of his obsessive attempts to stay thin. In the early 1900s, some people turned to the Tapeworm Diet as a disturbing shortcut to weight loss. Then there was the Sleeping Beauty Diet of 1970, which involved being heavily sedated to avoid cravings and prevent eating. Through this lecture we will discover All Information About the different types of diets.

# Pharmacy Education:

## Future of African Higher Education

**Prof. Amany El-Sharif**

*Vice President of Pan African University and Dean of Faculty of Pharmacy Al-Azhar University, Egypt*

Higher education is globally considered the driving force for development. In this regard, African nations launched several initiatives to build quality higher education and to meet the needs of the 4IR. A global development in higher education has demonstrated the critical need for communication technologies in modern day teaching and learning.

According to The UN S.G. policy Brief 'the pandemic has created severe disruption in the world's education systems in history and is threatening a loss of learning that may stretch beyond one generation of students. By 2030, the Skills of the graduates will be hardly meet Job market. Learning Outcomes of Virtual Education in Africa should be assessed. How to develop the capacity of staff especially in the medical schools on virtual medical education?

Another burden is the financial challenge of African countries towards Education needs, how should they respond? The disruption brought about by the pandemic right is broadening the gaps of inequalities in African HE institutions both within and across countries. Contributions of the African Diaspora to support Higher Education should be encouraged. Africa HE should lead the continent towards achievement of AU 2063 Agenda of "*The Africa we want*". Different ways of learning should be encouraged to empower graduates, preserve the planet, build shared prosperity, and foster peace. Resilience education system should be developed and roles of all stakeholders including governments, H.E.Is., Society should be defined.

## Online Pharmacogenomics and Personalized Medicine Postgraduate Program: A Program for the Future

**Prof. Ahmed Wahid**

*Head of Pharmaceutical Biochemistry Department, Faculty of Pharmacy, Alexandria University, Egypt*

Towards the end of the last century the expression of 'personalised medicine' has come to life. This simply means the right drug for the right patient with the right dose. We all now understand that the difference between any individuals regarding their DNA sequence is only about 0.1%. In spite of the fact that this is really a tiny figure, it is enough to lead to important effects on disease susceptibility and progression.
Although the healthcare community in Egypt and Lebanon has identified the need for academic educational programs on pharmacogenomics and personalised medicine, yet there has been no appreciable effort done in either country so far to fill this gap. Even the awareness of such programs is low. There exists no higher educational degree for pharmacogenomics in Egypt or Lebanon. Thus, there is a pressing need to implement this personalized medicine educational program in core training of pharmacists and physicians in the region. Moreover, there are very few programs in Egypt or Lebanon that make use of online education using IT and e-laboratories. This kind of smart learning programs facilitate the education process and make it suitable for the greatest numbers of target groups outside the Egyptian and Lebanese borders.
Identification of the proper drugs for specific patient phenotypes will heighten the drug efficacy, lessen expected adverse outcomes, increase cost effectiveness and elevate public confidence in marketed pharmaceuticals. Herein, we design a novel diploma/master program in pharmacogenomics and personalised medicine.

# ACPE International Accreditation of Pharmacy Education

**Mr. Michael Rouse**

*Accreditation Council for Pharmacy Education, Chicago, Illinois, USA*

Throughout the world, pharmacists' roles are evolving to meet public health demands, especially with regard to safe, effective and responsible medication use. This trend is driving governments and academic institutions to re-evaluate pharmacy education and the methods for evaluating, assuring and improving the quality of that education. In response to the steady and growing demand from global stakeholders including governments, professional organizations, quality assurance bodies, colleges and schools of pharmacy, and providers of continuing education and continuing professional development, the Board of Directors of the Accreditation Council for Pharmacy Education (ACPE) – an independent, autonomous organization – established its International Services Program (ISP) in 2011. With over 80 years history in degree program accreditation, ACPE has gained extensive experience in the field and it is keen to share the benefit of this experience with institutions in other countries, recognizing that patients around the world will benefit from better educated and trained pharmacists.

The ISP offers consultation, training, and professional degree program certification to international stakeholders who seek guidance related to quality assurance and advancement of pharmacy education. The expertise, global perspectives, staff resources, and formal processes within the ISP support international stakeholders to advance pharmacy education and quality in their respective countries. The mission of ISP is to promote, assure, and advance the quality of pharmacy education internationally to improve patient care through safe and effective medication use, and its vision is that quality-assured pharmacy education and training prepares graduates throughout the world for expanded roles to optimize safe and effective medication use and improve patient care.

To differentiate what it is doing in the USA from what it is offering to degree programs outside the USA, ACPE adopted the term "certification" rather than "accreditation." Certification Quality Criteria ("standards"), intended to be globally applicable and not degree-specific, were developed with broad-based input. Policies and procedures – as comprehensive and rigorous as those for accreditation - and an application process were established. Five degree programs (from Saudi Arabia, India and Northern Cyprus) have been certified and additional applications have been received.

The presentation will describe the purpose, philosophy, and key principles behind ACPE's certification program, and summarize the application process and requirements for the self-study, report, documentation and data. The rationale behind compliance definitions and the determination of compliance will be explained to stress ACPE's primarily focus on quality improvement. Finally, the terms and requirements for maintenance of certification will be outlined.

## Pharmaceutical Technology and Nanomedicine:

# Drug Delivery Across Biological Barriers for Combatting Infectious Diseases

**Prof. Claus-Michael Lehr**

*Helmholtz Institute for Pharmaceutical Research Saarland (HIPS),*
*Saarland University, Department of Pharmacy, Germany*

**Introduction**

Infectious diseases are on the raise and increasing challenge to human health with mortality rates predicted to soon exceed those of cancer and other diseases. While antimicrobial resistance is increasing, the number of new antibiotics and even the number of companies engaging in those is decreasing. Besides the need for new targets and molecules for anti-infective compounds, such as e.g. pathoblockers, there is also a need to deliver those across biological barriers preventing access to the target site. Relevant barriers in this context are the body's outer epithelia, in particular of the gut, the skin and the lung, but also host cell membranes, the bacterial cell envelope as well as non-cellular barriers, such as mucus and bacterial biofilm.

**Modelling the gram-negative bacterial cell envelope**

Because of their complex structure consisting of an inner lipid bilayer, some hydrophilic periplasmic space, and an asymmetric outer membrane, the cellular envelope of gram- negative bacteria represents a very tough biological barriers when it comes to delivering novel pathoblockers, such as e.g. *P. aeruginosa* quorum sensing inhibitors (PQSI) to their intra-bacterial site of action. Rebuilding the structure of this barrier on a Transwell® setup, we found some encouraging predictivity for actual *in bacterio* uptake and bioavailability. More recently, we have further improved this model by using 3D-printed polymeric hydrogels to mimic the outer membrane porins, and by coating membranes using bacterial extracellular vesicles (ECV's) containing active bacterio- specific transporters, respectively.

**Non-invasive delivery of antigens and drugs via skin hair follicles**

Studies on the safety of topically applied nanomaterials had revealed, that nanoparticles do not cross the stratum corneum, but show some substantial penetration into the skin hair follicles. This led us to the hypothesis, that the same pathway could also be used to deliver antigen to the dendritic skin without otherwise impairing the skin barrier. In several studies im mice, we could indeed demonstrate some significant cellular and humoral immune response to the model antigen ovalbumin. In addition, this pathway also holds interesting perspectives for the targeted delivery of drugs for the treatment of hair follicle diseases, such as alopecia areata.

**Pulmonary Delivery of anti-infective nano-assemblies against biofilm-forming bacteria**

To study the cellular interactions of drugs and nanoparticles after deposition in the deep lung, our group has pioneered human alveolar epithelial cell models, including primary cells and as cell lines. More recently, we are moving towards microfluidic devices and more complex co-cultures, allowing to mimic the air-blood-barrier also in state of inflammation and bacterial infection. As we could show in such systems, novel self-assembling nanocarriers capable to co-deliver Tobramycin and modern PQSI may allow to significantly reduce the dose of the antibiotic for completely eradicating the bugs and thus to reduce the risk of inducing antimicrobial resistance.

# Impact of Nanobiotechnology on the Future of Medicines: The Road Toward Precision Medicines–Case Studies

**Prof. Shaker Mousa**

*Professor of Pharmacology, Executive VP and chair of PRI at Albany College of Pharmacy and Health Sciences, USA.*

Over the past decade, evidence from the scientific and medical communities has demonstrated that nanobiotechnology and nanomedicine have tremendous potential to affect numerous aspects of cancer and other disorders in term of early diagnosis and targeted therapy. The utilization of nanotechnology for the development of new Nano-carrier systems has the potential to offer improved targeted delivery through increased solubility and sustained retention and more importantly active targeting. One of the major advantages of this innovative technology is its unique multifunctional characteristics. Targeted delivery of drug incorporated nanoparticles, through conjugation of site-specific cell surface markers, such as tumor-specific antibodies or ligands, which can enhance the efficacy of the anticancer drug and reduce the side effects. Additionally, multifunctional characteristics of the Nano-carrier system would allow for simultaneous imaging of tumor mass, targeted drug delivery and monitoring **(Theranostics)**.

A summary of recent progress in nanotechnology as it relates to nanoparticles and drug delivery will be reviewed. Nano Nutraceuticals using combination of various natural products provide a great potential in diseases prevention. Additionally, various Nanomedicine approaches for the detection and treatment of various types of organ specific delivery, vascular targeting, and vaccine will be briefly discussed. Additionally, novel Ligand-Drug Conjugates and Ligand conjugated Nano loaded with active Pharmaceuticals versus Antibody-Drug Conjugates will be briefly highlighted.

# Multifunctional Nano-Platforms for Biomedical Applications

**Prof. Mamoun Muhammed**

*KTH Royal Institute of Technology, Sweden*
*and IGSR, Alexandria University, Egypt*

It is now abundantly clear that Nanotechnology plays an important role in future technological development in the biomedical area. The merge of Nanotechnology and medical science offers novel solutions and unprecedented approaches for treating diseases and biological disorders. Major breakthroughs are within smart drug delivery systems, bio-diagnostics and early discovery of diseases, improved implants, visualization, and targeting tissues and organ for regeneration and repairs, etc.

Several types of nanomaterials are used as theranostic agents. Multifunctional nanoparticles have many important biomedical applications such as, controlled drug delivery, tissue-engineering, diagnostics, and visualization agents. Several components can be incorporated into the nanoparticles-matrix to achieve specific functions, e.g., reporters or visualization agents (MRI contrast agents, quantum dots) while superparamagnetic nanoparticles which can be used for magnetic targeting, heat generation, or localization of the nanoparticles to deliver their payload (therapeutics, genes, DNA) to given tissues. More complex systems may also include components responsive to external environment, e.g., temperature, pH, magnetic field, etc. The surface outer layer of the nanoparticles is constructed to be a conjugation platform to which several other molecules can be attached, e.g., targeting peptides, fluorescence compounds, etc., whereas the residual surfaces should be blocked in order to avoid undesirable binding to other molecules in the biological systems. Nanofibers are another form of nanosystems that have shown several biomedical applications e.g., in wound therapy and healing. Examples of some of these systems are to be presented.

# Pharmaceutics Informatics: A Magical Tool to Advance the Drug Formulation and Delivery Research

**Prof. Rania Hathout**

*Head of Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Ain Shams University, Egypt*

The word “informatics” includes a lot of tools such as: softwares, data mining, artificial intelligence, meta-analysis, machine learning, natural language processing, optimization and cloud computing. The use of any of these aforementioned tools solely or in combinations in the field of drug delivery and formulation introduces a new term which could be named “Pharmaceutics Informatics”. This novel approach can revolutionize the drug formulation and delivery field leading to dramatic reduction in the resources costs and the time of development of new drug formulations.

Machine learning methods are a branch of artificial intelligence that utilizes certain software algorithms in order to make computers “learn” and to make hard and critical decision functions from representative data samples. With the advent of the internet and the enormous growth of data that are obtained from huge number of sources, the recent advances in various statistical and programming tools and the continuous innovations in machine learning algorithms have resulted in a rapid increase in new applications in the different areas of pharmaceutics and drug delivery disciplines. Over the past 20 years, this new approach of data analysis has been extensively used in drug development and delivery.

Machine learning methods offer several advantages and applications over the other conventional statistical methods. First, the majority of these methods can model nonlinear relationships that are hard-to-model using the common quantitative structure-bioavailability or structure–property relationships methods. Second, they can model incomplete data or nontrending data and the users do not have to suggest any models or particular deigns before use. In other words, no restrictions are encountered while implementing machine learning algorithms where all types of data whether binary classification, multiple classes and continuous data can be analyzed and modeled. And finally, these methods can they offer. Integrating the machine learning methods into drug delivery saves costs, resources, time, and effort.

In this talk, different types of the machine learning methods together with a new approach utilizing bioinformatics and proteomics that were exploited in drug delivery aspects and applications will be demonstrated and discussed. These methods are currently considered important elements of the new approach of computer-aided drug formulation design (CADFD) and computer- aided pharmaceutical technology. The cross-disciplinary integration of drug delivery and machine learning methods as a branch of artificial intelligence may shift the paradigm of pharmaceutical research from experience-dependent investigations to data-driven studies.

# The Evolving Landscape of Genetic Therapeutics: How Nanomedicine Comes to the Rescue.

**Assist. Prof. Samar El Achy**

*Nanomedicine Laboratory at Center of Excellence for Research in Regenerative Medicine and its Applications (CERRMA), Faculty of Medicine, Alexandria University, Egypt*

Decoding of the human genome, has unraveled numerous canonical molecular pathways having great significance in cancer and chronic diseases. Recent advancements in the development of genomic high-throughput platforms have fuelled genome-wide approach to mine novel biomarkers and paved the way for better diagnostics and the discovery of promising therapies. The technology of using nucleic acid-based therapeutics is powerful, as it enables precise modulation of the expression of genes known to be involved in disease progression and can thereby be used for precision medicine. DNA and mRNA are used to induce a specific gene of interest, whereas siRNA and miRNA are used for silencing and modulation of specific genes. The sequence of nucleic acids can further easily be modified to enable patient-specific treatments and can encode essentially any gene involved in specific molecular pathways, or oncogenes, to facilitate treatments of otherwise so-called "undruggable" tumors. Accordingly, nucleic acid therapeutics can be designed to target specific genes involved in cell proliferation, migration, invasion, apoptosis, as well as inflammation, including gene editing correction using CRISPR-Cas9. Gene therapy using free nucleic acids has a great potential to deal strategically with specific genes up- and down regulated in cancer and disease. However, their therapeutic effect is limited due to poor cell uptake, lower potency, instability in circulation, immune surveillance, off-target toxicity and tumor-inducing insertional mutagenesis, and the need to trespass extra- and intracellular barriers for successful delivery. The bioavailability of nucleic acid-based therapeutics has been tremendously enhanced with advancements in nanotechnology. Clinical gene therapy depends upon the delivery methods used, either viral or non-viral delivery. Non-viral delivery systems including nanoparticles based delivery offer numerous advantages over the viral methodologies primarily; relatively safer, less adverse immune responses, easier fabrication in large amounts, and can be easily adapted by incorporation of ligands for targeting particular cell types. Nanoparticles can be game changer for gene therapeutics, as they can be employed as effective carrier of specific drug/gene to improve the circulation time, enhance bioavailability, reduce the chances of immune system based recognition, and deliver the gene regulator accurately. Currently employed pharmaceutical nanocarriers, like micelles, liposomes, nanoemulsions, polymeric nano-particles, etc. amongst which few have already entered clinic, whilst others are ongoing preclinical development, exhibit a variety of advantageous characteristics. Herein, we discuss the mechanisms of nanoparticle-targeted drug delivery, recent advancement of therapeutic strategies of nanoparticles based carriers for siRNA, miRNA, and gene augmentation therapies. We also discuss the future prospects and challenges of nanoparticle gene therapeutics. Additionally, a brief overview of our research experience in nanoparticle gene therapeutics at the Center of Excellence for Research in Regenerative Medicine and its Applications (CERRMA) at the Faculty of Medicine, Alexandria University, Egypt.

## Dynamic Organ-on-a-Chip Models: Bringing Bio-relevance to In Vitro Evaluation of Nanoparticles

**Assist. Prof. Hagar Labouta**

*College of Pharmacy, University of Manitoba, Canada*

Microfluidics, manipulation of fluids at the sub-millimetre scale, has given rise to biomimetic systems called organ-on-a-chip to evaluate therapies under conditions mimicking in vivo dynamic conditions and the microstructures of biological barriers. My talk will focus on our research on evaluating nanotherapies using dynamic organ-on-a-chip models. We will focus on two novel models developed in our lab. We will highlight recent results from the Labouta Lab on the use of placenta-on-a-chip models for screening safe therapies during pregnancy. We have also developed a vessel-on-a-chip model using vascular endothelial cells subjected to a shear stress within the physiological range. Using this model, we examined the effect of wall shear stress on the interaction of nanoparticles with the endothelium in regards to cell viability, cell internalization of nanoparticles, as well as their effect on the cell transcriptome. The results of this work will direct future studies towards the use of in vitro approaches for improving in vitro-in vivo correlation.

# Recent Advances in Microbiology, Immunology and Biotechnology:

## Egypt and Global Pandemics and Local Epidemics

**Prof. Soad Farid Hafez**

*Department of Microbiology & Immunology, Faculty of Medicine, Alexandria University, Egypt.*

## Anti-microbial Stewardship: A Pharmacy Perspective

**Prof. Abdullah Al Balushi**

*Dean of School of Pharmacy, Oman College of Health Sciences, Oman.*

## Pharmacomicrobiomics: Microbes as drug dealers!

**Prof. Ramy Karam Aziz**

*Head of the Microbiology and Immunology Research Program at the Children's Cancer Hospital of Egypt 57357 and Department of Microbiology and Immunology, Faculty of Pharmacy, Cairo University, Egypt.*

Even before the official discovery of microbes and the foundation of microbiology, microbes have been a source of food and medication. With fermentation and other classical biotechnological approaches, microbes were also a major source of drugs. Antibiotics, vaccines, and enzymes are among the many drugs of microbial origin, whether with traditional culture-based methods or later via recombinant DNA technology. Meanwhile, another under-appreciated property of microbes is their wide metabolic potential and their remarkable ability to modify drugs, by potentiation, transformation, inactivation, or detoxification. With the advancement in analyzing the human microbiome, the role of human microbial communities in modifying drugs pharmacokinetics and pharmacodynamics is becoming a promising research field. Pharmacomicrobiomics and toxicomicrobiomics are systematic attempts to assess the human microbiome effects on the action, fate, and toxicity of administered drugs, and will be discussed in detail.

# Host Glycan Binding To SARS-Cov-2 Spike Protein and its Role in Viral Infectivity and Cell Entry

**Assoc. Prof. Amr EL-Hawiet**

*Department of Pharmacognosy, Faculty of Pharmacy, Alexandria University, Egypt*

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a member of the coronavirus family, was responsible for the global outbreak of Coronavirus Disease since 2019 (COVID-19). SARS-CoV-2 is believed to rely on a combination of angiotensin-converting enzyme 2 (ACE2) and glycans to bind and infect the lungs, as well as other tissues and organs. Using catch-and-release electrospray ionization mass spectrometry (CaR-ESI-MS) screening of defined and natural glycan libraries, revealed that the recombinant receptor-binding domain (RBD) of SARS-CoV-2 S-protein recognizes several different classes of glycan structures. Specifically, oligosaccharides containing sialic acid, with preference for the oligosaccharide of monosialylated gangliosides (GM1 and GM2). For both pseudotyped and authentic SARS-CoV-2 virus, ACE2-dependent viral entry was diminished by at least two-fold when sialic acid levels were decreased by pre-treatment of cells with neuraminidase or a sialyltransferase inhibitor. Despite the significant involvement of glycans in SARS-CoV-2 infection, very little is known about the modulatory effect of different glycans as human milk oligosaccharides (HMOs) and ABH blood group antigens on binding of SARS-CoV-2 S protein to the ACE-2 receptor on the target cells. Exploring the possible allosteric effect of purified HMOs, natural libraries of HMOs, gangliosides and ABH glycans on SARS-CoV-2 binding to ACE2 receptor using mass photometry (MP), ESI-MS binding measurements and pseudotyped viral infection assay will be included in the talk.

## Drug Discovery:

# Synthesis, Biological Evaluation, and Molecular Modeling Simulations of New Heterocyclic Hybrids as Multi-Targeted Anti-Alzheimer's Agents

**Prof. Hussein El-Subbagh**

*Department of Medicinal Chemistry, Faculty of Pharmacy, Mansoura University, Egypt*

The widespread and the recognition of the multifactorial nature of Alzheimer disease (AD) increased the demands for multi-targeted directed ligands (MTDLs) to overcome possible drug-drug interactions of the combination therapy, and to acquire superior therapeutic profile than single targeted molecules. Two main scaffolds namely: pyrazolopyridine and tetrahydroacridine (THA) were used to synthesize four different series of integrated multi-targeted synthons possessing ChE (*h*AChE or *h*BuChE), $A\beta_{1\text{-}42}$ aggregation inhibition potency, in addition to optimum metal chelating capability. Structure modifications were performed to 9-amino function of THA core of tacrine and the pyrazolopyridine scaffolds linked to a variety of cyclic secondary amines directly or using amide spacers or ethylamine bridge or engaging THA with pyrazolopyridine to produce hybrid compounds. Different 9-amino substitutions improved the *in vitro h*AChE activity of 7- or 6,7-disubstituted THA derivatives. Compounds **16** and **28** proved to be multimodal anti-AD agents as they were potent *h*AChE inhibitors, in addition, they could bind with the amino acids of the peripheral anionic site (PAS) affecting Aβ aggregation and hence Aβ-dependent neurotoxicity especially compound **16** which was almost twofold more active than donepezil. Furthermore, both compounds directly inhibited $A\beta_{1\text{-}42}$ self-aggregation and chelated bio-metals such as $Fe^{2+}$, $Zn^{2+}$ and $Cu^{2+}$ preventing reactive oxygen species (ROS) generation by Aβ and its oxidative damage in the brain regions of AD patients. Compound **28** had superior privilege by its dual ChE activity resulting in better cognitive improvement. Compounds **16** and **28** showed acceptable relative safety upon hepG2 cell line and excellent BBB penetration with wide safety margin as their $LD_{50}$ were higher than 120 mg/kg.

# Marine Natural Products in Drug Discovery: Current Status and Future Prospects

**Prof. Diaa Youssef**

*Department of Natural Products, Faculty of Pharmacy, King Abdulaziz University, KSA*

Historically, natural products from terrestrial plants and soil microorganisms have played an important role in cancer chemotherapy. A review concluded that, natural products and their derivatives are represented by 26% of the total newly approved drugs (1355 NCEs) between 1981 and 2010, and another 24% are synthetic natural product mimics or contain natural product pharmacophores. Of the remainder, 15% are biological macromolecules such as peptides, 6% are vaccines, and only 29% are totally synthetic. With the anticancer drugs, the number of natural or naturally inspired agents is 74.9% of the total approved anticancer drugs. This fact clearly reflects the significance of natural products for drug discovery and development. Important examples of anticancer compounds from plants include the Vinca alkaloids from the periwinkle plant *Vinca rosea*, the epi analogs of podphyllotoxin from *Podophllum peltatum*, paclitaxel from *Taxus brevifolia* and camptothecin analogs, topotecan and irinotecan. Examples from microbes include anthracyclines such as adriamycin and daunomycin, actinomycin D, bleomycin and mitomycin C. Nonetheless, if natural products are to continue to make important contributions to cancer chemotherapy, new groups of organisms or organisms that have evolved under unique environmental pressures are most likely to provide the chemical diversity required to find novel agents. Discoveries in the past 60 years indicate that our oceans may provide the pharmaceuticals for the next millennium. The marine environment has provided an abundant supply of natural products with a diverse array of structures and bioactivities including antimicrobial, immunosuppressive and anticancer agents. The ocean covers over 71% of the earth's surface and constitutes more than 90% of the inhabitable space on the planet. An estimated 50–80% of all life on earth resides in the ocean and it is home to 32 out of 33 known animal phyla, 15 of which are exclusively marine. More than 38,000 natural products have been discovered in the marine environment over the past 60 years. From the continuing progress in the area of MNPs, 17 approved drugs and additional 29 agents are currently in different phases (I-III) of clinical trials have been discovered. These molecules are either natural products, tailored natural products or are molecules inspired from the structure of natural products. Marine organisms largely obtained from shallow-water, tropical ecosystems are the major sources of MNPs. In this presentation, current status of marine natural products in drug discovery, challenges, and future prospects will be presented.

# Behind The Scenes of Symbiotic Relationships: Novel Insights as Revealed Using metabolomics in Plants, Sea Corals and Humans

**Prof. Mohamed Farag**

*Department of Pharmacognosy, Faculty of Pharmacy, Cairo University, Egypt*

In symbiotic associations, there is a constant molecular complexity that allows for the establishment and maintenance of such ecological relationship. Metabolomic profiles have enabled us to explain symbiotic associations in terms of their underlying molecules and interactions between the symbiotic partners. Here, we define metabolomics as ‘‘a systematic analysis of metabolite structures, concentrations, pathways and fluxes, and molecular interactions within and among organisms as a function of the environment.’’ This talk provides an overview of metabolomics and discusses its complementary role within system biology of three different symbiotic relationships in plants, marine derived soft corals and lastly human gut microbiota. In plants, we present a procedure for metabolome-based volatiles profiling approach in soil bacteria termed PGPR for the identification of bioactive agents that could be directly applied as biocontrol agents. Results presented shall illustrate how interestingly can volatiles analyses in PGPR lead to valuable information relative to PGPR beneficial effect in planta that could ultimately lead to their better field exploitation. Coral reef biologists have attributed much of the increase in coral mortality to coral bleaching subsequent to elevated seawater temperatures concurrent with a release of the algal endosymbont living inside corals. Metabolomics was applied for the first time in corals to assess the metabolic response of individual partners and how each host/symbiont system responds separately to environmental stress. A unique change in natural products patterns of each partner was observed in response to a variety of environmental stimuli. These marker metabolites may act as stress indicators which reflect the metabolic processes tuned during such stress events. Lastly, a scenario as to how gut microbiota interact with different dietary food using in vitro culture and the outcome on human health is presented for the first-time using metabolomics.

# Multi-target Directed Ligands (MTDLs) as a Powerful Medicinal Chemistry Strategy to Combat Complex Scenario Disorders

**Assoc. Prof. Ahmed Belal**

*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Alexandria University, Egypt*

Complex scenario disorders are characterized by an intricate network of intertwining molecular pathways, that are full of redundancies and compensatory mechanisms. Hence, the single-molecule-single-target approach proved in many instances to be insufficient or even counterproductive. Our lab, among many others, has adopted the idea of simultaneous modulation of closely related biological targets implicated in highly networked disorders by single molecular designs that contained carefully designed hybridized pharmacophores and/or privileged scaffolds. We published a series of glitazone-like compounds that proved to be effective against adipose tissue inflammation, which is involved in metabolic syndrome, via modulating COX-2, 15-LOX and PPARγ. Based on the SAR published in this study plus the pharmacophoric structural features that we extracted from co-crystallized ligand X-ray Crystallography, we designed other MTDLs with both modified and enhanced pharmacological profiles, which will be briefly discussed in the talk. In another publication, we reported a series of tacrine-like derivatives that proved to be effective Cholinesterase, COX-2 and 15-LOX inhibitors, within the context of Alzheimer's disease. The later study's findings served as the foundation for the development of further MTDLs for neurodegenerative illnesses, which will once more be covered in the session. Finally, we will discuss the cutting-edge PROteolysis TArgeting Chimera (PROTAC) technology as a multitargeting technique and provide a brief overview of our experiments in this new field.

## Medical Imaging for Discovering and Monitoring Drugs

**Dr. Ahmed Gharib**

*National Institutes of Health, USA*

Medical imagining is essential in drug discovery, testing, and validation of effects on end organs. Hence, it is crucial to understand the imaging strategies that can be used toward these goals. This presentation will discuss current imaging methods that help in drug discovery. These include magnetic resonance spectroscopy and positron emission tomography. Such methods allow targeting and measuring specific metabolic and biological events that are affected by drugs, thus helping to facilitate their effective development and speedy instruction to the markets.

## New Strategies and Targets for Antibiotic Drug Discovery

**Dr. Omar EL-Halfawy**

*Department of Chemistry and Biochemistry, Faculty of Science, University of Regina, Canada*

Infectious diseases pose a serious health problem with a considerable social and economic burden. Antimicrobial resistance is on the rise, where existing antibiotics fail to treat infections, whereas the antibiotic discovery pipeline has stalled in the last three decades. New and alternative approaches are required to address the current antibiotic crisis. This talk will discuss our search for new antibiotic resistance and virulence targets that we may exploit to discover novel antimicrobial solutions. It will also cover how chemical genomic approaches can expedite such efforts and enable the understanding of the mode of action of newly discovered bioactives.

## Thinking Green:

### Climate Change and Global Health: Impacts, Awareness, Preparedness, and Response

**Dr. Radwa Ewaisha**

*Department of Microbiology and Immunology, Faculty of Pharmacy, Alexandria University, Egypt*

The world is rapidly warming as a direct result of human activities, resulting in melting ice, rising sea levels, and increasing climate variability. The impacts of climate change are unfolding before our eyes, and they are expected to have a substantial impact on human health. This includes illnesses and deaths from severe weather events such as heat waves and floods; increased incidence and prevalence of vector-, water-, and food-borne diseases as well as allergies and respiratory diseases; food and water insecurity; and a huge toll on mental health. Public health preparedness to these unprecedented changes is a critical challenge. An effective response is of paramount importance to raise awareness; reduce risk, illnesses, and fatalities; and avoid overwhelming the healthcare systems. This talk reviews some of the health impacts of climate change and discusses a framework for global health preparedness and response.

### The Three Major Environmental Issues and Ways to Combat Them

**Dr. Nagwa Essam ElDin**

*Therapeutic and Public Health Consultant.*
*Assistant Governor, Rotary District 2451 -Egypt 2022-2023.*

# Bridging the gap between academia and practice: A Clinical Pharmacy Perspective

## Integrating Clinical Expertise into Students Classroom

**Dr. Noha Alaa Hamdy**
*Lecturer of Clinical Pharmacy, Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, Alexandria University.*
*noha.alaaeldine@alexu.edu.eg*

## Clinical Pharmacy Tricks in Cardiology Management

**Rasha Wafaie Mahmoud Elsorady, PharmD**
*Doctor in Clinical Pharmacy, Logistics of Hospital Management Masters Degree*
*Head of Clinical Pharmacy Internal Medicine Units Alexandria Main University Hospital.*
*Rasha.Elsorady@gmail.com*

## Nephrology Polypharmacy Management: Clinical Pharmacy Perspective

**Engy Mahmoud Emam, PharmD**
*Clinical Pharmacy and Hospital Management Diploma,Biochemical Analysis Diploma*
*Senior Clinical Pharmacist at Internal Medicine at AMUH*
*Supervisor of Clinical Pharmacy Department at Alexandria University Students Hospital*
*Engyemam2005@gmail.com*

## Empowering Pharmacists as Psychoeducators to Fight Stigma Against Mental Disorders and Improve Treatment Outcomes: From Theory to Clinical Practice

**Nancy Ali Mahfouz, PharmD**
*Senior Clinical Pharmacist - Departement of Neuropsychiatry, Alexandria University Hospitals.*
*Head of the Clinical Pharmacy Department, Nariman University Hospital.*
*nancy_mahfouz84@yahoo.com*

## Clinical Pharmacy Approach in HCV Management with Kidney Transplantation

**Enas Abdelaziz Mohamed; PharmD, BCPS, Biostatistics Diploma.**

# Clinical Pharmacy Practice in Alexandria University Hospitals

## Uncommon Septic Arthritis Case Presentation in Pediatrics: Clinical Pharmacy Interventions

**Clinical Pharmacist Heba Sabry**
*Supervisor of Clinical Pharmacy in Alexandria University Children Hospital.*

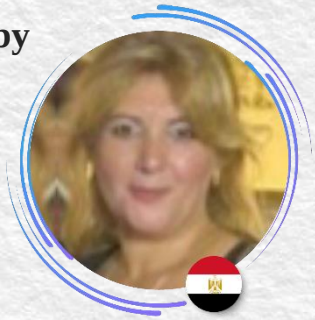
## A Case of Postsurgical Complications in Hepatic Patient

**Clinical Pharmacist Esraa Alaa**
*Clinical Pharmacist at AMUH, Surgery Department.*

## Nutritional Intervention in Acute Necrotizing Fasciitis: Case Presentation

**Clinical Pharmacist Nancy Ahmed Sorour**
*Clinical Pharmacist at Nutrition Support Unit at AMUH*
&
**Clinical Pharmacist Rowan Gadelkarim**
*Clinical Pharmacist at Nutrition Support Unit at AMUH*

## Focus on Updated Treatment Guidelines for UTI (Caused by Antimicrobial Resistant Organisms) with Presentation of Cultures Related to Urological Cases (ex Perinephric Abscess)



**Clinical Pharmacist Mariam Maher Karam**
*Supervisor of Clinical Pharmacy at Urology Department & DIC (AMUH)*

## Students' Oral Presentations:

### Benzenesulfonamido Hydrazones as Open Chain Analogs of Celecoxib: Design, Synthesis, Biological Evaluation and *In Silico* Studies

***Presented by:*** Ola A. Elbadry and Eman A. Hassanin
***Supervisor:*** Assoc. Prof. Ahmed Belal and Assoc. Prof. Perihan Elzahhar

### Role of Glycogen Synthase Kinase-3β as a Modulator of Canonical WNT Signaling in Adipose Tissue Dysfunction in Obesity and Related Metabolic Disorders

***Presented by:*** Ahmed S. Khalifa, Amr Y. Seddik and Esraa G. El-Nagar,
***Supervisor:*** Prof. Ahmed El-Yazbi

### Management of Coagulopathy Problems in Critically Ill Cancer Patients

***Presented by:*** Esraa M. Rashed and Reem M. Mohamed
***Supervisor:*** Dr. Noha Alaa Hamdy

### Using Different Techniques in Analyzing the Biomarkers Found in DNA Damage

***Presented by:*** Ayat M. Mohamed
***Supervisor:*** Assoc. Prof. Amira El-Yazbi

# Workshops

# Palliative Care

## Role of Pharmacists in the Palliative Care Team

**Dr. Horeya Mohamed Ismail**
*Pharmacist Specialized Universal Network of Oncology (SUN), Alexandria University.*

## Communicating Effectively and Gaps in Oncology

**Dr.Waleed Hamdy Nafae**
*MBBCH, MSc, PhD*
*Head of Palliative Care Units in Ayady4040 and Shefaa Alorman.*

## End of Life Care Issues

**Dr. Mahmoud Foudeh**
*Consultant in Oncology and Palliative Care Medicine,*
*Chairman of Jordanian Society of Pain and Palliative Care*
*FRCS, MS Oncology (London Univ.) American Board pain & Palliative Medicine.*

Open discussion through real cases:

How could palliative care help?
1. metastatic cancer ovary with extensive peritoneal and omental deposits inoperable unresectable with intestinal obstruction.
2. Metastatic chondrosarcoma with neurotoxicity hyperalgesia diagnosis and treatment.

# Science Communication for Researchers

**Science Journalist Bothina Osama**
*Regional Coordinator of SciDev.Net for the Middle East & North Africa Region, and the Editor in Chief of the Arabic Edition.*

**Science Journalist Rehab Abd Almohsen**
*Awarded Science Journalist, Media Trainer, and Co-author of Media Handbook: Water Cooperation and Conflict.*

**What is the main focus of our session?**

Part one:
How should researchers communicate their research?
How to write a press release to disseminate your work?
And how to do a fruitful interview with journalists?

Part two:
How do science stories publish process work?
How fact-checking works?
And what is the definition of a “good science story”?

**Why this session is important?**

There is a growing understanding among scientists that visibility in the media is important and responding to journalists as a professional is a duty, but we can see that there is still an obvious gap between science and media.

This needs to change by informing our future-to-be scientists on how to communicate their work and how to talk to media, and how media itself is working?

Our decision-making and conduct is influenced by what we read, see or hear. And many parts of our lives, from the food we eat to our quality of sleep, can in some way be linked back to scientific research.

And if readers understand what accurate, balanced science journalism should look like, they'll be able to distinguish the good stories from the not-so-good ones and make informed choices.

# PROFESSIONAL POSTERS

# Pharmacotherapy, Pharmacogenomics & Precision Medicine

# PHS 201: Metformin, Pioglitazone, Dapagliflozin and Their Combinations Ameliorate Manifestations Associated with NAFLD in Rats via Anti-inflammatory and Anti-fibrotic Mechanisms

**Hager H. shaaban[1]*, Ahmed I. El-Mallah[1], Ahmed F. El-Yazbi[1,2,3], Ahmed W. Mahmoud[4]**

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Non-alcoholic fatty liver disease (NAFLD) is an important health threat that is strongly linked to components of metabolic syndrome. Significantly, several of the available anti-diabetic drug classes demonstrate a considerable anti-inflammatory effect, and hence might be of benefit for NAFLD patients. Here, we used a rat model of diet-induced NAFLD to examine the potential effect of metformin, pioglitazone, dapagliflozin and their combinations on NAFLD manifestations. Rats were fed an atherogenic diet containing 1.25% cholesterol, 0.5% cholic acid and 60% cocoa butter for 6 weeks, causing a number of metabolic and hepatic impairments including insulin resistance, dyslipidemia, systemic inflammation, increased hepatic oxidative stress and lipid peroxidation, resulting in hepatic steatosis, lobular inflammation, as well as increased markers of liver inflammation and hepatocyte apoptosis. Drug treatment started at the third week of NAFLD induction and continued for three weeks ameliorated the observed metabolic impairment, and also functional and structural manifestations of NAFLD. Specifically, anti-diabetic drug treatment reversed markers of systemic and hepatic inflammation, as well as hepatic fibrosis. Our findings propose that anti-diabetic drugs with a potential anti-inflammatory effect can ameliorate the manifestations of NAFLD, and may provide a therapeutic option for such a condition that is closely associated with metabolic diseases. The detailed pharmacology of these classes in aspects linked to the observed impact on NAFLD requires to be further investigated and translated into clinical studies for tailored therapy specifically targeting NAFLD.

**Keywords:** NAFLD, metabolic syndrome, Metformin, Pioglitazone, Dapagliflozin.

# PHS 202: Protective Effects of Selenium Nanoparticles Against Vancomycin Induced Nephrotoxicity in Experimental Rats

**Eman T. Mehanna[1]*, Samar S. Khalaf[2], Mohamed M. Hafez[3], Noha M. Mesbah[1], Dina M. Abo-Elmatty[1]**

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*[2]Department of Biochemistry, Faculty of Pharmacy, Heliopolis University, Cairo, Egypt.*
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Nephrotoxicity is the major limiting factor for the clinical use of vancomycin (VCM) for treatment against multi-resistant Gram-positive bacteria. The present research aimed to investigate the ability of selenium nanoparticles (SeNPs) to protect against VCM-induced nephrotoxicity in rats. Experimental rats were divided into five groups; the first was the normal control, the second was treated with VCM (200 mg/kg twice/day, i.p.) for 7 days. The third, fourth, and fifth groups were treated orally with SeNPs (0.5, 1, and 2 mg/kg/day); respectively. SeNPs were administered for 12 days before VCM, 1 week simultaneously with VCM, and for another 1 week after its administration. Levels of malondialdehyde (MDA), inducible nitric oxide synthase (iNOS), nitric oxide (NO), tumor necrosis factor-alpha (TNF-α), and kidney injury molecule-1 (KIM-1) were significantly increased in kidney tissue after VCM administration. Expression of adenosine 5'-monophosphate-activated protein kinase (AMPK), Bcl-2 associated X protein (Bax), caspase 3 and caspase 9 in kidney tissue was significantly increased, while the antioxidant enzymes, mitochondrial complexes, the ATP levels and B-cell lymphoma protein 2 (Bcl-2) were decreased in kidney in the VCM-treated rats compared to the normal control group. Treatment with SeNPs significantly decreased levels of MDA, iNOS, NO, TNF-α, and KIM-1 in the kidney tissue. Administration of SeNPs also downregulated the expression of the proapoptotic agents and enhanced the activities of the antioxidant enzymes and the mitochondrial enzyme complexes in the kidney. In conclusion, SeNPs alleviated VCM-induced nephrotoxicity through their anti-oxidant, anti-inflammatory, anti-apoptotic and mitochondrial protective effects.

**Keywords:** Vancomycin; Selenium nanoparticles (SeNPs); Mitochondrial complexes; Anti-apoptotic.

# PHS 203: The Hepatoprotective and Nephroprotective Effects of Lipopolysaccharide from Rhodobacter sphaeroides Against Ethanol-Induced Toxicity in Experimental Rats

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Lipopolysaccharide from Rhodobacter sphaeroides (LPS-RS) is a potent toll-like receptor 4 (TLR4) antagonist that attenuates TLR-4 mediated inflammation. Furthermore, it has an antioxidant activity. This study aimed to investigate the protective effects of LPS-RS against ethanol-induced hepatotoxicity and nephrotoxicity in experimental rats. The study involved an intact control group, LPS-RS group, two groups were given ethanol (3 and 5 g/kg/day) for 28 days, and two other groups (LPS-RS + 3 g/kg ethanol) and (LPS-RS + 5 g/kg ethanol) received a daily dose of LPS-RS (800 µg/kg) before ethanol. Ethanol significantly increased the expression of nuclear factor kappa B (NF-κB) and levels of malondialdehyde (MDA), tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) in the liver tissue and decreased anti-oxidant enzymes. Hepcidin expression was downregulated in the liver, with increased serum levels of ferritin and iron. Prior-administration of LPS-RS alleviated the increase in oxidative stress and inflammatory markers, and preserved iron homeostasis markers. In the kidney, administration of ethanol caused significant increase in the expression of NF-κB and the levels of TNF-α and kidney injury markers; whereas LPS-RS + ethanol groups had significantly lower levels of those parameters. In conclusion; this study reports anti-oxidant, anti-inflammatory and iron homeostasis regulatory effects of the TLR4 antagonist LPS-RS against ethanol induced toxicity in both the liver and the kidney of experimental rats.

**Keywords:** alcoholic liver disease; hepcidin; kidney injury molecule-1; lipopolysaccharide from Rhodobacter sphaeroides; nuclear factor kappa B; toll-like receptor 4.

# PHS 204: Effect of α7-Nicotinic Receptor Allosteric Modulator PNU-120596 on Motor Dysfunction and Neuroinflammation in 6-OHDA Rat Model

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Parkinson's disease (PD) is the second most common neurodegenerative disorder and a leading cause of disability. The current gold standard for PD treatment, L-Dopa, has limited clinical efficacy and multiple side effects. Evidence suggests that activation of α7 nicotinic acetylcholine receptors (α7nAChRs) abrogates neuronal and inflammatory insults. Here we tested whether PNU-120596 (PNU), a type II positive allosteric modulator of α7 nAChR, has a critical role in regulating motor dysfunction and neuroinflammation correlated with the associated PD dysfunction. Neuroprotective mechanisms were investigated through neurobehavioral, molecular, histopathological, and immunohistochemical studies. PNU reversed motor incoordination and hypokinesia induced via the intrastriatal injection of 6-hydroxydopamine and manifested by lower falling latency in the rotarod test, short ambulation time and low rearing incidence in the open field test. Tyrosine hydroxylase immunostaining showed significant restoration of dopaminergic neurons following PNU treatment, in addition to histopathological restoration in nigrostriatal tissues. PNU halted striatal neuroinflammation manifested as a suppressed expression of JAK2/NF-κB/GSk3β accompanied by a parallel decline in the protein expression of TNF-α in nigrostriatal tissue denoting the modulator anti-inflammatory capacity. Moreover, the protective effects of PNU were partially reversed by the α7 nAChR antagonist, methyllycaconitine, indicating the role of α7 nAChR modulation in the mechanism of action of PNU. This is the first study to reveal the positive effects of PNU-120596 on motor derangements of PD via JAK2/NF-κB/GSk3β/ TNF-α neuroinflammatory pathways, which could offer a potential therapeutic strategy for PD.

**Keywords:** Parkinson's disease, Nicotinic receptor, Positive modulator, Neuroinflammation.

# PHS 205: Apocynin Abrogated Methotrexate-Induced Testicular Toxicity in Rats: Crosstalk Between Oxidative Stress, Inflammation, and Molecular Signal Expression

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Male reproductive toxicity is becoming of growing significance due to clinical chemotherapy usage. Methotrexate (MTX) is an anti-folate used on a large scale for different tumors and autoimmune conditions. Despite its wide clinical use, MTX is associated with severe testicular intoxication. The exact underlying mechanism is unclear, So, our study was conducted to explore the pathogenesis mechanism of MTX-induced testicular damage and the potential testicular protective effects of apocynin (APO) on testicular injury induced by single i.p. MTX (20 mg/kg). Animals were assigned into four groups: normal- group (0.5% carboxymethyl cellulose; CMC) for 10 days, APO-group (single daily dose of APO (50 mg/kg, P.O.) for 10 days, MTX-group (a single i.p. dose of 20 mg/kg ) at the end of the 5th day of the experiment, and APO+MTX-group where APO was administered for 5 consecutive days before MTX injection and 5 days after. Interestingly, as compared to rats given MTX alone, co-administration of MTX with APO demonstrated multiple beneficial effects evidenced by a marked increase in testosterone, FSH, and LH and significantly restored testes histopathological alterations. Mechanistically, APO restored antioxidant status through up-regulation of Nrf2, cytoglobin, PPAR-γ, SIRT1, AKT, and p-AKT, while effectively lowering Keap-1. Moreover, APO significantly attenuated inflammation by down-regulating NF-κB-p65, iNOS, and TLR4 expressions confirmed by in-silico evidence. Additionally, network pharmacology analysis, a bioinformatics approach, was used to decipher various cellular processes' molecular mechanisms. In conclusion, the current investigation proves the beneficial effects of APO in MTX-associated testicular damage through activation of cytoglobin, Keap-1/Nrf2/AKT, PPAR-γ, SIRT1, and suppressing of TLR4/NF-κB-p65 signal. Our data collectively encourage extending the investigation to the clinical setting to explore APO effects in MTX-treated patients.

**Keywords:** Apocynin; Methotrexate; Keap-1/Nrf2/AKT; iNOS/NF-κB/TLR4; Computational pharmacology.

# PHS 206: The Diabetogenic Effects of Chronic Supplementation of Vitamin C or E in Rats via Modulating Transcriptional Machinery of Lipid Metabolism

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The chronic administration of vitamin C and E can differentially disrupt hepatic insulin molecular pathway in rats. Hence, this study evaluated their effects on lipogenesis in the liver and adipose tissue and investigated the possible involvement of microRNA (miR)-22/29a/27a in the induced impaired glucose tolerance. Wistar rats were orally supplemented with vitamin C (100, 200, and 500 mg/kg) or vitamin E (50, 100, and 200 mg/kg) for eight m onths. Vitamin C or E at the highest doses significantly altered liver weight and index, serum and hepatic lipids, adiponectin, and liver enzymes; besides their reported unfavorable effect on glucose homeostasis. Vitamin C and E negatively affected peroxisome proliferator-activated receptor coactivator-1 (PGC-1α), sterol regulatory element-binding protein (SREBP)-1c/-2, miR-22/29a/27a expression, and adipose perilipin 1 to different extents, effects that were supported by the histopathological examination. The current study provides a deeper insight into the findings of our previous study and highlights the detrimental effects of chronic vitamins supplementation on lipid metabolism. Overall, these findings emphasize the damage caused by the mindless use of supplements and reinforce the role of strict medical monitoring, particularly during the new COVID-19 era during which numerous commercial supplements are claiming to improve immunity.

**Key Words:** Vitamin E; Vitamin C; microRNAs; PGC-1α.

# PHS 207: Diosmin Nanocrystals Alleviate Imiquimod Induced Psoriasis in Rats via Modulating TLR7,8/ NF-κB/Micro RNA-31, AKT/mTOR/P70S6K Milieu and Tregs / Th17 Balance

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Diosmin is a flavonoidal compound characterized by highly challenging physicochemical properties. There wasn't enough attention paid for using diosmin topically in spite of its strong anti-inflammatory and antioxidant properties. The aim of this work is the development and characterization of diosmin nanocrystals using anti-solvent precipitation technique to be used for topical treatment of psoriasis. Evaluation of different stabilizers with different concentrations to achieve the most stable nanocrystals was studied. Results revealed that diosmin nanocrystals stabilized with hydroxypropyl methylcellulose (HPMC E15) in weight ratio (diosmin:polymer 1:1) could reach the desired particle size (276.9±16.49 nm); provided the promising colloidal properties and higher drug release profile. In-vivo assessment was carried out to evaluate and compare the activities of diosmin nanocrystals gel using 3 different doses and diosmin powder gel in alleviating imiquimod induced psoriasis in rats and investigating their possible anti-inflammatory mechanisms. Herein, 125 mg of 5% imiquimod cream (IMQ) was applied topically for 5 consecutive days on the shaved backs of rats to induce psoriasis. Diosmin nanocrystals gel especially in the highest dose used offered the best anti-inflammatory effect. This was confirmed by causing the most significant mitigation in the psoriasis area severity index (PASI) score and the serum inflammatory cytokines levels (IL17A, IL23, and IL22). Furthermore, it was capable of maintaining balance between Th17 and Treg cells by decreasing the immunohistochemical expression of RORG and increasing that of FOXP3. Moreover, it tackled TLR7/8/NF-κB, AKT/mTOR/P70S6K and elevated the TNFAIP3/A20 (negative regulator of NF-κB) expression in psoriatic skin tissues. Also, it abrogated the tissue expression of PCNA, BCL-2 and miRNA-31 level. This highlights the role of diosmin nanocrystals gel in tackling imiquimod induced psoriasis in rats via modulating TLR7,8/NF-κB/miRNA-31, AKT/mTOR/P70S6K milieu and Tregs/Th17 balance. Therefore, it is suggested that diosmin nanocrystals gel could be a novel promising therapy for psoriasis.

**Keywords**: Imiquimod induced Psoriasis; Diosmin nanocrystal gel; Th17/Treg balance; TLR7/8/NF-KB/miR-31 trajectory; AKT/mTOR/P70S6K trajectory.

# PHS 208: Free Fatty Acids as Key Modulators of Macrophage-Induced Inflammation in Metabolic Diseases

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The escalating prevalence of metabolic disorders, such as obesity, type 2 diabetes, and metabolic syndrome, is attributed to the higher consumption of western-type diets. Increased fatty acid intake, being major components of these diet styles, is a risk factor for the development of these metabolic disorders and their cardiovascular complications. Interestingly, free fatty acids (FFAs) could serve as a common instigator of several inter-linking inflammatory pathways underlying the common pathology of these disorders. Saturated FFAs, especially palmitate, are proposed as key contributors to insulin resistance and important immune modulators of adipose tissue (AT) inflammation, a mechanism that triggers the progression of metabolic disease and vascular dysfunction. Such a pro-inflammatory milieu in adipose tissue can be triggered by FFAs, either through direct stimulation of surface immune receptors on adipocytes, most important of which is toll-like receptor 4 (TLR4), or through promoting a phenotypic switch of adipose tissue-resident macrophages from an anti-inflammatory M2 to a pro-inflammatory M1 phenotype with insulin desensitizing actions. In fact, FFA-induced AT inflammation, in presence of insulin resistance and an impaired fat metabolism, may also trigger paracrine release of FFAs from adipocytes to neighboring tissues, thereby entering a self-exacerbating loop that aggravates inflammation. As such, the close proximity of the perivascular AT layer to the vascular layer augments the proinflammatory effects of FFAs on the endothelium, which culminates in the impairment of the endothelial vasodilatory responses. Moreover, atherosclerotic lesions of the vascular walls are also thought to be exacerbated by saturated FFAs, through enhancing macrophages' uptake of oxidized low-density lipoproteins and modulation of plaque instability. In this review, we aim at summarizing the mechanisms involved in the FFA-mediated inflammatory changes underlying metabolic and vascular deterioration, hence highlighting the importance of studying agents with anti-inflammatory potential to halt inflammatory processes involved in the progression of metabolic disorders.

**Key Words:** free fatty acids; macrophages; adipose tissue inflammation; toll-like receptors; endothelial dysfunction.

# PHS 209: Nicorandil Reduces Morphine Withdrawal Symptoms, Potentiates Morphine Antinociception, and Ameliorates Liver Fibrosis in Rats

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Chronic liver disease (CLD) is a serious medical condition affecting patients globally and pain management poses a unique challenge for clinicians. ATP-sensitive potassium channels (KATP) are widely expressed in nociceptive neurons and hepatic fibrotic cells. We tested the hypothesis whether morphine, the gold standard analgesic and nicorandil, KATP channel opener, alone and in combination possess hepatoprotective and antinociception effect and could alter morphine induced physical dependence. Male Wistar rats were injected with CCl4, 40%, 2mg/kg i.p., twice weekly for five weeks to induce hepatic fibrosis. Nicorandil (15mg/kg/day, p.o.) was administered for two weeks. Antinociception was evaluated in two pain models namely: tail flick test and the formalin test. Withdrawal signs were recorded in morphine-dependent rats. Assessment of antinociception, physical dependence and fibrotic biomarkers, oxidative stress markers were performed in parallel with histopathological examination of liver tissues. Morphine exerted antinociceptive effects in both animal models of pain in a dose dependent manner. The analgesic doses of morphine alone, insignificantly reduced the degree of liver injury. Nicorandil alone protected against liver damage as evident by decreased liver index, serum ALT, AST, hyaluronic acid, hydroxyproline content, hepatic MDA and increased SOD levels with concurrent histopathological improvement of fibrosis and steatosis scores. Surprisingly, nicorandil combined with morphine, potentiated the hepatoprotective effect of morphine. Nicorandil alone produced antinociception in the formalin model, but not in the tail flick test, however, the combined therapy produced persistent analgesia compared to morphine alone as evident by reduced EC50 of morphine in combined regimen. Additionally, nicorandil augmented morphine analgesia in both pain models and markedly decreased withdrawal signs in morphine-dependent rats. Together, the data showed for the first time, the hepatoprotection and augmented antinociception mediated by nicorandil-morphine combination in CCl4-induced liver fibrosis in rats via antioxidant and antifibrotic mechanisms. Moreover, nicorandil ameliorated withdrawal signs in morphine dependent rats in CLD. Thus, combining nicorandil with morphine could be a safe and effective pain-managing approach in patients with liver fibrosis.

**Keywords**: Opioids, nicorandil, antinociception, liver injury, hepatoprotection.

# PHS 210: Evaluation of the Combined Antitumor Effect of Pioglitazone and the Tyrosine Kinase Inhibitor Dactolisib in Experimental Models of Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is one of the most lethal malignancies worldwide. This study addresses potential crosstalk between two major signaling pathways; phosphatidylinositol-3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR) and Peroxisome Proliferator Receptors gamma (PPAR-γ) in different experimental models of HCC. In achieving our goal, we used; Dactolisib, as a dual kinase inhibitor of PI3K/AKT/mTOR, pioglitazone and GW9662, PPAR-γ agonist and antagonist respectively. For the *in-vitro* study, the $IC_{50}$ was determined for HCC cell line (Hep-G2) treated with dactolisib, pioglitazone, and GW9662. Several biochemical parameters were determined on treated-cell lysates to evaluate potential keystones of probed crosstalk. For the *in-vivo* study, mice with diethylnitrosamine-induced HCC were treated for 21 days with dactolisib and/or pioglitazone in the presence and absence of GW9662 (10, 20, and 1mg/kg, respectively). The anti-apoptotic proteins Mcl-1and survivin were assessed immunohistochemically. The *in-vitro* study confirmed the potential chemotherapeutic inhibitory effect of the combined therapy of dactolisib with pioglitazone in presence of GW9662, which entailed the in-vivo results. This was further clarified by decreasing the PI3K/p.Akt cue along with MAPK, p-STAT-3, and HGF levels to enhance apoptosis by an increase in caspase-3 level. Additionally, they inhibited hypoxic-angiogenic growth factors (HIF-1α, VEGF), cell cycle progression factor (Cyclin-D1), and inflammatory cytokines (TNF-α). Moreover, downregulation of the anti-apoptotic proteins (Mcl-1 and Survivin) levels. The best effect was mediated by the combination regimen that surpassed the effect of either drug alone. Our results highlighted the potential chemotherapeutic effects because of the pivotally increased inhibition of PI3K/AKT/mTOR involving PPAR-γ-dependent and independent manners. Co. administration of Pioglitazone and its antagonist GW9662 over Dactolisib permits achieving dactolisib therapeutic outcomes at lower levels with subsequent reduction of its reported toxicity. Therefore, this novel combination therapy may represent promising adjuvant targeted chemotherapy to enhance HCC management.

**Keywords:** PI3K/AKT/m-TOR, PPAR-γ, HCC, Dactolisib, Pioglitazone, GW9662.

# PHS 211: Biochemical and Molecular Studies on the Healing Effect of Some Celecoxib-Related Compounds on Induced Liver Injury in Experimental Animals

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Liver fibrosis is a natural immune response that is highly conserved and coordinated wound healing process that aims to maintain the integrity of liver through simultaneous inflammation, remodeling and tissue repair. The causes of liver fibrosis are multifactorial including hepatitis C, non-alcoholic fatty liver, alcoholic liver diseases and autoimmune diseases. Owing to the fact that liver fibrosis is one of the leading causes of morbidity and mortality worldwide and the lack of presence of approved antifibrotic drugs for human use, a pressing need to discover a novel drug presented itself. Several studies were conducted aiming at repurposing of the famous nonsteroidal anti-inflammatory drug Celecoxib (a selective COX-2 inhibitor) to prove its potential fibrolytic effects on liver fibrosis induced by carbon tetrachloride ($CCl_4$) in rats. Three novel bipyrazole compounds (**HR1-3**) structurally related to celecoxib of proven potential anti-inflammatory activity were employed in the current study aiming to discover a new drug candidate to treat liver fibrosis induced by $CCl_4$ in rats. The fibrolytic effects of the three candidates (**HR1-3**) were investigated through histopathological tests in addition to some biochemical tests including the determination of oxidative stress markers as well as liver function tests. Moreover, biomolecular tests for the assessment of inflammatory biomarkers such as C-reactive protein and Tumor necrosis factor alpha, as well as other parameters such as Transforming growth factor beta-1, alpha smooth muscle actin and Tissue inhibitor of metalloproteinases-1 were also performed using ELISA, RT-PCR and immunohistochemical techniques. Finally, an *in silico* molecular docking study was conducted in order to investigate the possible binding mode of the three tested compounds with the active site of some biological targets. Collectively, the results revealed that the fluorinated analog (**HR3**) showed a comparable fibrolytic effect to that of the reference standard drug (Celecoxib), making it a potential candidate for treating liver fibrosis.

**Keywords:** Liver fibrosis, Celecoxib, Bipyrazoles, COX2, ELISA, RT-PCR.

# PHS 212: Celecoxib-Based Fused Ring Derivatives: Therapeutic and Molecular Roles in Animal Model of Induced Liver Fibrosis

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Liver Fibrosis can be life-threatening if left untreated as it may lead to serious, uncurable complications. The common therapeutic approach is to reverse the fibrosis while the intervention is still applicable. Celecoxib, a non-steroidal anti-inflammatory drug, has been proved to exhibit some antifibrotic properties being effective in decreasing the fibrotic score in induced fibrotic liver of rats. Herein, we report the synthesis, molecular docking, biological, biochemical, and molecular evaluation of three novel methoxylated pyrazolo[3,4-d] pyrimidines as antifibrotic agents in comparison to celecoxib. Liver fibrosis was induced in male Sprague–Dawley rats via CCl4 injection for six weeks followed by oral treatment with celecoxib or one of the three methoxylated pyrazolo[3,4-d] pyrimidines for other six weeks. The levels of plasma alanine aminotransferase (ALT), aspartate aminotransferase (AST), and liver homogenate oxidative stress markers (lipid peroxidation and reduced glutathione levels) were determined. Histopathology was performed using H&E staining and Masson Trichrome stains, and immunohistochemical analysis was performed for alpha smooth muscle actin (α-SMA). The expression levels of tumor necrosis factor alpha (TNF-α) and tissue inhibitor of metalloproteinase 1 (TIMP-1) were detected by ELISA technique. The results revealed that the analog (E)-4-(2-(3,4-dimethoxy-benxylidene)hydrazinyl)-1-phenyl-1H-pyrazolo[3,4-d]pyrimidine (dimethoxy-derivative) showed significant inhibition of CCl4-induced elevations in plasma ALT and AST, in addition to a reduction in the antioxidative stress properties by restoring the redox equilibrium . This dimethoxy derivative has also shown an observable decrease in the fibrotic score and α-SMA positive area. In addition, a marked reduction in the level of TNF-α and TIMP-1 was detected indicating anti-inflammatory and antifibrotic characteristics. The same dimethoxy-derivative exhibited the greatest activity in all the previously mentioned parameters compared to the reference drug celecoxib and the other two analogs. Collectively, dimethoxy-derivative could be considered as a promising antifibrotic candidate.

**Keywords:** Liver fibrosis, Celecoxib, Fused pyrazoles, Inflammation parameters, ELISA.

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# PHS 213: Antioxidant and Antifibrotic Effect of Cilostazol, Silymarin and Their Combination on Carbon Tetrachloride-Induced Liver Fibrosis in Rats

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Hepatic fibrosis (HF) is an outcome of chronic liver damage of different etiologies. Cilostazol, a vasodilator, is used particularly in intermittent claudication therapy. Silymarin, a hepatoprotective flavonoid, modulates experimental hepatic fibrosis. It is the initial study that has dealt with assessing cilostazol, silymarin and their combination in experimental liver fibrosis modulation. For induction of HF, male albino rats were injected intraperitonealy with carbon tetrachloride $CCl_4$ twice a week for 8 weeks. Drug treatment was given for further 28 days post-induction with daily oral doses of Silymarin (100mg/kg), Cilostazol (30mg/kg) and their combination. Hepatic fibrosis was assessed by measuring serum levels of hepatic enzymes, serum bilirubin and fibrosis markers (tumor necrosis factor α and transforming growth factor β1). Markers of oxidative stress (MDA, GSH, and GPx activity), were also evaluated in the liver besides the histopathological examination of the liver specimens. $CCl_4$ injection resulted in marked hepatic fibrotic transformation and oxidative stress. The results revealed that the combination exhibited the superior therapeutic potential in hepatic fibrosis treatment in this study. The current study provides an evidence for the promising antifibrotic effects of the two drugs cilostazol and silymarin and their combination. Interestingly, cilostazol was observed to be better than silymarin in lessening fibrosis and inflammation.

**Key words:** Hepatic fibrosis, Silymarin, Cilostazol, transforming growth factor β.

# PHS 214: Combination of Thioridazine and Sorafenib Potentiates Anti-Tumor Effect in HepG2 Cell Line

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Hepatocellular carcinoma (HCC) is a leading cause of death worldwide with a remarkable rise among patients with chronic liver disease. The first line of systemic therapy for the advanced stage is sorafenib, but with unfortunately a limited therapeutic outcome. Therefore, there is an urgent need to develop alternative systemic therapies to improve patients' outcomes. In the current study, thioridazine, an antipsychotic drug, was combined with sorafenib in HepG2 cell line to investigate the possible mechanisms to augment its therapeutic efficacy. Four groups were used: control, sorafenib, thioridazine and sorafenib+thoridazine. Cytotoxicity, apoptosis, DNA double strand breaks (DSBs), angiogenesis, inflammation and metastasis were assessed, in addition to some mediators of PI3K/AKT/mTOR and RAF/MEK/ERK pathways. Compared to the actions of either drug alone, the combination of sorafenib and thioridazine resulted in enhanced inhibition of cell growth, augmented levels of DSBs and increased apoptosis. Combination index analysis illustrated a synergistic growth inhibitory effect with reduced doses of sorafenib and thioridazine; 2.6 and 1.88, respectively. Furthermore, the combination regimen showed marked blockade of both PI3K/AKT/mTOR and RAF/MEK/ERK pathways. Consequently, levels of vascular endothelial growth factor, nuclear factor kappa-B-p65, E-cadherin and N-cadherin were notably reduced in the combination therapy. These findings highlight that the stronger effect obtained with lower doses of both drugs, in combination, suggests this regimen to be a potential therapeutic approach for the treatment of HCC.

**Keywords:** Hepatocellular carcinoma, Thioridazine, Sorafenib, Combination.

# Clinical Pharmacy Practice & Patient Care

# PHS 301: Possible Neuroprotective Effects of Newer Antidiabetic Drugs in Patients Attending Diabetes Clinics in Alexandria

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It is becoming more widely accepted that neuroinflammatory alterations and the related change in cognitive impairment are consequences of type 2 diabetes mellitus. This study examines the effects of dipeptidyl peptidase-4 (DPP-4) inhibitors and/or sodium glucose cotransporter-2 (SGLT2) inhibitors in combination with metformin on cognitive deterioration in type 2 diabetes patients. By conducting a prospective observational cohort study, we are comparing type 2 diabetic patients on SGLT2 inhibitors and/or DPP-4 inhibitors in combination with metformin with a control group receiving metformin alone. In addition to a group of healthy non-diabetics to serve as a baseline reference, both groups will have their cognitive function and inflammatory markers tested at baseline and six months after the follow-up. With a mean age of 58.07 ± 5.48 years, a total of 80 individuals (33 men and 49 women) have been recruited and the study started in early March 2022. Based on baseline data, it was shown that diabetic patients (diabetic for an average of 15.22 ± 8.40 years) had impaired cognitive function, with an average Montreal Cognitive Assessment score of 18.69 ± 4.92 compared to 20.38 ± 4.63 in the healthy subjects. Furthermore, there was evidence of higher inflammatory markers in the diabetes patients, with CRP levels at 7.40 ± 7.93 mg/L compared to 3.79 ±3.42 mg/L in the healthy subjects and IL-6 levels at 7.71 ± 8.40 pg/mL compared to 3.02 ± 1.50 pg/mL in the healthy subjects. Follow-up with patients is underway to measure the same parameters at the end of the follow-up period. Additionally, proteomic and glycomic serum profiling will be done in control and treated individuals, followed by a full network analysis to elucidate the probable pathways connected to the observed metabolic and cognitive abnormalities.
Trial registration: ClinicalTrials.gov NCT05347459

**Keywords**: Type 2 diabetes, novel antidiabetics, cognitive dysfunction, inflammatory status.

# PHS 302: Impact of Psychiatric Pharmacists on Designing Practice-Based Educational Materials for Pharmacy Students to Overcome Malpractices in Psychiatry: A Quasi-Experimental Study

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Pharmacy education has shown a drastic change during the past decade. The evolving role of clinical pharmacists in the healthcare team necessitates parallel improvement in pharmacy education and individual speciality integration in pharmacy curricula. Improving the quality of psychiatric pharmacy practice demands bridging the gap between academia and clinical practice by clinical pharmacists. This aims to empower pharmacy graduates to overcome malpractices in psychiatry and fight stigma against mental illness. A quasi-experimental study was initiated to evaluate the impact of a practice-based course on pharmacists' knowledge. The course was designed by a PharmD psychiatric pharmacist (first author) and delivered to candidates of the postgraduate Doctor of Pharmacy degree, Faculty of Pharmacy, Alexandria University. A sum of 42 questions were reviewed and validated by three consultant psychiatrists. Questions are categorised to assess pharmacists' knowledge about different domains in psychiatric pharmacy practice such as psychoeducation and misconceptions in mental health, dealing with side effects of psychotropic drugs, tapering strategies and individualization of treatment. Scores of the intervention group are compared to those of community and hospital pharmacists' who did not receive a similar practice-based and patient-oriented educational material. This study expands the role of practitioners in academia to prepare pharmacy graduates for the increasing challenges in daily practice.

**Keywords**: Psychiatric pharmacist, malpractices, psychiatry, practice-based educational materials, pharmacy students, academia, PharmD.

# PHS 303: OSCE for the First Time in the Community Pharmacy Practice Course for Assessment of Students Clinical Competencies, Faculty of Pharmacy, Alexandria University, Egypt

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Since pharmacy profession has become patient-oriented more than being product-oriented, clinical skills assessment of pharmacy students has become a crucial issue. Objective structured clinical examination (OSCE) has been described as gold standard for clinical assessment since 2002. It is considered as a tool to simulate real situations that occur in real-life working environment. It focuses on clinical skills rather than basic knowledge which necessitates its incorporation in students' educational program and curriculum. In the fall 2021 semester, 192 students at the 3rd year pharm D clinical program at the faculty of Pharmacy, Alexandria University in Egypt, have been enrolled into a wide variety of OSCE stations during their tutorial sessions. With the help of tutorials supervisors, OSCE stations were designed to be individualized, of 7-mins duration, three times through the semester, for each student with a pre tutorial handouts. Scenarios involved cases of referral, OTC product selection, drug-related adverse effects and patient education about medical devices use (e.g. Inhalers) covering different minor ailments, smoking cessation, drug-related adverse effects and device patient education. Evaluation rubrics included student's self-introduction, communication skills, systematic ordered flow of thinking (following Quest Scholar Mac), appropriate information retrieval and how to end up properly with the patient. 89.4% of students were excellent in Confidence- body language and eye contact with only 3.5% showed some weakness. 87.71% used appropriate language and communication skills, 3.5% were good and 5.6 were weak. 68.42% greeted patient appropriately while 29.82% did not do that well enough with only 50.87% asked about exclusion criteria (Alarming signs). Although OSCE experience was time consuming, demanding great number of well experienced teaching assistants and subjected to bias, it was the first time to do it in the community pharmacy practice and it highlighted the weakness of some students in clinical skills and guided staff members to better design more experiential courses.

**Keywords**: OSCE, Community pharmacy practice, clinical skills, experiential course.

# PHS 304: A Prospective Descriptive Study to Evaluate the Impact of Clinical Pharmacist in Antiplatelet Utilization and Safety in Coronary Heart Disease Patients

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**Aim:** To evaluate the interventions associated with integration of a clinical pharmacist for antiplatelets best utilization and safety as multidisciplinary team approach is recommended to improve patient outcomes. **Methods:** prospective observational study on coronary heart diseases patients (stable angina, unstable angina, MI, post PCI or post CABG) on antiplatelets therapy (single antiplatelet; SAPT, or dual antiplatelet; DAPT) at governmental and private hospitals. Detailing pharmacist-initiated interventions targeting pharmacotherapy optimization (Dose, duplicate and interactions), also adverse effects detection, and hospital re-admission (re-event of coronary insufficiency). Collecting patients' data by interviews and hospital records using validated check list. Statistical software IBM SPSS software package version 20.0, The Kolmogorov-Smirnov was used to verify the normality of distribution of variables, Mann Whitney test was used to compare between two categories for not normally distributed quantitative variables. Kruskal Wallis test was used to compare different categories for abnormally distributed quantitative variables. Spearman coefficient was used to correlate between quantitative variables. Linear Regression was used to detect the most affecting factor for affecting DAPT score and Precise DAPT. Significance of the obtained results was judged at the 5% level, calculate sample size by G Power3. **Results:** There is a significant correlation between cardiac related readmission and Precise DAPT score (P=0.013). A statistically significant correlation is found between smoking and DAPT score (p=0.015) but not with precise DAPT (P=0.152). Also a significant linear association exists between DAPT type and DAPT score, for Aspirin + Clopidogrel (P=0.010) (95%CI=-1.000 (-1.754 – -0.246), Aspirin + Ticagrilor (P=0.012) (95%CI= 1.001 (0.228 – 1.774). The highly significant influencing variable in both scores, is the dose value, for DAPT score (P=0.038), Precise DAPT (P=0.001). The distribution of Myocardial infarction as cardiac related readmission and smoking are higher in males than females without statistically significant difference (P=0.08), (P=0.39), the absence of adverse effects and bleeding events is statistically significant in DAPT score (P=0.041, 95%CI=1.706 (0.071 – 3.341) & precise DAPT score (P=0.002, 95% CI= -15.95 (-25.832 – -6.074). **Conclusions:** Impact of a clinical pharmacist within cardiology department generated substantial pharmacotherapy optimization which improve the medication adherence, safety and clinical outcomes. Our study suggests pre-calculating DAPT and precise DAPT for all patients before treatment and commitment on DAPT period administration may decrease re-admission rate of patients.

**Keywords**: coronary artery diseases, re- admission; clinical pharmacist; Precise DAPT score, DAPT score.

# Drug Analysis & Quality Control

# PHS 401: Application of Inexpensive Bioluminescent Probe in the Sensitive Determination of DNA Damage Induced by Some Commonly Used Sunscreens

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Sunscreens (SSs) are highly applied all over the world on large areas of human body. Benzophenone chemical group constitute a major part in most SSs. Benzophenones are reported to induce changes in nucleic acids upon UV-irradiation. These alterations may potentially lead to DNA mutation, cell apoptosis, and eventually skin cancer. This work compares the kinetics of the induced DNA damage by some SSs after UV-irradiation. Six commonly used SSs; 4-t-butyl-4-methoxy dibenzoyl methane, 4-methoxycinnamic acid, 2-hydroxy-4-methoxy- benzophenone (BZ-3), Dibenzoyl methane, 2,2′-dihydroxy-4-methoxy benzophenone (BZ-8) and p-methyl- benzoic acid; are investigated. In this work, terbium chloride bioluminescent genosensor is used for sensitive, simple and inexpensive determination of induced DNA-damage. Results reveal that only BZ-3 and BZ-8 induced DNA-damage upon UV-irradiation that are confirmed by both absorption spectroscopy and viscosity measure- ments. Moreover, viscosity studies indicated the possible intercalation of the SS into DNA prior to initiation of DNA damage. Furthermore, the potency of BZ-3 and BZ-8 to induce DNA damage upon UVA irradiation was assessed on calf thymus DNA. The low cost of the proposed bioluminescent genosensor allows it to be an automatic simple process for the investigation of any DNA-drug interactions without the need of coupling with other analytical methods.

**Keywords**: DNA-Damage, Sunscreens, Terbium luminescent probe, Absorption spectroscopy, Viscosity measurements, UV-Irradiation

# PHS 402: Economic Electrochemical Sensors for the Selective Determination of Eszopiclone in Presence of its Alkaline Degradation Product: Greenness Appraisal Using Analytical Eco-Scale and GAPI

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Electrochemical-ion-selective-sensors offer green, rapid, economic and simple analytical-tool in pharmaceutical industry, control processes, physiological measurements and environmental monitoring. In this study, two sensors were introduced for eszopiclone (EZP) determination in presence of its alkaline degradant and other relevant interferents either in pure-form or pharmaceutical formulation using drug-ion-exchanger association complex fabrication technique. Two different ion-exchangers were used and compared, potassium tetrakis (4-chlorophenyl) borate (K-TpClPB) in sensor 1 and sodium tetraphenyl borate (Na-TPB) in sensor 2. Such sensors showed superior performance at pH 3.5 over a wide-range of EZP concentration. According to the obtained results, the utility of K-TpClPB as an ion exchanger in the development of sensor 1 provided better sensitivity and selectivity than Na-TPB, used in the development of sensor 2, showing higher Nernstian slope and faster response. The proposed method greenness was also assessed using GAPI and analytical Eco-scale. Furthermore, the selectivity of the proposed sensors towards different interferents was evaluated using three approaches of separate solution methods (SSMs) and one approach of matched potential method (MPM) providing an accurate and realistic deduction of the electrode selectivity parameters. Low cost, short analysis-time, direct drug determination in turbid and colored solutions, and greenness of the proposed sensors allow their use for routine analysis in quality-control laboratories.

**Keywords:** Eszopiclone, Ion Selective Electrode, Tetraphenylborate, Tetrakis, Nitrophenyl octyl ether, Greenness assessment.

# PHS 403: Simultaneous HPTLC Densitometric Determination of Amoxicillin, Metronidazole, and Famotidine Ternary Mixtures: A Promising Protocol for Eradicating *H. pylori*

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GIT disorders continually strike many people, and they constitute a heavy burden to healthcare providers. Infection with *Helicobacter pylori* is known to be pandemic, with an estimated prevalence of approximately 50% of the world's population, being recognized as the primary cause of gastric carcinogenesis. In an attempt to eradicate such infection, different triple therapy protocols have been proposed. Among which are combinations of proton pump inhibitors (e.g omeprazole), histamine-2 receptor antagonists (e.g. famotidine), along with antibiotics (e.g. amoxicillin). In this work, a sensitive and accurate high performance thin layer chromatography (HPTLC) method was developed and validated for the simultaneous determination of amoxicillin, metronidazole, and famotidine in bulk powder and laboratory prepared combined-tablet mixtures. Complete separation of the cited compounds was achieved using pre-coated silica gel HPTLC plates with a mixture of methanol: chloroform: toluene: water: glacial acetic acid (5:2:1.5:0.5:0.1 v/v/v/v/v) as the mobile phase. Densitometric detection of the developed bands was performed at 280 nm for amoxicillin and famotidine and 300 nm for metronidazole. The developed method was fully validated according to the ICH guidelines. Good linearity, correlation coefficient of 0.9991, was obtained in the concentration ranges 0.1-1.6 µg band$^{-1}$, 0.1-0.9 µg band$^{-1}$ and 0.1-0.9 µg band$^{-1}$ for amoxicillin, metronidazole, and famotidine, respectively. The proposed method allowed the determination of the cited compounds with relative errors and standard deviation values not exceeding 2% indicating high degree of accuracy and precision, respectively. Since the suggested method allowed the determination of the three compounds in combined tablets with high degree of selectivity, accuracy, precision, with cost-effectiveness, it could be used for regular quality control. Moreover, the applicability of the proposed method was extended to the determination of the ternary mixture in simulated gastric juice.

**Keywords**: HPTLC, Multicomponent analysis, Amoxicillin, Metronidazole, Famotidine, *H-pylori*

# PHS 404: Green Spectrophotometric & Fluorimetric Versus HPTLC Assay of Remdesivir; The FDA Approved Covid-19 Antiviral

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Covid-19 can be misdiagnosed with mild flu-like symptoms but may rapidly progress into pneumonia and respiratory distress leading to hypoxial and/or embolic death. The viral inexorable pandemic has resulted in worldwide lockdowns and has exceeded 1.2 million deaths before the end of 2020. Drug manufacturing companies are in fierce scientific, as well as political rivals to authorize anti-Covid agents. U.S. Food & Drug Administration (FDA) previously approved the first antiviral "Remdesivir" for hospitalized Covid-19 cases. Thus, Remdesivir (RDV) determination in pure or formulated forms endears an accurate and robust assay. This study presents three different assay methods to detect and quantify RDV in bulk and its injection dosage form. Method I and II are based on direct measuring of the maximum absorbance and relative fluorescence intensity of the drug, respectively. Method II is an HPTLC-based technique, using ethanol and water only as a green & environmental-friendly mobile phase. The proposed methods have reached down the micro level determination and are validated and tested for all performance parameters to be ready for their use in RDV routine analysis in quality control labs. The three methods' greenness had been assessed by the known "Green analytical procedure index" to prove that the three methods are eco-friendly and fulfill the recommendations of green chemistry.

**Keywords:** Remdesivir, Covid-19, FDA, Spectrophotometry, Spectrofluorimetry, HPTLC and Green.

# PHS 405: Sustainable Kinetic Degradation Study of the First Oral Approved Anti COVID 19 Drug Molnupiravir Using HPLC-DAD with LC-MS-UV Degradation Characterization: Comparable Whiteness and Greenness Appraisal

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SARS-CoV-2 virus triggered a worldwide crisis, with world nations putting up massive efforts to halt the spread. Molnupiravir (MLN) was the first oral, direct-acting antiviral drug approved for nasopharyngeal SARS-CoV-2 infection with favorable safety and tolerability profile. The study aims at MLN assessment under different stress conditions using NaOH, HCl, neutral, $H_2O_2$, dry heat and sun light. Thus, a fast, efficient, and selective HPLC-DAD method was developed for MLN determination in the presence of its forced degradation products, followed by a novel kinetics degradation investigation. The stationary phase was Agilent HC-C18 analytical column (150 x 4.6 mm, 5 µm) with mobile phase consisting of deionized water and acetonitrile in an isocratic elution 75:25, v/v, respectively. The detection wavelength using DAD was set at 236 nm. The total run time was 5 min and 20-µL injection volume. The linearity range was 0.1–100 µg/mL with LOD and LOQ equal 0.034 & 0.1 µg/mL, respectively. According to a detailed stress stability investigation, MLN is extremely vulnerable to alkali hydrolysis and less so to acid and dry heat. In contrast, MLN was discovered to be stable under conditions of oxidative, neutral, and sunlight-induced deterioration. By investigating the rates of acid and alkali hydrolysis degradation, it was found that the kinetics followed a pseudo first-order model. LC-MS-UV was used to suggest the mechanism of the stress conditions' degradation route. As with the parent drug, MLN, the proposed Degradation Products (DPs') toxicities were evaluated using ProTox-II and determined to be negligibly harmful. The effective analysis of MLN in commercial pharmaceutical formulations without interference by usual capsule excipients or likely degradation products demonstrates the utility of the HPLC-DAD method as a stability-indicating tool. Our proposed method for MLN determination after greenness and whiteness appraisal was shown to be superior compared to the reported methods for MLN analysis.

**Keywords**: kinetic Degradation, LC-MS-UV, Molnupiravir, Shelf-life, Whiteness.

# PHS 406: Spectrophotometric Determination of Ternary Mixture of Beta-Carotene, Vitamin C and Vitamin E

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Liver plays an important role in the vitality and maintenance of the internal balance in the human body as it regulates metabolism, blood volume, detoxification and excretion of many endogenous and exogenous compounds. Hepatoprotective agents are gaining much attention due to their efficiency in controlling liver diseases. In addition, antioxidants have radical-scavenging role that defend the body against oxidative stress induced by active oxygen species and free radicals. Beta-carotene (B-CAR), Vitamin C (VIT C) and Vitamin E (VIT E) have very important role in disease prevention and maintaining health as hepatoprotective agents and antioxidants. In the analysis of their mixture, although direct spectrophotometric technique is suitable for the determination of B-CAR in the presence of VIT C and VIT E, it is not possible to determine both drugs using the same spectrum due to spectral interference. Therefore, first and second derivative spectra for the mixture have been calculated and it was found that VIT C can be successfully resolved from interfering spectra in the first derivative spectrum while VIT E can be determined without any interference in the second derivative spectrum. The present study was able to develop a combination of three spectrophotometric methods for simultaneous determination of B-CAR, VIT C and VIT E in their ternary mixture in the presence of co-formulated adjuvants in their pharmaceutical preparations without prior clean-up procedures. The developed direct spectrophotometric, 1$^{st}$ derivative spectrophotometric and 2$^{nd}$ derivative spectrophotometric methods have succeeded in quantitation of B-CAR, VIT C and VIT E in concentration ranges of 0.68-6, 3.4-53.6 and 3-24 $\mu gmL^{-1}$, respectively with correlation coefficient values exceeding 0.999. Application of the developed methods to laboratory-prepared mixtures proved the accuracy of the methods with the obtained recovery values of 100.87± 0.88, 99.86± 1.32 and 101.3± 0.95 for B-CAR, VIT C and VIT E, respectively.

**Keywords:** Spectrophotometry, First derivative, Second derivative, Laboratory-prepared mixture, Hepatoprotective, Antioxidants, Beta-carotene, Vitamin C, Vitamin E.

# PHS 407: HPLC-DAD Determination of Two Antiemetic Binary Mixtures Used as Supportive Care to Cancer Patients

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A simple chromatographic-diode array detection (DAD) method was developed for analysis of two antiemetic binary mixtures frequently used to control chemotherapy induced- vomiting. The two mixtures are composed of Dexamethasone (DEX) with either Metoclopramide (MET) (mixture 1) or with Ondansetron (OND) (Mixture 2). Chromatographic separation was achieved using a C18 ODS GL Sciences® column (4.6 × 250 mm × 5 µm), with isocratic elution of the mobile phase composed of acetonitrile and 50 mM phosphate buffer of pH 4.5 (adjusted using phosphoric acid) in a ratio of (26:74 %) v/v. The mobile phase was pumped at a flow rate of 1.0 mL/min. The DAD was set at 240, 277, 302 nm to determine DEX, MET and OND, respectively, and quantification of the analytes was based on peak area measurement. This method was conducted to analyze the two antiemetic binary combinations in spiked plasma samples with good recovery values after simple protein precipitation. The proposed chromatographic method was validated in accordance with FDA guidelines including linearity (correlation coefficients > 0.999), range, precision, accuracy, selectivity & robustness. All results proved the potential applicability of the proposed HPLC method as an analytical tool for further pharmacokinetic and bioequivalence studies for the two co-administrated drugs in each mixture.

**Keywords**: Dexamethasone, Metoclopramide, Ondansetron, HPLC-DAD and Plasma.

# PHS 408: Development of a White HPLC-DAD Method for Simultaneous Determination of Sulfacetamide Sodium and Two of Its Impurities Together with Three Co-formulated Drugs in Ophthalmic Solutions

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A white HPLC-DAD method has been developed and validated for the simultaneous determination of Phenylephrine (PHE), sulfacetamide sodium (SAC), Fluorometholone (FLU), Prednisolone acetate (PRD) and SAC pharmacopeial impurities in presence of benzalkonium chloride (BNC) as a preservative in ophthalmic solution. The separation of the cited compounds was achieved on Agilent C18 column (4.6 x 250 mm, 5 µm p.s.) under gradient elution conditions of mobile phase ratio and flowrate. The mobile phase composed of acetonitrile (HPLC grade), methanol (HPLC grade) and buffer solution (0.01 M sodium dihydrogen orthophosphate dihydrate, pH adjusted to 3 with orthophosphoric acid). The determination was carried out at 212, 240 and 260 nm. The proposed analytical procedure was validated according to the International Conference on Harmonization (ICH) guidelines in terms of linearity, limits of detection and quantitation, accuracy, precision, selectivity, and robustness. Good linearity was proved by the high values of correlation coefficients (r) were not less than 0.99994. Sensitive determination of the cited compounds was carried out within the concentration ranges of 20-400 µg/mL for PHE and SAC, 20-300 µg/mL for FLU and PRD and 2-100 µg/mL for sulfanilamide and dapsone (SAC pharmacopeial impurities). The proposed method was successfully applied for the determination of the cited analytes in pharmaceutical ophthalmic solutions without interference from co-formulated excipients and preservatives. Moreover, evaluation and comparison of the proposed method's greenness and whiteness with previously published methods was performed.

**Keywords**: Sulfacetamide sodium; Impurities; Co-formulated drugs; HPLC-DAD; Whiteness-study.

# PHS 409: Integrative Genomic and Metabolomic Strategy for Quality Assessment of German chamomile (*Matricaria recutita* L.) and its Differentiation from Toxic Adulterants

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German chamomile (*M. recutita* L.) is amongst the most consumed herbals worldwide in either raw or processed state. *German chamomile* is prone to intentional/unintentional adulteration owing to its wide range of pharmacological activities. Tiered barcode authentication was approached for discrimination of G. chamomile from its morphological resemble; *Anthemis cotula* L. and the common *Senecio* weeds; *Senecio desfontainei* Druce and *Senecio vulgaris* L. Three plastid loci (matK, rbcL & intergenic spacer psbA- trnH) and two nuclear spacers (ITS & ITS2) were targeted. ITS2 revealed the maximum discriminatory power reflecting the genetic diversity among the studied plants in a well-correlative manner to morphological, botanical, and genetic characteristics, with enhanced sequencing feasibility and success rate. For deep insights, chemical profiling was implemented via HPTLC-image analysis, tracking and quantifying quality, and toxicity markers to guarantee effectiveness and safety. Flavonoids and phenolic acids were screened as quality markers for *M. recutita* L. while anthecotulide (sesquiterpene lactone) and senecionine (pyrrolizidine alkaloid) were accounted as toxicity contributors for *A. cotula* L. and *Senecio* species, respectively. Furthermore, distinguishable coumarin accumulation patterns across the studied plants could be valuable for their differentiation. In conclusion, the proposed genomic and metabolomic integration represents a comprehensive quality control protocol that can be accomplished as paramount routine analysis of German chamomile.

**Key words:** *Matricaria recutita*, authentication, adulteration, ITS2, quality and toxicity markers.

# PHS 410: Environmentally Benign Carbon Nano Dots as a Luminescence Probe for Quantification of Palladium (II) Chloride Impurity in Naproxen

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Green shades of "The 2030 Global Green Agenda" have directed the analysts into a peaceful relationship with their surrounding environment. Natural resources, clean energy, green solvents are in commitment with Earth's sustainability. Hazardous inorganic chemical reagents are in gradual replacement by nanoscale reactive species of green origins. In this sense, the present study utilizes nano Carbon Dots, synthesized from garlic peels as natural precursor, with a modified surface activity "multiple active chromophore". The latter act as potent fluorogenic scavengers for optical nanosensing of Palladium traces in the anti-inflammotary Naproxen drug substance. Palladium traces are found in Naproxen bulk as synthesis-related impurity. Higher ingested levels increase the risk of debilitating diseases in the human body. Stoichiometric reaction between Palladium traces and the dots' active surfaces was quantified indirectly along the linear spectral diminish of carbon dots luminescence. The proposed methods involve quantitative fluorescence quenching of carbon dots at 432 nm upon excitation at 375 nm and absorption peak at 250 nm upon addition of studied palladium chloride. The results obtained were in good agreement according to the Stern-Volmer equation along the linear range of 49.63 nM - 5.01 mM palladium chloride. The procedures that were developed were validated in accordance with the ICH guidelines.

**Keywords**: Quantum dots, Fluorescence Quenching, Synthesis Impurity, Quality Control.

# PHS 411: A Comparative Study of Different Spectrophotometric Methods for the Analysis of Binary Mixtures of Novel Oral Anticoagulants with Rosuvastatin

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The significant importance of the binary mixtures of the novel oral anticoagulants (NOACs); Apixaban (APX), Edoxaban tosylate (EDX) and Rivaroxaban (RIV) with the lipid lowering drug Rosuvastatin calcium (ROS) resides in their co-prescription to cardiovascular patients for prophylaxis from stroke. The present work deals with the development, validation and application of several simple and direct spectrophotometric methods for the analysis of the novel oral anticoagulant drugs with Rosuvastatin (ROS) in their binary mixtures. The proposed methods involved (a) first, second and third derivative spectra, (b) treatment of the absorbance ratio spectra using derivative or difference functions, (c) treatment of zero-order spectra using delta absorbance method followed by derivative function. APX in mixture 1 with ROS was assayed using second derivative (D2) spectra method, absorbance difference ratio (R.D) method and first derivative ratio (D1R) method with no interference from ROS, while EDX in mixture 2 with ROS was determined using first derivative (D1) spectra, absorbance difference ratio (R.D) method, first and second derivative of delta Absorbance (ΔA) method. In the third mixture consisting of RIV and ROS, RIV was assayed using third-order (D3) spectra and absorbance ratio difference (R.D). ROS was assayed by first derivative (D1) in both mixtures 1 and 2, second derivative (D2) in mixture 3 and the derivative of delta Absorbance (ΔA) method in mixture 2. Linear regression lines were obtained with excellent correlation coefficients. The developed methods were successfully applied to the analysis of the drugs in their synthetic mixtures and in their dosage forms. The mean percentage recoveries were within acceptable range with % RSD and Er % that didn't exceed 2 %. The methods were validated according to ICH guidelines parameters and showed good performance in terms of linearity, precision, accuracy, sensitivity and stability. A comparative study was finally conducted by performing the ANOVA test.

**Keywords**: Novel oral anticoagulants, Rosuvastatin, Spectrophotometric analysis, ANOVA test.

# Medicinal Chemistry Advances: Molecular Modeling & Drug design

# PHS 501: Design, Synthesis, and Biological Evaluation of Some Novel 1,2,3-Triazole Derivatives as Potential Antifungal and Anticancer Agents

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Invasive fungal infections (IFI) have increased dramatically in recent decades. Such infections, in large part, are due to an increase in the number of immunocompromised patients because of aggressive therapies, such as cancer chemotherapy. Moreover, due to the wide spread of resistant fungal strains, the majority of presently available antifungal agents are diminishing their effectiveness. On the other hand, the high mortality rates engaged with the rising number of diverse types of cancers, have triggered an unrivaled level of research aiming at finding out new lead structures that might be beneficial in designing novel antitumor agents. Consequently, there is an urgent demand for the discovery of novel unconventional antifungal and anticancer agents with high selectivity and minimum side effects. Herein, we report the design, synthesis and molecular docking studies of novel phenylethyl-1,2,3-triazoles to be evaluated for their antifungal and/or cytotoxic potentials. Most compounds proved to be active as antifungal members against C.albicans clinical isolate strains. Docking of the targeted compounds with the active site of CYP51 (the primary target of azole antifungal agents) demonstrated a superior binding profile relative to fluconazole. Additionally, the targeted compounds were evaluated for their cytotoxicity against three cancerous cell lines; lung A549, colon CaCo2, and breast MCF7 as well as normal lung fibroblasts (Wi-38) using MTT assay. Compounds 3b, 5, 6, 7, and 9 were the most active with a broad-spectrum anticancer activity against the three tested human cancer cell lines with $IC_{50}$ values comparable to the reference drug docetaxel. Collectively, compounds 6, 7, and 9 could be considered as promising dual antifungal-anticancer candidates.

**Key words:** Triazole, antifungal, anticancer, Cyp51 inhibitors.

# PHS 502: Design, Synthesis and Biological Characterization of Histone Deacetylase 8 PROTACs with Anti-Neuroblastoma Activity

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Because reversible acetylation and deacetylation play a role in controlling the chromatin structure, they are among the most studied posttranslational modifications (PTMs). They are regulated by histone acetyltransferases (HATs) and histone deacetylases (HDACs). Generally, the 18 mammalian HDACs known to date are divided into two families that are subdivided into four classes. While classes I, II and IV depend on $Zn^{2+}$ for their catalytic activity, class III members are $Zn^{2+}$-independent and require nicotinamide adenine dinucleotide as cofactor. HDAC8 is a unique class I $Zn^{2+}$-dependent HDAC whose overexpression was significantly correlated with the advanced stage of neuroblastoma, the most common childhood extracranial solid tumour, and its metastasis. However, its knockdown in cultured neuroblastoma cells led to proliferation inhibition, and induction of cell cycle arrest and differentiation. As a result, selective HDAC8 inhibition or degradation is a promising therapeutic strategy in neuroblastoma. In the work presented we designed a pool of bifunctional proteolysis targeting chimeras (PROTACs) based on previously published HDAC8 inhibitors by our group with good inhibitory activity. Various degradation machinery recruiting units in addition to different linker types and lengths were employed to investigate their effect on the degradation profile of the synthesized PROTACs. The degradation ability of the synthesized degraders was demonstrated through testing them on SK-N-BE(2)-C neuroblastoma cells and the determination of the protein levels of HDAC8 and the acetylation level of its substrate SMC3. From the synthesized heterobifunctional molecules only two cereblon (CRBN)-based PROTACs, namely CRBN_1b and CRBN_1e, resulted in strong HDAC8 degradation connected with SMC3 acetylation. They also exhibited good selectivity against HDAC1 and HDAC6. Moreover, they presented good anti-neuroblastoma activity coupled with enhanced phenotype differentiation. In future work, the developed PROTACs will be used to investigate the physiological functions of HDAC8 in other cancer cells.

**Keywords**: histone deacetylases; HDAC8; proteolysis targeting chimera; neuroblastoma.

# PHS 503: Design, Synthesis, Biological Evaluation and Molecular Docking Study of Novel Pyrazine Derivatives as Potential Anticancer Agents Targeting FAK Enzyme

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Focal adhesion kinase (FAK) is a non-receptor tyrosine kinase that plays a vital role in regulating cancer cell survival, proliferation, migration, and angiogenesis. Aiming to explore new potent inhibitors, a series of pyrazine-heteroaryl hybrids was designed and synthesized. The newly synthesized compounds were evaluated for their *in vitro* anti-proliferative activity against human liver (HUH-7), lung (A549) and breast (MCF-7) cancer cell lines, in addition to their cytotoxic activity against normal lung cell line (WI-38) to predict their safety profiles. The most active and selective compounds were further screened for their inhibitory activity against FAK. Cell cycle analysis and the apoptotic mechanism of compounds (**4f** and **7c**) through caspase-3 activation were also investigated. Results indicated that compounds **(4d, 4f, 7a, 7c, 8, 11, 14, 15** and **17c)** displayed significant anti-proliferative activity as well as high selectivity towards the tested cancer cell lines (SI>2). Among them, compounds **(4f** and **7c)** potently inhibited FAK enzyme with $IC_{50}$ values of 27.95 and 50.98 nM, respectively, comparable to GSK-2256098 as a reference drug. According to flow cytometric cell cycle analysis, compounds **(4f** and **7c)** triggered pre G1 apoptosis and caused cell cycle arrest at S phase. They also exhibited an increase in the expression level of caspase-3 enzyme. Molecular docking study of compounds **(4f** and **7c)** into FAK's active site was performed to elucidate its possible binding modes and to provide a structural basis for the further structural guidance design of FAK inhibitors. Collectively, these data support that compounds (**4f** and **7c)** could serve as lead compounds for FAK-targeted anticancer drug discovery.

**Keywords***:* FAK inhibitor, Anti-cancer, Pyrazine analogs, Molecular docking, Apoptosis.

# PHS 504: Design, Synthesis and Anticancer Evaluation of Some New Purine Derivatives as Potential EGFR Inhibitors and Apoptotic Inducers

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Cancer is a leading cause of death worldwide and a multifactorial disorder involving complicated molecular mechanisms and pathways. Lung and breast cancers are the most common types affecting men and women, respectively. In the past years, EGFR inhibition laid the foundation for many targeted cancer therapies. Even more, the implications of high levels of EGFR gene expression have been extended to increased cancer aggressiveness, angiogenesis, in addition to resistance to chemotherapy and radiotherapy. Hence, we present the design and synthesis of some new purine derivatives comprising 8-hydrazinyl, thiosemicarbazide and substituted sulfanyl moieties to evaluate their anticancer activities along with their EGFR inhibition and activation of apoptosis as possible mechanisms of action. Biological evaluation results revealed that most of the tested compounds exhibited no cytotoxic effects on WI38 normal cells. It was also found that twelve compounds exhibited potent anticancer activity against lung cancer cell line (A549) whereas sixteen compounds were highly active against breast cancer cell line (MCF-7), compared to 5-FU. EGFR inhibition data showed that two compounds were potent EGFR inhibitors compared to erlotinib. Flow cytometric analysis of cell death for the most active compounds using annexin V/propidium iodide revealed that they induced apoptosis in treated MCF-7 cell lines. In addition, they induced a remarkable increase in BAX and caspase 9 levels and a decrease in Bcl-2 level. They also significantly induced mitochondrial cytochrome c release and were able to exhibit overexpression of p53. Docking studies indicated that these compounds showed favorable binding interactions with EGFR active site. Also, *in silico* predictions proved their suitability as hits or drug-like. Accordingly, these purine derivatives might serve as structural leads amenable for modifications into new potent anticancer agents.

**Keywords:** Purine, Anticancer, Epidermal growth factor receptor (EGFR), Apoptosis.

# PHS 505: O-Alkylation of 2-Pyridone Derivatives as PIM-1 Kinase Inhibitors: Design, Synthesis, Anticancer Evaluation, Kinetic and *In-Silico* Studies

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New O-alkyl derivatives of the 2-pyridone were designed and synthesized as PIM-1 kinase inhibitors. Compounds **4c** and **4f** showed potent *in-vitro* anticancer activity against myeloid leukemia (NFS-60), liver cancer (HepG-2), prostate cancer (PC-3) and colon cancer (Caco-2) cell lines and low toxicity against normal human lung fibroblast Wi-38 cell line. Flow cytometric annexin V/propidium iodide analysis elicited that, compound **4c** and **4f** showed high percentage of annexin-stained apoptotic cells in the four tested cancer cell lines. Moreover, compounds **4c** and **4f** significantly induced caspase 3/7 activation in HepG-2 cell line. Furthermore, these compounds showed potent PIM-1 kinase inhibitory activity. Kinetic studies using Lineweaver–Burk double-reciprocal plot indicated that compounds **4c** and **4f** are both competitive and non-competitive inhibitors for PIM-1 kinase enzyme. In addition, in-silico physicochemical and molecular docking studies were consistent with the biological and kinetic studies.

**Keywords**: pyridine, anticancer and PIM-1 kinase.

# PHS 506: The First-in-Class COX-2 Targeted Protein Degrader Endowed with Antineoplastic Activity

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Targeted protein degradation (TPD) has manifested itself as a New Promising Therapeutic Paradigm in Drug Discovery. Among TDP tools and of particular interest to this work, PROteolysis Targeting Chimera (PROTAC) technology relies on a unique ability of degrading target disease-promoting proteins instead of inhibiting them, resulting in "chemical knockouts". This is accomplished by utilizing the ubiquitin-proteasome natural machinery. On the other hand, the link between inflammation and cancer development is widely understood. Besides, A growing body of research demonstrated that COX-2 is a validated target for cancer chemotherapy. Hence, we used this knowledge to design and synthesize a COX-2 targeted protein degrader for anticancer outcomes. Its identity has been elucidated by different spectroscopic techniques. Our degrader (CTP) was evaluated for cytotoxicity in breast and colorectal cancer cell lines (MCF7, MDA-MB-231, Caco-2 and HCT-116). It exhibited anticancer activity with single to two-digit nanomolar $IC_{50}$ values in comparison to two-digit micromolar $IC_{50}$s for celecoxib. CTP is currently being tested for its capability to induce degradation of COX-2 enzyme in cancer cell lines, that are highly expressing this enzyme, by Western blotting. Further confirmation for targeted degradation will be provided by measuring the expression levels of downstream proteins such as PGE2 and VEGF by ELISA. Moreover, the effect of the degrader on cell migratory potential will be assessed. As a conclusion, we aim that this work will introduce the notion of chemical degradation of inflammatory targets into the realm of PROTACs, to provide a distinct perspective into their anticancer activities rather than their traditional inhibition.

**Keywords:** Cancer, PROTAC, COX-2, Western blotting.

# PHS 507: Redefining the Scope of Application of 1,2,3-Triazole Glitazones in Metabolic Disorders: Simultaneous Modulation of COX-2, PPARγ and Carbonic Anhydrases

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Diabetes right now is perceived as a multifaceted disease implicating the interplay of metabolic, cardiovascular, immune and low-grade inflammatory components. Hence, it stands to reason that a multitarget-directed ligand (MTDL) strategy, would be beneficial to target different lines of defense of the disease such as PPARγ, COX-2 and carbonic anhydrase enzymes. This could be achieved by merging bioactive pharmacophores for these targets into two newly synthesized series namely; 1,2,3-triazole thiazolidinedione/rhodanine hybrids and some derived thiazolone-based molecules. This work is considered as an interesting extension for our previous work in this arena, however, this study is additionally exploring the role of inhibition of carbonic anhydrase enzymes in an anti-diabetic context. Biological evaluation of the target compounds revealed significant *in vitro* COX-2 inhibitory activities with submicromolar $IC_{50}$ values (0.05-0.4 μM) and reasonable selectivity indices COX-1/COX-2. Then, assessment of CA inhibitory activities against isoforms I, II and IV showed varying degrees of activity. Intriguingly, twelve compounds demonstrated potent inhibition against the tumor-associated isoform CA IX with *Ki* values in the range of 21.8-32.1 nM, compared to 25 nM for acetazolamide. *In vitro* glucose uptake assay, using rat hemi-diaphragm model, for sixteen compounds revealed that four compounds showed comparable or higher glucose uptake than pioglitazone without insulin and considerably higher uptake with insulin. Moreover, PPARγ functional reporter gene assay verified the partial agonistic activity of the latter compounds towards PPARγ with $EC_{50}$ values of 2.4-11 μM. *In vivo* anti-inflammatory and anti-diabetic activities in animal models, for representatives of the most active compounds, are now being evaluated. Besides, molecular docking simulation study was carried out to explore the possible binding modes/affinities behind the observed activities. Considering the aforementioned data, this series could provide a promising foundation for the development of multi-target anti-diabetic agents.

**Keywords:** Diabetes, multitarget-directed ligand, PPARγ, COX-2, carbonic anhydrase.

# PHS 508: New Tetrahydropyrimidine Derivatives as Potential Antitubercular Agents and TMPK Inhibitors

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Several new tetrahydropyrimdine derivatives were designed, synthesized and evaluated for their antimycobacterial activity. Thirteen compounds were tested for their antimycobacterial activity against *Mycobacterium tuberculosis* strain $H_{37}R_v$. The results revealed that **seven** of those compounds exhibited moderate to strong antimycobacterial activity (MIC ranging from 5.86 to 29.66 µM) compared to pyrazinamide (MIC 50.77 µM) and ethambutol (MIC 7.64 µM). Molecular Docking studies into Thymidine Monophosphate Kinase (TMPKmt) enzyme have been conducted using Molecular Operating Environment software (MOE 2019), where reasonable binding interactions have been identified and effective overall docking scores have been recorded.

**Keywords**: tetrahydropyrimdine, *Mycobacterium tuberculosis,* Thymidine Monophosphate Kinase, Molecular Operating Environment.

# Natural Products in Drug Discovery

# PHS 601: Effect of Ultraviolet-B Radiation and Dark Incubation on *Morus alba* L. Leaves Revealed via SWATH-Based Quantitative Proteomic Analysis

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Morus alba is a woody shrub of the family Moraceae and has a long history of use in traditional medicine. Ultraviolet-B (UV-B) radiation, as a kind of abiotic stress factor, affected the growth and secondary metabolism in M. alba. Previous studies indicated that the contents of several secondary metabolites such as moracin N and chalcomaricin were significantly increased under high level UV-B radiation and dark incubation in M. alba leaves. To reveal the response mechanism under UV-B radiation and dark incubation in M. alba leaves sequential window acquisition of all theoretical fragment-ion spectra (***SWATH***) mass spectrometry (MS) -based quantitative proteomic analysis was performed. Totally, 716 proteins were identified and quantified in the control, UVB (UV-B radiation for 15 min), and UVD (UV-B radiation for 15 min then dark incubation for 36 h.) groups. Among them, 123 proteins and 96 proteins were identified as differentially abundant proteins in UVB group and UVD groups, respectively. Proteins related to photosynthesis, amino acid biosynthesis, and tocopherol biosynthesis were significantly altered in UVB group, while proteins related to the biosynthesis of phenolic compounds were significantly altered in UVD group. In addition, the abundances of proteins involved in the ubiquitin-proteasome system (UPS) were significantly increased in both UVB and UVD groups, indicating that UPS combined with secondary mechanism participated in the resistance to UV-B radiation and dark incubation. The obtained results provide novel insight into the effects of high level UV-B radiation on M. alba leaves and on the strategies used for maximizing the chemical constituents and the medicinal value of the M. alba leaves.

**Keywords.** Ultraviolet-B, Proteomic SWATH, *Morus* leaves, Phenylpropanoids.

# PHS 602: Green Extraction of Terpene Lactones and Ginkgolic Acids from *Ginkgo biloba* Using Natural Deep Eutectic Solvents: Optimization Through Experimental Design and HPTLC-MS Analysis

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In this research, a green extraction approach was applied to enhance terpene lactone output while minimizing ginkgolic acid yield from *Ginkgo biloba* L. leaves. The objective of the conducted study is to quantify and compare the extractability of different mixtures of natural deep eutectic solvents (NADES) in comparison to conventional solvents. HPTLC-MS technique was established and validated for the simultaneous detection of terpene tri-lactones and ginkgolic acids in *Ginkgo biloba* samples. For bilobalide, ginkgolide A, ginkgolide B, ginkgolide C, ginkgolide K, ginkgolide J, and ginkgolic acid, the detection limits were 0.791, 0.850, 0.868, 0.785, 0.763, 0.871, and 0.622 µg/band, while the quantitation limits were 2.399, 2.576, 2.632, 2.380, 2.313 µg/band, respectively. In comparison to methanol, ethanol, and water, the extraction capability of 15 distinct deep eutectic solvents (DES) combinations were investigated using ultrasonic-aided extraction. The findings showed that DES 2 (Choline chloride, ascorbic acid) displayed the best overall ginkgolide extraction yields. On the other hand, in the case of ginkgolic acids, DES 2 exhibited significantly lower extraction quantities showing 4.7 and 5.5-fold decrease compared to methanol and ethanol, respectively. To achieve the optimum extraction conditions, Box Behnken design for optimization experiments were employed and indicated that the extraction yield of ginkgolides was substantially impacted by water % (C, $p<0.0001$; $C^2$, $p<0.0001$), and after that ultrasonication temperature (B, $p<0.0001$; $B^2$, $p<0.0001$), with ultrasonication temperature having a larger influence on the extraction yield of ginkgolic acids. An ultrasonication time of 36.63 minutes, a temperature of 55.77°C, and a water content of 33.66 %v/v were found to be the ideal circumstances for extraction.

**Keywords**: *Ginkgo biloba*, NADES, choline chloride, Ginkgolides, Ginkgolic acids, Box-Behnken design.

# PHS 603: Phytochemical Profile, Anthelmintic Activity, and Antimicrobial Activity of Two *Pinus* Species: Effect of Altitudinal Variation

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Active components from natural sources are the current focus in most pharmacological research to provide new therapeutic agents for clinical use. Essential oils from the *Pinus* species have been traditionally used in medicine. This study aimed to investigate the chemical profile of two *Pinus* species, *Pinus halepensis* L. and *Pinus pinea* Mill, from different altitudes in Libya and study the effect of environmental conditions on the biological activities of essential oils. Clevenger apparatus was used to prepare the essential oils by hydrodistillation. Chemical profiling of the obtained essential oils was done using GC/MS. Anthelmintic and antimicrobial activities were tested against the earthworm *Allolobophora caliginosa*, gram-positive bacteria, gram-negative bacteria, and fungi. Essential oils analyses resulted in the identification of 48 compounds. Monoterpene and sesquiterpene hydrocarbons are remarked as the major classes in all four studied essential oils especially in *P. pinea* from low altitude (Pp-2) (36.27 & 33.16%) respectively. However, *P. pinea* from the high altitude (Pp-1) is found to be rich in oxygenated monoterpenes (23.36%). Conversely *P. halepensis* (Ph-1& Ph-2) essential oils from both altitudes are rich in Oxygenated diterpenes (33.99 & 22.78%) respectively. All studied essential oils from the *Pinus* species exhibited a remarkable anthelmintic activity compared to the standard piperazine citrate drug. Though, *P. halepensis* essential oil from low altitude (Ph-1) was the most active. *Pinus halepensis* from both altitudes (Ph-1& Ph-2) showed broad-spectrum antimicrobial activity against all tested microorganisms; but also low altitude have the greatest antimicrobial activity; whereas *Pinus pinea* was only effective against *Escherichia coli*. From these findings, one can conclude that there are variations between all studied samples. The essential oil compositions are affected by environmental factors showing that the low altitude has more impact on the phytochemical constituent, which consequently affects the anthelmintic and antimicrobial activity.

**Keywords**: essential oils; environmental conditions; GC/MS; *Pinus halepensis* L.; *Pinus pinea* Mill.

# PHS 604: Phytochemical Screening and Anti-*Heliobacter pylori* Activity of Volatile Oil Isolated from the Leaves of *Salvia officinalis*

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*Salvia officinalis* is a medicinal plant well known of its astonishing reputation as an antimicrobial agent. In this study we aimed to screen the active constituents present in the aerial parts, to isolate the essential oil and to investigate its activity against a reference strain of *Heliobacter pyroli.* Phytochemical chemical tests were used among which were, Molich's, dragendorff's, Modified Bontrager's and Salkowski and Lieberman's for the screening of carbohydrates, alkaloids, anthraquinones and steroids respectively. The screening tests indicated the presence of volatile oil, carbohydrates, sterols, tannins, and flavonoids but the anthraquinones and alkaloids were absent. The volatile oil of the dried aerial parts was prepared by hydro distillation with a yield of 1.9% oil. The *in vitro* antibacterial activity of the oil was determined against *Helicobacter pylori* using microtiter XTT assay, as well as measurement of minimum inhibitory concentration. The results showed inhibitory activity against the test bacteria with MIC 15.63 µg/mL for the reference isolates compared to the standard antibiotic clarithromycin MIC 1.95 µg/mL.

**Keywords:** *Salvia officinalis*, Essential oil, Phytochemical screening, *H. Pyroli*, antibacterial, clarithromycin.

# PHS 605: Chemical Characterization Coupled to Chemometric Analysis for the Identification of *Red Sage (Lantana camara L.) Cultivars* and Determination of Anti-COVID-19 Biomarkers

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*Lantana camara* L. (Verbenaceae) is a widely spread plant that was traditionally used in treating several ailments including rheumatism and leprosy. Despite its historical role in relieving respiratory diseases, limited studies mentioned its probable inhibition to respiratory viruses especially after the striking spread of SARS-COV2 infections and flare up of its mortality rates. This study aimed to investigate the inhibitory activity of different plant cultivars to SARS-COV2 and clarify their mechanisms of action from the metabolomics viewpoint in addition to biomarkers determination related to such activity using UPLC/MS/MS coupled to *in-vitro* studies and chemometric analysis. Chemical profiling of different cultivars *via* UPLC-MS/MS was accomplished for metabolites identification. Principle component analysis (PCA) and orthogonal projection to latent structures (OPLS) models were built using SIMCA® followed by cytotoxicity and SARS-COV2 inhibitory activity testing. Detected biomarkers were docked into RNA-dependent RNA polymerase - a potential target pocket - to investigate their interaction patterns using Schrodinger® suite. UPLC/MS analysis of different cultivars yielded 47 metabolites, most of them were triterpenoids and flavonoids. PCA plots revealed that inter-cultivar factor has no pronounced effect on the chemical profiles of extracts except for Drap d'or cultivar flowers and leaves extract as well as for Chelsea gem cultivar leaves extract owing to their distinctive chemical components. All extracts showed 50% cytotoxicity at concentrations more than 30 µg/ml indicating their safety on these cells. Leaves and flowers extracts of Chelsea gem cultivar, flowers extracts of spreading sunset and Drap d'or cultivars were the most promising inhibitors to viral plaques exhibiting $IC_{50}$ values of 3.18, 3.67, 4.18 and 5.01 µg/ml, respectively. OPLS analysis discriminated them as cluster A extracts and related their promising SARS-COV2 inhibitory activities to the presence of twelve biomarkers which were dominantly or exclusively present in these extracts. Molecular docking of the active biomarkers against RdRp revealed that isoverbascoside exhibited higher docking score of -11.378 Kcal/mol when compared to remdesivir (-5.75 Kcal/mol), thus can serve as a promising anti-COVID candidate.

**Keywords:** *Lantana camara* L., Chemometrics, COVID-19, UPLC/MS.

# PHS 606: Anticoagulant Activity of Some Medicinal Plants Through Targeting Factor Xa Reveals Licorice Flavonoids as Potential Leads

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Traditional natural products enclose a wealth of anticoagulants that can be prospected for new selective factor Xa (FXa) inhibitors. Bioactivity guided evaluation of three well known plants; *Glycyrrhiza glabra (*licorice), *Olea europaea* (olive) and *Trifolium alexandrinum* (berseem clover) was conducted using *in-vitro* inhibitory assay of coagulation factor X. The investigated plants showed factor X inhibitory effects with $IC_{50}$ values of 0.363, 0.729, and 0.866 mg/mL, for licorice roots, trifolium aerial parts, and olive leaves, respectively. Evaluation of licorice and trifolium solvent fractions revealed that licorice ethyl acetate fraction and trifolium butanol fraction are the most active ones with % inhibition of 97.93 ± 0.019% and 73 ± 0.042%, respectively. Ten flavonoids were isolated and identified from licorice roots using bioactivity guided approach, of which the four compounds, liquiritin, 3,3',4,4'-tetrahydroxy-2 methoxychalcone, naringenin 5-*O*-glucoside and 7-hydroxy-4'-methoxyisoflavone pointed out as promising FXa inhibitors. These compounds showed $IC_{50}$ values of 5.15, 10.43, 12.5 and 17.71 µM, sequentially. The identified compounds could be provided as promising candidates for future optimization and design of potent, selective nature based FXa inhibitors.

**Keywords:** Anticoagulants, Factor Xa inhibitors, licorice, trifolium, flavonoids.

# PHS 607: Immunomodulatory Potentially Active Markers of the Herbs and Roots of Echinacea Species; Metabolomic Discrimination

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Echinacea species roots and aerial parts are considered among the most popular plants used worldwide for management of common cold and other upper respiratory infections. This study aims at revealing the immunomodulatory biomarkers amid the diverse metabolites in the roots and herbs of the most widely used Echinacea species; *E. purpurea, E. angustifolia* and *E. pallida*. UPLC-QqQ-MS-based metabolomic approach was implemented for comprehensive investigation of the relative amount of chemical constituents resulting in the identification of 56 metabolites. PCA and HCA revealed that *E. angustifolia* root was separately segregated from all other samples, with cynarin and 2-undecene-8,10-diynoic acid isobutylamide being the main secondary metabolites contributing to such a clustering pattern. Further, determination of immunomodulatory discriminatory metabolites among the tested roots and herbs of the three Echinacea species was attempted through construction of an OPLS-DA model which revealed that, with exception of *E. pallida* in which both roots and herbs were clustered together reflecting the similarity in their immunomodulatory activity, the roots of Echinacea species possessed similar immunomodulatory response in comparison to the herbs which were relatively less efficient as immunomodulators. Correlation analysis indicated that 8,11-dihydroxy-2,4,9-dodecatrienoic acid isobutylamide, dicaffeoyl quinic acid, echinacoside and 8-hydroxy-pentadeca-(9E,13Z)-dien-11-yn-2-one were positively correlated to upregulation of the RELA pathway while 2-undecene-8,10-diynoic acid isobutylamide, dodeca-2,4,8,10- tetraenoic acid isobutylamide and dicaffeoyl quinic acid, were positively correlated to the upregulation of NFKB1. The results also indicated that the immunomodulatory effect of polyenes is correlated to the upregulation of IL6 production and downregulation of RELA and NFKB1 pathways. Meanwhile, alkylamides immunomodulatory effect is correlated to upregulation of IL6, NFKB1 and NO production.

**Keywords**: Echinacea, UPLC/QqQ/MS, Immunomodulation, Inflammation, Metabolomics.

# PHS 608: An Integrated Approach for Exploring Anticancer Molecular Mechanisms of Egyptian Propolis Using Network Pharmacology, Molecular Docking and In Vitro Analyses

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Cancer is one of the predominant causes of death worldwide. The new trend nowadays is to exploit natural products with the hope of developing new anticancer agents with fewer side effects. Propolis is one of these natural products which showed effectiveness in cancer treatment. The aim of this study is to understand the multi-level mechanism of action of propolis constituents in cancer treatment using an integrated approach of network pharmacology-based analysis, molecular docking and in vitro cytotoxicity testing. An inhouse database of one hundred chemical constituents from Egyptian propolis was compiled and assessed for its ADME properties using the QikProp module in the Schrodinger software. STITCH, UniProt, STRING, KEGG and DAVID databases were used for construction of constituent-target gene, gene-pathway, and constituent-target gene-pathway networks with the aid of Cytoscape 3.8.2. The network pharmacology-based analysis showed that the hit propolis constituents related to cancer targets were genistein, luteolin, benzoic acid, quercetin and vanillic acid, whereas the main cancer associated targets were CYP1A1, CYP19A1, ESR1, NOS3, CASP3 and AKT1. Twenty-four cancer-related pathways were recognized where the most enriched ones were pathways in cancer and estrogen signaling pathway. The most enriched biological processes involved in the mechanism of action of propolis constituents in cancer treatment were negative regulation of the apoptotic process and the metabolic process and negative regulation of cellular glucuronidation. Molecular docking analysis of the top hit compounds against the most enriched target proteins in the constructed networks was carried out using the Maestro interface of the Schrodinger software. Among hit compounds, quercetin and genistein exhibited the most stabilized interaction. Finally, confirmation of the potential anticancer activity of propolis was assured by in vitro cytotoxicity testing of propolis extract on human prostate cancer (DU-145), breast adenocarcinoma (MCF-7) and colorectal adenocarcinoma (Caco-2) cell lines. This study presents deeper insights about propolis molecular mechanisms of action in cancer for the first time using an integrated approach of network pharmacology, molecular docking and in vitro testing. Further extensive in vivo and clinical studies are required to confirm the anti-cancer potential of the concluded top hit natural compounds.

**Keywords**: Propolis; network pharmacology; cancer; molecular docking, quercetin.

# PHS 609: Fighting COVID-19 via NTPase/Helicase Enzyme Targeting: An In Silico Study

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Since the end of 2019, COVID-19 has been threatening the lives of millions and the efficacy of global health care systems, which paved the way for it to be the primary concern of global scientific research. Although many COVID-19 vaccines have been produced, the search for medications for it is well under way through targeting both host and viral proteins that participate in the viral pathogenesis. The NTPase/Helicase enzyme plays an important role in viral genome replication depending on the energy derived from NTP hydrolysis. In this virtual screening study, the NTPase binding site of SARs-CoV 2 non-structural protein 13 (PDB code:5RL9) was targeted using a database of 1012 natural compounds in a molecular docking study, followed by the prediction of the physico-chemical, pharmacokinetics, and toxicological properties for the best four hits using the SwissADME and ADEMTlab servers. For validation of the system, three reported ATPase inhibitors with IC50 of 6, 57, and 115 µM, were docked using the same protocol, which could predict their activity well since the resulted scores were 6.82, 6.2, and 6.01 kcal/mol, respectively. According to the affinity score, the top four compounds were L-arabino-Hexitol, 1,5-dideoxy-6-C-[2-(5-oxazolylmethyl)-4-oxazolyl]-, 6-heneicosanoate, (6R) (-8.29 kcal/mol), Pentagalloylglucose (-8.2 kcal/mol), Epigallocatechin gallate (-7.42 kcal/mol), and Tribuloside (-7.31 kcal/mol). Interestingly, the top four compounds showed remarkable affinity scores compared to the three standard compounds. These findings indicate that natural products could be a valuable source for active compounds against COVID-19, but more in-vitro and in-vivo studies are needed.

**Keywords**: COVID-19, Molecular Docking, COVID-19 NSP13, ADMET.

# PHS 610: Screening of Pancreatic Lipase Inhibitory Activity of Some Selected Medicinal Plants

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Obesity is a global health problem. It is also known to be a risk factor for the development of metabolic disorders: type 2 diabetes, systemic hypertension, cardiovascular disease, dyslipidemia, and atherosclerosis. The rich potential of nature to combat obesity has not been fully explored yet. Several phytochemicals have been investigated for their potential as lipid lowering agents. In this study, 7 plants were screened to test their anti-obesity activity using para nitrophenyl palmitate as a substrate in *in-vitro* spectrophotometric inhibitory assay of porcine pancreatic lipase (PPL; triacylglycerol lipase, Type II). Inhibition of the pancreatic lipase was chosen as the criteria for therapeutic efficacy since such inhibition would serve two functions. It would provide an adjunctive therapy to the pharmacological agents and would minimize systemic adverse reactions by acting locally in the GI tract. The seven Egyptian plants are: *Cymbopogon citratus, Alhagi maurorum, Hibiscus sabdariffa* L., *Ziziphus spina christi*, *Olea europaea* L., *Lawsonia inermis* and *Thymelaea hirsuta*. The selection of these plants was based on their previous ethnopharmacological uses in treatment of diseases such as: obesity, hyperlipidemia and diabetes, as well as the limited literature on lipase inhibition activities of these plants. It was observed that the alcoholic extract of *Ziziphus spina christi* showed the most significant lipase inhibitory activity with a 93 % inhibition, followed by *Thymelaea hirsuta* extract (70 % inhibition). Further isolation, identification and characterization of phytoactive compounds responsible for anti-lipase action is required to evaluate the full therapeutic potentials of these plants.

**Keywords**: Anti-obesity; Pancreatic lipase; Plant extracts; Screening; Lipase inhibitor.

# PHS 611: Biologically Active Compounds from the Red Sea Sponge *Negombata corticata*

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Members of the genus *Negombata* (formerly *Latrunculia*) are characterized by elaboration of diverse classes of secondary metabolites such as macrolides, the alkaloids discorhabdins, terpenes and terpenoidal peroxides, peptides and many others. Latrunculins possess different biological properties including anticancer, antiviral, antibiotic, anti-angiogenic, anti-migratory, and microfilament-disrupting activities. As a part of our development continuous interest to identify biologically active drug leads from the Red Sea organisms, the Red Sea sponge *Negombata corticata* was studied. Two new analogs of latrunculin A with modified ring system, 6,7(Z)-latrunculin A (**1**), 6,7(Z)-18-*epi*-latrunculin A (**2**) along with latrunculin A (**3**). Structural determinations of the compounds were accomplished by analyses of their HRESIMS and 1D and 2D NMR spectral data. The compounds displayed significant activities against HCC1806, HCC1937and MBA-MB-231 cell lines. Furthermore, the compounds displayed potent actin-disrupting activities in A10 cells. In conclusion, latruculins could serve as scaffolds for the of novel antitumor drug candidates.

**Keywords**: Marine sponge, *Negombata corticata*, macrolides, actin-disrupting activity.

# PHS 612: Cytotoxic Diketopiperazine Alkaloids from the Marine-Derived Fungus *Penicillium* species

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Marine-derived fungi represent a vigorous source of alkaloids with the diketopiperazine backbone. 2,5-Diketopiperazines represent the smallest cyclic dipeptides that contain a six-membered ring with two amide linkages where the two nitrogen atoms and the two carbonyls are at opposite positions. 2,5-Diketopiperazines are represented in structurally diverse groups of secondary metabolites with significant bioactivities such as antimicrobial, antitumor, analgesic, and many other biomedical indications. Significant antitumor diketopiperazines include the anti-microtubule phenylahistins, the cell cycle inhibitors tryprostatins, the chaetocins, which inhibit the lysine-specific histone methyltransferase and the ardeemins with heir reversal effects on multiple drug resistant (MDR) phenotype. As a part of our continuous interest to identify biologically active drug leads from the marine-derived fungi, the Red Sea derived-fungus *Penicillium* species was investigated. Two new diketopiperazine alkaloids, penicillipizines A (**1**) and B (**2**), along with several reported diketopiperazines alkaloids (**3-6**) are isolated and characterized. Structural determinations of the compounds were accomplished by interpretation of their NMR and MS spectral. The compounds displayed significant activities against HCT 116 and HeLa cell lines.

**Keywords**: Marine fungus, *Penicillium* species, diketopiperazines, growth inhibitory activity.

# PHS 613: Phytochemical Profiling and Effect of Raw and Dried Ginger Extracts on Inflammations and Insulin Resistance in Type 2 Diabetes Compared to Metformin

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Diabetes mellitus (DM) is the ninth major cause of death worldwide, making it a major challenge to health-care systems. Diabetes is a chronic inflammatory condition in which there is an augmented level of inflammatory mediators such as interleukin that leads to insulin resistance and disease progression. Nuclear factor kappa-B (NF-κB) is a key mediator involved in the inflammatory process through multiple mechanisms, including contribution in reactive oxygen species (ROS) production and inducing nitric oxide synthase (iNOS). Even though various medications have been created to treat type-2 DM, interest in using natural remedies to treat type-2 DM has been increasing. This study aimed at comparing the effect of metformin, one of first-line treatment options, to the effect of alcoholic extract of fresh ginger prepared by cold maceration in addition to extract of oven dried ginger. Our results showed that raw ginger extract improved the glucose homeostasis and the lipid profile, comparable to those of metformin. These findings were supported by a decrease in the expression of the genes for NF-κB, iNOS and COX-2 as inflammatory markers, in addition to decrease gene expression of Protein tyrosine phosphatase-1B (PTP1B) and mir-29a expression as markers of insulin signaling. Constituents of ginger extract responsible for activity were investigated using LC-Tandem MS and chemometric multivariate data analysis, which revealed the wholistic action of ginger owing to different components as gingerols, shogaols and paradols.

**Keywords:** Diabetes, Ginger, Metformin, inflammation, LC-MS/MS, gene expression.

# PHS 614: Exploring the Anti-*Helicobacter pylori* Urease and Human $H^+/K^+$-ATPase Activity of *Jacaranda mimosifolia* Using Metabolomics and Molecular Docking

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*Helicobacter pylori* urease and human $H^+/K^+$-ATPase are among the main causes of peptic ulcers. The current study deals with the phytochemical investigation of various organs (*leaf*, fruit, seed, and bark) of *Jacaranda mimosifolia D.* Don. UPLC-MS/MS analysis allowed identification of 53 compounds where flavonoids, quinoids, and triterpenoids represented the major identified metabolites. Multivariate statistical analysis (principle component analysis (PCA), hierarchical cluster analysis (HCA)-heat map, orthogonal partial least squares-discriminate analysis (OPLS-DA), orthogonal projection to latent structures (OPLS), and coefficient plots of the OPLS model) was implemented to investigate in-between and within-class discrimination of the different organs of *Jacaranda mimosifolia D.* Don. The obtained extracts were tested for their inhibitory activities against Helicobacter pylori urease and human $H^+/K^+$-ATPase enzymes. Fruit extracts showed the highest biological activity against the urease enzyme, whereas leaf extracts exhibited significant inhibition against the $H^+/K^+$-ATPase enzyme. OPLS-DA model coefficients revealed isoquercitrin and rutin as the main biomarkers for the detected anti-urease and $H^+/K^+$-ATPase activities, respectively. Molecular docking simulations were utilized to gain more insights into the interaction modalities of the identified metabolites with the active sites of urease and $H^+/K^+$-ATPase enzymes.

**Keywords:** *Jacaranda mimosifolia;* Anti-ulcer; Chemometrics*;* Molecular docking; UPLC/MS/MS; Urease and $H^+/K^+$-ATPase inhibitory activity.

# PHS 615: *Callisia fragrans;* A Promising Anti-inflammatory Herb

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The ethanolic extract of *Callisia fragrans* aerial parts showed a significant strong *in vivo* anti-inflammatory and *in vitro* antioxidant activities with a high *in vivo* gastrointestinal safety profile and a very low *in vitro* cytotoxicity on peripheral blood mononuclear cells (PBMCs) with an $IC_{50}$ > 1000 µg/ml. The alcoholic extract of *C. fragrans* has been analysed by HPLC coupled to multiple-stage Linear Ion-Trap and Orbitrap High-Resolution mass spectrometry in negative electrospray ionisation mode (LC-ESI/LTQOrbitrap/MS/MSn). By this approach, it was possible to putatively identify 13 compounds, mainly organic acids, flavonoids, one steroid and one hydroxy-coumarin. Luteolin 6-C-glucopyranosyl-7-O-glucopyranoside, luteolin-8-C-glucopyranosyl-7-O-rhamnopyranoside, luteolin-6-C-glucoside and isoorientin 7-O-[6''-feruloyl]-glucoside were detected for the first time in *C. fragrans* and family Commelinaceae.

**Keywords**: *Callisia fragrans*, anti-inflammatory, *in vivo*, LC-ESI/LTQOrbitrap/MS/MSn.

# PHS 616: HPTLC-Mass Spectrometry-Multivariate Image Analysis for Folate Content During Different Stages of Germination in Legumes

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Folate or vitamin B9 is not synthesized in humans therefore the major sources are legumes and green leafy vegetables. Folate deficiency is a global problem may result from poor dietary intake. Inadequate intake of folate during pregnancy increases the risks of abortion, low birth weight, In addition, cardiovascular diseases, and a range of cancers. Food processing can cause considerable losses of folate. the aim of our study was very challenging for designing an appropriate method for folate determination in plant sprouting due to the instabilities, different forms and low concentrations of folate. The five folate species: 5- methyl tetrahydrofolate, tetrahydrofolate, pteroyl glutamate, 5-formyl tetrahydrofolate and 10-formyl tetrahydrofolate were quantitatively determined in legumes seeds and sprouts by a newly developed and validated high performance thin layer chromatography method. High resolution plate imaging hyphenated to mass spectrometry was exploited for fingerprint analysis of tested samples. Results indicated that germination of all seeds resulted in a 2.5–4 fold increase in the content of total folates as well as the individual vitamers. The total amount of folate reached a maximum on the fifth day in the case of black-eyed peas (861 µg/100 g Fresh Weight), white beans (755 µg/100 g FW) and brown lentils (681 µg/100 g FW). 5- methyl tetrahydrofol was found to be the most dominating folate species reaching its maximum content in day 5 sprouts of black-eyed peas (490 µg/100 g FW).

**Keywords**: folate-sprout-black peas-legumes.

# PHS 617: The Synergistic Chemotherapeutic Effect Between Galloylquinic Acid Compounds and Doxorubicin in a Solid Ehrlich Carcinoma Model Through the Modulation of the Notch Signaling Pathway

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Aims: This study aims to investigate the potential synergistic effect of the combined treatment of galloylquinic acid compounds from Copaifera lucens with doxorubicin via the modulation of the Notch pathway in solid Ehrlich carcinoma-bearing mice model. Methods: The solid tumor model was induced by subcutaneous inoculation of Ehrlich carcinoma cells in the right hind limb of mice, after serial syngeneic cell passages in the peritoneal cavity. Sixty mice were allocated into five groups including treated groups with galloylquinic acid compounds, doxorubicin, and their combination. Normal and tumor control groups were also assigned. Tissue homogenates were collected to measure the levels of the Notch-1, Hes-1, Jagged-1, TNF-α, IL-6 and VEGF, as well as SOD, MDA, and GSH. Histopathological and immunohistochemical examinations of tumor or control tissues were also performed for the levels of NF-κB p65, cyclin D1 and caspase 3 activity. Key findings: Our results showed that the combined treatment of galloylquinic acid compounds with doxorubicin significantly decreased the levels of the Notch-1, Hes-1, Jagged-1, TNF-α, IL-6, VEGF, NF-κB p65, and cyclin D1 in tumor tissues. Moreover, the compounds induced cancer cell death as evidence by increasing the caspase 3 activity, and they possessed potent inhibitory effects on oxidative stress. Conclusion: Galloylquinic acid compounds exhibited promising antineoplastic effects and promoted the chemosensitivity of doxorubicin, mainly by modulating the Notch signaling pathway and its downstream effectors. These compounds may be considered in solid tumors treatment for improving the efficacy and reducing the side effects of chemotherapeutic agents.

**Keywords:** Solid Ehrlich carcinoma; Notch-1; Jagged-1; NF-κB p65; Caspase 3; Copaifera lucens; Galloylquinic acid.

# PHS 618: Phytochemical Investigation of Selected Plants Grown in Egypt and Libya with Potential Antiviral Activity

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The flora of Egypt and Libya are among the richest flora in north Africa. The current study focuses on the chemical profiling of *Artemisia herba-alba* and *Thymus capitatus* collected from Egypt and Libya using liquid chromatography/mass spectrometry (LC/MS) and gas chromatography/mass spectrometry (GC/MS) analyses. The selected plants are rich in diverse secondary metabolites as essential oils, flavonoids, lactones and phenolics. They are extensively used in North Africa traditional medicine mainly for their antihyperglycemic, anti-inflammatory and potent antimicrobial properties in gastrointestinal and respiratory tract illnesses. 46 and 50 compounds were detected in the Egyptian and Libyan *Thymus capitatus* ethanolic extracts while 56 and 39 compounds were identified in the Egyptian and Libyan *Artemisia herba-alba ethanolic* extracts, respectively. The essential oils analysis revealed the presence of 15, 17, 17 and 8 compounds in Egyptian and Libyan *Artemisia herba-alba* and *Thymus capitatus,* respectively. Evaluation of the anti HSV1 activities of the studied extracts showed that the Egyptian *Thymus capitatus* ethanolic extracts was the most potent extract with more than 200-fold reduction in the viral PFU. The obtained results supported the wide folk medicine use of the studied plants as potent antimicrobial agents in north Africa and encouraged further investigation Egyptian *Thymus capitatus* metabolites as promising anti HSV1 agents.

**Key words:** *Artemisia herba-alba, Thymus capitatus,* LC/MS, GC/MS, Herpes simplex virus.

# PHS 619: The Use of Regular and Greener HPTLC Approaches for Determination of Colchicine in Pharmaceutical Formulations, and *Colchicum autumnale* Different Extracts

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Colchicine is an alkaloidal compound that is commonly obtained from *Colchicum autumnale* Pleniflorum (L.) (family: Colchicaceae). Colchicine is used in the treatment of gout. It has also been found to show anti-inflammatory, antimitotic, and anticancer activity and is used in the treatment of Mediterranean fever. Recently, colchicine has also been investigated in the treatment of SARS-COVID-19. In the literature, there is a scarcity of greener analytical approaches for colchicine analysis. As a result, efforts were made in this study to develop and validate a greener reversed-phase high-performance thin-layer chromatography (HPTLC) technique for colchicine analysis in traditional extracts and ultrasonication-based extracts of commercial Unani formulations, commercial allopathic formulations, and *Colchicum autumnale* Pleniflorum (L.) obtained from Egypt and India. This new technique was compared to the regular normal-phase HPTLC method. The greenness profile of both methods was estimated using the Analytical GREENness (AGREE) approach. In the 100–600 and 25–1200 ng/band ranges, regular and greener HPTLC procedures were linear for colchicine analysis, respectively. For colchicine analysis, the greener HPTLC method was more sensitive, accurate, precise, and robust than the regular HPTLC method. For colchicine analysis in traditional extracts and ultrasonication-based extracts of commercial Unani formulations, commercial allopathic formulations, and *C. autumnale* obtained from Egypt and India, the greener HPTLC method was superior in terms of colchicine content compared to the regular HPTLC method. In addition, the ultrasonication-based extracts procedure was superior to the traditional extracts procedure for both methods. The AGREE scores for regular and greener reversed-phase HPTLC methods were found to be 0.46 and 0.75, respectively. The AGREE results showed an excellent greener profile of the greener HPTLC method over the regular HPTLC technique. Based on several validation criteria and pharmaceutical assay findings, the greener HPTLC method is regarded as superior to the regular HPTLC approach.

**Keywords:** Colchicine; greener HPTLC; ultrasonication-based extracts; Comparative Evaluation.

# PHS 620: Pseurotin A as a Novel Dual Inhibitor of PCSK9 Secretion and Interaction with LDL Receptor for the Control of Breast Cancer Progression and Recurrence

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Hypercholesterolemia has been documented to drive hormone-dependent breast cancer (BC) progression and resistance to hormonal therapy. Proprotein convertase subtilisin/kexin type-9 (PCSK9) regulates cholesterol metabolism through binding to LDL receptor (LDLR) and targeting the receptor for lysosomal degradation. Inhibition of PCSK9 is an established strategy to treat hypercholesterolemia. Pseurotin A (PS) is a unique spiro-heterocyclic γ-lactam alkaloid isolated from the fungus *Aspergillus fumigatus*. Preliminary studies indicated that PS lowered PCSK9 secretion in cultured HepG2 hepatocellular carcinoma cells, with an $IC_{50}$ value of 1.20 μM. Docking studies suggested the ability of PS to bind at the PCSK9 narrow pocket that accommodates LDLR. Surface plasmon resonance (SPR) showed PS ability to inhibit the PCSK9-LDLR interaction at a concentration range of 10-150 μM. PS showed dose-dependent reduction of PCSK9, along with increased LDLR levels in hormone-dependent BT-474 and T47D BC cells. In vivo, daily oral 10 mg/kg of PS suppressed the progression of the hormone-dependent BT-474 BC cells in orthotopic nude mouse xenograft model. Immunohistochemistry investigation of BT-474 breast tumor tissue proved the PS ability to reduce PCSK9 expression. PS also effectively suppressed BT-474 BC cells locoregional recurrence after primary tumor surgical excision. Western blot analysis showed decreased PCSK9 expression in liver tissues of PS-treated mice compared to vehicle-treated control. PS treatment significantly reduced PCSK9 expression and normalized LDLR levels in collected primary and recurrent breast tumors at the study end. Inhibition of tumor recurrence was associated with significant reduction in plasma level of the human BC recurrence marker CA 15-3 in treated mice. Histopathological examination of various PS-treated mice organs indicated lack of metastatic tumor cells and any pathological changes. PS is a novel first-in-class PCSK9-targeting lead appropriate for the use to control hormone-dependent BC progression and recurrence.

**Keywords:** Breast cancer; Hypercholesterolemia; PCSK9, LDLR; Pseurotin A; Recurrence.

# PHS 621: UPLC-MS/MS Metabolomics Comparative Study to Unravel Intraspecies Variability and Anticancer Biomarkers of Various Pomegranate Fruit Cultivars (*Punica granatum* L.) and Their Waste By-Products

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**BACKGROUND**: The peels and pulp of pomegranate fruits are typically discarded and regarded as industrial waste despite the fact that the various parts of the fruit are thought to contain a potent blend of bioactive components. The peel, pulp, seed, and juice of various pomegranate fruit cultivars were analysed using ultra-performance liquid chromatography coupled with triple quadrupole mass spectrometry (UPLC-QqQ-MS) to determine any potential differences between the fruits and their waste products as potential sources of functional constituents. **RESULTS**: Multivariate anlaysis including orthogonal projection to latent structure-discriminant analysis (OPLS-DA) coefficient-plot showed enrichment of phenolic compounds such as punicalagin and ellagic acid derivatives in pulp samples while seeds class was enriched in phlorizin, catechin and quercetin, juice class showed abundance of naringenin and pelargonidin-3-pentoside while peels were enriched in anthocyanins and flavonoids including cyanidin diglycoside, quercetin and luteolin glycosides. Although the juice samples of almost all tested cultivars showed remarkable cytotoxic activity, the pulp samples, particularly the Manfalouti cultivar, exhibited the most potent [half maximal inhibitory concentration (IC50) = 2.367 ± 0.14 µg/mL in MCF-7, IC50 = 3.854 ± 0.23 µg/mL in Hep-G2 cell lines]. OPLS models were constructed for determination of cytotoxicity-associated metabolites among where the coefficients plots revealed tannins; granatin A, ellagic acid derivatives, punicalagin α and β, in addition to anthocyanins and phenolic compounds; cyanidin diglycoside, quercetin, phlorizin, 3-O caffeoylquinic acid, naringenin and liquiritin were more pertinent with cytotoxicity of the different parts of pomegranate fruit. **CONCLUSION**: The study outcomes allow for the full usage of the resources of pomegranate fruit including its industrial waste as sources of bioactive compounds.

**Keywords:** pomegranate fruit parts; cultivars; UPLC-QqQ-MS; cytotoxicity; industrial waste.

# PHS 622: Comparative Metabolomics Examination of Bioactive Metabolites of the Leaves of Distinctive Trigonella Species: Relationship Survey of α-Amylase and α-Glycosidase Inhibitory Impacts

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Trigonella plants are semiarid crops grown all over the planet where their seeds and leaves are commonly utilized in cosmetic, medical and therapeutic purposes. Despite substantial research on the seeds, comprehensive study of *Trigonella* leaves extracts has not been documented. In this work, chemical profiling of *T. foenum-graecum, T. maritima, T.* hamosa *and T. stellata* leaves extracts using UHPLC-QqQ-MS, where the relationship between the bioactive elements of the leaves and their in-vitro α-amylase and α-glycosidase inhibitory potential was investigated through employment of integrated metabolomics and chemometric analyses. 50 compounds were identified with saponins, flavonoids and pterocarpans being the most abundant classes in all extracts while amino acids accumulated exclusively in *T. foenum-graecum*. Orthogonal projection to latent structure discriminant analysis models coefficients plots revealed hamoside B, sarsaponin, and trigocoumarin were correlated positively to *T. hamosa* leaves while, quercetin, quercetin hexoside, and isoschaftoside, were correlated to *T. stellata*. Oxovaleric acid, trigraecum, and trigoneoside were correlated positively to *T. maritima* class. Further, the amino acids hyroxyisoleucine and ketoleucine, and the alkaloid trigonelline correlated strongly to *T. foenum-graecum*. The recognition of inhibitory α-amylase and α-glycosidase discriminatory metabolites was investigated through OPLS discriminatory model construction along with correlation coefficients analysis which depicted that 4-hydroxyisoleucine, trigonelline and hamoside B were the main constituents positively correlated to α-amylase inhibitory acivity while quecetin, quercetin hexoside and isoschaftoside possessed the highest positive correlation to α-glycosidase inhibitory effect. This research lays the groundwork for future research into the antidiabetic potential of the leaves of different *Trigonella* species which were revealed to be valuable sources of bioactive chemical compounds.

**Keywords:** *Trigonella* leaves, antidiabetic, chemometrics, metabolomics, correlation analysis.

# PHS 623: Molecular Authentication of Medicinal Plants from Family *Moraceae* Using RAPD, ISSR, SCAR and DNA Barcodes

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Morus species are well known for their pharmacological activities, such as antiviral, antimicrobial, anticancer, antioxidant, anti-inflammatory, antihyperlipidemic, and anti-diabetic. To ensure the medicinal and nutritional value, precise identification is crucial among Morus species. In the current study, the diversity of the two morphologically and chemically related *Morus alba* L. and *Morus nigra* L. was assessed. Molecular techniques as random amplified polymorphic DNA (RAPD), Inter simple sequence repeat (ISSR), and DNA barcoding regions, including three plastid loci (mat K, rbcL, and psbA-trnH) and two nuclear spacers (ITS and ITS2) were implemented. DNA barcoding failed to differentiate between the studied species. Out of fifty-five screened ISSR primers, seven were able to produce reproducible and clear polymorphic profiles with variable number of amplified fragments of variable sizes. Twenty-seven RAPD primers were evaluated, 121 fragment were produced of which 119 were polymorphic accounting for 98.3% polymorphism. The number of amplified bands varied from 4 to 10 ranging in size from 100 to 700 bp. Sequence characterized amplified region (SCAR) marker was developed based on reproducible banding pattern obtained by RAPD primer OPG-03. The polymorphic band was sequenced and specific primer was designed to develop a SCAR marker approximately 558 bp exclusively for *M. nigra*. The SCAR marker showed 100% success in differentiating authentic *M. nigra* and *M. alba*. The proposed protocol was successfully implemented on fifty commercial *M. nigra* samples collected from different Egyptian markets.

**Keywords**: *Morus* species, DNA barcoding, RAPD, ISSR, and SCAR.

# PHS 624*: Withania somnifera*: A Review of its Chemistry and Biological Activities

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*Withania somnifera* Dunal, also known as 'Ashwagandha or Indian Ginseng' is a wonder herb that belongs to family Solanaceae. It is a well-known genus of perennial herbs or shrubs with flowers, especially in Indian Ayurvedic medicine, occurring in North Africa, India, Israel, and Europe. Great interests in *Withania somnifera* led to the identification, characterization, and isolation of bioactive compounds for their biological activities. Steroidal lactones, withanolides, alkaloids, tannins, flavonoids and flavanol glycosides have been isolated from leaves, roots, stems and fruits of *Withania*. It also possesses different activities including anti-microbial, anti-inflammatory, antistress, anti-hepatotoxic, nootropic, anti-convulsant, antioxidant, anti-carcinogenic, antigenotoxic, immunomodulatory, hematopoietic, cardioprotective and anti-Parkinson's activities. Present review summarizes the phytochemistry and pharmacological advances of *Withania* reported in literature.

**Keywords:** Steroidal lactones, Ayruvedic medicine, Ashwagandha, Withanolides, Anticancer.

# PHS 625: Digitally Optimized HPTLC Imaging-MS/UV Multivariable Approach for Precise Prediction of Antihyperglycemic Markers from Bee Propolis in Combination with Palynological Analysis

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An integrated method for standardization of propolis using chromatographic, spectroscopic, palynological and biological analyses was implemented in this study. Digitally-enhanced HPTLC images using dual visualization approach with four image analysis software packages adopting different digitalization algorithms were comparatively evaluated i.e.; Sorbfil TLC View®, ImageJ®, JustTLC® and Gel Analyzer®. ImageJ® and Gel Analyzer® showed superior figures of merits in case of flavonoids and phenolic acids quantitation, respectively. Unsupervised and supervised multivariable pattern recognition models were constructed for comprehensive discrimination between the three propolis types (blue, orange and green) collected from various geographical locations worldwide. HPTLC-ESI-MS was utilized for precise identification of the discriminatory phytoconstituents. Fingerprint-efficacy relationship analysis was conducted via an Orthogonal Projection to Latent Structure multivariate model to unravel the bio-efficient markers in terms of α-glucosidase and α-amylase inhibition as main targets. 3,4-Dimethoxycinnamic acid, caffeic acid, isoferulic acid, rosmarinic acid, and quercetin were found to be the main health-relevant markers. A complementary fast, simple and readily available UV spectroscopic method using aluminium chloride as bathochromic shift reagent was used as an independent method for prediction of aforementioned biomarkers using a validated Partial Least Squares Regression model. In addition, palynological analysis was implemented to determine the botanical origin of Egyptian propolis for the first time. Twenty-eight pollen types assigned to 13 families were identified, with Asteraceae being the highest representative one. The investigated samples lacked dominant pollen types, which reflected the multifloral origin of Egyptian propolis. Identification of plant sources of propolis, which directly affect its chemical composition and subsequently its biological efficacy represents an integral part of its standardization.

**Keywords:** Image analysis; Palynological analysis; HPTLC-MS; Multivariate analysis; UV spectrophotometry; Propolis.

# PHS 626: Hazard Use / Misuse of *Mentha pulegium* During Pregnancy: Study of Endogenous and Metabolic Profiling

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Pregnant women usually turn to natural products to relieve pregnancy-related ailments which might pose health risks. Mentha pulegium L. (MP, Lamiaceae) is a common insect repellent, and the present work validates its abortifacient capacity, targeting morphological anomalies, biological, and behavioral consequences, compared to misoprostol. The study also includes untargeted metabolite profiling of MP extract and fractions thereof viz. methylene chloride (MecH), ethyl acetate (EtOAc), butanol (But), and the remaining liquor (Rem. Aq.) by UPLC-ESI-MS-TOF, to unravel the constituents provoking abortion. Administration of MP extract/fractions, for three days starting from day 15th of gestation, affected fetal development by disrupting the uterine and placental tissues, or even caused pregnancy termination. These effects also entailed biochemical changes where they decreased progesterone and increased estradiol serum levels, modulated placental gene expressions of both MiR-(146a and 520), decreased uterine MMP-9, and up-regulated TIMP-1 protein expression, and empathized inflammatory responses (TNF-α, IL-1β). In addition, these alterations affected the brain's GFAP, BDNF, and 5-HT content and some of the behavioral parameters escorted by the open field test. All these incidences were also perceived in the misoprostol-treated group. A total of 128 metabolites were identified in the alcoholic extract of MP, including hydroxycinnamates, flavonoid conjugates, quinones, iridoids, and terpenes. MP extract was successful in terminating the pregnancy with minimal behavioral abnormalities and low toxicity margins.

**keywords:** Mentha pulegium (pennyroyal); Abortion; UPLC metabolite profiling; micro-RNA; MMP-9.

# PHS 627: LC/MS/MS Analysis for Valorization of Mesquite (*Prosopis juliflora* (Sw.) DC.) By-products Using and Investigation of Their Anti-inflammatory Action

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Mesquite (*Prosopis juliflora* (Sw.) DC.) is widely used in food, biotechnology, pharmaceutical, and cosmetic industries. Every part of mesquite is used for medicinal purposes. In this work, stems, leaves, flowers and pods of *P. juliflora* were chemically profiled via UPLC/MS/MS analysis for their valorization as forest by-products with tentative identification of 44 metabolites. Multivariate statistical analysis was implemented to investigate in-between and within class discrimination of the different parts of mesquite where stems and leaves extracts were separately segregated indicating great variation in their chemical profile, while pods and flowers were clustered together. *Ex-vivo* anti-inflammatory activity of the tested extracts on four pro-inflammatory markers (TNF-$\alpha$, IL-1$\beta$, IL-6 and INF-$\gamma$) were performed where stems extracts showed significant inhibition to the tested cytokines. Orthogonal projection to latent structures (OPLS) models and coefficient plots of each pro-inflammatory marker unraveled the important functional constituents that positively correlated to inhibitory activity of each cytokine. 3'-oxojuliprosine, isojuliprosine, and palmitic acid have high coefficient correlation values regarding inhibiting TNF-$\alpha$ and IL-1$\beta$ pro-inflammatory markers, where they showed spatial correlation to flowers extracts. Meanwhile, stems and leaves were spatially correlated to downregulation of IL-6 and INF-γ levels with retusin-7-neohesperidoside, tryptamine and schaftoside, being the most significant coefficients. Results indicate the possible use of different parts of mesquite a potential source of functional components as high-value-added byproducts.

**Keywords:** Mesquite, LC/MS/MS, Multivariate analysis, anti-inflammatory action.

# PHS 628: Egyptian Propolis Composition in Context to its Major Pharmacological Uses: Unveiling its Antioxidant, Anti-viral and Anti-inflammatory Activities *In-Vitro*

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Propolis, a honeybee product that varies in its chemical composition as per the climate, geographical source, bees hive and plants surrounding the hive. In this current study, 70 % hydroethanolic extract of the Egyptian propolis (PE) was prepared for both chemical profiling as well as biological studies. The PE extract exhibited potent anti-inflammatory activity on LPS stimulated RAW 264.7 cell line with iNOS dose dependent protein expression inhibition (western blot). Also, it recorded effective anti-viral activity on $H_1N_1$ influenza and 229E Corona viruses. Total phenolics and flavonoids were assessed on the PE extract. The chemical profiling of PE proved its enrichment with flavonoids class using LC-MS/MS. The HPLC-PDA results revealed propolis enrichment with chrysin followed by galangin. Total phenolics and flavonoids results of PE sample were recorded *ca.* 180.8±0.11 µg GAE/mg and 158.7±0.15 µg QE /mg), respectively. The Egyptian propolis was enriched mainly with flavonoids chrysin, galangin and pinocembrin using LC-MS/MS. HPLC-PDA results revealed the enrichment of PE with chrysin and galangin *Ca.* 18.8 and 17.5 mg/g PE extract, respectively. The biological studies conducted on 70% hydroethanolic extract of Egyptian propolis revealed effective antioxidant results using different assays *viz.* DPPH and ABTS recording $IC_{50}$ 46.52±1.25 and 11.74±0.26 µg/mg, respectively while FRAP assay recorded 445.29±29.9 µM eq./mg Trolox equivalent. Promising antiviral activities ($IC_{50}$) on both $H_1N_1$ influenza and 229E Corona viruses *Ca.* 10.35 and 11.39 µg/mL, respectively using cytopathic effect inhibitory assay (crystal violet). The anti-inflammatory activity on LPS stimulated RAW 264.7 cell line recorded promising $IC_{50}$ 38.1 µg/mL with iNOS dose dependent protein expression inhibition (western blot). The Egyptian propolis recorded effective antioxidant, anti-inflammatory and anti-viral activities *in-vitro*. The potent biological activities would be correlated to its chemical profiling being enriched with flavonoids class.

**Keywords:** Egyptian Propolis, LC-MS/MS, HPLC-PDA, Antioxidant, Anti-viral and Anti-inflammatory.

# Pharmaceutical Technology & Nanomedicine

# PHS 701: Elaboration of Oral Trans-Resveratrol-Loaded Nanocochleates for Fighting Against Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is a prevalent liver cancer representing the fourth most lethal cancer world-wide. Trans-Resveratrol (T-R) possesses a promising anticancer activity against HCC. However, it suffers from poor bioavailability because of the low solubility, chemical instability, and hepatic metabolism. Herein, we developed T-R-loaded nanocochleates using a simple trapping method. Nanocarriers were optimized using a comprehensive *in-vitro* characterization toolset and evaluated for the anticancer activity against HepG2 cell line. The optimized T-R-loaded nanocochleates demonstrated monodispersed cylinders (163 nm and 0.25 PDI) and high negative ζ-potential of -46.6 mV along with superior entrapment efficiency (99.7%), good drug payload (45.3 mg/g) and utmost product yield (98%). This nanoplatform exhibited a controlled biphasic pattern with minimal burst followed by sustained release for 72 h and its lyophilized formula was maintained physically and morphologically stable after a long period of storage. Significant enhancements of Caco-2 transport and *ex-vivo* intestinal permeation over liposomes, with 1.8- and 2.1-fold respectively, were observed. Nanocochleates showed significant reduction of 24-h $IC_{50}$ values compared to liposomes and free T-R. Moreover, an efficient knockdown of anti-apoptotic (Bcl-2) and cancer stemness (NANOG) genes was demonstrated. To the best of our knowledge, we are the first to develop T-R-loaded nanocochleates and scrutinize its potential in suppressing NANOG expression, 2-fold lower, compared to free T-R. According to these auspicious results, nanocochleates represent a promising nanoplatform to enhance T-R oral permeability and augment its anticancer efficacy in the treatment of HCC.

**Keywords:** Trans-Resveratrol; Nanocochleates; *Ex-vivo* Permeation; Caco-2 Permeation; Hepatocellular Carcinoma; HepG2 cells; Apoptosis; NANOG.

# PHS 702: Genistein Loaded Phytosomes: Novel Approach for Hepatocellular Carcinoma Oral Treatment

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Genistein (Gen) is one of the most potent soy isoflavones used for hepatocellular carcinoma (HCC) treatment. Low aqueous solubility and first-pass metabolism are the main obstacles resulting in low Gen oral bioavailability. The current study aims to introduce phytosomes as an approach to improve Gen solubility, protect it from metabolism by complexation with phospholipids (PL), and get used to PL in Gen lymphatic delivery. Different forms of PL namely: Lipiod® S100, Phosal® 53 MCT, and Phosal®75 SA were used in phytosomes preparation GP, GPM, and GPL respectively. The effect of formulation components on Gen absorption, metabolism, and liver accumulation was evaluated following oral administration to rats. Cytotoxicity and cellular uptake studies were applied on HepG2 cells and *in-vivo* anti-tumor studies were applied to the DEN-mice model. Results revealed that GP and GPL remarkably accumulated Gen aglycone in hepatic cells and minimized the metabolic effect on Gen. They significantly increased the intracellular accumulation of Gen in its complex form in HepG2 cells. Their cytotoxicity is time-dependent according to the complex stability. The enhanced *in-vivo* anti-tumor effect was observed for GP and GPL compared to Gen suspension on DEN-induced HCC in mice. In conclusion, Gen-phytosomes can represent a promising approach for liver cancer treatment.

**Keywords**: Genistein, Chylomicron induction, Oral bioavailability, Tissue biodistribution, Hepatocellular carcinoma.

# PHS 703: Phenytoin Crown Ether Nanovesicles for Healing of Corneal Ulcers

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Drug repositioning is an important drug development strategy as it saves the time and efforts exerted in drug discovery. Since, re-epithelization of the cornea is a critical problem, we envisioned that the anticonvulsant, phenytoin sodium can promote re-epithelization of corneal ulcers as it was repurposed for skin wound healing. Herein, our aim is to develop novel crown ether-based-nanovesicles "Crownsomes" of phenytoin sodium for ocular delivery with minimal drug induced-irritation and enhanced efficacy owing to "host-guest" properties of crown ethers. Crownsomes were successfully fabricated using span-60 and 18-crown-6 and characterized for their size, morphology, polydispersity index, zeta-potential, drug loading efficiency, conductivity and drug release. Crownsomes exhibited favorable properties such as formation of spherical nanovesicles of 280 ±18 nm and -26.10 ± 1.21 mV surface charges. Crownsomes depicted high entrapment efficiency (77 ± 5%) with enhanced and controlled release pattern of phenytoin sodium. The optimum crownsomes formulation ameliorated ex vivo corneal drug permeability (1.78 fold than drug suspension) through corneal calcium extraction ability of 18-crown-6. In vivo study was conducted utilizing alkali induced corneal injury rabbit model. Clinical and histopathological examination confirmed that crownsomes exhibited better biocompatibility and minimal irritation due to complex formation and drug shielding. Further, they enhanced corneal healing indicating their effectiveness as a novel drug delivery system for ocular diseases.

**Keywords:** 18-Crown-6; Crownsomes; Corneal Ulcer; Phenytoin Sodium.

# PHS 704: Prodigiosin-Surfactin Nanomicelles: A New Nanobiotechnological Anticancer Combination

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Surfactin, a cyclic lipopeptide biosurfactant produced by *Bacillus subtilis,* exhibits anticancer activity. Its amphiphilic nature leads to self-assembly into nanomicelles which may act as novel drug carrier. This study aimed at developing an anti-cancer combination based on surfactin nanomicelles for the delivery of prodigiosin, a lipophilic secondary bacterial metabolite, as anticancer agent. Prodigiosin was produced from *Serratia marcescens,* extracted and characterized by standard methods. Surfactin nanomicelles were prepared by a vortex/sonication method involving heat at 50$^{o}$C and loaded with prodigiosin. Prodigiosin-surfactin nanomicelles were characterized for colloidal properties, morphology (TEM), entrapment efficiency (EE%), and storage stability at 4$^{o}$C. The anticancer activity of prodigiosin-surfactin nanomicelles in comparison with prodigiosin and surfactin solutions was evaluated using two human breast cancer cell lines, MCF-7 and MDA-MB 231 by the MTT. Results indicated the formation of spherical nanomicelles (TEM) with a mean diameter 227.5±52.3 nm, PDI 0.453±0.12, and zeta potential-27.3±2.4, relatively high prodigiosin loading (EE%), and retention of colloidal properties upon storage for 2 weeks at 4$^{o}$C. Cell viability data indicated cytotoxicity of prodigiosin and surfactin to both breast cancer cell lines, though lower activity was observed against MDA-MB 231 cells. Interestingly, the anticancer activity of surfactin nanomicelles surpassed that of surfactin solution. Loading prodigiosin into nanomicelles resulted in the formation of a synergistic nanocombination against both cell lines allowing for 1.4-fold and 7.7-fold reduction in the dose of prodigiosin and surfactin, respectively. Findings provided evidence for the potential of surfactin nanomicelles as novel nanobiotechnology-based drug nanocarrier, capable of enhancing the activity of anticancer activity of their drug payload.

**Keywords**: Prodigiosin, Biosurfactant, Nano-self assemblies, Breast Cancer.

# PHS 705: Biopolymer Based Tetrahydrodiferuloylmethane Nanoparticles Loaded Buccal Wafers with the Potential of Prolonged Residence and Drug Release for Local Treatment of Buccal Cavity Disorders: Formulation Development and In-Vivo Assessment

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Buccal cavity disorders (BCDs) are a serious public health problem starting from gum diseases reaching to oral cancer. Conventional dosage forms like bioadhesive tablets, ointments, pastes and gels are commonly affected by physiological factors which can reduce their contact with the mucosa and hence their therapeutic efficacy. In recent years wafers with their good mouth feel, compatibility, stability, and higher bioavailability, have succeeded to meet the expectations as an advancement to oral films. Polymers compose the majority of wafer formulation, either single or in blends to obtain the desired properties. Carrageenans (CG) are a natural sulphated polysaccharide with a wide range of biological activities which make them appealing biopolymers for drug delivery. Tetrahydrodiferuloylmethane (TF), a curcumin metabolite with similar pharmacological activity but of superior solubility and stability at physiological conditions, which makes it more accessible in-vivo. The current study aimed to develop and characterize CG-based bioadhesive composite wafers loaded with TF nanoparticles (TF-NP) with the potential of prolonged in-vivo residence and drug release for effective local treatment of BCDs. TF-NP were optimized in terms of their colloidal properties and incorporated in CG based wafers. In-vitro characterization of TF-NP loaded wafers was performed in terms of mechanical, and bioadhesive parameters. In-vivo performance in human volunteers regarding residence time and drug release in human saliva was also performed. The obtained results showed that the TF-NP loaded wafers exhibited acceptable flexibility, excellent bioadhesion properties. In-vivo assessment confirmed prolonged wafer residence and sustained release of TF therapeutic concentration in saliva up to 10 hours. This significantly emphasizes the appreciable role of the formulated TF-NP loaded wafers in enhancing TF solubility while achieving both prolonged residence and controlled drug release. Therefore, the current work represents a coherent approach for delivering TF in a promising drug delivery system capable of effective local treatment of BCDs.

**Keywords**: buccal cavity disorders; wafer; local treatment; nanoparticles.

# PHS 706: A Novel Strontium Decorated Mebendazole Nanosystem for Bone Marrow Targeting: Formulation Development and In-Vivo Evaluation

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Treating bone metastasis is extremely challenging as it necessitates sufficiently high chemotherapeutic doses to reach the diseased bone marrow in an effective therapeutic magnitude. As a result, bone marrow targeting has become an indispensable requirement. Bisphosphonates have been used successfully in the active targeting of therapeutics to treat bone metastasis. However, their long-term use had many drawbacks. Consequently, finding new bone targeting moieties or ligands that do not have the disadvantages of bisphosphonates has become an important issue to address. Despite its limiting physicochemical properties, several clinical trials strongly recommend mebendazole (Meb) repurposing for inhibiting cancer progression and metastasis. Therefore, the objective of this work was to combine mebendazole with strontium as a novel targeting ligand in a single nano-delivery system with dual activity for treating bone metastasis and enhancing bone regeneration. The nano-delivery system was designed and impact of Meb concentration as well as solvent system composition were investigated and optimised. Optimization criteria were colloidal properties and entrapment efficiency. On the other hand, in-vivo assessment of anti-tumor efficacy, bone osteolysis inhibition, bone regeneration and toxicity in adult female BALB/c mice were also performed. The results revealed that the optimum formulation showed proper physicochemical properties regarding particle size (123.78±4.05 nm), zeta potential (-32.88±3.20 mv) and entrapment efficiency (92.5±2.08 %). The in vivo results demonstrated that in comparison with non-targeted formulations; Sr decorated Meb nanosystem showed superior anti-tumor efficacy (98.30%) with significant percent necrosis and granulation tissue formation reaching to 100 % together with zero % residual tumor. Furthermore, the X-ray imaging revealed a significant mineralized bone formation in which the bone was completely rebuilt similar to a normal healthy one. As a result, the developed strontium decorated Meb nanosystem represents a novel targeted platform capable of dual functionality through antitumor potential and bone regenerative effect.

**Keywords:** metastasis, bone marrow, mebendazole, strontium.

# PHS 707: Novel Fucoidan Coated Fisetin-Loaded Liposomes for Oral Cancer Management: *In-Vitro* Optimization and *In-Vivo* Studies

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Fisetin suffers from low solubility and poor absorption. Accordingly, it is necessary to develop nanosystems to improve fisetin clinical potential and enhance its anti-cancer activity. Therefore, this work aimed at preparing novel fisetin-loaded liposomes coated with fucoidan to mitigate the drug drawbacks and enhance its bioavailability. Liposomes were prepared with phospholipid (lipoidS-100) using the ethanol injection technique. Optimized formulation showed a suitable particle size (256 ± 2.82 nm), zeta potential (-26.7 ± 0.05) and entrapment of fisetin (93 ± 2.5%). Physical stability of the selected formulation was investigated by monitoring any changes in particle size, zeta potential and drug entrapment efficiency upon storage for 6 months in 4°C. Cellular uptake and *in-vitro* cytotoxicity studies were carried out for the selected nanoformulation on oral squamous cell carcinoma cell line. The effect of the selected nanoformulation was assessed on different oral squamous cell carcinoma serum biomarkers. In addition, the anti-tumor effect of this formulation against oral cancer induced in rats was evaluated. Loading of fisetin within the liposomes coated with fucoidan showed significantly enhanced anticancer activity compared to the drug suspension indicated by significant decrease of all serum markers levels. Furthermore, the treatment group demonstrated significantly superior caspase-3 levels within the oral tumors in comparison with untreated positive control rats. In conclusion, fisetin-loaded liposomes coated with fucoidan could be considered as a promising nanoplatform for oral cancer treatment.

**Keywords:** Fisetin, Fucoidan, Liposomes, Oral carcinoma.

# PHS 708: Formulation of Regenerative Brushite Cement Scaffold Loaded with Quercetin-Phytosomes for Repair of Bone Defects

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Quercetin (QT) is a natural compound that is found in many vegetables, fruits, and seeds. Its potential role in enhancing osteogenesis and improving bone regeneration with significant osteo-inductive and angiogenic properties had been reported. However, its poor stability and solubility have limited its clinical use. The key to this problem is to formulate QT within simple and easily prepared nano-systems. Phytosomes (PHY) are nano-vesicles that are easily formulated by formation of a phyto-phospholipid complex. They can improve the delivery and bioavailability of natural drugs. The aim of this work was to formulate a biodegradable, biocompatible and regenerative scaffold to enhance the healing of orthopedic fractures. Therefore, the potential use of a synthetic bone substitute as calcium phosphate cement (CPC) loaded with formulated QT can fulfil the urgent need to repair bone defects and face orthopedic challenges. In this work, self-setting brushite CPC was selected as an artificial bone graft. For the first time, the CPC scaffolds were loaded with lyophilized QT-phytosomal formulations. *In vitro tests* included the optimization of both QT-phytosomal formulation and blank CPC. The optimized formulations were characterized both *in vitro* and *in vivo* in a rat femur bone defect model. The addition of phytosomes did not deteriorate the CPC properties. An adequate setting time, porosity and mechanical strength were maintained within drug-loaded cement. Moreover, the scanning electron microscope confirmed the maintenance of nano-system integrity within cement. The *in vivo* study showed the superiority of QT-PHY CPC compared to crude QT-CPC in enhancing bone healing. This was confirmed using histological and histomorphometric studies that showed the formation of a significantly higher percent of mature lamellar bone in phytosomal group. In conclusion, QT-PHY /CPC are promising lipid nano-composite materials that could enhance bone regeneration.

**Keywords**: Brushite, Quercetin, Phytosomes, regeneration.

# PHS 709: Repurposed Deferoxamine-Loaded Bioactive Chitosan Alginate Nanoparticles for Diabetic Pressure Ulcers Treatment

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Chronic poorly healing diabetic wounds represent a major medical and social challenge. In this area, drug repurposing has become an interesting and attractive approach that offers relatively reduced development costs and time, compared to the development of entirely new drugs. Deferoxamine (DFO), an iron chelator mainly used clinically for the management of acute and chronic iron overload is currently being investigated for its wound healing potential. However, its high water solubility and short half-life call for a topical delivery system that would maximize its wound healing potential and provide a sustained release profile. In this study, DFO was encapsulated, by emulsion-cross linking method, in a positively or negatively charged chitosan alginate nanoparticles (NPs), which had already proven to enhance wound healing. The size, surface charge and release profile of the formed NPs was evaluated, in addition to Fourier-Transform infrared spectroscopy characterization. Positively charged DFO-loaded NPs were evaluated in vivo for their pressure ulcers-healing effect using diabetic rats. These NPs demonstrated higher wound healing efficiency, compared to DFO solution or blank NPs, regarding healing rates, re-epithelialization, granulation tissue maturation, neovascularization, and collagen formation. These results suggest that the use of a bioactive carrier can maximize the wound healing efficacy of DFO while using a relatively low dose of the drug.

**Keywords**: chitosan, alginate, deferoxamine, diabetic pressure ulcers, repurposing.

# PHS 710: Microneedles: A New Horizon for Pediatric Drug Delivery

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Conventional dosage forms pose many challenges for the pediatric population. Oral solutions may not mask the bitter taste of drugs, and children and parents equally dislike painful injections. Hence, researchers have long worked on developing delivery systems that improve the bioavailability of poorly soluble drugs yet have good patient acceptability and adherence. Microneedles (MNs) are tiny needles that transpierce the stratum corneum with minimal invasiveness and pain while creating temporary channels across the skin and delivering drugs systemically. This technology combines the convenience of transdermal delivery with the efficiency of injections to deliver small molecules, macromolecules, and vaccines. We aimed to design, fabricate and characterize a dissolving MN (DMN) system for effective drug delivery for pediatrics while selecting an optimum therapeutic application that covers unmet needs. Our work was guided by clinicians' perspectives on pediatric drugs that can benefit from such technology. Polydimethylsiloxane (PDMS) MN molds were fabricated via stereolithography. The mold produces a 5x5 MNs array; each needle of a 500µm height, 300µm base width, and 1500µm needle interspacing. Different polymers were screened for biocompatibility, forming DMNs with good mechanical strength and easy manufacturing. DMNs were fabricated using the micromolding method using different polymer concentrations. The fabricated systems were visually examined for integrity and strength via insertion test and microscopy. The survey of 57 pediatricians of various subspecialties generated a set of proposed medications, mostly analgesics, antibiotics, diuretics, and antihypertensives. We successfully produced a stable DMN patch from hyaluronic acid (HA). Concentration was found to affect the integrity and insertion properties of created patch. Patches prepared at 1-1.25% w/w concentrations have shown to be stable with adequate mechanical strength. We believe that our developed system of HA DMNs is a promising platform for drug loading and delivery for different pediatric applications.

**Keywords:** dissolving microneedle, hyaluronic acid, pediatric, transdermal delivery.

# PHS 711: Anticancer Probiotic / Carbon Dots Fluorescent Bio-Hybrid for Imaging-Guided Intracellular Delivery

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Bacteria including probiotics and their respective structures are presently under active investigation as biological drug carriers that may overcome some limitations of biomaterial-based drug delivery systems. Combination of bacteria with nanomaterials may lead to bio-hybrids having unique therapeutic potentials. Our objective was to combine *Lactobacillus plantarum* (LP) probiotic with carbon dots (CDs) fluorescent nanoparticles to develop a bio-hybrid for imaging-guided anticancer drug delivery using the secondary bacterial metabolite, prodigiosin (PG), as anticancer agent. Heat killed LP (HKLP) was combined with CDs prepared from D-glucose to generate inactivated fluorescent LP cells. These were loaded with PG obtained from the bacteria *Serratia marcescens*. The developed biohybrid was characterized for LP structural integrity by TEM and PG release properties. Cytotoxicity was assessed using human colon cancer Caco-2 and A459 lung cancer cell lines and intracellular PG delivery was assessed by laser confocal microscopy (LMC). Finally, potential PG target genes were identified by bioinformactic analysis. Results indicated the formation of fluorescent PG/CDs-HKLP with high LP membrane integrity and stability under different release conditions as affirmed by TEM imaging. Cytotoxicity data revealed a significant increase in PG anticancer activity by loading into CDs-HKLP which was associated with intracellular PG delivery as verified by LCM imaging. Bioinformatics analysis revealed that PG mainly binds to kinases (31%), family A G-protein coupled receptors (17%) and other enzymes (15%), suggesting interference of PG with the signaling cascade at different levels. Identified molecular targets included those related to inflammation and immune response as well as those contributing to growth signaling. In conclusion, findings provided evidence for the aptitude of the PG-CDs-HKLP biohybrid as a potential anticancer biomedicine that combines the safety, bioactivity, and inherent affinity of HKLP to colon and lung cells, CDs bioimaging function and PG anticancer activity.

**Keywords**: Probiotics, Carbon dots, Prodigiosin, Cytotoxicity

# PHS 712: Limonene-Based Nanostructured Lipid Carriers Azithromycin-Loaded *In-Situ* Gel: Potential Platform to Overcome Clinically Isolated *Methicillin-Resistant Staphylococcus aureus* Ocular Infection

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*Staphylococcus aureus (S. aureus)* is the main pathogen that causes serious ocular infection as endophthalmitis and keratitis. The major obstacle in managing S.aureus infection is antibiotic resistance, as illustrated by the development of methicillin-resistance S.aureus (MRSA) strains. D-limonene is the main constituent of oil extracted from citrus peel, which has been known for its antibacterial effect. Thereby, the current work attained to fabricate an effective *in-situ* ocular limonene-based nanostructured lipid carriers (NLCs) gel to improve azithromycin (AZ) solubility and efficacy against and *methicillin-susceptible S. aureus* (MSSA) and MRSA-associated ocular biofilm infection. NLCs, consisting of limonene and Gelucire® as an oily phase and Labrasol® and labrafil® as an aqueous phase, were prepared by cold microemulsion technique and characterized regarding size, polydispersity index, surface morphology, and the state of AZ within NLCs. Besides, *in-vitro* antimicrobial susceptibility was assessed on biofilm-forming MSSA and MRSA strains via kinetics of killing and biofilm assay. The *in-situ* based NLCs gel was developed using Poloxamer® and hydroxypropyl methyl cellulose (HPMC) and assessed based on physicochemical characteristics, *in-vitro* release, *ex-vivo* transcorneal permeation through ocular sheep, and its ocular safe profile using HET-CAM test. NLCs displayed a nanometric size of 77.42±0.82 nm, unimodal size distribution, and spherical shape with improved eradicating efficacy of MRSA biofilm, where the MIC and MBC of AZ-loaded NLCs were 4 µg/ml and 64 µg/ml, respectively, significantly less than that of AZ alone which were 16 µg/ml and 128 µg/ml, respectively. NLCs-based *in-situ* gel exhibited 1.25-fold enhancement in *ex-vivo* transcorneal permeability compared to the control *in-situ* gel with a safe ocular profile revealing zero irritation index compared to 9.87 for the positive irritant group (1%w/v sodium lauryl sulfate). Therefore, AZ-loaded limonene-based NLCs *in-situ* gel is considered as a promising platform against resistant bacterial strains with superior safety and efficacy.

**Keywords:** Azithromycin, *In-situ* gel, Limonene, *Methicillin-resistant staphylococcus aureus*, Nanostructure lipid carriers.

# Microbiology, Immunology & Biotechnology

# PHS 801: Genomic Insights into a Colistin-Resistant Uropathogenic *Escherichia coli* Strain of O23:H4-ST641 Lineage Harboring *mcr-1.1* on a Conjugative IncHI2 Plasmid from Egypt

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The reintroduction of colistin, a last-resort antibiotic for multidrug-resistant pathogens, resulted in the global spread of plasmid-mediated mobile colistin resistance (*mcr*) genes. Our study investigated the occurrence of colistin resistance among *Escherichia coli* isolated from patients with urinary tract infections admitted to a teaching hospital in Egypt. Out of 67 isolates, three isolates were colistin-resistant, having a minimum inhibitory concentration of 4µg/mL and possessing the *mcr-1* gene. A double mechanism of colistin resistance was detected; production of *mcr-1* along with amino acid substitution in PmrB (E123D and Y358N) and PmrA (G144S). Broth mating experiments inferred that *mcr-1* was positioned on conjugative plasmids. Whole-genome sequencing of EC13049 indicated that the isolate belonged to O23:H4-ST641 lineage and to phylogroup D. The *mcr-1*-bearing plasmid corresponded to IncHI2 type with a notable similarity to other *E. coli* plasmids previously recovered from Egypt. The unbanned use of colistin in the Egyptian agriculture sector might have created a potential reservoir for the mcr-1 gene in food-producing animals that spread to humans. More proactive regulations must be implemented to prevent further dissemination of this resistance. This is the first characterization of *mcr-1*-carrying IncHI2:ST4 plasmid recovered from *E. coli* of a clinical source in Egypt.

**Keywords:** colistin resistance; *mcr-1*; multidrug resistant uropathogenic *E. coli*; IncHI2 plasmid; whole genome sequencing; Egypt.

# PHS 802*: In vitro* Assessment of the Antiviral Activity of Lectin Extracted from *Pleurotus ostreatus* Mushroom Against Herpes Simplex Virus, Hepatitis B Virus, and Hepatitis C Virus Infection

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Viruses cause many serious outbreaks and pandemics around the world, resulting in high mortality rates and economic problems. Lectins are carbohydrate-binding proteins of non-immunologic origin with antiviral properties against both RNA and DNA viruses. This study tested the antiviral properties of the purified lectin from *Pleurotus ostreatus* mushroom (POL) against different viruses. The half-maximal inhibitory concentration ($IC_{50}$) of the anti-HIV reverse transcriptase was 0.97 µM. Using infectivity assays, the $IC_{50}$ values of POL against HBV using treatment and blocking mechanisms were 0.043 and 0.015 µM, respectively. The blocking and neutralizing $IC_{50}$ values for HCV were 0.06 and 0.05 µM, respectively. Additionally, the binding percentage to CD81 was 58.80% and the $IC_{50}$ of the targeting to the scavenger receptor class B-type I (SR-B1) was 10 nM. The $IC_{50}$ of the HCV-NS3/4A (non-structural ¾A) protease inhibitor and anti-HBV-polymerase were 10.98 and 4.22 nM, respectively. The inhibitory effect of POL against herpes HSV-1 and HSV-2 was studied using plaque reduction and cell viability assays. Besides antiviral activity, POL showed anticancer effect against hepatoma cell lines and inhibits their proliferation at low $IC_{50}$ values. These findings offer vital insights into the way that POL inhibits HIV, HSV, HBV and HCV infection.

**Keywords:** Mushrooms; Lectins; Antiviral; HCV; HBV; HSV; HIV.

# PHS 803: Whole Genome Characterization of the High-Risk Clone ST383 *Klebsiella pneumoniae* with a Simultaneous Carriage of *bla*$_{\text{CTX-M-14}}$ on IncL/M Plasmid and *bla*$_{\text{CTX-M-15}}$ on Convergent IncHI1B/IncFIB Plasmid from Egypt

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Egypt has lately witnessed the emergence of multidrug-resistant (MDR) *Klebsiella pneumoniae* posing a serious healthcare challenge. The accelerated dissemination of *bla*$_{\text{CTX-M}}$ genes among these MDR *K. pneumoniae*, particularly *bla*$_{\text{CTX-M-14}}$ and *bla*$_{\text{CTX-M-15}}$, was noted. In this study, we investigated the occurrence of *bla*$_{\text{CTX-M-IV}}$ among *K. pneumoniae* recovered from the laboratory of a major hospital in Alexandria. The 23 tested isolates showed an MDR phenotype and *bla*$_{\text{CTX-M-IV}}$ gene was detected in ≈22% of the isolates. Transformation of plasmids harboring *bla*$_{\text{CTX-M-IV}}$ to *Escherichia coli* DH5α chemically competent cells was successful in 3 out of 5 tested *bla*$_{\text{CTX-M-IV}}$ -positive isolates. Whole genome sequencing of K22 indicated that the isolate belonged to the high-risk clone ST383 showing a simultaneous carriage of *bla*$_{\text{CTX-M-14}}$ on IncL/M plasmid, pEGY22_CTX-M-14, and *bla*$_{\text{CTX-M-15}}$ on a hybrid IncHI1B/IncFIB plasmid, pEGY22_CTX-M-15. Alignment of both plasmids revealed high similarity with those originating in the UK, Germany, Australia, Russia, China, Saudi Arabia, and Morocco. pEGY22_CTX-M-15 was a mosaic plasmid demonstrating convergence of MDR and virulence genes. The emergence of such plasmid with enhanced genetic plasticity constitutes the perfect path for the evolution of *K. pneumoniae* isolates causing invasive untreatable infections especially in a country with a high burden of infectious diseases like Egypt. This necessitates an imperative countrywide surveillance to monitor the prevalence of these superbugs with limited therapeutic options.

**Keywords:** *Klebsiella pneumoniae*; whole genome sequencing; high-risk clone ST383; *bla*$_{\text{CTX-M-14}}$; *bla*$_{\text{CTX-M-15}}$; convergence of resistance and virulence.

# PHS 804: Evaluation of the Antimicrobial and Anti-inflammatory Activity of Selected Probiotics Isolated from Dietary Supplements *In Vitro* and *In Vivo*

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Probiotics, and their derived components as cell free supernatants (CFS), are gaining a solid reputation owing to their prodigious health promoting effects. In this study, three probiotic strains were isolated from dietary supplements which were *Lactiplantibacillus plantarum*, *Lacticaseibacillus rhamnosus*, and *Pediococcus acidilactici*. This study aims to investigate the antimicrobial, antibiofilm and anti-inflammatory activities of the isolated probiotic strains as well as their CFS. The antimicrobial activity of the isolated probiotics was assessed against some standard indicator strains using the agar overlay method. The isolates showed moderate to strong growth inhibition of the tested indicator strains. Using the time-kill assay, the CFS of *L. rhamnosus* or *P. acidilactici* showed a synergistic activity when combined with ceftazidime or gentamicin antibiotics against *Staphylococcus aureus* or *Escherichia coli* pathogenic isolates. Moreover, the neutralized CFS of the isolated probiotics exhibited an antibiofilm effect, assessed by the crystal violet assay, through hindering the biofilm formation of the tested *S. aureus* and *Pseudomonas aeruginosa* clinical isolates in addition to *P. aeruginosa* PAO1 strain. Finally, the anti-inflammatory activity of *L. plantarum* and *L. rhamnosus*, together with their CFS, was studied in the carrageenan-induced rat paw edema model. The increase in the paw swelling was monitored by a Vernier caliper, and the inflammatory changes in the paw tissue sections were revealed by histopathological examination. Generally, the cell cultures of the two tested probiotics moderately suppressed the acute inflammation induced by carrageenan compared to indomethacin. Additionally, the studied CFS relatively reduced the inflammatory changes compared to the inflammation control group but less than that observed in case of the probiotic cultures treated groups. In conclusion, the tested probiotics, as well as their CFS, have promising antimicrobial and anti-inflammatory activities. Thus, their potential use as biotherapeutics for bacterial infections and inflammatory conditions is worthy of further investigation.

**Keywords:** Cell free supernatant – Antimicrobial - Antibiofilm - Anti-inflammatory - Time-kill assay - Crystal violet assay - Carrageenan-induced rat paw edema model - Histopathological examination.

# PHS 805: Engineering a Microbial Cell Factory for Production of Monoterpenoids

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Terpenoids belong to the largest class of natural products that have long marveled researchers with their structural diversity and wide range of applications. Monoterpenoids, in specific, are an interesting subgroup of this class, with over 55,000 different compounds and various applications such as drugs, food flavors, fragrances, raw materials in cosmetics, biofuels and cleaning agents. Nevertheless, the majority of terpenoids are produced in low yields, and their extraction is usually labor-intensive and requires considerable consumption of natural resources. In addition, chemical synthesis is problematic due to their complex structures. A promising alternative method is production of terpenoids in microbial hosts, microbial cell factories formed of metabolically and genetically modified organisms (GMOs). Various microorganisms have been engineered for such purpose such as the yeast *Saccharomyces cerevisiae*, gram-negative *Escherichia coli*, and gram-positive *Bacillus subtilis*. This research aims at engineering a platform microorganism for biosynthesis of valuable monoterpenoids. That entails studying the step-by-step biosynthesis pathway of the target monoterpenoids in their native plant sources and mimicking such pathway in the host organism through genetic and metabolic engineering. *B. subtilis* possesses an inherent pathway that produces the C5 building blocks of all terpenoids. This pathway was overexpressed to increase the supply of the building blocks. Then, the necessary genes required for the biosynthesis of the target monoterpenoids will be introduced from the plant source into *B. subtilis*. Followed by that, the engineered strains will be screened for production of the monoterpenoids. Based on literature review, six monoterpenoids were selected namely, cineole, sabinene, linalool, limonene, camphene and geraniol. Plant sources were collected followed by total RNA extraction then reverse transcription. Primers were designed and used for amplification of the target genes from the total cDNA of the plant sources. These genes will be inserted in integrative pDR111 plasmid and introduced into *B. subtilis*. The goal is to direct the industry toward an alternative affordable method for production of terpenoids in general and monoterpenoids in particular.

**Keywords:** Monoterpenoids, Microbial cell, Genetic engineering, Metabolic engineering.

# PHS 806: Serum Immune Profiling for Early Detection of Cervical Disease

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Worldwide estimates from the International Agency for Research on Cancer indicate that approximately 528,000 new cases and 270,000 deaths per year are attributed to cervical cancer worldwide. The disease is preventable with HPV vaccination and with early detection and treatment of pre-invasive cervical intraepithelial neoplasia, CIN. Antibodies (Abs) to HPV proteins are under investigation as potential biomarkers for early detection. To detect circulating HPV-specific IgG Abs, we developed programmable protein arrays (NAPPA) that display the proteomes of two low-risk HPV types (HPV6 and 11) and ten oncogenic high-risk HPV types (HPV16, 18, 31, 33, 35, 39, 45, 51, 52 and 58). Arrays were probed with sera from women with CIN 0/I (n=78), CIN II/III (n=84), or invasive cervical cancer (ICC, n=83). Abs to any early (E) HPV protein were detected less frequently in women with CIN 0/I (23.7%) than women with CIN II/III (39.0%) and ICC (46.1%, $p<0.04$). Of the E Abs, anti-E7 Abs were the most frequently detected (6.6%, 19.5%, and 30.3%, respectively). The least frequently detected Abs were E2-Abs in CIN 0/I (1.3%) and E1-Abs in CIN II/III (1.2%) and ICC (6.6%). HPV16-specific Abs correlated with HPV16 DNA detected in the cervix in 0% of CIN 0/I, 21.2% of CIN II/III, and 45.5% of ICC. A significant number (36 – 76%) of E4, E7, L1, and L2 Abs had cross-reactivity between HPV types. HPV protein arrays provide a valuable high-throughput tool for measuring the breadth, specificity, and heterogeneity of the serologic response to HPV in cervical disease.

**Keywords**: Antibodies; HPV; cervical cancer; cervical intraepithelial neoplasia; NAPPA; protein microarrays; serology; early detection.

# PHS 807: Code Red: Resistance and Co-carriage of Staphylococci in the Nasal Cavity

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Background: Staphylococci are commensals of the skin and mucous membranes of humans, yet they can also cause serious infections. The most common colonization site is the anterior nares. We are investigating the antimicrobial resistance patterns among different staphylococcal species isolated from anterior nares of healthy pharmacy students and the effect of co-carriage of more than one isolate on the isolates' biofilm formation capacity. Methods: Nasal swabs collected in 2019 were cultivated on nutrient agar, mannitol salt agar and DNase agar for isolation. Isolates were identified using biochemical tests and VITEK 2 automated system. Antibiotic susceptibility was determined using disc diffusion method. D-test was used to determine the prevalence of the inducible Macrolide-Lincosamide-Streptogramin B ($iMLS_B$) phenotype. Biofilm formation was screened using the crystal violet method; and some biofilm-related genes were studied using the Polymerase chain reaction. Results: Out of 196 samples, 103 isolates were obtained, of these 34 were non-duplicate *S. aureus* and 69 were non-duplicate Coagulase Negative Stapylococci (CoNS). The highest resistance among the isolates was to fusidic acid (54.8% and 79.7%, respectively), followed by azithromycin at 26.5% and 52.2% for *S. aureus* and CoNS, respectively. Methicillin resistance was detected among 35.3% of *S. aureus* and 39.19% of CoNS. About 94% of *S. aureus* and and 55% of CoNS isolates displayed the inducible $MLS_B$ phenotype. Seven (20.6%) *S. aureus* isolates were co-carried with CoNS, and six (17.6%) *S. aureus* isolates co-occurred with other *S. aureus* isolates. Twelve (17.4%) CoNS isolates co-occurred with other CoNS isolates. In over 80% of the cases, *S. aureus* co-carried with other isolates formed moderate to strong biofilms. Conclusions: In our study, nasal staphylococci displayed a high level of multidrug resistance and biofilm formation. We recommend education about personal hygiene habits and proper antibiotic use guidelines to limit spread of infections caused by once-commensal isolates.

**Keywords**: CoNS, *S. aureus*, Biofilm formation, Co-occurrence.

# PHS 808: Modulating Breast Cancer Tumor Microenvironment for Effective Immunotherapy: Tackling Immune Evasion, Autophagy and Cancer Stem Cells

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Breast cancer tumor microenvironment (TME) is a complex, heterogenous milieu that includes an interplay between different types of cells such as cancer cells, cancer stem cells, fibroblasts, endothelial and immune cells in addition to different immune-mediating cytokines. Evasion of apoptosis and immune surveillance, upregulated autophagy and cancer stem cells (CSC) maintenance are essential vital processes involved in tumorigenesis, tumor survival, invasion and treatment resistance within the TME. Thus, targeting TME with immune-supportive strategies is considered as one of the most promising approaches for fighting cancer. The current work aimed at targeting apoptosis, autophagy and cancer stem cells as well as modulating the immune surveillance within the TME by different strategies. Fresh tumor tissue samples excised from breast tumor after radical mastectomy were cultured separately in presence of either TRAIL or anti-IL8 monoclonal antibody or anti-IL6 monoclonal antibody or recombinant FAS molecules or blocked Fas - peripheral blood mononuclear cells (PBMCs) (using anti-Fas mAb). A significant increased level of caspase 3 (indicator of apoptosis), decreased expression of CD 44 (CSCs marker) and inhibition of autophagy marker LC3B were observed within the different designed breast tumor tissue culture systems compared to the breast tumor tissues cultured alone. Accordingly, we can consider each strategy in the current work as a promising proposed immunotherapeutic strategy for breast cancer.

**Key words:** Breast cancer, Autophagy, Cancer stem cells, Apoptosis.

# STUDENT POSTERS

# PHS 101: Coupling Reactions and the Advances in Drug and Drug Delivery Systems Syntheses

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Due the infinite diversity in the types of chemical reactions and their variable tunable conditions, they are highly sensitive to the slightest change that may affect the duration of the reaction, the amount of yield produced and the purity of the products. These are considered the major problems that are faced during the chemical syntheses of new drugs and drug delivery systems. Coupling reactions are the most common bioconjugation reactions that lead to formation of new chemical link which can be C-C, C-O or C-N bonds. This happens by activating the first molecule through an addition step to a metal catalyst; e.g. Palladium or a coupling reagent; e.g. N, N- Diisopropyl carbodiimide and N-ethyl- N-(3 dimethyl aminopropyl) carbodimide hydrochloride. Then the second molecule undergoes trans addition to the catalyst\coupling center in the activated species and eliminating the functional groups of the starting molecules. Finally, regenerating the catalyst or the coupling reagent occurs and formation of new bond between the starting molecules happens giving the organic product. In recent years, many coupling reactions have found their way into pharmaceutical industry to play a vital role in the development of bio-therapeutics and chemical biology approaches. Coupling reactions have participated in the synthesis of many drugs; for example: dexamethasone (anti-inflammatory drug), chitosan iodoacetamides (promising hemostatic agent) and caparratriene (a highly effective in the treatment of leukemia) and in the synthesis of many drug delivery systems such as polymeric nanoparticles and silk fibroin/sodium alginate composite. Altogether, coupling reactions have proved to possess the ability to synthesize drugs, modify proteins, nucleic acids, and carbohydrates opening many doors to wide range of drug synthesis methods, ground-breaking targeted therapies and imaging methods.

**Keywords:** Bioconjugation reactions, Coupling reactions, Drug synthesis, Drug delivery systems.

# PHS 102: Using Different Techniques in Analyzing the Biomarkers Found in DNA Damage

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Free radicals can be defined as the reactive species of nitrogen, oxygen, and chlorine. Such free radicals cause oxidation to biomolecules including proteins and nucleic acids which ultimately causes various diseased conditions. Recently, we can predict and know more about diseases using biomarkers that result from the oxidative damage caused by free radicals. Using different techniques, such as GC, LC and electrophoretic techniques, can help in measuring the amount of damage done by free radicals. Free radicals and oxidative damage contribute to aging, inflammation, diabetes, and cancer. The hydroxyl radicals are considered to be the most common radicals to cause DNA damage. Hydroxyl radicals generate a different range of base and sugar modification products that can affect mutagenesis, aging, and carcinogenesis. Between all the purine and pyrimidine bases in the DNA, guanine bases are the most susceptible ones to be oxidized as they present the lowest oxidation potential of the four bases. The addition of a hydroxyl group to the eight position of the guanine molecule results in generating the oxidized nucleoside 8-hydroxy-2'-deoxyguanosine (8-OHdG) which, together with the base 8-hydroxyguanine (8-OHGua), constitutes the most widely studied biomarker of oxidative DNA damage; both have specificity, potent mutagenicity, and relatively exist in high amount in the DNA. In this work, we will present the effect of different analytical methods that include chromatographic and electrophoretic techniques in measuring the biomarkers and detecting oxidative damage to one of the main macromolecules like oxidized DNA.

**Keywords**: biomarkers, free radicals, DNA damage, analysis.

# PHS 103: Epidemiology of Carbapenem Resistant Gram-Negative Pathogens from Egypt During the Last Decade

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Antimicrobial resistance continues to increase while the pipeline for new antibiotic development is drying up. After only eight decades of antibiotic use, bacterial infections that once were easily treated are becoming untreatable. Beta-lactams are by far the most used antibiotics worldwide and include the penicillins, cephalosporins, monobactams and carbapenems. Carbapenems are last resort agents to treat infections caused by multidrug resistant (MDR) Gram-negative pathogens (e.g. *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Escherichia coli*). Recently, increasing numbers of carbapenem resistant Gram-negative pathogens represent an ongoing public-health problem of global dimensions i.e. carbapenem-resistant isolates are emerging at an alarming rate. This type of antimicrobial resistance, especially when mediated by transferable carbapenemase-encoding genes, is spreading rapidly causing serious outbreaks and dramatically limiting treatment options. **Aim:** The aim of the current study is to explore the epidemiology and prevalence of carbapenem resistance among Gram-negative isolates from Egypt during the last decade using online survey and literature review. **Method:** Published articles from Egypt related to the epidemiology of carbapenem resistance among Gram negative during the last decade were collected through internet-based search in specialized journals and official scientific web sites (e.g. Scopus, PubMed, etc.) and the obtained data were statistically analyzed. **Results:** The rates of carbapenem resistance among Gram negative pathogens and the prevalence of certain carbapenemases encoding genes are different between Egyptian governorates. No significant relationship between the rates of resistance and timing or area of isolates' collection was observed. **Conclusion:** The emergence carbapenem resistant Gram-negative pathogens reached worrisome levels. The overuse and misuse of carbapenems should be avoided. Antimicrobial stewardship program should be strictly applied for the rational utilization of carbapenems.

**Key words:** Carbapenem resistance, gram negative, prevelance, carbepenemases.

# PHS 104: Analytical Methods for Accurate Determination of Anti-Covid-19 Drug Therapies

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According to the statistics of World Health Organization (WHO), about 596.87 million confirmed coronavirus cases and 6.45 million deaths had been reported. Since SARS-CoV-2 started in Wuhan in December 2019, it turned into a global pandemic. Remdesivir (RMD) is the first U.S. Food and Drug Administration (FDA) approved antiviral drug for the treatment of coronavirus in pediatrics and adults with different disease severities, ranging from mild to severe, in both hospitalized and non-hospitalized patients. Various drug regimens are used in SARS-CoV-2 therapy, all of which rely on the use of antiviral agents including Ritonavir (RTN)/ Nirmatrelvir (NTV) combination, Molnupiravir (MLP) and Favipiravir (FVP). Optimizing analytical methods for selective and sensitive quantification of the above-mentioned drugs in pharmaceutical dosage forms and plasma samples is a must in the current pandemic. Several analytical techniques were reported for the estimation of antivirals used in SARS-CoV-2 therapy. Chromatographic methods include Thin Layer Chromatography (TLC) densitometry, High Performance Thin Layer Chromatography (HPTLC), Revered Phase-High Performance Liquid Chromatography (RP-HPLC), RP-HPLC using Diode Array Detector (DAD), High Performance Liquid Chromatography using Mass Spectrometer (LC-MS/MS) or Ultraviolet detectors (LC-UV), same in Ultra High Performance Liquid Chromatography (UPLC-MS/MS) or (UPLC-UV) and Micellar Liquid Chromatography (MLC). Spectroscopic methods include Paper Spray Mass Spectrometry (PS-MS), UV-Spectrophotometry, and spectrofluorimetry. Here we will focus on the clarification of trendy, simple, rapid, accurate, precise, sensitive, selective, and eco-friendly analytical methods used for the analysis of anti-Covid-19 drugs in dosage forms and plasma samples.

**Keywords:** Covid-19, human plasma, dosage forms, chromatography and spectroscopy.

# PHS 105: Various Analytical Methods for the Detection of Volatile Organic Compounds as Biomarkers in Breath

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Manifold metabolic processes occurring within the human body create a wide variety of volatile organic compounds (VOCs). A large number of VOCs may be useful in diagnostics because they can provide valuable information on health conditions, such as infections or metabolic diseases. Breath is a rich mixture containing numerous VOCs at trace amounts, such as hydrocarbons, alcohols, ketones, aldehydes, esters or heterocycles. Such VOCs varies in quantities or even may be produced according to the patient's health condition. Some of them are directly linked to certain diseases. Exhaled breath analysis is a non-invasive, painless and non-stressful method proposed for clinical application. Therefore, breath analysis is a very useful tool for clinical diagnostics, therapy monitoring and control of metabolic or biochemical cell cycle products. Many efforts are made to fully and accurately describe traditional and modern techniques used to determine the components of breath. Examples of such techniques are GC with different detectors, MS, optical sensor and laser spectroscopic detection techniques. The techniques were compared in terms of design, function and also detection limit of different volatile organic compounds. Such wide range of sensitive analytical methods for detection of biomarkers in the breath at the ppbv or pptv levels can be applied to help the process of medical diagnosis. This study will provide an update on the most recent developments in breath analysis used to diagnose various diseases using high-quality equipment.

**Keywords:** volatile organic compounds, biomarkers, breath analysis, sensitive analytical methods.

# PHS 106: Development and Implementation of a Mobile Application "IMMUNO-PLANT" at the Nephrology Department, Alexandria Main University Hospital

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Making decisions concerning immunosuppressants used in organ transplantation is one of the most arduous challenges that physicians in Alexandria Main University Hospital (AMUH) are constantly facing. IMMUNO-PLANT is an effective comprehensive mobile application that was developed to provide them with consensuses that numerous studies came to in an accessible, time-saving way. It also includes the doses and adverse effects of these drugs in chronic kidney diseases and different dialysis modalities. Over three months**,** the difficulties facing physicians and clinical pharmacists who work at AMUH when using immunosuppressive agents in kidney diseases and transplantation patients were collected through electronic pre-surveys and face-to-face interviews. The aim was to evaluate their satisfaction with the information currently available in this field, their experience with such drugs and the importance of clinical pharmacists in improving their use. The responses reinforced the need for the application, some examples were Azathioprine causing bone marrow depression and rituximab causing hypersensitivity. Thereafter, trusted scientific information about dose modifications and adverse effects of twelve immunosuppressant classes, and the management of the most prevalent adverse effects of nine kidney transplantation immunosuppressives were overviewed in tertiary references; The Renal Drug Handbook 5$^{th}$ Edition and Renal Pharmacotherapy, 2$^{nd}$ Edition; 2021. Drug monographs; as PDR and Lexicomp were used, also pertinent studies published in PubMed, ScienceDirect, Research Gate, Elsevier, Springer and journals; as The American Journal of Transplantation. IMMUNO-PLANT was then developed and is currently available for iOS and android. Finally, the application was evaluated by a post survey, it was found to be highly effective, trusted and gives evidence-based fruitful knowledge by more than 80% of users, more than 90% would recommend it to their colleagues. Immuno-plant effectively offers organized scientific information to not only nephrologists but all healthcare workers using immunosuppressants.

**Keywords:** immunosuppressants, nephrology, renal transplant, IMMUNO-PLANT.

# PHS 107: Plastics Recycling: Challenges and Opportunities

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Plastics are inexpensive, lightweight and durable materials, which can readily be moulded into a variety of products that find use in a wide range of applications. As a consequence, the production of plastics has increased markedly over the last 60 years. However, current levels of their usage and disposal generate several environmental problems. Out of all the environmental hazards that our planet faces every day, pollution due to plastic industry takes the first place in killing our planet. There is a rising awareness of the severity of the plastic waste problem, and the implications of plastics accumulation in the environment. A major portion of plastic produced each year is used to make disposable items of packaging or other short-lived products that are discarded within a year of manufacture. In addition, because of the durability of the polymers involved, substantial quantities of discarded end-of-life plastics are accumulating as debris in landfills and in natural habitats worldwide. Plastics recycling is one of many solutions that have been proposed, that can be broadly defined by their relative simplicity, into primary, secondary, and tertiary processes. However, all the used recycling methods still can't deal with micro-plastics problem that badly affect the marine life and human beings every day. Several methods have been developed for the sampling, extraction, purification, identification, and quantification of microplastics in complex environmental matrices. Large microplastic particles can be sorted manually and identified through chemical analysis; however, sample preparation for small microplastic analysis is usually more difficult. Here, we intend to summarize recent research trends on the subject.

**Keywords:** Plastics, Recycling, Pollution, detection.

# PHS 108: Antimicrobial Activity of Chitosan Coated Silver Nanoparticles Against Multidrug-Resistant Bacteria

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The increase in multidrug-resistant (MDR) bacteria represents a true challenge in the pharmaceutical and biomedical fields. There is a great demand for research on the development of new potential antibacterial compounds. This study aimed to investigate the antibacterial effect of chitosan coated silver nanoparticles against multi drug-resistant bacteria. In this *in-vitro* experimental study, environmentally benign silver nanoparticles were synthesized using commercially purchased shrimp-shell chitosan as a capping agent. The synthesized chitosan-silver nanoparticles (Ch-AgNPs) were characterized by different methods of identification. The *in-vitro* cytotoxic activity of Ch-AgNPs was assessed using MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assay. The antimicrobial activity of (Ch-AgNPs) was evaluated against MDR *Escherichia coli, Klebsiella pneumonia, Pseudomonas aeroginosa, Acinetobacter baumannii and* methicillin-resistant *Staphylococcus aureus* (MRSA) using minimal inhibitory concentration (MIC) by broth microdilution assay. Results are still pending in the ongoing process.

**Keywords:** Chitosan-silver nanoparticles; Cytotoxicity; Antibacterial; MDR; MIC.

# PHS 109: Anti-obesity Products and COVID-19: A Cross-Sectional Study

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Obesity and COVID-19 are at the top of nowadays health concerns with significant crosstalk between each other. COVID-19 pandemic negatively affected healthy life-style and increased obesity prevalence. Thus, there was a surge in anti-obesity products (AOP) intake, even without medical consultation. Herein, we evaluated how the pandemic has affected slimming products efficacy and safety in patients seeking weight reduction at an urban, weight management centre in Alexandria, Egypt. In addition, the effect of AOP on COVID-19 infection severity was also appraised to detect whether AOP can alter COVID-19 host cell entry mechanisms (such as; Angiotensin-Converting-Enzyme-2 (ACE2) pathways) and subsequently affect infection severity. Patients were invited to complete anonymous survey. The survey assessed self-reported changes in weight, the use of AOP following issuance of social distancing/stay-at-home policies in 2020. Another inclusion criterion is being infected by COVID-19 during the course of receiving the AOP. A total of 462 participants completed our anonymous questionnaire between 16$^{th}$March-2022 and 16$^{th}$June-2022. Most of participants were females (450; 98.4%) with BMI ranging 24.98-58.46. Surprisingly, all participants administered AOP in all its forms without medical consultation. Of them, only 21.2% received FDA-approved AOP and the remainder received herbs with known slimming properties or non-FDA approved drugs. About 42% of patients participated in our survey got infected with COVID-19 during the course of treatment. Patients reported alterations in AOP efficacy and side effects following COVID-19 infection. Further, severity of COVID-19 symptoms were affected by the AOP. In conclusion, some administered slimming products used by participants maintained their efficacy and others showed decreased efficacy when continued post COVID-19 infection. In addition, some products developed more side effects post infection. In most cases, the use of AOP or herbs prior to or during the course of COVID-19 infection resulted in beneficial outcomes and patients experienced mild to moderate symptoms.

**Keywords**: COVID-19; Obesity; Anti-obesity Products; Angiotensin Converting Enzyme-2

# PHS 110: Triple Negative Breast Cancer Overview and Burden

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Cancer starts when cells begin to grow out of control. It ranks as a leading cause of death and an important barrier to increasing life expectancy worldwide. According to estimates from the World Health Organization (WHO) in 2019, cancer is the second leading cause of death below the age of 70 years in 112 of 183 countries after cardiovascular diseases. This study aims to highlight the epidemiological status for TNBC in Egypt along with the current diagnosis and treatment plan implemented in the region. In addition to spreading awareness for the general public. Globally, Cancer comprises an estimated **19.3 million** new cancer cases and almost **10.0 million** cancer deaths occurred in 2020. Breast cancer is a type of cancer that starts in one or both breasts and can spread to other organs. It has surpassed lung cancer as the most commonly diagnosed cancer, with an estimated 2.3 million new cases (11.7%), followed by lung (11.4%), colorectal (10.0 %), prostate (7.3%), and stomach (5.6%) cancers. About **1 in 8** women are diagnosed with breast cancer during their lifetime. Breast cancer is the 5$^{th}$ leading cause of cancer-related death comprising around 6.9% of all cancers. The global cancer burden is expected to grow to be **28.4 million** cases in 2040, a 47% rise from 2020. Triple negative breast cancer is an aggressive Subtype that accounts for 12-25% of all breast cancer cases. It lacks known surface receptors (Estrogen, Progesterone, Human epidermal growth factor HER2) making it unresponsive to the hormonal therapy. It has high metastatic potential and poor 5-year survival rate reaching 12%. Recently, it has been divided into 6 molecular subtypes, having relatively different features. Proper diagnosis and Subtyping to TNBC would direct the physician in his medication choice, adhering to the best medical practice, improving the prognosis.

**Keywords**: Molecular Subtype; Triple-negative breast cancer; Therapeutic target; Prognosis.

# PHS 111: Hospital Acquired Infection Caused of MRSA in Egyptian Hospital Prevalence and Treatment Options

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*Staphylococcus aureus* (*S. aureus*) is a Gram-positive facultative anaerobe that colonizes specific parts in human body. *S. aureus* causes various hospital-acquired and community- acquired infections. It is a pathogen with serious virulence and associated high morbidity. The emergence of many multidrug-resistant (MDR) strains especially methicillin-resistant *S. aureus* (MRSA) makes *S. aureus* related to many life-threatening infections. It can cause a wide range of illnesses ranging from minor skin infections, scalded skin syndrome, and abscesses, surgical wound infections following surgery to life-threatening diseases such as pneumonia, meningitis, osteomyelitis, endocarditis, toxic shock syndrome, bacteraemia, and sepsis. **Aim:** This study aimed to explore the prevalence and consequences of hospital-acquired infections caused by MRSA in Egypt during the last decade. In addition, alternatives and non-conventional treatment options to combat serious MRSA infections were suggested. **Method:** Published articles from Egypt related to the epidemiology of hospital-acquired MRSA during the last decade and non-conventional treatment options were collected through internet-based search in specialized journals and official scientific web sites (e.g. Scopus, PubMed, etc.) and the obtained data were statistically analyzed. **Results:** the prevalence of hospital-acquired MRSA infections has reached worrying levels in some areas in Egypt all over the last decade. These increased levels may be due irrational use of antimicrobial agents. Also, non-conventional treatment options have significant role in reducing treatment failure and resistance to antibiotic therapy. **Conclusion:** Over the last few decades, a significant rise in the prevalence of MRSA strains around the world has become a matter of concern and imposes serious economic costs on patients and health care. So finding alternatives and non-conventional therapy options to treat infection caused by MRSA to treat high prevalence of MRSA and disseminate antimicrobial resistance which leads to treatment failure, deterioration of disease and healthcare costs. Antimicrobial stewardships should be applied to reduce MDR pathogens.

**Keywords:** Hospital-acquired infection, MRSA, prevalence, Alternative and non-conventional treatments option.

# PHS 113: Extending the Therapeutic Utility of Celecoxib: Multi-target Modulators of COX-2, PPARγ and Tumor Associated Carbonic Anhydrase

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Metabolic diseases, such as type 2 diabetes, are becoming growingly prevalent and have a significant influence on global public health. It is widely acknowledged that chronic inflammation is a hallmark of metabolic disease. In this regard, diabetes-associated inflammation causes complications such as nephropathy, neuropathy, and retinopathy. Accumulating evidence reported that Such complicated disorders are preferably managed by multitarget modulators. In this work, we adopted a pharmacophoric hybridization strategy capitulating on a celecoxib analog merged with some propargyloxy benzylidene rhodanine/thiazolidinediones through 1,2,3-triazole linker. The resulting assembly is designed to modulate three inflammatory targets namely; COX-2, PPARγ and carbonic anhydrases. A common denominator for this set of molecular targets is their ability to address inflammation. Biological evaluation of this series of compounds will include testing of inhibitory activities against COX-1 and COX-2 enzymes as well as assessment of their safety profile based on their COX-1/COX-2 selectivity indices. Furthermore, PPARγ reporter gene assay will be conducted to confirm their partial agonistic activities. Besides, inhibitory activities against tumor associated-carbonic anhydrase enzymes will be assessed. Also, in vivo anti-inflammatory activity will be tested in an animal model. Docking simulations will be carried out in order to elucidate the binding affinities towards the studied targets. Taken together, this series is anticipated to serve as a powerful contribution to the currently existing anti-inflammatory agents.

**Keywords:** Metabolic diseases, Celecoxib, PPARγ, COX-2, carbonic anhydrase.

# PHS 114: Benzenesulfonamido Hydrazones as Open Chain Analogs of Celecoxib: Design, Synthesis, Biological Evaluation and *In Silico* Studies

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Pharmacotherapy for chronic inflammatory illnesses and persistent pain from varied origins remains a major obstacle. These conditions place a significant financial, social, and medical burden on society. Consequently, there is an imperative necessity to identify novel anti-inflammatory agents with new mechanisms of action and fewer adverse effects. In this work, it was tempting to design and synthesize some benzenesulfonamido hydrazones as open chain analogs of celecoxib by the condensation reaction of some functionalized acetophenone derivatives with (4-sulfamoylphenyl)hydrazine hydrochloride. Design of the resulting compounds was guided by computer-assisted drug design techniques such as flexible alignment and molecular docking simulations using celecoxib as a reference. The resulting hydrazones were designed to bear some properly selected functional groups, that could be utilized as building synthons in other synthetic drug discovery approaches. The target compounds will be characterized by several spectroscopic techniques such as 1H-NMR, C13-NMR, and mass spectroscopy. The purity will be also assessed by HPLC analysis. Biological evaluation of the target hydrazones will entail the evaluation of their COX-1 and COX-2 inhibitory activities together with determination of their selectivity indices COX-1/COX-2, in comparison to celecoxib. Hopefully, this series of hydrazones could provide us with some functionalized COX-2 inhibitor scaffolds capable of being derivatized into more bioactive anti-inflammatory agents. Moreover, their synthetic routes could serve as a foundation for the development of more versatile open chain analogs of celecoxib for further medicinal chemistry diversification strategies.

**Keywords:** Anti-inflammatory, Celecoxib, COX-2, Computer-assisted drug design techniques.

# PHS 115: Evaluation of Effectiveness and Shortcomings of Targeted Therapy for Breast Cancer patients

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Breast cancer is an abnormal cell growth that develops in the breast and can spread throughout your body and destroy healthy body tissue. Despite cancer being the second leading cause of death globally, survival rates for many cancer types are increasing as a result of progress in cancer screening, therapy, and prevention. Breast cancer is the most frequently diagnosed cancers among women, it can also affect men. As of 2021, it accounted for 12% of all annual new cancer cases worldwide, making it the most prevalent cancer in the world according to WHO. Breast cancer can begin in different parts. Ductal cancer, which starts in the milk duct epithelium, accounts for 85% of cases. Lobular cancer, which starts in the lobules of the glandular tissue of the breast, accounts for 15% of cases. Invasive ductal carcinoma constitutes around 80% of all breast cancer cases (IDC). In most cases there are no symptoms however it can be detected by screening mammogram, it might be felt as a lump in the breast. The stage of IDC is determined by the cancer characteristic that helps the doctors in identifying the best treatment option. Surgery, chemotherapy, and targeted therapy are all forms of treatment. Targeted therapies are generally less harmful to healthy cells than chemotherapy. It targets specific characteristics of cancer cells such as HER2 gene. Enhertu, Physego are HER2 inhibitors used to treat all stages of HER2-positive breast cancer. Newer class CDK4/6 is used to treat metastatic cancer that has spread to bones or liver such as Ibrance, Kisqali. Through computer-aided drug design, which accelerates the development process, we hope to increase the efficacy of these medications while lowering their adverse effects and costs.

**Keywords**: Breast cancer, breast cancer statistics, invasive ductal carcinoma, new targeted therapy, downsides.

# PHS 116: In Silico Computational Study to Identify Potential Dual Acting SARS-CoV-2 Proteases Inhibitors: Two Birds with One Stone

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The quick identification of therapeutic candidates is crucial due to the growing worries regarding the rapid rise of COVID-19 globally. An enormous amount of work has been put into finding potential new medications to treat SARS-CoV-2 illness. Remdesivir is the only approved FDA drug targeting Mpro. thus, there is a strong demand for drug repurposing which appears to be highly impressive for developing effective medications quickly. Inhibition of the major proteases (Mpro and PLpro) is considered one of the primary options for COVID-19 treatment among all suggested research guidelines. Our research group aims to perform a computational study to predict potential candidates for the treatment of SARS-Cov-2 with dual inhibitory activity towards Mpro and PLpro. We investigated in silico activity of twenty analogs of indole-peptidomimetic candidate with Mpro ($IC_{50}$ = 1.72 μM) and PLpro ($IC_{50}$= 67 μM) from PubChem database inhibitors of Mpro (6LU7) and PLpro (7JIW). The molecular docking study was performed using BIOVIA-Discovery Studio 2020. Furthermore, structure-insilico activity relationship was established to get insights on the essential pharmacophoric features of the retrieved compounds. ADME study were conducted to identify the analogues with drug like properties. The results illustrated that several analogues afforded good binding affinity towards Mpro and PLpro which indicates these compounds may possess promising Mpro and PLpro inhibitory-like activity.

**Keywords**: Papain-like protease (PLpro), Main protease (Mpro), COVID-19 drug candidates, Molecular Docking.

# PHS 117: Pain Management in Non-Cancer Patients

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Pain is still one of the most challenging prevalent problems, pain is classified into two categories: acute and chronic, depending on its duration and time course, acute pain is defined as "pain which has a sudden onset with varied intensity lasting for less than six months"and Chronic pain is defined as "pain that lasts for more than six months which may or may not have an underlying pathology to explain the patient's suffering", there is also another classification according to the origin of pain into nociceptive pain and neuropathic pain, pain management is complex due to several causes, including the mechanisms of pain, classification, individualization, knowledge, psychological and social factors, pain management is well known since many decades, It has been improved a lot lately and is starting to involve plenty of diverse methods. Certainly, the management of pain is a multidisciplinary task, and it depends on the origin of the pain.

**Keywords:** pain management, acute pain, chronic pain, nociceptive pain, neuropathic pain.

# PHS 118: Statins' Repurposing: Cancer Treatment and Recent Formulations

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Drug repurposing involves the exploration of new uses for existing drugs, which effectively reduces the drug development timeline and its cost. We aim to illustrate some published data for statins' repurposing formulations used in cancer treatment. **Atorvastatin** (ATS) with vinpocetine optimized solid lipid nanoparticles for hepatic cancer therapy showed acceptable particle size, stability, % EE and controlled growth of melanoma B16 F10 cell lines. In another study, the impact of mannitol as a binder to improve the inhalation deposition of the ATS dry microparticles was examined for treatment of lung cancer. For inhalation therapy, the formula's particle size and aerosol performance met the criteria. Compared to the free AVT, the cellular uptake of the AVT-mannitol formula in A549 cells was enhanced. **Simvastatin** (SIM) nanoparticles were evaluated for the treatment of colorectal cancer by combining pH-sensitive and timed-release approaches of the polymeric coat. The coated capsules had no release in the gastric media. The cytotoxic effect of the SIM nanoparticles was increased compared to the free SIM. In another study, blended polymeric films containing SIM and resveratrol (RSV)showed a cytotoxic synergistic effect of RSV and SIM in melanoma cell lines. Repurposing **lovastatin** (LV)cytotoxicity against the tongue carcinoma HSC3 cell line using the eucalyptus oil (Eu)-based nanoemulgel carrier was optimized. Nanoemulsion had an acceptable droplet size and stability index. The *in vitro* cell viability studies revealed the synergistic cytotoxic effect of LV and Eu on cancer cells. For **rosuvastatin**, the optimized self-nano-emulsifying formula for hepatocellular carcinoma showed an acceptable globular size, stability, and increased cell death by both apoptosis and necrosis. Challenges for repurposing include drug re-formulation that differs from that is originally approved by the FDA, the delivery system, and the route of administration. Thus, studying drug pharmacology and the intended way of repurposing is recommended.

**Keywords**: Repurposing, Statins, formulations, cancer.

# PHS 119: Human Gut Microbiota: A Constant and Changing Choreograph

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Gut microbiota consists of a diverse microbial community, including bacteria, viruses, archae and eukaryotes that colonize the human gastrointestinal (GI) tract and interact with the human body in multiple ways in health and diseased states. These interactions are complex to the point that the host and its microbiota are together considered a “superorganism”. Each individual possesses a unique microbiota profile that develops as early as birth or even in-utero. Likewise, within each individual the composition of the gut microbiota may vary with age and life incidents. Imbalance in the gut microbiota composition, known as dysbiosis, has been linked to multiple metabolic disorders. In this review we describe the main families that comprise a healthy human gut microbiota and highlight the variation in relative abundance of several taxa of the gut microbiota in diseased conditions. We also explain the different factors affecting this microbial profile such as the anatomical region of GI tract, the mode of delivery (vaginal vs C-section), aging, hormones, lifestyle, antibiotic exposure and diet. Furthermore, we focus on the metabolic products of these organisms as a possible route of interaction between the microbiota and the host shedding light on the current understanding of the link between dysbiosis and several metabolic pathological conditions. The effect of the produced metabolites on different physiological and pathological pathways will be discussed, in an attempt to pinpoint the metabolites that can be targeted as diagnostic biomarkers for the determination of propensity to develop diseases in as-of-yet healthy individuals.

**Keywords**: Microbiota, Composition, Metabolites, Metabolic disease, Biomarker.

# PHS 120: Antibiotic Use Tracking Application

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The irrational and widespread use of antibiotics caused pathogens to develop resistance to their action. Antibiotic resistance is making treatment of infectious diseases more difficult. In Egypt, many people consume antibiotics unwisely, due to lack of awareness and the availability of most antibiotics on the shelf without the need for a prescription. In order to set up surveillance of antibiotic use, we are designing a prototype mobile application to track antibiotic consumption in the community. The application will track antibiotics purchase rate as well as how they are being consumed by the patients. To incentivize the patients to use the application, it will be equipped with a built-in alarm system to remind the patients to take the antibiotic on time as well as a reminder of the dose they need to take to avoid missing doses. This was based upon the results of a survey conducted to assess what tools patients need to improve their drug compliance. To start using the application, the patient needs to set up a profile that can be updated by the pharmacist at the time of antibiotic purchase. As such, the application will track the classes and volumes of antibiotics consumed in the community, in addition to helping patients comply with their dosing regimen. That profile will also contain patient diagnosis, site of infection and patient co-morbidities such as: diabetes, hypertension and liver or kidney dysfunction in addition to the concomitant identifying the presence or absence of a culture and the result of the culture if present. On the other hand, the de-identified usage data collected by the application will provide public health surveillance tools to determine the actual rates of antibiotic use in the community. This is an integral step towards the design of antimicrobial stewardship plans to limit further evolution of antibiotic resistance.

**Keywords**: antibiotic, antibiotic tracking, antibiotic resistance, mobile application, health authorities, healthcare.

# PHS 121: Association Between Different *Staphylococcus aureus* Virulence Factors and Their Pathogenicity to Host Cells

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*Staphylococcus aureus* is a gram-positive bacterium that can be either commensal or pathogenic to humans and animals. The rising trends of antibacterial resistance in this species due to the indiscriminate use of antibiotics threaten our ability to treat the various clinical conditions that it causes. Targeting the virulence factors used by these bacteria to cause diseases is a promising alternative approach to treat resistant infections. The aim of this study is to determine the relative prevalence of different virulence factors among staphylococcal clinical and commensal isolates belonging to different genotypes and to link them to the isolates' pathogenesis. We analysed whole genome sequencing data to determine the presence or absence of several virulence factors genes at the Deoxyribonucleic acid (DNA) level. Moreover, we investigated the pathogenic potential of the collected isolates to the host cells using different cell culture infection models; bacterial adhesion of the various isolates was investigated in an A549 lung cell line and the adherent bacterial cells were counted. Cytotoxicity was assessed using the MTT assay on the same cell line. Here, we show the relationship between each of the virulence factors and how they contribute to host pathogenicity. Moreover, we provide a comprehensive analysis of the difference between commensal and clinical staphylococcal isolates in terms of their virulence and cytotoxic effects. Our data indicate the importance of exploring new anti-virulence strategies as an alternative and emerging approach to treat drug resistant *S. aureus.*

**Keywords:** Staphylococcus aureus, Antibacterial resistance, Pathogenicity, Adhesion, Cytotoxicity, Cell culture, A549 cell line.

# PHS 122: PAMT: Online Pain Assessment and Management Tool

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Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”. Mostly, pain is underestimated by healthcare providers. In addition to lack of pain assessment leading to poor management which negatively affects patient’s outcomes, quality of life, and satisfaction. According to recent study by GSK (2020), One third of the population is in pain every day and 1 in each 5 suffers chronic pain for population under 30 years old. Pain is not restricted to age and disease. However, women, older persons, and rural residents are significantly more likely to report pain. Therefore, the purpose of this review was to create a helpful tool for healthcare providers through online platform (PAMT) which uses recent guidelines and monographs to assess and ease managing patient’s pain. This platform focuses on all Pain relievers with its different classes Anti-inflammatory (NSAIDS and Paracetamol), Opioids, Antidepressants, and Adjuncts (anticonvulsant, muscle relaxant). It starts with assessing the pain type and intensity, then forwarded to a checklist with patient’s history to help choosing the best drug for each case with its indicated dose taking into considerations the dose modifications for renal or liver impairment. Another important feature is to check the interactions and side effects to give results with a suggested list of appropriate medication for each case.

**Keyword**: Pain, Pain assessment, Pharmacological pain management, Pain relievers, Medical online platform.

# PHS 123: Antibiotic Use in the Community, A Reason for Concern? Results from Alamein, Egypt

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In most low to middle-income countries, community pharmacies are considered the patients' first destination for seeking healthcare; and the pharmacist is considered a haven for pharmaceutical advice. In Egypt, antibiotic use is under-regulated, and patients can purchase antibiotics with or without a prescription. Many patients present to the pharmacy complaining from various infectious disease symptoms and ask for the pharmacist' advice on which antibiotic to take. Yet, many more self-prescribe antibiotics. We are conducting a cross-sectional study on 10 pharmacies representing the main drug purchase outlets in Alamein, Egypt to assess antibiotic dispensing patterns. Clinical pharmacy students observed antibiotic dispensing patterns in the participating pharmacies for three hours and/or interviewed pharmacists/pharmacy assistants at each pharmacy to collect data on antibiotic dispensing. About 37% of the patients presenting to the pharmacies purchased antibiotics based on a prescription, 30.5% of the patients took antibiotics based on pharmaceutical advice and the rest of the patients self-prescribed the antibiotics. Analyzing the antibiotics in demand in the participating pharmacies revealed that β-lactams were the most demanded class at 56%, followed by the fluoroquinolones at 16.5%. It was noteworthy that none of the patients purchased polymyxins, a class of agents considered last resort options to treat multidrug resistant infections. Two-thirds of the patients purchased antibiotics on medical or pharmaceutical advice. We recommend education programs targeting the general public to raise awareness about antibiotic misuse hazards and to promote safer antibiotic use patterns, particularly in rural areas.

**Keywords**: Pharmacy; Dispensing; Antibiotics; Cross-sectional.

# PHS 124: Toxicological Events, Their Occurrence and Prevention: An Awareness Campaign

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**Introduction**: Poisons are proved to contribute significantly to the mortality and morbidity rate of the general populations. There are diverse factors that contribute to the epidemiology of toxicological events which differs from one country to another such as educational, socioeconomic levels and availability of certain poisons. Therefore, special epidemiological surveillance for each country is necessary to determine the problem according to which preventive measures can be taken. Due to the significant impact of this issue we aim to raise the public awareness towards common pharmaceutical & household toxidromes. **Methods:** The aim of our project is to assess the knowledge of population about handling most common toxicological events, to correct any misconceptions about managing toxicological events and to increase the safety measures against toxins or toxidromes. Identification of toxicological events of highest occurrence was based on retrospective information gathered from several studies conducted in Egypt and other countries as well. **Results:** The main goal of the campaign is to analyze the knowledge of the general population regarding the handling and prevention of toxicological events and correcting the correcting the misconceptions of handling toxicity patients. This is achieved due to the analysis of the difference between males and females in regard to occurrence of toxicological incidents. In addition, a correlation between certain age groups and toxidromes had been made. Altogether lead to the provision of a brief but effective awareness concerning common poisons and how to prevent the occurrence of toxicological events. **Conclusion:** Toxicological events are considered to be representing a threat to public health. In addition, it represents an economic burden. Ingestion was the main route of poisoning and suicidal poisoning predominated. Corrosives and detergents were the most commonly involved toxic substances while centrally acting drugs topped the list of drug poisoning.

**Keywords:** Epidemiological Surveillance, Preventive Measures, Public Awareness, Toxidromes.

# PHS 125: Role of Glycogen Synthase Kinase-3β as a Modulator of Canonical WNT Signaling in Adipose Tissue Dysfunction in Obesity and Related Metabolic Disorders

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Individuals with the metabolic syndrome are at higher risk for the development of cardiovascular disorders. The latter is related to visceral adipose tissue dysfunction and the existence of a crosstalk between adipose tissues and the cardiovascular system. In the metabolic syndrome, adipose tissue dysfunction has been linked, at least in part, to increased hypertrophy, reduced vascularization, and hypoxia of adipocytes, precipitating in a pro-oxidative and pro-inflammatory environment. The canonical wingless-type mammary tumor virus integration site family (WNT) signaling pathway involves activation of β-catenin which drives its translocation to the nucleus and is reported to inhibit adipogenesis. Canonical WNT signaling is also implicated to play a role in mature adipocyte hypertrophy and browning of white adipose tissues. Several modulators of the canonical WNT signaling have been discovered to play a role in the pathogenesis of metabolic disease. Glycogen Synthase Kinase-3β (GSK-3β) belongs to β-catenin degradation complex and its expression is thus associated with the induction of adipogenesis. GSK-3β was reported to be increased in obesity and related metabolic disorders and its inhibition was linked to improved insulin resistance. Interestingly, the latter was shown to be related not only to suppressed differentiation of adipocyte precursors but also to reduced visceral adipose tissue inflammation secondary to altered macrophage and secretory profiles. Elevation of GSK-3β could thus present a link between adipose tissue dysfunction and the development of cardiovascular disease in the metabolic syndrome.

**Keywords:** GSK-3β, metabolic syndrome, adipogenesis, adipose tissue inflammation.

# PHS 126: Psoriasis from the Point of View of Patients and Healthcare Professionals: A Survey and Awareness Study

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Psoriasis is a chronic inflammatory skin disease presenting as red scaly plaques in the form of patches with no joint involvement. It has significant effects on the quality of life due to its psychological and social consequences and employability as well. There are varieties of treatment options including topical, phototherapy and biological systemic or non-systemic treatments. We had the opportunity to collect data about the opinion of different involved personnel like pharmacy students, patients and healthcare professionals specialized in the field of dermatology especially the treatment of psoriasis. An electronic survey was conducted including questions about the etiology of disease, symptoms, diagnostic tests, treatment, and patients' compliance to therapy protocols. This study aims to using the data obtained from the survey and utilize it to hold an awareness campaign targeting patients in addition to healthcare/pharmacy students aiming to increase the patient's quality of life by spreading awareness about psoriasis so that these patients will not be rejected or exposed to bullying. Awareness also aims to accentuating patient's acceptability to the disease and the treatment.

**Keywords**: psoriasis, phototherapy, scaly dermatosis, patients.

# PHS 127: Prevalence of COVID-19 Infection, Acute Symptoms, and Vaccine Acceptance in a Representative Egyptian Cohort

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The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2), is an unprecedented global health crisis. Since its outbreak at the end of 2019 until September 2022, there have been more than 600 million confirmed COVID-19 cases and more than 6.5 million deaths, worldwide. In Egypt, there have been more than 510 thousand confirmed cases and more than 24 thousand deaths since the beginning of the outbreak. People who fall sick with COVID-19 most probably experience mild to moderate symptoms and recover without special treatment. However, COVID-19 can lead to serious illness and even death. Additionally, some people remain sick even after the end of the acute course of the infection and can develop a disability. Thus, further studies are needed to understand the epidemiology of COVID-19 in Egypt in order to help guide the implementation of successful preventive measures. There have been limited studies that report antibody prevalence in vaccinated individuals, and they are mostly restricted to select vaccine types. Our objective was to compare the responses of individuals vaccinated against COVID-19 with any of the major vaccine types available worldwide and to study their effectiveness to protect against subsequent infection and disease severity. Using personal interviews, we show the rate of infection as well as the prevalence of acute COVID symptoms in a representative sample of the Egyptian population. Moreover, we illustrate the acceptance rate of different COVID-19 vaccines and the coverage of different vaccine types administrated in Egypt. Altogether, our study helps answer many questions related to the current pandemic and sheds the light on the protective role of the seven different COVID-19 vaccines available worldwide.

**Keywords:** SARS-Cov-2, vaccines, Egypt, COVID-19.

# PHS 128: AI in Drug Discovery: Advances and Assessment

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Drug discovery is a complex, multi-step, resource-intensive procedure that moves from target identification to lead identification then lead optimization, and finally candidate selection. Despite the fact that in 2019 the pharmaceutical industry spent $83 billion on R&D, yet almost 90% of drugs fail to reach clinical trials, contributing to large capital losses. Nowadays, a multitude of computational methods is routinely applied by the vast majority of major research organizations and pharmaceutical companies to accelerate the speed of drug discovery innovation. Furthermore, a wide variety of tools from the fields of data science and machine learning has been adopted by the drug discovery community to deal with the issue of handling the large amount of data generated with any meaningful drug discovery project, forming the basis of what we know today as the field of Cheminformatics. In a nutshell, Cheminformatics links computational information and chemical data. Since introduced in 1998 by Brown FK, Cheminformatics aims to utilize information science to solve problems in the field of chemistry to make better and faster decisions in drug discovery. In this work, we summarize some state-of-the-art Cheminformatics methods and their applications in drug discovery along with presenting some examples of works that have been conducted using these methods, demonstrating their potential to reform the paradigm of drug discovery. Additionally, we present some advantages and limitations with respect to the currently used methods. This aims to familiarize researchers and medicinal chemists with these new technologies and their benefits, also their great impact on collaborative research, as most of these methods are open access and with minor modifications, they can fit any experiment, saving time and effort.

**Keywords**: AI, drug discovery, cheminformatics, algorithms.

# PHS 129: Pharmacist Survey on Their Knowledge and Use of Herbal Supplements in Egypt

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Herbal medicine has long been a hot commodity within the Egyptian populace, with its earliest use dating back as early as the ancient Egyptians. Community pharmacists are at the forefront of healthcare consumerism and therefore, are in direct contact with the masses. In some communities, pharmacists are recognized as the sole healthcare provider available. As such, and due to the ever-increasing demand of herbal medicine, it is vital that pharmacists' knowledge regarding herbal supplements are kept in check. An anonymous, interview-based structured survey was conducted to assess pharmacists' personal/professional practice, recommendation pattern and knowledge. It has been found that herbal supplements are sold at all pharmacies, and many consider it an important source of the pharmacy's revenue. The majority of pharmacists surveyed denied asking patients about their medical history prior to dispensing a herbal supplement. Moreover, pharmacists rarely asked for a prescription when dispensing a herbal product. The work at hand sheds light on the shortcomings of Egyptian community pharmacists when it comes to herbal supplements; there is significant room for improvement. We can fill the gap present through workshops and educational courses.

**Keywords:** Herbal supplement, Community pharmacist, Pharmacist knowledge, Pharmacist survey, Complementary and alternative medicine.

# PHS 130: In Silico Repurposing of FDA-Approved Anthelmentics Niclosamide and Nitazoxamide in Treating Covid19 and Their Comparability with Approved Antivirals

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The 2019 Coronavirus Disease (COVID-19) is a highly contagious illness that have infected a lot of people causing high rates of morbidity worldwide turning mostly to a pandemic. The disease is caused by SARS-CoV-2 virus resulting in severe acute respiratory syndrome, hyper-inflammatory response, vascular damage, angiogenesis, and thrombosis. The recently discovered disease has drawn researchers to find an actual cure including different pharmacological classes such as; Antiviral medicines, inflammatory inhibitors, low-molecular-weight heparins and hyper-immune immunoglobulins. However, no treatment has shown extreme efficacy in curing the disease. There is an urgent need for the discovery of new medications to treat and control the spread of this illness where new SARS-CoV-2 variants are continuously developing. Numerous therapy modalities have been investigated for COVID-19 treatment, some of them showed promising results and the others might have been tried out of desperation. Niclosamide and Nitazoxanide, The FDA-approved anthelminthic medications, have been shown to be effective against several viral infections with nanomolar to micromolar potency, including SARS-CoV, MERS-CoV, ZIKV, HCV, and human adenovirus. This finding suggests the drugs' potential as Antiviral agents. Also, Many antiviral drugs with different mechanisms have shown great efficacy in treating COVID-19 such as: Molnupiravir, Remdesivir and Nirmatrelvir. In this brief study, we assure Niclosamide's and Nitazoxanide's potential clinical application in the management of COVID-19 in addition to drawing a comparison between both Anthelmentics and Antiviral agents and their ability to treat the virus. By reducing the time and expense involved, computer-aided drug design has contributed to the acceleration of the drug discovery and development process. We aim to improve the drugs' downsides digitally and by simulation to enhance its efficacy for future synthesis and release into the market with their latest potentiality.

**Keywords**: covid 19, anthelmentic repurposing, niclosamide, nitazoxamide, antiviral comparison, in silico drug design and improving downsides.

# PHS 131: Management of Coagulopathy Problems in Critically Ill Cancer Patients

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Coagulopathy is a critical condition in patients with cancer. Thrombocytopenia could be induced by chemotherapy or radiation or as a result to specific types of cancer as leukaemia. A challenge comes when patients are critically ill existing in Intensive care unit (ICU) where exposure to infection is common. Infection activates neutrophils producing thrombosis, resulting in sepsis- induced disseminated intravascular coagulation (DIC). The latter is also associated with malignancy. The prevalence of DIC in advanced malignant diseases is 21%. Thus, bleeding risk due to thrombocytopenia together with the probability of thrombosis makes the decision about prophylactic anticoagulant as well as anticoagulant for treatment challenging. Our project aims at determining the prevalence of coagulopathy among critically ill cancer patients in Alexandria medical university hospital. As well as that following up patients' lab tests including the following markers: PT-INR, PTT, WBCs, Serum albumin. Also, determining the best approach concerning suitable drug and adverse reactions for managing thrombocytopenia and DIC in different patients. We are also willing to estimate physicians' knowledge about best approaches for management followed by physician education by means of either newsletters or through onsite sessions. Furthermore, we are aiming at assessing the effectiveness of our project through collecting data about the changes our project made in ICU clinical practice. For the sake of patient safety and drug efficacy, a balance between risk of bleeding and thrombosis will be provided through valid scores including SIRS, ISTH and HEP scores.

**Keywords**: Thrombocytopenia; Cancer; Critically ill; Guideline.

# PHS 132: Stress Complications

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Walking into everyday life, we experience worry and fear in different scenarios, that eventually result in our bodies acting differently from how they're destined to; these actions are all a response to what we call Stress. Stress is a condition of an emotional or physical tension that results from any situation that gets you out of your comfort zone. But what if the body constantly reacts as if there's a giant animal chasing you? there comes the major problem; chronic stress. It can be manifested by variable signs that mainly take place due to the release of a hormone called "Cortisol", which ultimately contributes to shifting of neural connections in different parts of the brain, suppressing the immune system's effectiveness, leading to cardiovascular abnormalities etc. Consequently, these functional changes contribute to further major complications and diseases. Chronic stress is classified into different classes, such as; Emotional stress (difficult emotions such as anger, sadness, or frustration), Environmental stress (where you live and work), Relationship stress (how you relate to friends, family, co-workers, partners and Work stress (challenges and pressures related to your job). In this study, we elucidated the specific mechanisms of how stress affects different body parts and the linkage between different respiratory disorders and chronic stress. In addition, we imparted the difference between chronic stress, anxiety disorders and how they can overlap leading to further mental complications such as depression. We adopted the use of a questionnaire in our research to anticipate the knowledge of the public regarding the hazardous effects of chronic stress. Furthermore, we discussed the relationship between the physical and psychological states, and what adaptive responses can worsen or improve the symptoms of stress. All in all, because chronic stress is so prolonged, it can have a detrimental impact on your health and well-being if left untreated. However, different treatment options exist, and, according to the results of the questionnaire, there's a reasonable number of the public audience that recently became aware of the coping mechanisms and how to deal with different stressors, especially after the experience of the COVID-19 Pandemic.

**Keywords:** Stress, cortisol, mental and physical state, complications.

# PHS 133: Appropriate Medication Prescription for Hemodialysis Patients: Development of New Criteria

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End stage kidney disease (ESKD) patients on maintenance hemodialysis (MHD) have multiple comorbid conditions that often require pharmacologic therapy. The complex medication regimens and polypharmacy in those patients may cause many unfavorable drug related problems (DRPs) that may result in reduced quality of life, higher cost of care, morbidity, and mortality. There is little information about potentially inappropriate prescribing (PIP) in patients on dialysis. Several studies tried to implement criteria designed mainly for identification of PIP in geriatrics such as criteria of Screening Tool of Older Person's inappropriate Prescription (STOPP)/Screening Trial to Alert Doctor to Right Treatment (START), or the Beers Criteria. These criteria can offer a framework for the development of tools for PIP management for the dialysis population. The aim of this study is to assess the PIP in ESKD patients on MHD and to develop new criteria designed specifically for dialysis patients. In this single center, cross-sectional study, we recruited adult patients who had received outpatient HD for at least 3 months. We reviewed medical records reviewed to identify PIP according to the explicit tools Beers list and STOPP/START criteria, implicit tools as Medication Appropriateness Index, and specific renal guidelines and recommendations. Data were collected, analyzed, and used to develop new criteria designed specifically for hemodialysis patients. Our findings revealed the need for specific tools for PIP management for patients on hemodialysis. We developed the first criteria for identification and management of PIP in hemodialysis patients. We added sections for topics not covered by other criteria, such as anemia, hyperkalemia, and vaccination. Implementation of this criteria can decrease the risk of DRPs and improve patient's quality of life.

**Keywords**: Hemodialysis; potentially inappropriate prescribing; polypharmacy; geriatrics.

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