مؤتمر الكويت الدولي السابع للصيدلة

7th Kuwait International Pharmacy Conference

(KIPC 2019)

5-7 March, 2019 - Salwa Al-Sabah Hall

Marina Hotel, Kuwait

Theme: Medicines – From discovery and delivery to optimal use
Under the Patronage of President of Kuwait University

www.KIPC2019.com

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General Information

Conference Date & Venue
5-7 March, 2019 at Salwa Al-Sabah Hall; Marina Hotel, Kuwait

Inaugural Ceremony
5th March, 2019: 4.00 pm by the Prof. Hussein Ahmed Al-Ansari; Honourable President of Kuwait University

Plenary Lectures, Workshops & Exhibitions
5-7 March, 2019 at Salwa Al-Sabah Hall; Marina Hotel, Kuwait

Gala Dinner
5th March, 2019; 7.00 pm at Salwa Al-Sabah Hall; Marina Hotel, Kuwait

Conference Closing Ceremony
7th March, 2019; 4:30 – 5:00PM: Closing Ceremony - Marina Hotel

Registration Desk
For registration and any enquiries or assistance, please proceed to the Registration Desk near the Salwa Al-Sabah Hall; Marina Hotel, Kuwait

CME/CEPD Credits
Registration Number: 001639/LABI. /Mar19; Cat 1

Title of Activity:	7th Kuwait International Pharmacy Conference
Scheduling:	March 5-7, 2019
CME Organizer:	Dr. Jamshaid Iqbal

CME/CPD Credits:

Lectures:	*Category 1: 15 Credits*
Poster Presentations:	*Presenting Author: 1 credit*
	Co-author: 0.5 credit

Chairperson's Welcome Message

On behalf of the organizing committee, it is my pleasure to welcome you to attend the 7th Kuwait International Pharmacy Conference, scheduled during March 5-7, 2019 at Salwa Al-Sabah hall, Marina Hotel, Kuwait. This year's theme of this biannual conference will be: Medicines – from discovery and delivery to optimal use. The conference, composed of two tracks, will include contemporary issues and developments from basic pharmaceutical sciences to pharmacy practice.

This three day event will be dedicated to cover a wide spectrum of sessions related to drug discovery and development as well as pharmacy practice, and will feature keynote forum, plenary sessions, presentations, panel discussions, poster session, and a workshop. We are delighted to have 13 outstanding international speakers from distinguished universities/institutions in Canada, USA, UK, Germany, Saudi Arabia, and Oman, in addition to several local speakers from Kuwait University and Ministry of Health. Therefore, this congress will provide a unique opportunity to gain new knowledge, exchange experience and establish contacts.

We hope that you will consider attending and contribute to the success of this meeting.

We look forward to seeing you all in Kuwait and wish you a pleasurable experience!

Sincerely,
Fatma Al-Awadhi, B.Pharm., Ph.D.
Chairperson of the organizing committee
Assistant Professor
Department of Pharmaceutical Chemistry
Faculty of Pharmacy, Kuwait University

Message from Dean

Dear Colleagues,

It is my pleasure to welcome you to Kuwait. The seventh international congress of our Faculty of pharmacy brings together the science and the practice that makes our profession unique. Medicines are complex therapeutic modalities and pharmacists today are uniquely trained in fundamental research to understand this complexity and to optimize their usage in an evidence-based manner. They are the medication therapy experts. The conference opens a window on the major scientific disciplines that are the underpinning of pharmacy like pharmaceutical chemistry, pharmaceutics and pharmacology. International and local speakers will bring their research to life, for the advancement of knowledge and improvement of lives. In addition, the conference will offer a unique opportunity for local and international speakers to discuss the state of pharmacy practice in the country and to develop a series of recommendations to support its evolution in Kuwait. As Kuwait is moving towards ambitious goals in its 2035 New Kuwait vision, scientific research and relevant education will be at the core of this transformation. We hope that this blend of science and its application, as well as the challenges that face the evolution of pharmacy practice in Kuwait will appeal to you so that we can count on your active participation. I wish all participants a great congress and I hope that the social activities will continue to bring us closer together and improve our international collaborations in science, education and the support of the professional evolution.

Pierre Moreau, B.Pharm., Ph.D.
Professor and Dean; Faculty of Pharmacy
Health Sciences Center; Kuwait University

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Chairperson; Department of Pharmaceutical Chemistry
Faculty of Pharmacy

Prof. Pierre Moreau
Dean; Faculty of Pharmacy

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Co-Chair; Department of Pharmacology and Therapeutics

Dr. Bedoor Qabazard
Chair sub-committee;
Department of Pharmacology and Therapeutics

Dr. Sarah Al-Ghanem
Chair sub-committee; Department of Pharmacy Practice

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Member; Department of Pharmacy Practice

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Member; Department of Pharmacology and Therapeutics

Prof. Pierre Moreau
Member; Department of Pharmacology and Therapeutics

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Director, Centre for Medical Education

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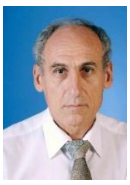
Ms. Leya Jacob Computer Engineer	**Ms. Mariam Saleh Al-Najadah** Medical Secretary

International Speakers

Prof. Ahmed Al-Jedai *Deputy Minister for Therapeutic Affairs, Ministry of Health, Riyadh, Saudi Arabia*	
Prof. Hendrik Luesch *College of Pharmacy, University of Florida, USA*	
Prof. Raymond John Andersen *University of British Columbia, Canada*	
Prof. Rolf Müller *Helmholtz Institute for Pharmaceutical Research Saarland, Germany*	
Prof. Shaker A. Mousa *Albany College of Pharmacy and Health Sciences, USA*	
Prof. Zubin Hosie Austin *Leslie Dan Faculty of Pharmacy, University of Toronto, Canada*	
Prof. Fars Alanazi *College of Pharmacy, Kind Saud University, Saudi Arabia*	
Prof. Nigel Pyne *Strathclyde Institute for Pharmacy and Biomedical Sciences, University of Strathclyde, UK*	
Prof. Susan Pyne *Strathclyde Institute for Pharmacy and Biomedical Sciences, University of Strathclyde, UK*	
Prof. Gamal Eldin Harisa *College of Pharmacy, Kind Saud University, Saudi Arabia*	

Dr. Abdullah Al-Sultan *College of Pharmacy, Kind Saud University, Saudi Arabia*	
Dr. Alison Thomson *Strathclyde Institute for Pharmacy and Biomedical Sciences, University of Strathclyde, UK*	
Ph. Thamna Al Shibani *Clinical Pharmacist, Oman*	
Ministry of Health Speakers	
Dr. Haifa Hamid Glom Ali *Quality Physician at the Safety Department*	
Dr. Monther Al-Sharekh *Head, Nephrology Unit Chest Hospital, Kuwait*	
Dr. Reem Al-Essa *Inspection Dept, Ministry of Health, Kuwait*	
Dr. Mohammed Al-Enezi *Life Sciences Academy, Kuwait*	
Dr. Saja Almatrook *Ministry of Health, Kuwait*	
Ph. Donia Bastaki *Head of Drug Registration Kuwait Drug and Food Control Administration*	
Ph. Nour Al-Khalaf *Pharmacist, KOC hospital, Kuwait*	
Ms. Rania Azmi *President, "Fadia Survive & Thrive Association - Supporting Cancer Patients" and Wharton Board*	

Kuwait University Speakers

Prof. Ahmed El-Hashim *Faculty of Pharmacy, Kuwait University*	
Prof. Jassim Al-Hassan *Faculty of Science, Kuwait University*	
Prof. Kamal Matar *Faculty of Pharmacy, Kuwait University*	
Prof. Ludmil Benov *Faculty of Medicine, Kuwait University*	
Prof. Oludotun Phillips *Faculty of Pharmacy, Kuwait University*	
Prof. Yunus Luqmani *Faculty of Pharmacy, Kuwait University*	
Dr. Fouzi Mouffok *Faculty of Science, Kuwait University*	
Dr. Jacinthe Lemay *Faculty of Pharmacy, Kuwait University*	
Dr. Khaled Orabi *Faculty of Pharmacy, Kuwait University*	
Dr. Mohammed Al-Enezi, *Life Science Academy, Kuwait*	

Dr. Maitham Khajah *Faculty of Pharmacy, Kuwait University*	
Dr. Pierre Mourue *Dean, Faculty of Pharmacy, Kuwait University*	
Dr. Mohsen Hedaya *Faculty of Pharmacy, Kuwait University*	
Dr. Noha Nafee *Faculty of Pharmacy, Kuwait University*	
Dr. Salah Waheedi *Faculty of Pharmacy, Kuwait University*	
Dr. Sarah Al-Ghanem *Faculty of Pharmacy, Kuwait University*	
Dr. Suleiman Al-Sabah *Faculty of Medicine, Kuwait University*	
Dr. Willias Masocha *Faculty of Pharmacy, Kuwait University*	
Ph. Asmaa Al-Haqan *Faculty of Pharmacy, Kuwait University*	

Program at a glance

Tuesday **March 5th , 2019**	**Wednesday** **March 6th , 2019**	**Thursday** **March 7th , 2019**
04:00 pm – 7.00 pm Registration	08:00 am – 9.00 am Registration	08:00 am – 9.00 am Registration
04.00 pm – 4.45 pm **Opening Ceremony**	09.00 am – 12.00 pm **Morning Parallel Session**	
4.45 pm - 5.00 pm **Opening of Poster Exhibitions with Refreshments**	12.15 pm – 1.30 pm **Lunch Break**	
5.00 pm – 7.00 pm **Keynote Addresses 1, 2**	1.30 pm – 4.30 pm **Afternoon Parallel Session**	1.30 pm – 4.30 pm **Workshop by invitation**
7.00 pm - 9.00 pm **Gaala Dinner**	4.30 pm - 6.30 pm **Poster Session**	4.30 pm – 5.00 pm **Closing Ceremony**

Scientific Program

The KIPC 2019 conference will have two tracks.

- First Track - Pharmaceutical Sciences to advance our knowledge and understanding of medicines
- Second Track - Pharmacy Practice aiming to understand the evolution of clinical pharmacy in the region and worldwide and help to advance pharmacy profession in the country

Day 1- Tuesday March 5, 2019

4:00 pm – 7:00 pm	**Registrations**	
4:00 pm – 5:00 pm	**Opening Ceremony & Exhibitions**	
4:00 pm – 4:05 pm	National Anthem	
4:05 pm – 4:15 pm	Introductory Remarks	Dr. Fatma Al-Awadhi; Conference Chairperson
4:15 pm – 4:30 pm	Patronage Speech	Prof. Hussein Al-Ansari; President of Kuwait University
4:30 pm – 4:45 pm	Welcome Address	Prof. Pierre Moreau; Dean, Faculty of Pharmacy
4:45 pm – 5:00 pm	**Opening of Poster Exhibitions with Refreshments**	
	Keynote Forum	
5:00 pm – 6:00 pm	Title: Current and Future Impact of Pharmaceutical and Life Sciences on Global Health Care	Prof. Shaker Mousa, USA
6:00 pm – 7:00 pm	Title: Highlights of the 9Ps to Expand Practice	Prof. Zubin Austin, Canada
7:00 pm – 9:00 pm	**Dinner**	

Day 2- Wednesday March 6, 2019

8.00 am – 9.00 am	**Registration**		
9:00 am – 12:00 pm	**Morning Parallel Sessions**		
Expanding the chemical space for drug discovery		**Regulatory framework to support pharmacy practice**	
Time	**Lectures**	**Time**	**Lectures**
9:00 am – 9:45 am	**Prof. Raymond Andersen,** Canada Title: Chemical Genetics Approach to the Discovery of Terrestrial and Marine Natural Product Drug Leads	**9:00 am – 9:45 am**	**Prof. Ahmed Al-Jedai,** Saudi Arabia Title: Pharmacy Practice in the Gulf; Challenges and Future Outlook
9:45 am – 10:15 am	**Prof. Hendrik Luesch,** USA Title: Natural Products from Marine Cyanobacteria as Starting Points for Drug Discovery and Development	**9:45 am – 10:00 am**	**Dr. Saja Almatrook,** Kuwait Title: Regulatory and Legal Framework of Pharmacy Practice in Kuwait
		10:00 am – 10:15 am	**Dr. Salah Waheedi,** Kuwait Title: Pharmacist Code of Ethics in Kuwait
10:15 am – 10:30 am	**Coffee Break**		
10:30 am – 11:00 am	**Prof. Rolf Müller**, Germany Title: Basic Microbiology, Chemistry and Synthetic Biotechnology to Identify and Characterize Antibiotics from Microbes	**10:30 am – 10:45 am**	**Dr. Reem Al-Essa,** Kuwait Title: Requirements and Roles of the Regulatory Bodies in Inspecting Pharmacy Practice in the GCC
11:00 am – 11:35 am	**Prof. Jassim Al-Hassan**, Kuwait Title: Exciting Discoveries Utilizing Materials from the Skin of the Catfish Arius Bilineatus, Val. in the Novel Treatment of Diseases That are Unresponsive to Conventional Treatment	**10:45 am – 11:00 am**	**Prof. Pierre Moreau**, Kuwait Title: Development of a Cadre for Clinical Pharmacists
11:35 am – 11:55 am	**Dr. Khaled Orabi**, Kuwait Title: The Role of Natural Products in Modern Medicine	**11:00 am – 12:00 pm**	Panel discussion
11:55 am – 12:15 pm	**Prof. Oludotun Phillips**, Kuwait Title: Oxazolidinone as a Scaffold for Drug Discovery		
12:15 pm – 1:30 pm	**Lunch Break**		

1:30 pm – 4:30 pm	**Afternoon Parallel Sessions**		
Biomaterials and biotechnology in drug discovery and delivery		**Importance of education in supporting and evolving practice**	
Time	**Lectures**	**Time**	**Lectures**
1:30 pm – 2:15 pm	**Prof. Shaker Mousa**, USA Title: Impact of Nanobiotechnology on the Future of Medicine: The Road from Nanomedicine to Precision Medicine	**1:30 pm – 2:15 pm**	**Prof. Zubin Austin**, Canada Title: The 9Ps to Support the Evolution of Pharmacy Practice with a Focus on Education
2:15 pm – 2:45 pm	**Prof. Ludmil Benov**, Kuwait Title: Targeted Delivery of Reactive Species for Anticancer Therapy	**2:15 pm – 2:30 pm**	**Dr. Sarah Al-Ghanem,** Kuwait Title: Kuwait Change in Curriculum
2:45 pm – 3:15 pm	**Dr. Fouzi Mouffok,** Kuwait Title: New in vivo Method for PH Probing using MRI Modality for Cancer Early Detection and Post-Chemo and Radiotherapy Patient Respond to Treatments	**2:30 pm – 3:00 pm**	**Ph. Asmaa Al-Haqan**, Kuwait Title: CPD Regulations, Requirements and Audits
3:15 pm – 3:30 pm	**Coffee Break**		
3:30 pm – 3:50 pm	**Prof. Gamaleldin Harisa,** Saudi Arabia Title: Nano-Erythrocyte Membrane-Chaperoned 5-Fluorouracil Liposomes as Biomimetic Delivery Platforms to Target Liver Cancer Cells	**3:30 pm – 3:45 pm**	**Dr. Jacinthe Lemay,** Kuwait Title: CPD Needs for MOH Pharmacists in Kuwait
3:50 pm – 4:10 pm	**Dr. Nuha Nafee,** Kuwait Title: Nanomedicine for Pulmonary Drug Delivery	**3:45 pm – 4:00 pm**	**Dr. Mohammed Al-Enezi**, Kuwait Title: LSA's Model of CPD Offer and Delivery
4:10 pm – 4:30 pm	**Prof. Fares Alenezi,** Saudi Arabia Title: Nanotechnology Based Solid Dosage Form for Enhancing Dissolution and Oral Bioavailability	**3:55 pm – 4:30 pm**	Panel discussion
4:30 pm – 6:30 pm	**Poster Session**		

7th Kuwait International Pharmacy Conference: KIPC 2019
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Day 3- Thursday March 7, 2019

8.00 am – 9.00 am	**Registration**		
9:00 am – 12:00 pm	**Morning Parallel Sessions**		
Target identification and mode of action studies		**Expanding the scope of pharmacy practice**	
Time	**Lectures**	**Time**	**Lectures**
9:00 am – 9:45 am	**Prof. Nigel Pyne**, UK Title: Structural Guided Drug Discovery using Sphingosine Kinase with Therapeutic Indications in Various Diseases	**9:00 am – 9:25 am**	**Dr. Haifa Hamid Glom Ali**, Kuwait Title: Accreditation Standards for Pharmacists
		9:25 am – 9:45 am	**Prof. Ahmed Al-Jedai,** Saudi Arabia Title: Clinical Pharmacy Initiatives in Saudi Arabia
		9:45 am – 10:00 am	**Ph. Thamna Alshaibani,** Sultanate of Oman Title: Pharmacist-Led Clinical Services: the Oman Experience
9:45 am – 10:15 am	**Dr. Maitham A Khajah,** Kuwait Title: Angiotensin 1-7 (Ang 1-7), a Potential Target for the Management of Inflammatory Bowel Disease (IBD)	**10:00 am – 10:15 am**	**Ph. Nour Al-Khalaf,** Kuwait Title: Kuwait Experience in Peer-Referencing
10:15 am – 10:30 am	**Coffee Break**		
10:30 am – 11:00 am	**Prof. Ahmed El-Hashim**, Kuwait Title: Unraveling the Mechanisms of Cough	**10:30 am – 10:45 am**	**Dr. Monther Al-Sharekh,** Kuwait Title: Kuwait: Physician Perception and Demand of Clinical Pharmacists in Kuwait
11:00 am – 11:25 am	**Prof. Susan Pyne**, UK Title: Targeting Sphingolipids as a New Therapeutic Approach to Treating Obesity and Type 2 Diabetes		
11:25 am – 11:50 am	**Prof. Yunus Luqmani**, Kuwait Title: Why do Cancers Metastasise?	**10:45 am – 11:00 am**	**Dr. Rania Azmi,** Kuwait Title: Patient Expectations of Pharmacists as a Driver for Expansion of the Profession
11:50 am – 12:15 pm	**Dr. Suleiman Al-Sabah,** Kuwait Title: Molecular Pharmacology of Incretin Receptors	**11:00 am – 12:00 pm**	Panel discussion
12:15 pm – 1:30 pm	**Lunch Break**		

1:30 pm – 4:30 pm	**Afternoon Parallel Sessions**		
Target identification and mode of action studies (continue)		**Recommendations to Support the Clinical Pharmacy in Kuwait** **Facilitated by: Dr. Sarah Al-Ghanem; Prof. Pierre Moreau, Dr. Jacinthe Lemay, Dr. Abdullah Al-Bassam**	
1:30 pm – 1:50 pm	**Dr. Willias Masocha,** Kuwait Title: Targeting the Endocannabinoid System for Management of Chemotherapy-Induced Neuropathic Pain: Preclinical Studies	**1.30 pm – 4.30 pm**	**Workshop by invitation:** Objective**:** Drafting recommendations to support an expanded scope of pharmacy practice in Kuwait Discussion of the recommendations
Towards optimal use of drugs			
1:50 pm – 2:35 pm	**Dr. Alison Thomson,** UK Title: TDM, Population Pharmakokinetics and Optimal Use of Medicines		
2:35 pm – 3:05 pm	**Dr. Kamal Matar**, Kuwait Title: Therapeutic Drug Monitoring of Busulfan in Kuwait		
3:05 pm – 3:35 pm	**Dr. Abdullah Al-Sultan,** Saudi Arabia Title: TDM of Antimicrobials		
3:35 pm – 3:50 pm	**Coffee Break**		
3:50 pm – 4:10 pm	**Dr. Mohsen Hedaya**, Kuwait Title: Pharmacogenetic Testing: A Tool for Optimizing Drug Therapy		
4:10 pm – 4:30 pm	**Ph. Donia Bastaki,** Kuwait Title: Biosimilars and Biologics: What Data do Regulators Need?		
4:30 pm – 5:00 pm	**Closing Ceremony and Awards**		

Opening Ceremony Lectures

Shaker A. Mousa, PhD, MBA, FACC, FACB
Professor of Pharmacology, Executive Vice President, and Chairman;
The Pharmaceutical Research Institute, ACPHS, Albany, NY USA

Current and Future Impact of Pharmaceutical and Life Sciences on Global Health Care

Pharmaceutical sciences combine a broad range of scientific disciplines that are critical to the discovery and development of new drugs and therapies. Those disciplines, varied over the years with various degrees of emphasis depending on the era, including pharmacology, biochemistry, physiology, molecular biology, immunology, toxicology, pharmaceutics, biopharmaceutics, pharmaceutical chemistry (medicinal chemistry), analytical chemistry, pharmacognosy, phytochemistry, microbiology, and other related life sciences.

Pharmaceutical sciences can also be broadly classified into the following functional categories, with many specialized fields within each category. Those categories include: drug discovery and design, high-throughput screening and human genome sequencing, drug delivery, formulations, pharmacodynamics, pharmacokinetics and drug disposition, pharmacogenomics, drug development, cost-effectiveness (pharmacoeconomic), pharmacovigilance, regulatory affair, nanomedicine, and biopharmaceuticals.

The future of pharmaceutical, biopharmaceutical and life Sciences in 2020-2030 and beyond will be accelerated by a number of emerging technologies in favor of major improvement in global healthcare. While discovery using genome-based technologies has accelerated, these have only begun to be adopted into clinical medicine. Orphan drugs for rare diseases, gene therapy, human genome sequencing, and early disease diagnosis for the (3Ps) prediction, prevention, and personalization. Example of those technologies include: big data, bioinformatics and data analytic, the applications of the human genome project and Precision medicine are poised to have an impact on health care delivery, global healthcare and patients quality of life.

The different era of pharmaceutical and life science's contributions to global healthcare will be highlighted.

Prof. Zubin Austin
Professor and Koffler Chair in Management, Leslie Dan
Faculty of Pharmacy, University of Toronto, Canada

Highlights of the 9Ps to Expand Practice

What does it take to change practice? How can educators, policy makers, regulators, and employers support the evolution of practice change in a profession? For many years, the pharmacy profession has discussed the need for and importance of practice change and expansion. Recently, in many countries, regulation and legislation have changed to allow pharmacists to engage in expanded practice activities such as prescribing, vaccinating, and medication review/reconciliation. However in most of these countries, there is evidence that front-line community pharmacists are resistant to change and do not willingly take on new roles, responsibilities and responsibilities. As a result, well-intentioned regulatory or educational attempts to change and expand practice appear to fail in the real world.

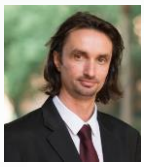
This presentation will review recent research from Canada examining the question of practice change in pharmacy and what it takes to motivate and support front-line pharmacists to take on new responsibilities and expand practice. Based on this research, a model was developed to help educators, regulators, employers, and others understand how to best implement practice expansion and change. This 9Ps of Practice Change model suggests the following are all essential to support pharmacists: 1) permission, 2) process pointers, 3) practice/rehearsal, 4) positive reinforcement, 5) personalized attention, 6) peer referencing, 7) physician acceptance, 8) patients' expectations and 9) professional identity supportive of a truly clinical role. One theme that did not emerge was payment, or remuneration, as a specific or isolated motivational factor for change.

Legislation alone is not implementation; education by itself is not motivation; telling pharmacists to change will not be sufficient. The 9Ps of Practice Change model can provide useful insights into the psychology and practical issues associated with change management in pharmacy and can help stakeholders across the pharmacy profession better manage the complex environment of practice expansion.

Prof. Raymond Andersen
Departments of Chemistry and Earth, Ocean & Atmospheric Sciences,
University of British Columbia, Vancouver, B.C., Canada

A chemical genetics approach to the discovery of marine natural product drug leads

The secondary metabolites found in marine organisms represent an extremely rich source of novel chemical diversity for academic drug discovery and chemical biology programs. Our group at UBC has amassed a sizable library of crude extracts from marine sponges, other marine invertebrates, and cultured marine microorganisms collected in many of the world's oceans. In collaboration with biologists, this crude extract library has been screened for activity in cell-based and pure enzyme assays designed to identify promising marine natural product lead compounds for the development of drugs. Bioassay-guided fractionation of crude extracts and extensive spectroscopic analysis has been used to identify the structures of pure natural products active in the assays. Biology-oriented chemical synthesis has been undertaken to probe the SAR for new natural product pharmacophores that we have discovered and to provide material for *in vivo* testing in animal models. We have used Click chemistry probes and protein x-ray diffraction analysis to study the interactions of bioactive natural products with their molecular targets. Several new drug candidates for the treatment of cancer, inflammation, type II diabetes, and infectious diseases have emerged from this research program. Four of them have progressed to phase II/III clinical trials in humans and others are in preclinical evaluation/development. The lecture will present some highlights from our academic 'Drugs from the Sea' and chemical biology research in the area of bacterial and viral infectious diseases.



Prof. Hendrik Luesch

Department of Medicinal Chemistry and Center for Natural Products, Drug Discovery and Development (CNPD3), University of Florida, USA

Natural Products from Marine Cyanobacteria as Starting Points for Drug Discovery and Development

Marine cyanobacteria serve as a rich source of novel bioactive secondary metabolites. Our chemical investigations have yielded novel marine natural products that act on a range of therapeutically relevant targets. A requisite for their development into therapeutics is the detailed characterization of their mechanisms of action, along with solving the supply problem. An integrative platform of pharmacological, genomic and proteomic profiling assisted us in understanding their activities on the cellular and molecular level. Total synthesis, structure-activity relationship studies and medicinal chemistry campaigns for prioritized compounds allowed us to fine-tune activities and improve selectivity profiles.

Prof. Rolf Müller, Germany
Helmholtz Institute for Pharmaceutical Research Saarland, Germany

Basic Microbiology, Chemistry and Synthetic Biotechnology to Identify and Characterize Antibiotics from Microbes

Amongst the well-established bacterial producers myxobacteria have a great track record for the discovery of entirely new natural product scaffolds exhibiting promsing bioactivities[1]. This is at least in part due to the fact that they have been much less studied in the past in comparison to other traditional sources such as actinomycetes and bacilli. Nevertheless, the issue of rediscovery is a major hurdle for myxobacterial extracts as well. I will disucss recent results from our efforts to culture previously uncultured myxobacteria and to connect phylogentically distant clades to novel metabolites by metabolome and genome mining[2]. Examples of novel and genetically engineered natural products in preclinical development as broad spectrum antibiotics exhibiting novel mode of action(s) will be shown [3,4,5,6] In addition, I will show examples of heterologous expression of myxobacterial compounds yielding producer strains making production of lead compounds for pharmaceutical development feasible[7].

1. Herrmann, J., Abou Fayad, A. and Müller R. (2017) Natural products from myxobacteria: novel metabolites and bioactivities, Nat. Prod. Rep., 34 (2):135-160.
2. Hoffmann, T., Krug, D., Bozkurt, N., Duddela, S., Jansen, R. Garcia, R., Gerth, K., Steinmetz, H. and Müller, R. (2018) Correlating chemical diversity with taxonomic distance for discovery of natural products in myxobacteria, Nat. Commun., 9 (1): 803.
3. Baumann, S., Herrmann, J., Raju, R., Steinmetz, H., Mohr, K.I., Hüttel, S., Harmrolfs, K., Stadler, M. and Müller, R. (2014) Cystobactamids: myxobacterial topoisomerase inhibitors exhibiting potent antibacterial activity, Angew. Chem. Int. Ed.,53 (52): 14605-14609.
4. Kling, A., Lukat, P., Almeida, D.V., Bauer, A., Fontaine, E, Sordello, S., Zaburannyi, N., Herrmann, J., Wenzel, S.C., König, C., Ammerman, N.C., Barrio, M.B., Borchers, K., Bordon-Pallier, F., Brönstrup, M., Courtemanche, G., Gerlitz, M., Geslin, M., Hammann, P., Heinz, D.W., Hoffmann, H., Klieber, S., Kohlmann, M., Kurz, M., Lair, C., Matter, H., Nuermberger, E., Sandeep T., Fraisse, L., Grosset, J.H., Lagrange, S. and Müller, R. (2015) Targeting DnaN for tuberculosis therapy using novel griselimycins, Science, 348 (6239): 1106-12.
5. Lesnik, U., Lukezic, T., Podgorsek, A., Horvat, J., Polak, T., Sala, M., Jenko, B., Harmrolfs, K., Ocampo-Sosa, A., Martinez Martinez, L., Herron, P.R., Fujs, S., Kosec, G., Hunter, I.S., Müller, R. and Petkovic, H. (2015) Construction of a new class of tetracycline lead structures with potent antibacterial activity through biosynthetic engineering, Angew. Chem. Int. Ed., 54 (13): 3937-40.
6. Hüttel, S., Giambattista, T., Herrmann, J., Planke, T., Gille, F., Moreno, M., Stadler, M., Brönstrup, M., Kirschning, A. and Müller, R. (2017) Discovery and total synthesis of natural
7. cystobactamid derivatives with superior activity against Gram-negative pathogens, Angew. Chem. Int. Ed., 56 (41): 12760-64.
8. Sucipto, H., Pogorevc, D., Luxenburger, E., Wenzel, S.C. and Müller, R. (2017) Heterologous production of myxobacterial α-pyrone antibiotics in Myxococcus xanthus, Metab. Eng., 44:160-170.

Prof. Jassim Al-Hassan
Biological Sciences Department; Faculty of Science, Kuwait University

Exciting Discoveries Utilizing Materials from the Skin of the Catfish Arius Bilineatus, Val. in the Novel Treatment of Diseases That are Unresponsive to Conventional Treatment.

The catfish Arius Bilineatus, Val., elaborates thick gel-like proteinaceous material through its epidermis when threatened or injured. This material is composed of 85% proteins and 13.4% lipids with 1.6% nucleic acid components and carbohydrates. Both the proteins and lipids are biologically active. We hypothesized that this proteinaceous material is for the protection of the catfish against injury. Our continued research activities proved that the secreted gel-like material has activities on blood, cellularity and contains enzymatic activities. Fractions and isolated compounds from catfish skin preparation (CSP) enhanced wound and diabetic ulcer healing, caused regeneration of crushed sciatic nerve in experimental animals, acted as anti-inflammatory and as anti-cancer against prostate, liver, pancreatic, lung, breast and skin cancer cell lines and acted on leukemic cells in synergism with Gleevec. Our recent preliminary research efforts proved that a fraction from CSP has interesting action on diabetes and regeneration of organs affected by diabetes. More interesting research results are being generated in collaboration with The University of Texas MD Anderson Cancer Center in Houston, TX, and the Sick Children Hospital Research Institute, University of Toronto, Canada.

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The Role of Natural Products in Modern Medicine

Natural products are the most successful source of potential drug leads, since they provide unique structural and pharmacological diversity in comparison to other avenues which mainly provide novel low molecular weight lead compounds. It is estimated that less than 10% of the world's biodiversity has been evaluated for potential biological activity, thus many more compounds await discovery. These products are derived mainly from plants, terrestrial microorganisms, marine macro- and micro-fauna, as well as synthetic or semi-synthetic compounds based on natural products.

Plants have been well documented for their medicinal uses since the dawn of history. Their ethnopharmacological properties have been used as a primary source of medicines for early drug discovery. Some studies showed that about 80% of almost the 130 plant-derived drugs were related to their original ethnopharmacological purposes. The knowledge associated with complementary and alternative herbal medicines has promoted further investigations of plants as potential medicines and has led to the isolation of many natural products that have been developed into pharmaceuticals.

The most famous example is acetylsalicylic acid which is derived from the natural product, salicin, which was isolated from willow tree (Salix alba). On the other hand, several phenanthrene alkaloids, including the painkiller morphine and the cough suppressant codeine, were isolated from the opium poppy (Papaver somniferum). The cardiotonic glycosides, digoxin and digitoxin isolated from foxglove (Digitalis purpurea), are yet other examples.

The anti-malarial drug quinine, approved by the FDA in 2004, was isolated from the bark of Cinchona succirubra, and had been used for centuries for the treatment of malaria and fever. Pilocarpine, from Pilocarpus jaborandi, has been used in the treatment of glaucoma. Additionally, an oral formulation of pilocarpine was approved by the FDA, in 1994, to treat xerostomia.

The most widely used breast cancer drug is paclitaxel, isolated from the bark of the Pacific Yew (Taxus brevifolia), and was approved for such indication by the FDA in 1992. Other examples of antitumor compounds include ingenol 3-O-angelate (Picato®), isolated from Euphorbia peplus and approved by the FDA in 2012 to treat actinic keratosis.

Other examples will also be mentioned including some from our laboratory.

However, there is a growing interest in developing products that contain mixtures of natural compounds from folkloric medicines. As an example, a defined mixture of components extracted from green tea (VeregenTM) has been approved by the FDA and has recently come on the market to treat external genital and perianal warts. Also, crofelemer (MytesiTM), a botanical oligomeric proanthocyanidin derived from the red latex of the Dragon's blood tree (Croton lechleri), was approved by the FDA to treat non-infectious diarrhea in AIDS patients.

In summary, natural products have played pivotal roles in drug discovery and development through; 1) providing a number of useful drugs that are difficult to produce commercially by synthetic means, 2) supplying basic compounds that may be modified slightly to render them more effective or less toxic, and 3) serving as prototypes for synthetic drugs possessing therapeutic activities as the originals.

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Oxazolidinone as a Scaffold for Drug Discovery

Introduction & Objectives: Oxazolidinone scaffold is part of the framework of some clinically useful antimicrobial, psychoactive, and anticoagulant agents. It also has anti-cancer and anti-thyroid activities. The objective of this study was to evaluate a series of triazolyl-oxazolidinones for anticonvulsant activity.

Methods: Eighteen oxazolidinones were evaluated using the NIH protocol on minimal clonic seizure (6Hz, 3sec) test. Test compounds (100 mg/kg) were pre-administered to mice (n=4) by i.p. injection and then challenged with current delivered through corneal electrodes to elicit psychomotor seizures, at varying times. Neurological toxicity was evaluated by rotarod test. The ED50 (n=8) of 6 compounds was determined with appropriate descriptive statistics. Compound PH192 with highest protective index (PI), was further evaluated in vivo using electrically-induced (6Hz and maximal electroshock (MES)) and chemically-induced (pentylenetetrazole (PTZ) 50 and 100mg/kg) rat seizure models.

Results: Nine of the tested compounds showed anticonvulsant activity, protecting between 1-3 mice out of 4. Of the 5 compounds further studied for ED50 evaluation, PH66 and PH192 were the most active with ED50 (± STD Err) values of 52.47 ± 0.52 and 34.03 ± 0.62 mg/kg, respectively. All 5 compounds showed good neurotoxicity profiles with 300 < TD50 < 750 mg/kg. The most active compound PH192 (ED50 of 34.5mg/kg) proved to be the least neurotoxic (TD50 >500 mg/kg) with a neuroprotective index of >14.7. When pretreated with 100 mg/kg of PH192 for 30 mins, about 75% (mice) and 66.6% (rats) were protected from 6 Hz-induced seizures, while 83.3% (rats) were protected from MES stimulation. PTZ at 50 and 100mg/kg injection produced seizures in all rats and 30 mins i.p. pretreatment with 100 mg/kg PH192 protected 80% rats from PTZ-induced seizures comparable to phenytoin (40mg/kg) protection.

Conclusion: PH192, though short acting, protects against both chemically- and electrically-induced seizures without obvious CNS side-effects.

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Impact of Nanobiotechnology on the Future of Medicine: The Road from Nanomedicine to Precision Medicine

Over the past few years, evidence from the scientific and medical communities has demonstrated that nanobiotechnology and nanomedicine have tremendous potential to profoundly impact 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 chemotherapeutic delivery through increased solubility and sustained retention. One of the major advantages of this cutting edge technology is its unique multifunctional characteristics. Targeted delivery of drug incorporated nanoparticles, through conjugation of tumor-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 specifically to nanoparticles and anticancer 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, vaccine, and impact of Nanoscafold in enhancing stem cell role in regenerative medicine will be briefly discussed.

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Targeted delivery of reactive species for anticancer therapy

With more than 14 million reported new cases and about 9 million deaths per year, cancer represents the hardest therapeutic challenge worldwide. Reactive species are a main cause for carcinogenesis, but are also widely used for cancer eradication. Hydrogen peroxide, hydroxyl radical, singlet oxygen, and other reactive species are commonly produced by anticancer therapeutics and are responsible not only for destruction of malignancies, but also for unwanted side effects. The best way to increase the efficacy and to limit the side effects of a drug, is to deliver it to a specific target. Cancerous cells commonly display alerted metabolism and preferential uptake of certain compounds, among them porphyrins. Porphyrin uptake by cancer cells is of special interest because porphyrins can act as photosensitizers (PS), absorbing energy of visible light and generating reactive species capable of killing cells. Since such species have short life in biological environment, PS-induced damage is limited to the close proximity of the PS. Modifications of the periphery of the porphyrin core produce molecules that can be delivered to different subcellular targets. Damage of such targets triggers specific cell death pathways which in turn define the overall organismal response. Experiments performed with porphyrin-based PSs revealed that overall charge, position and accessibility of charges, lipophilicity, three-dimensional shape, bulkiness, symmetry, and flexibility of a molecule, are the main factors which direct it to a particular cellular target.

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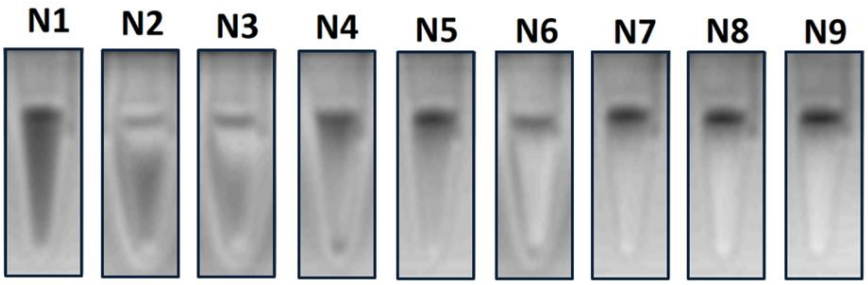
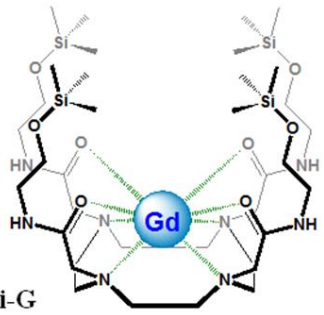
New in vivo Method for PH Probing using MRI Modality for Cancer Early Detection and Post-Chemo and Radiotherapy Patient Respond to Treatments

Determination of proton concentration and quantifying the number of protons in vivo are extremely vital in medical field. Due to the difficulty for in vivo pH probing, a few studies have been conducted towards this aim. However, very few investigations have been conducted to developed methods for lactic acid detection. Only two methods have developed 1) proton detection using chemical exchange saturation transfer magnetic resonance imaging (CEST MRI). 2) pH-sensitive poly-ion complex. Both techniques perform poorly at low concentration and showed a very low selectivity in-vivo toward lactic acid. Which makes them unfit for clinical use (cancer detection and monitoring patient respond to chemo and radiotherapy). Recently we developed a new process based on MRI smart contrast agent able to quantify and locate specifically proton atoms using MR Imaging as tool. The new contrast is based on pH sensitive Gd-DOTASi-Gd able to measure indirectly the pH of any given tissue with high precision and accuracy.



T_2-weighted *in vitro* MR Images using the new Gd(III)-DOTASi-G solutions at diffrent concentration of acid [H+].



Gd(III)-DOTASi-G

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Nano-Erythrocyte Membrane-Chaperoned 5-Fluorouracil Liposomes as Biomimetic Delivery Platforms to Target Liver Cancer Cells

Nano-erythrocyte coating has been developed as an interesting biomimetic platform to provide hybrid nano-carriers with innate functions to target liver cancer. This goal was achieved by coating nano-erythrocyte membranes (NEMs) onto 5-fluorouracil (5-FU)-loaded liposomes (LPs) to produce NEM-5-FU-LPs. This framework is used to promote the escape of 5-FU-LPs from degradation during systemic circulation. NEMs were obtained by hypotonic lysis of erythrocytes to produce ghost erythrocytes (GEs) followed by extrusion through polycarbonate membranes. Chimeric NEM-5-FU-LPs were fabricated via the fusion of NEMs and artificial LPs. The resultant chaperoned LPs were characterized based on particle size, morphology, entrapment efficiency (EE %), stability, protein content, phosphatidylserine exposure; their in vitro release profiles and cytotoxic efficacy were also determined. The present results revealed that 5-FU-LPs, NEM-5-FU, and NEM-5-FU-LPs exhibited nanosize, spherical shapes, and unimodal size distributions < 0.3. In addition, the vesicles presented a zeta potential with EE% of 24.6 to 30.7% and an appropriate stability for 3 weeks. NEM-5-FU-LPs retained the erythrocyte membrane proteins as confirmed by PAGE, and displayed a sustained release profile up to 48 h when compared to NEM-5-FU and the 5-FU solution. Moreover, hybrid NEM-5-FU-LPs induced a late cytotoxic effect after 48 h compared to the other formulations. Thus, mantling of 5-FU-LPs by NEMs could enhance vesicle controllability and their targetability to liver cancer cells.

Key words: 5-Flurouracil, liposome, nano-erythrocytes, chaperoned liposome, liver cancer

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Pulmonary nanomedicine between nanotheranostics and nanotoxicity

The unique aspects of nanocarriers endeavour innovative therapeutic strategies in particular for pulmonary diseases such as chronic obstructive pulmonary disease (COPD), lung cancer and cystic fibrosis. While numerous studies focused on diagnostic and therapeutic application of nanomaterials, parallel researches addressed the fate of inhalable nanocarriers and their possible health hazards. Herein, we will discuss the recent advances in nano-mediated drug delivery to the lungs as well as the role of nanoparticles in imaging and diagnostics. The potential of nanocarriers to cross challenging pulmonary physiological barriers will be highlighted. Meanwhile, special insights on the toxicological facets of both organic and inorganic nanoparticulate systems will be emphasized.

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Nanotechnology Based Solid Dosage Form for Enhancing Dissolution and Oral Bioavailability

Oral route is the most convenient and commonly used based on WHO industrial recommendation. This due to tremendous advantageous like ease of administration, high patient compliance, cost effectiveness, least sterility and high stability. However, this route is facing a major challenge which is the poor oral bioavailability. This depends on several factors and mostly due to low solubility and dissolution rate. The aqueous solubility of drug is often intrinsically related to drug particle size; as a particle becomes smaller, the surface area to volume ratio increases. The larger surface area allows greater interaction with the solvent which causes an increase in solubility. Thus, Nanosization is considered the most novel and promising approached to enhance aqueous solubility. Parameters that can influence the dissolution rate is illustrated as well as how the nanotechnology can enhance it. The major two ways of fabrication of nanoparticle are highlighted. More emphasis is on top-down technology. Particles in the nanometer size range have a strong tendency to agglomerate; thus stabilization of nanoparticles is discussed. Finally, cases studied are going to be presented and discussed.

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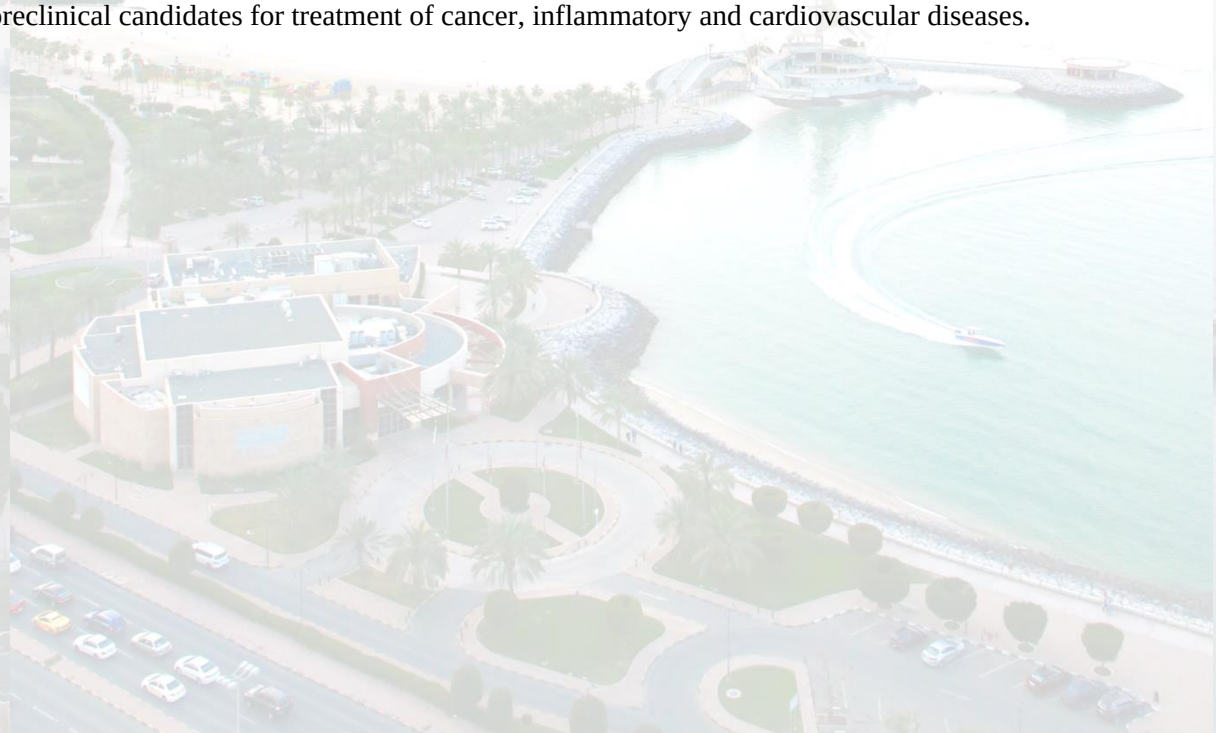
Structural Guided Drug Discovery using Sphingosine Kinase with Therapeutic Indications in Various Diseases

Sphingosine kinases (two isoforms termed SK1 and SK2) catalyse the synthesis of the bioactive lipid, sphingosine 1-phosphate (S1P) which can bind to a family of G protein coupled receptors (S1P1-5) and/or intracellular targets (e.g. histone deacetylases) to regulate many cellular responses in immune, neuronal and cardiovascular physiology. S1P is also involved in a number of disease pathologies, such as cancer, inflammation/autoimmune disease and cardiovascular disease including pulmonary hypertension and heart failure. Evidence will be presented to show that SK1 and SK2 are validated targets for therapeutic intervention in disease. Indeed, S1P is a therapeutic target as evinced by the introduction of the S1P1 modulator, fingolimod (GilenyaR) as the first oral treatment for relapsing and remitting multiple sclerosis. However, inhibitors of sphingosine kinases are yet to reach the clinic and only one SK2 inhibitor (YelivaR), with low potency and several 'off target' effects, is in clinical trials for oncology indications. The challenge is to produce isoform selective inhibitors of SK1 and SK2 such that therapeutic targeting of either one of the isoforms is achievable, thereby maintaining some S1P to preserve normal physiology and avoid deleterious side effects. By mapping isoform amino acid sequence differences for SK2 onto the available crystal structure of SK1, we have identified subtle structural variations between the two isoforms that has enabled the conversion of inhibitors with 100-fold selectivity for SK1 over SK2 through to equipotent SK1/SK2 inhibition and to reversed 100-fold selectivity for SK2 over SK1, with retention of nM potency. These findings will inform on the development of new isoform selective inhibitors as pharmacological tools to evaluate the role of sphingosine kinase in pathophysiology. Subsequent lead optimisation will develop preclinical candidates for treatment of cancer, inflammatory and cardiovascular diseases.



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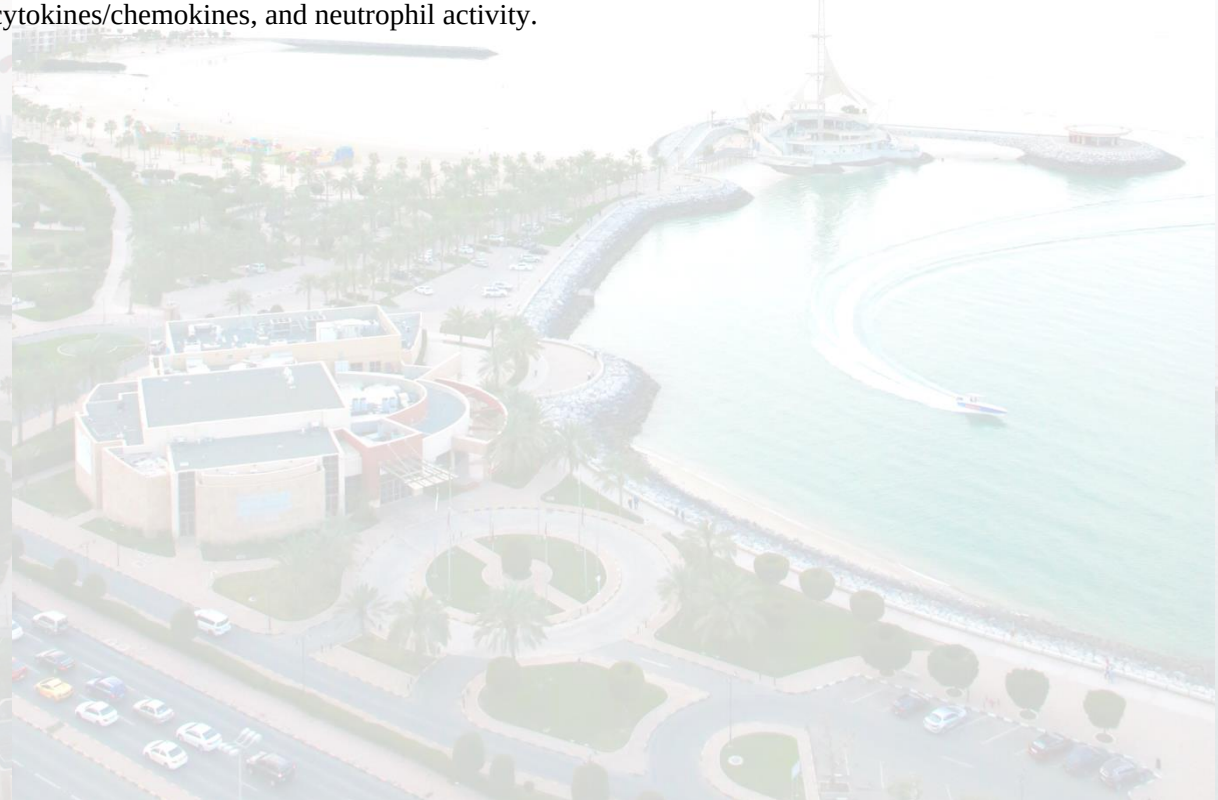
Angiotensin 1-7 (Ang 1-7), a potential target for the management of inflammatory bowel disease (IBD)

Background: there is an established role for angiotensin 1-7 (Ang 1-7) in the cardiovascular and renal systems with emerging evidence suggesting anti-inflammatory properties in various models of inflammation. Enhanced expression profile of the key enzyme responsible for Ang 1-7 production; angiotensin converting enzyme 2 (ACE2) was observed in patients with inflammatory bowel disease (IBD) suggesting a role in the disease pathogenesis. In the current study, we aim to demonstrate the role of Ang 1-7 in the pathogenesis of IBD by using the murine dextran sulfate sodium (DSS) colitis model. Methods: Ang 1-7 was daily administered at various doses (by i.p injection), or its endogenous levels was depleted (by using MAS1-R antagonist; A779) and colitis severity was determined at macroscopic and microscopic levels. The colonic expression/activity profile of ACE2, Ang 1-7, MAS1-receptor (MAS1-R), and various signaling molecules (p38 MAPK, ERK1/2, and Akt) were determined by western blot and immunofluorescence. The plasma levels of various cytokines/chemokines were also determined in response to Ang 1-7 treatment. In vitro effect of Ang 1-7 treatment on various neutrophil effector functions (apoptosis, chemotaxis and superoxide release) was also examined. Results: A779 treatment aggravated while Ang 1-7 treatment (particularly at 0.01-0.06 m/kg doses) reduced colitis severity through modulating the expression of the signaling molecules of MAPK family and PI3K, and reducing the circulating levels of several cytokines and chemokines, and neutrophil recruitment to the colonic tissue. Enhanced expression of ACE2, Ang1-7 and MAS1-R was also observed post-colitis induction. Ang 1-7 treatment significantly enhanced neutrophil apoptosis, while reduced neutrophil chemotaxis and superoxide release in vitro. Conclusion: Our results indicate important anti-inflammatory actions of Ang 1-7 in the pathogenesis of IBD through modulating the expression/activity of pro-inflammatory signaling molecules, circulating levels of cytokines/chemokines, and neutrophil activity.



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Unraveling the Mechanisms of Cough

Cough is one of the most common complaints for which sufferers seek medical assistance. Unfortunately, treatment options are limited and not very effective, particularly for cough subsequent to an upper respiratory tract infection. Nonetheless, our understanding of the pathways and mechanisms underlying cough has been gradually increasing over the last decade. Sensitization of the cough reflex has been identified as an important mechanism in chronic cough, where it can result from low level stimulation by chemical or mechanical stimuli and hence the term “cough hypersensitivity syndrome” (CHS) has been coined to reflect the increased cough response to sub-threshold airway stimulation. Whilst the mechanisms underlying CHS are not fully understood, there is evidence to suggest that sensitization occurs at both peripheral sensory nerves and within the central nervous system (CNS). Ex vivo and in vivo studies, using animal models of cough, show that exposure to allergens, ozone and inflammatory mediators results in both enhanced sensory nerve activation as well as cough. This has led to the identification of sensory nerves as being critical in the development of cough hypersensitivity. The role of the CNS in cough is less understood due to limited access and complexity of the CNS, and perhaps due to the general presumption of the airways as the primary site for cough sensitization. However, there is good evidence showing that the cough center nucleus solitarius (nTs) can undergo neuroplasticity. For example, exposure of guinea-pigs to cigarette smoke increases their cough response to citric acid. Additionally, central injection of several inflammatory mediators such as nerve growth factor and bradykinin have been shown to sensitize the cough reflex. Interestingly, this enhanced cough response can be inhibited by central administration of number of drugs such as neurokinin 1, TRKA, B2 receptor antagonists, in addition to TRPV1 and TRPA1 channel blockers. These findings suggest that neuroplastic changes in the CNS are, at least partly, responsible for the cough hypersensitivity and that this is can be pharmacological modulated. Therefore, better understanding of the central molecular mechanisms underlying cough hypersensitivity, will aid the development of more effective antitussive drugs.

Prof. Susan Pyne
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Targeting Sphingolipids as a New Therapeutic Approach to Treating Obesity and Type 2 Diabetes

Adipose tissue mass expansion in obese patient enhances the risk of metabolic syndrome, type 2 diabetes and cardiovascular diseases. This is associated with multiple molecular controls of lipid storage, adipocyte turn-over and endocrine secretion, which are altered. There is a role for ceramides and sphingosine 1-phosphate (S1P) in inducing adipose dysfunction. There are changes in ceramide biosynthesis, through the de-regulation of key enzymes which block insulin signaling and promote adipose inflammation. An important enzyme in this pathology is dihydroceramide desaturase (Degs1), which catalyses the introduction of a trans 4,5 double bond into dihydroceramides to form ceramides. The role of Degs1 in regulating adipogenesis, insulin sensitivity and catabolic autophagic processes will be discussed in the context of dysfunctional adipose function and inflammation. Particular focus will be on the recently discovered polyubiquitinated forms of Degs1, which exhibit opposing functions from the native form. The targeting of Degs1 with fenretinide promotes the ubiquitin-proteasomal degradation and loss of Degs1 which we propose fully recapitulates the phenotype of the Degs1 knockout in improving Akt signaling, insulin sensitivity and autophagy. Finally, the role of S1P in inhibiting adipogenesis and promoting inflammation will be discussed in the context of insulin resistance, with focus on the potential use of S1P2 receptor antagonists as a novel therapeutic approach to treating type 2 diabetes.

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Why do Cancers Metastasise?

While the mechanisms of tumour dissemination are being actively investigated, it is just as important to determine why metastasis occurs. What compels a tumour cell to leave an apparently secure and comfortable environment of a growing mass and expose itself to hazardous conditions open to attack from immune cells and antibodies both in the matrix and once they gain entry into the blood circulation? Hypoxic conditions leading to extracellular acidification are considered to facilitate metastasis, yet such cells are deep within the tumour far from the vascular network. It seems more likely that cells which metastasize would be located in an area of neovascularisation. Our hypothesis is that tumour metastasis is actually an active escape from a harsh environment of alkaline (not acidic) pH. Using breast cancer cell lines that have acquired endocrine resistance (through transition to a more motile mesenchymal-like phenotype), we have shown that these have the means to effect an escape from an imposed alkaline environment that will otherwise prove fatal to their survival. Unlike endocrine sensitive cells they display a protective reaction to increased pH that reduces extracellular contact by cellular contraction and rounding up of the cell (similar to that of a pre-apoptotic response), and the development of extensive locomotive membranous blebs that can presumably enable cellular migration.

Short exposure to pH < 8 results in a re-arrangement of cortical actin and a flow of associated proteins into blebs. Cytochalasin-D or blockers of Rho or MLCK or of Na+/K+ flux all inhibit both shape change and bleb formation at high pH. (not observed in normal breast cells), and could be an effective means of retarding metastasis, and therefore cancer mortality.

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Molecular Pharmacology of Incretin Receptors

The incretin hormones, glucose-dependent insulinotropic polypeptide (GIP) and glucagon like peptide-1 (GLP-1) are important regulators postprandial glucose tolerance, insulin and glucagon secretion as well as lipid metabolism and appetite. These biological functions make their receptors (GIPR and GLP-1R respectively) attractive targets in the treatment of both type 2 diabetes mellitus (T2DM) and obesity. However, the incretin effect is severely impaired in patients with T2DM and this is most probably due to a loss of response to GIP. So, while GLP-1R agonists are used clinically to treat diabetes and obesity, the use of GIPR agonists and antagonists remains controversial. Recent studies however suggest that simultaneous activation of GIPR and GLP-1R with a single peptide may provide superior glycemic and weight control than activation of GLP-1R alone.

GIPR and GLP-1R are closely related 'Family B' G protein-coupled receptors (GPCRs) and share a high degree of sequence similarity. In order to shed light on to why GLP-1R, but nor GIPR, remains responsive in T2DM we have compared their signaling properties in vitro. Originally identified for their role in desensitization, internalization and recycling of GPCRs, arrestins have since been shown to act as scaffolding proteins allowing GPCRs to signal in a G protein-independent manner. This has led to the concept of 'biased agonism' or 'functional selectivity', where ligands can favor a G protein-dependent pathway or an arrestin-dependent pathway. We have previously demonstrated, using various fluorescent and resonance energy transfer techniques, that GLP-1R can recruit arrestin but GIPR cannot [1]. More recently we have investigated the signaling properties of a recently reported 'dual incretin' receptor agonist (P18). Data generated from reporter gene and bioluminescence resonance energy transfer (BRET) assays suggest that P18 may act as a G protein-biased agonist. Finally, data generated from BRET saturation assays also suggest that GIPR and GLP-1R may also form functionally relevant hetero-dimers. Future studies will focus on the impact of receptor dimerization on cell signaling.

[1]. Al-Sabah S, Al-Fulaij M, Shaaban G, Ahmed HA, Mann RJ, et al. (2014) The GIP receptor displays higher basal activity than the GLP-1 receptor but does not recruit GRK2 or arrestin3 effectively. PLoS One 9: e106890.

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Targeting the endocannabinoid system for management of chemotherapy-induced neuropathic pain: preclinical studies

Chemotherapeutic drugs such as cisplatin, paclitaxel and vincristine, are fundamental in the treatment of various types of cancer. Unfortunately, these chemotherapeutic drugs can cause chemotherapy-induced neuropathy pain (CINP). Some of these drugs such as paclitaxel are associated with high incidence of peripheral neuropathy, around 71% of the patients of which 27% of these develop neuropathic pain. There is a dearth of effective drugs to treat this neuropathic pain. Use of cannabis or phytocannabinoids has been reported to improve pain measures in patients with neuropathic pain.

Phytocannabinoids and endocannabinoids, such as anandamide and 2-arachidonoylglycerol (2-AG), produce their effects via cannabinoid (CB) receptors. Endocannabinoids are synthesized in an “on demand” fashion and are degraded by various enzymes such as fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MGL).

Various studies, including those from our group, suggest that there are changes in gene and protein expression of endocannabinoid molecules in animal models of CINP. Analysis of endocannabinoid molecule expression in the brain, spinal cord and paw skin of mice using LC-MS/MS show that there is a specific deficiency of the endocannabinoids 2-AG and/or anandamide in the periphery during CINP.

Various drugs including endocannabinoids, inhibitors of FAAH and MGL, CB receptor agonists, desipramine and coadministered indomethacin plus minocycline have been found to either prevent the development and/or attenuate established CINP in a CB receptor-dependent manner.

The results available suggest that targeting the endocannabinoid system for prevention and treatment of CINP is a plausible therapeutic option. Further research is needed to find out if this approach has advantages over or can supplement already existing treatment options for CINP and if this can be translated into clinical applications.

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TDM, Population Pharmakokinetics and Optimal Use of Medicines

When optimising therapy for drugs with a narrow therapeutic range, healthcare professionals are faced with several challenges. Firstly, variability in pharmacokinetics means that guidelines for initial doses should be based on easily measured clinical characteristics, such as age, weight and renal function. Ideally, the pharmacokinetic parameters used to construct these guidelines should reflect the population of patients who will receive the drug in clinical practice. Over the past 30 years, computer tools that utilise population pharmacokinetic (PopPK) methodology have been used to identify such parameters and to help design dosage regimens that achieve target concentration-time profiles and exposures. However, obtaining quality data to support these analyses can be difficult. Within Glasgow, there is a long history of pharmacy involvement in therapeutic drug monitoring (TDM). An early MAP Bayesian program that was created to support TDM services facilitated data collection for PopPK analysis and the development of new guidelines to address gaps in knowledge or changes in practice. For example, PopPK methodology was used to create new vancomycin dosage guidelines for adult patients in response to a change in target concentrations.[1]

Before new guidelines are adopted into routine practice, agreement is required from decision-makers and an implementation plan should be in place. The Scottish Antimicrobial Prescribing Group (SAPG) was established in 2008 to promote the safe and effective use of antibiotics. In 2009, SAPG agreed national guidelines for the administration and monitoring of gentamicin and vancomycin.[2] A quality improvement project comprising a national survey, a point prevalence study and a qualitative study then examined the implementation process. These studies identified gaps in guideline adoption and enablers and barriers to effective implementation. To address the issues raised, the team modified the guidelines, developed online training resources, developed specialised prescribing forms and created online calculators. A recent repeat of the point prevalence study demonstrated clear improvements in guideline implementation.

Additional research studies have addressed issues highlighted by clinical pharmacists. For example, evidence was provided to support changing the guidelines to avoid administering vancomycin during the night and new guidelines were developed for vancomycin use in paediatric patients. Other challenges that are currently being examined involve amikacin dosage regimens for patients with mycobacterial infections and tobramycin dosage regimens for patients with cystic fibrosis. In some cases, these problems have been addressed through pharmacokinetic studies, in others, a quality improvement approach with a continuous cycle of small changes has been applied.

In conclusion, routine clinical practice generates a wealth of valuable data. Efficient capture and analysis of such data can help to develop new guidelines that solve clinical challenges but effective implementation of guidelines is necessary to ensure a positive impact on patient care.

1. Thomson AH, et al J Antimicrob Chemother, 2009;63:1050-1057.
https://www.sapg.scot/quality-improvement/hospital-prescribing/gentamicin-and-vancomycin/

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Therapeutic Drug Monitoring of Busulfan in Kuwait

Background: Busulfan (Bu) is an alkylating agent commonly used in preparative regimens for hematologic malignant and non-malignant patients undergoing hematopoietic stem cell transplantation (HSCT). An LC-MS/MS method for quantification of Bu in human plasma has been developed and fully validated to be used routinely for TDM of Bu.

Methods: A total of 55 patients with hematological (n=34) and non-hematological (n=21) malignancies received myeloablative Bu therapy prior to HSCT. Bu samples were analyzed by the present fully validated tandem mass spectrometric method.

Results: The method was validated over the concentration range of 25 – 2000 ng/ml (r > 0.99). Intra- and inter-run precision of Bu assay indicated good precision and accuracy. Stability of Bu in human plasma samples demonstrated that the drug was stable under the studied conditions. Based on the 1st dose AUC results, one third of hematologic malignant patients needed dose adjustment. However, in subsequent doses (5th, 9th, and 13th), 77%, 82% and 82%, respectively, achieved the target range of Bu AUC. Alternatively, after the 1st Bu dose, half of the non-malignant patients needed dose adjustment. Moreover, at 5th, 9th, and 13th doses, 71%, 67% and 86%, respectively, achieved the target range of Bu AUC.

Conclusion: The suitability of the developed method for routine TDM was demonstrated by measuring Bu in human plasma samples of patients who are going to undergo HSCT for various types of hematologic malignancies and non-malignancy conditions. The findings of the present study suggest that the pharmacokinetic profile of i.v. Bu varies in both groups.

Dr. Abdullah Al-Sultan
College of Pharmacy, Kind Saud University, Saudi Arabia

TDM of Antimicrobials

Optimizing the dosing of antimicrobials based on pharmacokinetics/pharmacodynamics (PK/PD) principles is critical to improve treatment outcome and decrease the development of resistance. One tool that is used to improve precision of dosing to attain these PK/PD targets is therapeutic drug monitoring (TDM). This tool is applied to assure antimicrobials drug concentrations are within the therapeutic window. It is commonly applied to vancomycin and aminoglycosides and sometimes to other classes of antimicrobials such as b-lactams, antifungals and antituberculous drugs. The aim of this presentation is provide an overview of antimicrobials PK/PD and how antimicrobials are classified as having time or concentration dependent killing. We will describe the different approaches to perform TDM for vancomycin and aminoglycosides. That includes topics such as trough VS AUC guided monitoring of vancomycin, Bayesian approaches for TDM, using nomograms VS two sample individualized approach for aminoglycosides. In addition, we will briefly discuss the role of TDM for other antimicrobials such as b-lactams and antituberculous drugs.

Dr. Mohsen Hedaya
Faculty of Pharmacy, Kuwait University, Kuwait

Pharmacogenetic Testing: A Tool for Optimizing Drug Therapy

The primary objective of pharmacogenetic testing is to provide information that can guide the selection of the optimal dose of the proper medication. This selection is based on the patient specific genetic predisposition to target those who will most likely respond and least likely develop adverse effects. Most of the clinically relevant pharmacogenetic information results from variation in the genes that code for drug metabolizing enzymes or those that alter the body's response to the drug. Over the past two decades, pharmacogenetic research has been generating information that supports the value of pharmacogenetic testing in optimizing drug therapy. This stimulated professional institutions and working groups such as The Clinical Pharmacogenetic Implementation Consortium (CPIC), Pharmacogenetic Knowledgebase (PharmGKB), and the Dutch Pharmacogenetic Working Groups and others to develop evidence-based guidelines for the implementation of pharmacogenetic testing in clinical practice. The development of these guidelines followed the established procedures for developing clinical guidelines. This include critical appraisal of the relevant scientific literature, input from researchers and clinicians with expertise in the subject, and extensive peer-reviewed approval process. Numerous guidelines for the implementation of pharmacogenetic testing in clinical practice has been published to guide practitioners in selecting the appropriate drug and optimal drug dose. Examples of the commonly utilized pharmacogenetic tests include the test for CYP2D6 expression level when prescribing codeine, tramadol, hydrocodone, and oxycodone. These opioid analgesics are metabolized by CYP2D6 to their pharmacologically active metabolites which can range in quantity from minute amount that does not produce any analgesic effect to large quantity that can cause toxicity, depending on CYP2D6 activity. Also, determination of UGT1A1 genotyping in metastatic colorectal cancer patients to predict the development of irinotecan toxicity. Reduction of the expression level of the enzyme UDP glucuronosyltransferase 1A1 can lead to slow metabolism of the active irinotecan metabolite (SN-38) and increase its toxicity. Evaluation of Thiopurine Methyl Transferase (TMT) genotype has been utilized to determine the individual's susceptibility to thiopurine toxicity, and for guiding thiopurine dosing. Furthermore, CYP2C9 and VKORC1 genotyping has been employed for guiding the initial selection of warfarin dose. Besides, CYP2C19 genotyping has been utilized for optimal dosing of the antiplatelet drug clopidogrel in patients undergoing percutaneous coronary interventions. This is in addition to other tests that can predict the response and remission rate in patients with major depressive disorders, and tests that can guide tailoring of psychotropic treatment. Despite the growing evidences supporting the usefullness of pharmacogenetic testing, its utility has been confined to specialized medical areas. Widespread integration of pharmacogenetic testing into routine clinical practice requires dissemination of evidences related to the clinical utility of pharmacogenetic tests that affect new and old drugs. Tackling regulatory and reimbursing issues related to pharmacogenetic testing is also important. Lastly, practitioners must be trained to interpret pharmacogenetic test results and to make use of these results in their drug-related decision making.

Ph. Donia Bastaki,
Head of Drug Registration Kuwait Drug and Food Control Administration
Kuwait

Biosimilars and Biologics: What Data do Regulators Need?

Scientific advances and modern technologies have initiated new areas for the effective treatment of human diseases that were previously beyond the scope of the classical pharmaceuticals containing chemically synthesized compounds as active ingredients.

Biologics are medicines made from living cells through highly complex manufacturing processes and must be handled and administered under carefully monitored conditions. Biologics are used to prevent, treat, diagnose, or cure a variety of diseases including cancer, chronic kidney disease, autoimmune disorders, and infectious diseases.

The cost of biological medicines is very high and hence came the need of biosimilar products. A biosimilar is a biological medicine highly similar to another already approved biological medicine. Biosimilars are approved according to the same standards of pharmaceutical quality, safety and efficacy that apply to all biological medicines.

A biosimilar demonstrates similarity to the reference product in terms of quality, safety and efficacy based on comprehensive comparability studies. Unlike small molecule generic drugs, biosimilar are large, complex protein molecules that cannot be identical to the reference product.
Despite the advances in the methods and techniques available today for the full characterization of biosimilars, limitations of some of these methods and techniques prompt the initiation of guidelines relevant to comparability of safety and efficacy. Therefore, Comparability studies are needed to generate evidence substantiating the similar nature, in terms of quality, safety and efficacy of the new biosimilar product.

The overall goal of the Kuwait Regulatory Authority is to ensure that only biological medicines and biosimilars of demonstrated quality, safety and efficacy are available in Kuwait.
Moreover, to reach the optimal use of biosimilars it is important to consider the concept of interchangeability and switching between reference biological product and its biosimilar.
It is essential to have a comprehensive post-marketing surveillance to detect safety risks, immunogenic, or adverse reactions with adequate pharmacovigilance activities for all drugs, including biologicals and biosimilars.

The presentation provides an overview of the regulatory requirements for biological medicines and biosimilars with an special focus on biosimilars in terms of assurance of clinical, non-clinical and quality similarities, highlighting the registration status of biologics and biosimilars in Kuwait.

Prof. Ahmed Al-Jedai
Deputy Minister for Therapeutic Affairs
Ministry of Health, Riyadh, Saudi Arabia

Pharmacy Practice in the Gulf; Challenges and Future Outlook

The healthcare system in the gulf region is very progressive and is ranked within the first 50 in the world. The population is estimated at 50 million with overwhelmingly young population and a median age of 30 years. With a population growth rate between 2-3%, the healthcare system faces major challenges. Similar to developed countries, cardiovascular disease and diabetes cause a huge health burden in the country. Pharmacy practice is continually evolving in the region and pharmacists have the opportunities to practice in a variety of settings. The number of pharmacists in the workforce and the evolving pharmacy education system are few of the challenges to the progress of the profession. This presentation will discuss the current status of the health care system and pharmacy practice in the GCC countries, challenges and future directions.

Dr. Saja Almatrook
Ministry of Health, Kuwait

Regulatory and Legal Framework of Pharmacy Practice in Kuwait

The field of pharmacy has significantly evolved during the past few years. In addition to medication dispensing, the role of pharmacists have expanded to include counseling, medication management services and clinical pharmacy, adding more responsibilities to pharmacists. Furthermore, pharmacy practice plays an important role in public health. Such diversified roles increased the demand for recruiting more pharmacists in both private and government sectors creating an urgent need to develop laws and legislations to regulate the practice of pharmacy to provide optimum health services with minimum errors.

The pharmacy practice in Kuwait was regulated in 1960 when the law No. 25 was introduced and enforced. In 1996 an emended law No. 28 was enforced to regulate the pharmaceutical profession by covering all pharmacy aspects related to the standard of practice and professional career. This law was further amended by law No. 30 in 2016. Such laws help pharmacists to address daily issues encountered during their practice and is considered an important reference guide for different clinical/ pharmacy issues.

In addition, other regulations were developed to manage three main aspects which are partly related to pharmacy practice, these are: laws regulating the sales and consumption of narcotics (Law No. 74 in 1983), laws regulating the sales and consumption of psychotropic substances (law no. 48 on 1987), and the law regulating advertisement of medicines and health products (Law No. 38 in 2002).

To further protect the public from the dangers of pharmacy malpractices and to improve patient-centered care, laws and regulations should involve various daily aspects relevant to the standards of professional conduct which needs to be well recognized and implemented by governmental institutions operating under the autonomy of the Ministry of Health.

Dr. Salah Waheedi
Faculty of Pharmacy, Kuwait University, Kuwait

Ethics for Pharmacists in Kuwait

Ethics understanding is an essential component of the professional characteristics of a pharmacist. Ethical standards have been set by regulatory organizations in developed countries around the world. However, to date, despite the time spent and efforts made by several pharmacists, the national code of ethics for pharmacists is still not published. Consequently, pharmacy students in Kuwait rely their learning about ethical standards on what has been set by other countries. Should we expect our graduates to comply with these ethical standards, even though they understand that these standards have not received the consensus by pharmacists or by their representatives in the country? Only recently, pharmacists in Kuwait have been given the opportunity to express their views over the International Pharmaceutical Federation (FIP) recommended ethical standards. This is an essential first step towards adopting these standards which promote patient centeredness and support advanced practice. A modern code of ethics, that sets the standards and provides pharmacists the compass to deal with ethical dilemmas, should be supported by regulatory authorities, professional organizations, and individual pharmacists. With a code of ethics, the regulatory authorities can hold members of the profession beyond the legal accountability. Professional organizations can use the ethical standards as a guide to provide professional support to their members. Also, individual pharmacists will realize soon that clear ethical standards lead to job satisfaction, and reduce work related stress and burnout.

Dr. Reem Al-Essa
Head of Government Inspection Administration,
Drug Inspection Administration, Drug and Food Control
Ministry of Health, Kuwait

The Roles and Responsibilities of the Regulatory Bodies in Auditing Pharmacy Practice within the GCC

Pharmacy Practice Audit is a formal review of operations and processes carried out by the responsible regulatory body to make sure that pharmacies are compliant with the national pharmacy rules and regulations set by the regulatory authority.

Since its inception, Kuwait Drug and Food Control (KDFC) has been the regulatory body to be the responsible sector within the Ministry of Health to ensure compliance with national laws and regulation governing the import, drug approval, market access, custom release, distribution, supply chain, dispensing, consumption, use of medicines and post-marketing surveillance. The responsible regulatory body for auditing/inspecting pharmacy practice is the Drug Inspection Administration. This study compares and contrasts between the roles and duties of the responsible regulatory bodies within the GCC State in auditing pharmacy practice to ensure compliance with pharmacy practice laws and regulation set within each member state.

A questionnaire was distributed to the person in-charge within each GCC regulatory body. The questionnaire was piloted with Bahrain first to ensure face validity, then with Kuwait to ensure content validity and feasibility. It was then distributed to the rest of the GCC Member States to be completed and returned for evaluation.

The results of the questionnaire showed similarities and differences between in the 6 regulatory settings and the methods carried out to ensure compliance with pharmacy regulations set by each Member State. Such similarities and differences revealed areas for improvement in the audit/inspection procedures carried out in Kuwait.

Prof. Pierre Moreau
Faculty of Pharmacy, Kuwait University

Development of a Cadre for Clinical Pharmacists

Purpose: In line with the advancement in pharmacy education worldwide and the current demand for clinical pharmacy services in Kuwait from pharmacists and Ministry of Health (MOH), our Faculty of Pharmacy started offering the add-on PharmD program from 2016. Since graduates of Medicine and Dentistry receive special cadre during their employment at MOH, financial and administrative incentives were needed to encourage pharmacists to enroll in the add-on PharmD program. Therefore, the purpose was to develop a modified cadre for clinical pharmacists that is deemed suitable and feasible to implement in Kuwait.

Method: An executive committee was created to develop a suggested cadre that may be applied to graduates of clinical pharmacy (PharmD) program. The committee makeup was: Vice president for Health Sciences (As the chairman of the committee); Assistant Undersecretary for Drug and Medical Affairs at the Ministry of Health; Assistant Vice President for Health Sciences; Dean of Faculty of Pharmacy; Dean of Faculty of Dentistry; and chairman of the PharmD planning committee (As the reporter of the committee). The executive committee were to meet several times and to review the current cadres for graduates of medicine, dentistry, and pharmacy programs and make their recommendations. The committee would then consult with the legal affairs office as well as with the Civil Service Commission (CSC) before making any suggestions.

Results: After consultation with CSC and the other members of the executive committee, it was decided to utilize the existing cadre for pharmacists in Kuwait (CSC decree No 30, 2012) and to modify it slightly such that graduates of accredited PharmD programs (and any other equivalent clinical pharmacy programs) would be hired on level 5 of the Pharmacy cadre directly (titled clinical pharmacist) while granting them clinical allowance ranging from 500-1200 KD depending on experience level and obtained credentials. Advancement and promotion within the clinical pharmacy cadre would require attainment of board certification in pharmacotherapy specialty (or any other equivalent of that board) as well as years of clinical pharmacy experience and supervision/training of clinical pharmacy staff. This suggested cadre was endorsed by the executive committee and sent to the CSC for approval since late 2016.

Conclusion: Approval of a special cadre for graduates of PharmD program is necessary to encourage these graduates and to promote the development of clinical pharmacy services in Kuwait, which are lacking in most hospitals. Further support is needed from the Minister of Health and high ranked government officials to recognize the importance of clinical pharmacists and their special services and to adopt this suggested cadre in Kuwait.

Prof. Zubin Austin
Professor and Koffler Chair in Management,
Leslie Dan Faculty of Pharmacy, University of Toronto, Canada

The 9Ps to Support the Evolution of Pharmacy Practice with a Focus on Education

Recent research in Canada has identified 9 key factors that appear to support practice evolution and change in pharmacy. These factors include: : 1) permission, 2) process pointers, 3) practice/rehearsal, 4) positive reinforcement, 5) personalized attention, 6) peer referencing, 7) physician acceptance, 8) patients' expectations and 9) professional identity supportive of a truly clinical role. One theme that did not emerge was payment, or remuneration, as a specific or isolated motivational factor for change.

This session will focus on how educators can interpret and apply this research to their work with students and practitioners to play an important role in fostering practice expansion. Through a series of interactive discussions, participants will have an opportunity to identify how the 9Ps of Practice Change can be applied at any level of pharmacy education, from undergraduate to postgraduate to continuing professional development. A key component of this session will be to provide participants with opportunities to discuss both content of change management education and teaching, learning, and assessment strategies that can be incorporated into curriculum design.

Dr. Sarah Al-Ghanem,
Faculty of Pharmacy, Kuwait University

Kuwait Change in Curriculum

Pharmacy is maturing as a clinical profession and presently is well positioned to transform itself from product-oriented to a patient-oriented profession and promotes the responsible use of medicines. Clinical pharmacy services provided through direct patient care that optimizes medication therapy and promotes health, wellness and disease prevention, are expanding worldwide. It requires extensive training to make the pharmacist the most knowledgeable health care professional when it comes to medicines and their optimal use. Therefore, all pharmacists must become agent of changes, and pharmacy education need to be the key leader of change to move the profession forward. Pharmacy education should prepare graduates to meet the demand of profession transformation and prepare them well for the increasing complex patient and medication therapy management. Currently, the practice of pharmacy in Kuwait is providing basic services of medicine dispensing to the population, with minimal clinical services in some hospitals. A recent (Spring 2015) needs assessment conducted by our Faculty has identified several services that are expected by the population and healthcare professionals (including pharmacists) to be provided by pharmacists but not adequately rendered by Kuwait pharmacists today.

Pharmacy curriculums are moving from Bachelors of Pharmacy (BPharm) to undergraduate Doctorates of Pharmacy (entry-to-practice PharmD) in several countries to better prepare future pharmacists to address those needs and offer a wider range of pharmacy services. Accordingly, the faculty of Pharmacy at Kuwait University undertook several initiatives and steps forward to adapt for the changes. A two years add-on-PharmD program has been offered since September 2016 on top of current BPharm as a transition stage. Our aim is to merge the 5-year BPharm with the 2-year add-on PharmD to create a 7-year entry-to-practice PharmD in the upcoming years. Keeping in mind the faulty vision to prepare graduates to engage in a stimulating career devoted to the optimization of medicine- based therapy to improve the health condition of patients in the State of Kuwait. To foster the development of proactive professionals, an environment where the responsibility of learning is shared between the students and the instructors has to be created, where autonomy and initiatives are expected from students. The program adapted competency based education delivered through active learning approach to allow candidates to develop defined competencies. In addition, assessment framework has been modify to allow measuring the progression of the students in their knowledge acquisition and competency development. Hence, the curriculum allow preparing the students to become life-long learners.

Ph. Asmaa Al-Haqan,
FIP Collaborating Centre, University College London,
School of Pharmacy, UK
Faculty of Pharmacy, Kuwait University, Kuwait

CPD Regulations, Requirements and Audits

Introduction: Global reports consistently urged the need for competent pharmacy workforce in order to ensure universal health coverage and the access to quality health services. The International Pharmaceutical Federation (FIP) led the creation of a developmental roadmap to facilitate the global transformation of pharmaceutical education and workforce by providing the appropriate strategic tools to support and develop quality-driven education at national levels. Building on the tools and strategies advocated by the FIP, the "Continuing professional development model (Co-ProDeM) was developed to guide a national pharmacy workforce transformation in Kuwait.

Methods: The Co-ProDeM was constructed based on the findings from: 1- a global evidence review of systemic factors influencing pharmacy continuing professional development and, 2- a comprehensive examination of pharmacists and CPD providers perspectives on professional development in Kuwait. A qualitative approach using focus group interviews was carried out with thirty three pharmacists practising in direct and non-direct patient care settings in Kuwait. In addition, semi-structured interviews with the three main pharmacy CPD providers in the country were conducted. Data from the literature review and the interviews were triangulated and analysed using the framework analysis method. The development of the model was also guided by the FIP workforce development goals that were built together to establish the milestones for impactful global development for pharmacy education, and on the conceptual global framework for quality assurance of pharmacy education that depicts the dynamic relationships between practice, regulation and education.

Results: findings showed that there are three main areas identified and are considered as the main building blocks for the development of a comprehensive CPD model for pharmacists. The first component of the Co-ProDeM is the development of foundation and advance competency frameworks to assist in adopting needs-based approach for education. Both, pharmacists and CPD providers agreed that lack of clear scope of practice and competency frameworks made it difficult for pharmacists to identify their learning needs and therefore made it difficult for them to decide on goals for career development. The second component is system of support incorporated in needs-based education strategic plans. Pharmacists mentioned the need for activating a system for support, as well as activating the role and leadership of higher authorities and professional and regulatory bodies for the implementation of an effective CPD strategies and policies. The third component is policies and regulations. This is important as national and international workforce development visions recognised the vital role of policies and regulation in implementing needs-based development approaches to professional development across all settings and stages of pharmacists career.

Conclusion: The Co-ProDeM was developed based on an evidence-based approach as well as the principles of sustainable health care improvement. The model aims towards achievement of national (New Kuwait 2035) as well as international strategic and sustainable development goals. This model would provide leaders and educators with a roadmap that would guide the pharmacy workforce development plans on a national level.

Dr. Mohammed Al-Enezi
Life Sciences Academy, Kuwait

LSA's Model of CPD Offer and Delivery

Life Science Academy (LSA) was established in 2013 under the umbrella of Kuwait Life Sciences Company and is funded by the Kuwait Investment Agency. Our mission is to promote continuous professional development (CPD) across all healthcare sectors and influence legislations and policies to match international standards and best practices. At our core, we believe in transforming healthcare leaders to advance patient care and inspire change in healthcare delivery. We focus on the development of healthcare professionals' knowledge, practices and skills by operating in collaboration with international top ranked universities/institutes and with regional and local experts to share latest practices in their field. Some of our partners include the American College of Clinical Pharmacy, Accreditation Council for Pharmacy Education, PharmExpert and Faculty of Pharmacy at Kuwait University. Over the recent years, we developed several trainings and CPD programs tailored to the needs of pharmacists. Some examples include basic life support for pharmacists, medication reconciliation, the pharmacist and patient-centered diabetes care, patient counseling for pharmacists and managing healthcare personnel. We continuously strive to meet the CPD needs of pharmacists and be a trusted CPD stakeholder in Kuwait.

Dr. Jacinthe Lemay,
Faculty of Pharmacy, Kuwait University, Kuwait

CPD Needs for MOH Pharmacists in Kuwait

In the context of developing a locally relevant doctorate pharmacy degree at Kuwait University, the Faculty of Pharmacy recently conducted several focus group meetings with various stakeholders and have identified five population needs, supported by eighteen pharmacy services. It remained to be determined whether practicing pharmacists felt ready to offer those services. Thus, the objective of this study was to determine the attitudes, practices and training needs regarding the identified services among pharmacists working in the Kuwait Ministry of Health hospitals. A cross sectional study using self-administered questionnaires among a total of 319 hospital pharmacists across secondary and tertiary care hospitals in Kuwait was conducted. In addition to demographics, participants answered 3 questions for each service: 1- how strongly they felt that pharmacists should deliver the services, 2- how often they offered them and 3- what was their current training need to offer or improve the service. Gaps were defined as the difference between those who believe pharmacists should offer the services and those who actually offer them. Results showed that the largest gap resides in the services that support the provision of pharmaceutical care (62.4%), followed by health promotion and education (59.2%), first-line healthcare access (51.8%), continuity of care (51.5%) and safe delivery of medicines (33.2%). There was a significant correlation between the gap and the need for training to be able to offer the services (rs=0.676; p=0.002), suggesting that continuing professional development (CPD) is essential to enable pharmacists to offer services that are needed by the population in Kuwait. Based on those results, Faculty of Pharmacy and Ministry of Health should collaborate to develop a CPD program focused on services that are expected by the population but currently inconsistently offered. This would meet the training needs of practicing pharmacists and ensure optimal use of medications and patient outcomes.

Dr. Haifa Hamid Glom Ali,
Quality Specialist, Quality and Accreditation Directorate, MOH Kuwait

Accreditation Standards for Pharmacists
Medication Management: Navigating through the Regulatory Requirements

Kuwait has collaborated with Accreditation Canada to introduce the accreditation program to Healthcare Organizations. Within the hospital's and primary care accreditation standards, "Pharmacy services" and "Medication management" modules are the two modules concerning medication management. Some of the Safety Required Areas (ROPs), which are high-priority areas and central to quality and safety, include medication reconciliation, control of concentrated electrolytes and look- alike, sound-alike medications. Currently, not all healthcare organization are implementing the medication reconciliation standard due to several barriers and obstacles including absence of electronic health record i.e. electronic medication prescription and electronic reconciliation forms which will facilitate the implementation of the medication reconciliation. Poor integration between the patient prescription and his laboratory profile and unavailability of "clinical decision support software" which will aid clinicians in decisions related to patient medications.

The standard regarding the control of concentrated electrolytes states that no concentrated electrolytes solutions should be stored in patient service areas, and commercially available premixed solutions should be used for electrolyte replacement when they are available; otherwise, the pharmacy prepares and dispense all infusions for electrolyte replacement therapy. The current practice in Kuwait is below the safety requirements: concentrated electrolytes are still stocked in large quantities in intensive and special care areas and due to pharmacies limited working hours in some hospitals, the general care areas are ordering concentrated electrolytes from special care units, which is against safety standard.

The accreditation standard regarding look alike sound alike medications (LASA) requires organizations to identify and manage risks associated with such medications. However, the current practice whether at the pharmaceutical companies or healthcare organization is not compatible with the safety requirement due to many reasons, like continued production and marketing of LASA medications, and development of multi strength medications in addition to products with different suffix descriptors. Moreover, at organizational levels, there are personal preferences of prescribers and unwillingness to conform to a limited formulary, the use of brand names instead of generic names when prescribing medication and lack of standard methodology and variation among care facilities when using text enhancing methods e.g. Tall-man lettering and in production of warning labels.

To overcome the barriers related to medication management, we need to empower the central pharmaceutical sectors and directorates to be more aware and involved in the safety requirement pertaining to medication management. In addition, we need to enhance the collaboration between the pharmaceutical services & other clinical entities at the central level to set the medication management guidelines according to the best practices &international safety standards. Participation and collaboration with the national and international regulatory, and advisory boards. Furthermore, we need to initiate the pharmacy and therapeutic committee whether at the central and/or organizational level, and to develop and improve the Electronic Health Information System and medication prescriptions.

Prof. Ahmed Al-Jedai
Deputy Minister for Therapeutic Affairs
Ministry of Health, Riyadh, Saudi Arabia

Clinical Pharmacy Initiatives in Saudi Arabia

Clinical Pharmacists play a critical role in direct patient care. This role has evolved over time with increased emphasis on collaborative care and patient interaction. Clinical pharmacists are uniquely trained on pharmacotherapeutics which allows them to provide comprehensive drug managements to patients and practitioners. There have been numerous reports to support the addition of clinical pharmacists to the clinical team with the conclusion that the addition of clinical pharmacy services in the care of patients generally results in improved care, with no evidence of harm. Clinical pharmacy started in Saudi Arabia in the mid-1970s where pharmacists initially provided basic pharmacy services to the team such as therapeutic drug monitoring, and drug information. The role has expanded to include designing, implementing and counseling patients on individualized drug regimens, designing therapeutic plans for complex medical regimens, monitoring for therapeutic success or failure and educating patients and health care professionals. In addition to, conducting clinical research and providing direct patient care in the clinic. This presentation will discuss the current status of clinical pharmacy in Saudi Arabia and initiatives to upgrade the profession to the next level.med Al-Jedai, Saudi Arabia

Ph. Thamna Alshaibani,
Sultanate of Oman
Clinical pharmacist, Head of pharmacy department, IRH, Oman

Pharmacist-Led Clinical Services: The Oman Experience

The practice of clinical pharmacy embraces the philosophy of pharmaceutical care; it blends a caring orientation with specialized therapeutic knowledge, experience, and judgment for the purpose of ensuring optimal patient outcomes. Clinical pharmacy is moving the pharmaceutical practice from medication oriented to patient care oriented. The role of clinical pharmacist underwent important changes in the last few years in Oman as their participation in direct patient care increased. Understanding the development of clinical pharmacy practice helped to establish new models of team-based care in Oman. They are now more specialized for specific services or complex care.

Ph. Nour Al-Khalaf, MSc, B. Pharm
Pharmacist, KOC Hospital, Kuwait

Kuwait experience in peer-referencing

Introduction: Clinical pharmacy is a health science discipline in which pharmacists provide patient care that optimizes medication therapy and promotes health, wellness, and disease prevention. Recently there is a dramatic changing in clinical pharmacy services in Kuwait. Peer referencing is considered as a significant tool for shaping attitudes and redirecting behaviors towards practice and clinical pharmacy profession.

Clinical pharmacy in Ahmadi Hospital: Clinical pharmacy services started in KOC hospital in 2014, led by 2 qualified clinical pharmacists to cover medical wards, then the service expanded to cover other wards and clinics.

Implementation: clinical pharmacist in Ahmadi hospital delivers clinical services by using different tools and electronic system, which allows the clinical pharmacist to provide patient care in effective and efficient manner. Clinical pharmacy services in Ahmadi hospital include the following services: medication reconciliation, Medication Therapy Management, ward round participation with multidisciplinary team, follow up evaluation, medications monitoring and documentations. Recently, clinical pharmacy services have expanded to include anticoagulation counselling clinic and medicine use review (MUR) clinic to cover outpatient setting. Moreover, Faculty of Pharmacy collaborated with KOC hospital for Pharm D students training program. The purpose of this program is to provide a structured, work-based training experience for students, enabling them to deliver safe and effective pharmaceutical care in internal medicine wards. Documentations in the electronic medical records in Ahmadi hospital is considered as an essential element for providing clinical pharmacy services and to address interventions for health care professionals.

Challenges and Barriers: Lack of group- based education, time constraints and shortage of personnel are some of the challenges facing current clinical practice in Ahmadi Hospital.

Conclusion: Sharing the clinical experience and challenges in day-to-day practice can be both bracing and informative to improve our profession. In addition, peer referencing is identified as an important motivational factor that help many pharmacists to improve their practice. Clinical pharmacy team will regularly review and audit the types of interventions performed for quality assurance purposes in Ahmadi Hospital.

Dr Monther Al-Sharekh
Head, Nephrology Unit Chest Hospital, Kuwait

Physician Perception and Demand of Clinical Pharmacists in Kuwait

It is well known the importance of clinical pharmacy in the hospitals. In outpatients or inpatients, for medications reconciliation or medications interactions. Examples of activities and services shared with pharmacist at our department are; development of catheter-related blood stream infections protocol, vancomycin dosing and monitoring guideline, participation in multidisciplinary meetings, and medication reconciliation service led by pharmacists. However, several challenges were notice which will be discussed further during the talk. I will talk about my experience in our center (Mubarak Al-Abdullah Al-Sabah Dialysis Center) after introducing the service of clinical pharmacy.

Dr. Rania Azmi, Kuwait
President, "Fadia Survive & Thrive Association- Supporting Cancer Patients" & Wharton Board

Patient Expectations of Pharmacists as a Driver for Expansion of the Profession

The current public perception of a pharmacist typically entails a neat person wearing a white coat while standing behind a counter dispensing medication, especially in less developed countries. By advocating at the pharmacist-patient level, this common perception could be reversed. Advocacy in its most basic form is simply promotion. Possibly the most difficult and important group to advocate to about the pharmacist role on the health care team is patient. This can be applied to simple dispensing, medication assessments, injections, pharmacist prescribing, over-the-counter recommendations and much more.

With the advancements in technology and communications across the world, patients are expecting pharmacists not only to inform them about prescribed medicines' side effects and how to take them besides making them aware of any drug interactions with their medication, but also to correct any public information they might acquire from unreliable sources (such as the data that lacks scientific evidence spreading via any social media platform).

As a result, patients are also expecting that the pharmacists would intervene in explaining and verifying the prescribed medicines with patients in order to help optimizing patient care.

It is essential to emphasize here that the oncology pharmacist is often one of the few team members who fully understands the safety, efficacy, pharmacologic, and financial components of patient care. Therefore, the patients' expectations are higher for this type of pharmacists compared to traditional or general pharmacists.

Also, recognizing that in recent few years Quality of life (QoL) has been viewed as a primary end point to assess the quality of care and management in oncology medicine, where oncology pharmacy is not an exception of that view. QoL is a multidimensional, multifaceted measure which refers to a patient's perception of general wellbeing, including psychological, cognitive, physical and social functioning. This adds to the complexity of the patients' expectations at least in oncology pharmacy.

Now, many pharmacists spend more time than ever in direct patient contact, explaining treatment goals, possible adverse effects, and safe and successful use of medications. However, such roles are still very random and driven by patients' inquiries rather than being an integral part of a standard pharmacist's practice.

Workshop by invitation:

Objective: Drafting recommendations to support an expanded scope of pharmacy practice in Kuwait

Discussion of the recommendations

Facilitated by: Dr. Sarah Al-Ghanem; Prof. Pierre Moreau, Dr. Jacinthe Lemay, Dr. Abdullah Al-Bassam

Poster Presentations

1
*Abbas A, Alshaibi S, Kattezhathu VS, Owusu Y, Awaisu A, Sankaalingam S: Profile of Drug-Drug Interactions in the Community Pharmacy Setting in Qatar

2
*Abdelkader N, Nasrallah L, Agouni A: In-Vitro Investigation of the Role of Protein Tyrosine Phosphatase 1B (PTP1B) in Endoplasmic Reticulum Stress-Induced Endothelial Dysfunction.

3
Abdelrahman AM, Al Suleimani YM, Shalaby A, Ashique M, Manoj P, Al-Saadi H, Ali BH: Effect of levosimendan, a calcium sensitizer, on cisplatin-induced nephrotoxicity in rats

4
Abdulraheem AI, Qasem JA: A study of the microbial content in non-sterile Pharmaceuticals by culture and PCR methods

5
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1

Profile of Drug-Drug Interactions in the Community Pharmacy Setting in Qatar

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Introduction:
Drug-drug interactions are very common in health care delivery settings and could compromise patient safety resulting in morbidity, mortality and an increase in the length of hospitalization. Limited data is available with regards to the prevalence of potential drug-drug interactions (pDDI) in Qatar. The objective of this study is to document the prevalence of (pDDI) and categorize them based on severity and risk rating and to identify factors that contribute to increased risk of DDI in Qatar.

Methods:
A quantitative cross-sectional observational retrospective study was conducted from October-December 2017. Prescriptions included in the study were legal and of patients of both genders that contained 2 or more prescribed drugs. The exclusion criteria were prescriptions that were in Arabic, illegible, incomplete, and included only 1 systemic medication. Potential drug-drug interactions were assessed using two databases: Micromedex® and Lexicomp® and were classified according to severity. Descriptive statistics using frequency and percentages, Pearson's Chi-square test and Cohen's kappa were used in this study.

Results:
The rate of pDDI among prescriptions (n=200) was 20.5% and 32.5% for Micromedex® and Lexicomp® respectively. There was moderate strength of agreement between the two databases (Cohen's Kappa = 0.698). More than 95% of the pDDIs were either in the moderate or major category of severity. However, the majority (78%) of pDDIs as assessed by Micromedex® were of major severity, while 58.8% of pDDIs were of moderate severity as reported by Lexicomp® (p-value<0.001). Importantly, the rate of pDDIs was more than 95% in prescriptions with 6 or more medications.

Conclusions:
There is a high rate of pDDIs among prescriptions dispensed in Qatar. The higher the number of concurrent medications in a prescription the higher is the rate of pDDIs. Although there is a moderate level of agreement between the two databases the extent of the discrepancy is significant. Thus, the databases used to check for pDDIs can also impact on patient safety in Qatar.

Key Words: pDDI; LexicompR

2

In-Vitro Investigation of the Role of Protein Tyrosine Phosphatase 1B (PTP1B) in Endoplasmic Reticulum Stress-Induced Endothelial Dysfunction.

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Introduction:
Type II diabetes Mellitus is associated with insulin resistance which induces endoplasmic-reticulum stress (ER-stress), and then leading to cardio-metabolic complications. ER-stress can result in cardiovascular disorders through endothelial dysfunction. Furthermore, researchers reported that a prototype from the PTPs superfamily which is known as PTP1B is a major regulator of insulin resistance. Recently, PTP1B was linked to ER-stress, and it was also thought to be involved in endothelial dysfunction. The aim of this study is to investigate the role of PTP1B inhibitor on ER-stress induced endothelial dysfunction.

Methods:
The study is designed to be in an in-vitro experimental setting using EA.hy 926 cell line. Four main groups were studied throughout the project; 1) No treatment (control). 2) DTT treated. 3) DTT+PTP1B inhibitor. 4) PTP1B inhibitor. Western blot was used to evaluate the effect of PTP1B inhibition on ER stress and on endothelial function. Alamar blue assay was used to assess the cell viability.

Results:
Western blot analysis of BiP showed significant increase in BiP expression in DTT and DTT plus PTP1B inhibitor groups as compared to control and PTP1B inhibitor (p-value < 0.05). While, the western blot results of CHOP, P-eNOS, and total eNOS, and the alamar blue assay showed no statistical significance.

Conclusions:
The study results indicated that the role of PTP1B inhibitor in endothelial dysfunction provoked by ER stress cannot be concluded. However, further investigations are required due to some limitations in this study and due to the bulk of evidence that supports the role of PTP1B.

Key Words: ER Stress; Protein Tyrosine Phosphatase 1B (PTP1B)

3

Effect of levosimendan, a calcium sensitizer, on cisplatin-induced nephrotoxicity in rats

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Introduction:
Background: Levosimendan is a positive inotropic agent with vasodilating properties. It increases the sensitivity of troponin C to calcium in cardiac cells, causes vasodilation by opening (ATP)-sensitive potassium channels in smooth muscle cells and possesses anti-inflammatory and antiapoptic effects. We investigated the effect of levosimendan on cisplatin (Cis)-induced nephrotoxicity in rats.

Methods:
Rats were divided into four groups (n = 6). The first and second groups received normal saline (control) and intraperitoneal (i.p.) cisplatin (6 mg/kg) on day 7, respectively. The third and fourth groups were given a single intraperitoneal (i.p.) injection of Cis on day 7 and levosimendan (1 mg/kg/day, orally) or vehicle for 10 days, respectively. At day 11, animals were anaesthetized and blood collected and kidneys removed. Another four groups were treated the same as the previous four groups to measure renal blood flow.

Results:
Cis significantly increased plasma urea, creatinine and neutrophil gelatinase associated lipocalin (NGAL) levels. In addition, Cis increased urinary albumin/creatinine ratio, N-Acetyl-β-D-Glucosaminidase (NAG) activity and reduced creatinine clearance. Cis also significantly increased the plasma concentration of plasma tumor necrosis factor–α (TNF-α) and significantly reduced antioxidant indices [catalase and superoxide dismutase (SOD)] and increased lipid peroxidation. Histopathologically, Cis caused remarkable renal damage compared with control. Moreover, Cis reduced renal blood flow. Levosimendan significantly ameliorated Cis-induced biochemical, histopathological and hemodynamic changes.

Conclusions:
Our results show that administration of levosimendan significantly reversed the biochemical, histopathological and hemodynamic indices of Cis-induced nephrotoxicity in rats. The protective effect of levosimendan is shown to be related to its anti-inflammatory and antioxidant effects.

Key Words: Cisplatin; Levosimendan; Nephrotoxicity

4

A study of the microbial content in non-sterile Pharmaceuticals by culture and PCR methods

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Introduction:
The objective of this work is to investigate the occurrence of microbial contamination of certain oral drugs by using polymerace chain reaciton. Oral drugs (non-prescriptional) shows to be frequently contaminated by microorganisms that can result in serious consequences to the patients health. We recently carried out a study of 5 Kuwaiti hospital community pharmacy units preparing non-prescriptional drugs in liquid dosage form (solution-suspension) that showed high level of bacterial and fungal contamination.

Methods:
The protocols for the study involved structured selection of representatives named of liquid dosage from some Kuwaiti hospitals, constitute microorganisms were elaborated and enumerated using standard microbiological protocols. Ten samples with five replicates of commercially available oral medications solution were obtained from retail pharmacy and clinical pharmacies in Kuwait. Samples of oral medication solutions were tested and spreads on agar media for culture development and for polymerase chain reaction amplification (PCR).

Results:
Eighty percent of contamination in Baby carminative and Magnesium Tri-silicate by culture and 100% of contamination in Baby carminative by PCR method was reported. Aldiya polyclinic from the central region reported high percent of contamination by culture (12%) and (16%) PCR when compares with other 4 polyclinics from the north and south regions. Samples tested replicates of ten oral drugs (including syrup, solution and suspension) each was examined of 50 samples tested by culture and PCR, produces positive results of 13 (26%), 7 (14%), 5 (10%) and 6 (12%), 9 (18%) and 3 (6%) by culture for bacteria, fungi and yeast respectively. E. coli, P. aeruginosa, S. aureus, A. niger and C. albican were identified by culture and PCR, among the five A. niger was reported high by culture (8%) and PCR (16%). E. coli, P. aeruginosa and S. aureus were sensitive to Potassium citrate, Adult carminative, Magnesium Tri-silicate (Basic compound), Expectorant and Belladona. A. niger and C. albican colonies were sensitive to Adult carminative, Baby carminative and Citric acid.

Conclusions:
Commonly available non-prescriptional drugs as oral medication solution have been shown to be frequently contaminated by microorganisms. This has possible adverse consequences of those who obtain drugs by oral medication. The uses of rapid PCR method provide reliable analysis for microbial evaluation.

Key Words: Microbiology; PCR; Drug;

5

Role of aquaporins in endocrine ressistant and sensitive breast cancer cell motility and invasion

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Introduction:
Anti-estrogen therapy, administered for >70% of breast cancer patients classified estrogen receptor (ER) +ve, is limited by development of drug resistance. Several ER-silenced cell lines exhibiting endocrine resistance and morphological change from epithelial to mesenchymal phenotype have been established to study this phenomenon. Their increased motility and invasive properties are accentuated by exposure to alkaline pH, with formation of dynamic plasma membrane blebbing through cytoplasmic streaming that may be sensitive to osmotic conditions controlled by aquaporins (AQPs), that modulate water movement. Four AQPs (1,3,4,5) have been reported to be modulated in several cancers and associated with disease progression so we investigated their role in motile functions in our breast cell lines.

Methods:
AQP expression/localization was examined by PCR, Western blotting. and confocal immunofluorescence in endocrine sensitive (YS1.2) and resistant (pII) breast cancer cells, and in normal epithelial cells of breast (MCF10A) or non-breast (HEK) origin. Effect of osmotic change on bleb formation was examined by live cell imager. AQP3 protein was knocked down by siRNA transfection.

Results:
Expression of the four AQPs varied in different cell lines and exhibited nuclear, cytoplasmic and membranous localisation. Osmotic change affected formation of blebs. In pII cells exposed to alkaline pH, there was translocation of AQP3 from the nucleus into the newly formed blebs. Expression of AQP3 protein was in the order YS1.2 > pII >MCF10A cells. SiRNA-mediated knockdown of AQP3 in pII and YS1.2 cells significantly reduced the motility and invasive behaviour of these cell lines and also reduced cellular blebbing in pII cells subsequently exposed to alkaline pH.

Conclusions:
These data suggest that AQP3 and possibly other aquaporins may participate in the processes leading to blebbing of endocrine resistant cells which we believe may be a mechanism that drives tumour metastasis.

Key Words: Breast cancer; Aquaporins; blebbing;

6

Phytochemical and Nephroprotective activity of Cichorium intybus L seed against Cisplatin induced toxicity

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Introduction:
Objective: The oxidative damage of cellular tissue by reacting active species causes various human diseases like cardiovascular disease, cancer, aging and nephropathy. The antioxidant supplements obtained from plants are useful to cure the oxidative damage in cells. Recently, attention has focused on phytochemicals as new sources of natural antioxidant and nephroprotective agent. The plant Cichorium intybus L., commonly denoted as chicory which belongs to family Asterac eae and geographically found in Asia and Europe. Chicory have medicinally active constituent like flavonoids, saponins tannins, alkaloids, inulin, sesquiterpene lactones, coumarins, vitamins, chlorophyll pigments and unsaturated sterols.Hence, in the present study methanolic extract of Cichorium intybus Linn seeds was evaluated for phytochemical screening and pharmacological activity against Cisplatin induced toxicity model in albino rats.

Methods:
Many standardization parameters of Cichorium intybus were analyzed. Standard method was adopted for the preliminary phytochemicals screening. Analysis of total phenolic and flavonoid contents, pesticides residues, aflatoxin & heavy metals were also performed. CAMAG- HPTLC system was used for fingerprinting of methanolic extract of Cichorium intybus L seeds. The slides of surface preparation of leaf were prepared for quantitative microscopic parameters. The air dried powdered plant materials were subjected for determination of physicochemical standardization. Phytochemical screening was performed for Presence/absence of phytopconstituents in the plant which was helpful development of analytical profile. The antioxidant potential was evaluated by DPPH method, H2O2 scavenging method and reducing power method. The pharmacological studies include acute toxicity studies were carried out according to OECD 423 guidelines and methanolic extract of selected plants methanolic extracts were found to be non toxic and nonlethal upto 3000mg/kg b.w

Results:
Phytochemical screening showed scavenging power (59µg/mL) at 100µg/mL concentration and 38µg/mL for Ascorbic acid. And methanolic extract of Cichorium intybus showed concentration dependent scavenging activity against hydroxyl radical. The IC50 value of methanolic extract Cichorium intybus was found to be 4.54µg/ml against standard ascorbic acid (IC50 2.50µg/ml) respectively. The total content 57.2 mg GAE/100 g & 5.61 mg QE/100 g phenolic compounds & flavonoids were respectively found in methanolic extract of Cichorium intybus. Heavy metal residue, pesticide residue & aflatoxin residue were totally absent in Cichorium intybus .The HPTLC method Toluene: Ethyl acetate: Formic acid (70:40:10 v/v) was found to be the best and gave good resolution with Rf 0.53 for quercetin acid and Rf 0.89 for quercetin. The proposed method was found to be precise, simple, specific and sensitive and can be used for quality control purposes of the plant Cichorium intybus seeds. Heavy metals concentrations were found to be within standard limits. Aflatoxins and pesticides residues were absent. Cichorium intybus L seeds methanolic extracts 600mg/kg revealed potent nephroprotective action against Cisplatin treated acute nephrotoxicity in male albino rats.

Conclusions:
It was concluded that the methanolic extract of Cichorium intybus (Chicory) is found to more effective and potent as an anti oxidant and nephroprotective against cisplatin induced nephrotoxicity which might prove beneficial in herbal industries for clinical trials as a potent Nephroprotective herbal drugs.

Key Words: Cichorium intybus L seeds; Chicory; Asteraceae;

7

Does Regular Consumption of Beetroot Improve Chemotherapy-Induced Anaemia In Cancer Patients?

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Introduction:
Cancer patients are at a high risk of developing anaemia either due to the nature of the disease or as a consequence of administering myelo-suppressive chemotherapeutic agents. This precipitates fatigue and general weakness. Cancer patients are seeking evidence-based knowledge about improving their dietary intake to manage chemotherapy side effects. Beetroot is a potent antioxidant and powerful source of dietary nitrates. Beetroot is considered a potential therapeutic treatment of heath conditions that are associated with inflammations and oxidative stress reactions. Also, it improves the endothelial function and iron level in the blood.

Methods:
In a comparative prospective study, 30 breast cancer patients with Invasive Ductal Carcinoma(IDC) who were candidates for a standard chemotherapy protocol[doxorubicin/cyclophosphamide+paclitaxel] were included. Patients were allocated to either consume beetroot juice[250ml/3-5times weekly], or no intervention[controls group]. The baseline haemoglobin level was documented and monitored throughout the study.

Results:
The baseline haemoglobin level was comparative in the two groups (Hb>10.5g/dL) indicating that all patients started as either non-anaemic or with mild-anaemia (p-value 0.1).However post-chemotherapy, the haemoglobin level was significantly higher in patients who had regular consumption of beetroot juice (p-value 0.00). While 13% of patients in intervention group had mild anaemia (Hb:10.1-11.9g/dL), 87% had moderate anaemia (Hb:8-10g/dL). None of these patients developed severe anaemia. Whereas the controls group had 40% mild anaemia, 53% moderate anaemia, and 7% developed severe anaemia(Hb:6.5–7.9g/dL).

Conclusions:
Cancer patients undergoing chemotherapy are at a high risk of developing anaemia, which worsen their quality of life. Beetroot juice consumption has shown to prevent severe or life-threatening anaemia by maintaining acceptable haemoglobin level, and reduce the risk of progressing mild-moderate anaemia.

Key Words: Anaemia; Chemotherapy; Beetroot;

8

Bioactivity-Guided Fractionation of *Ginkgo biloba* Extract and *In Vivo* Neurotherapeutic Evaluation: A New Evidence

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Introduction:
Ginkgo biloba is known to contain flavonoids and terpene trilactones called ginkgolides. Its extract (GBE) was documented to have neuroprotective effects on many neurological diseases such as Alzheimer's disease.

Methods:
Neuroprotective activity-guided fractionation protocol was applied on Ginkgo biloba leaves extract. The fractionation protocol and the purification of the ginkgolides were accomplished using different chromatographic techniques. To evaluate the neuroprotective effects, sixty Wistar male rats were randomly allocated into 6 groups: naive (n=6), sham (n=12), crush + normal saline (n=12), crush + GBE (n=6, 50 mg/kg, i.p.), crush + terpene trilactones-enriched fraction (TEGBE) (n=12, 50 mg/kg, i.p.), and crush + pure ginkgolide B (G-B) (n=12, 10 mg/kg i.p.). Treatments were given one hour following injury, and once daily for 14 days. Neurobehavioral tests, histomorphological examinations, and immunohistochemistry analysis of sciatic nerve and spinal cord were performed at weeks 3 and 6 post-injury. Additionally, Western blotting of GAP-43, GFAP and MBP was performed.

Results:
GBE, TEGBE, pure G-B were obtained. The effects of GBE and TEGBE were evaluated in comparison to that of the pure G-B in the crush sciatic injury model. GBE, TEGBE and G-B were shown to enhance neurobehavioral parameters and to protect the histological and the ultrastructural elements in sciatic nerve. Additionally, all treatments prevented spinal cord neurons from further deterioration following sciatic nerve injury. It was shown that G-B has the most significant potential effects among all treatments, nearly comparable to normal values.

Conclusions:
Bioactivity-guided fractionation afforded several fractions including TEGBE and pure G-B. GBE, TEGBE and G-B exhibit neurotherapeutic effects in the crush sciatic nerve injury model, where G-B showed the most neuroprotective outcome compared to other constituents. This study paves the way for more in-depth analysis of the involved mechanisms.

Key Words: Ginkgo biloba; Crush sciatic nerve injury; Neuroprotective;

9

Anti-apoptotic and Neuroregenerative Effects of Soluble Protein Fraction of the Epidermal Secretion from the Arabian Gulf Catfish following Sciatic Nerve Crush Injury in Rats

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Introduction:
Crush injuries occur from a traumatic compression of the nerve resulting in different degrees of neural damage. Significant cell death and axon degeneration occur as a result of this damage, leading to permanent functional deficits. Previous clinical trials showed that catfish skin preparations (CSP) have potent effects on chronic back pain and other neurological disorders. This study was designed to investigate the anti-apoptotic and neuroprotective effects of soluble protein fraction (SPF)-Fraction C (FC) derived from CSP on the sciatic nerve crush injury.

Methods:
Adult male Wistar rats were randomly assigned into five groups: SHAM, CRUSH, CRUSH+1.5mg/kg SPF-FC, CRUSH+3mg/kg SPF-FC, and CRUSH+4.5mg/kg SPF-FC. Rats underwent sciatic nerve crush surgery, followed by treatment with SPF-FC administered intraperitoneally (IP) for two weeks, and sacrificed at the end of the fourth week. All animals were assessed for sensory and motor neurobehavioral tests throughout the four weeks. Peripheral axonal regeneration was assessed through whole mount staining of sciatic nerve using axonal markers. The neuroprotective properties of the treatment on the spinal cord neurons were assessed using Cresyl violet staining, while the apoptotic pathway was assessed using Western blot, immunohistochemistry, and TUNEL techniques.

Results:
The results of this study showed that the IP administration of different SPF doses significantly ($p<0.05$-0.001) improved the neurobehavioral functions recovery of the nerve-injured groups. Visualization of sciatic nerve through whole mount staining revealed an increase in the axonal regeneration recovery with SPF-FC treatments. Moreover, SPF-FC treatments have neuroprotective effects on spinal cord neurons.

Conclusions:
Our results for the apoptotic pathway revealed that SPF-FC treatments reduce neuronal cell death resulting from sciatic nerve crush injury. The data suggest that SPF-FC reduces sensory and motor neurobehavioral deficits and enhances axonal regeneration recovery.

Key Words: Neuroregeneration; Nerve Injury; Catfish;

10

Knowledge and Attitude of Pharm D Students Regarding the Appropriate use of Antimicrobials

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Introduction:
Since the antibiotic therapy is considered more complex due to the incessant in developing epidemiology of infections, the role and importance of pharmacists in combating and managing infectious diseases become crucial. A strong basis about antibiotic therapy and resistance within the curriculum is important, as many pharmacy students will not have the opportunity to obtain advanced education through postgraduate training programs. The objective of this study is to investigate the knowledge and attitude of PharmD students regarding the appropriate use of antimicrobials.

Methods:
A cross-sectional, online validated survey aimed to assess pharmacy students' knowledge and attitude about appropriate antimicrobial use was conducted among the final year (graduating) pharmacy students.

Results:
Sixty graduating pharmacy students filled out the survey. Most of the students were male (66.7. %). Most of the PharmD students (71.6%) agreed that antimicrobials are overused and that antimicrobial resistance is a problem nationwide. Also, half of them face these apparent problems in hospitals where they had clinical rotations. Most of PharmD students (71.75%) believed that knowledge of antimicrobials is important in pharmacy career. However, only 55% of the students rated their pharmacy education about antimicrobials as useful or very useful. Students' mean correct knowledge score about the appropriate antimicrobials use was 3.1±1.4 which considered low.

Conclusions:
Pharm D students are aware of the importance of antimicrobial therapy and resistance, and familiar of the challenges about antimicrobial stewardship program. However, there is still low knowledge regarding antimicrobials appropriate use among our students.

Key Words: Antimicrobials, PharmD; Antibiotic Therapy

11

Influence of hypoxia on proliferative and migratory capacity of endocrine sensitive and resistant breast cancer cells

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Introduction:

Background: Metabolic behavior of tumor cells under hypoxic conditions found in the core of a tumor mass is influenced by the actions of hypoxia-induced factor (HIF). Breast cancer cells cultured under hypoxia display increased motile/invasive capabilities. However, to metastasize in vivo, hypoxic cells within the tumor core must penetrate layers of other cancer and non-cancer cells to gain access to vascular elements present nearer to the surface of the tumor mass. We have already demonstrated loss of endocrine control leads to increased motile and invasive behavior in vitro. Our aim in this study was to investigate the effect of hypoxia on breast cancer cells.

Methods:

Hypoxia was induced by culturing cells [MCF10A, PII, YS1.2] in a hypoxic chamber, or using chemical agents [cobalt chloride or deferoxamine]. HIF1α expression was measured using western blotting, ELISA and Immunofluorescence. Cell proliferation was measured using MTT assay. Cell motility and invasion were determined using scratch assay, live cell imaging and matrigel assays.

Results:

All experiments, performed in replicates, found that under hypoxic conditions, expression of HIF1α was significantly elevated in ER- cells ($P<0.001$) compared with ER+ or normal cells. In all cell lines, proliferation was inhibited whereas motility was increased, particularly in ER- cells ($P<0.001$). Also, ER- cells were able to penetrate and invade a dense layer of ER+ cells, as well as move out of a mixture of ER± cells ($P<0.05$). However, hypoxia did not increase the migration of ER- cells through a layer of basement membrane extract.

Conclusions:

Hypoxia increases the expression of HIF1α more in ER- cells which leads to higher cell aggressiveness and motility than in ER+ breast cancer cells, suggesting that hypoxic cells at the core of the tumor can penetrate layers of other cancer and non-cancer cells in order to gain access to vascular elements at the tumour periphery enabling them to metastasize.

Key Words: Hypoxia; Breast cancer; Endocrine resistant

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Assessment of safety culture in government hospitals in Kuwait - A cross-sectional study

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Introduction:
Background/Objectives: Safety culture assessments give an organization a basic understanding of its employee's perceptions and attitudes regarding the safety environment in their workplace. Assessing patient safety culture in secondary government hospitals in Kuwait, from the perspective of healthcare professionals helps to identify areas of weakness and strength in the context of patient safety.

Methods:
A descriptive cross-sectional study was conducted using a pre-tested self-administered questionnaire; Hospital Survey on Patient Safety Culture (HSOPSC) developed by the Agency for Healthcare Research and Quality (AHQR). Full-time medical staff working in the secondary government hospitals in Kuwait was considered eligible to participate in the study. Descriptive statistics were used to analyze the data.

Results:
A total of 445 medical staff were approached and asked to partake in the study, of which 427 agreed to participate giving a response rate of 95.9%. The mean positive response rate (PRR) for the 12 patient safety culture dimensions of the HSOPSC survey was 61%. The dimension with the highest score was 'Teamwork Within Units', followed by 'Organizational Learning- Continues Improvements' and 'Feedback and Communication About Error'. In comparison, the lowest score was demonstrated in the dimension 'Nonpunitive Response to Errors', which received the lowest PRR of 32.3% followed by the dimensions of 'Staffing' and 'Communication Openness' with scores of 45.9% and 47.4%, respectively. Other areas of weakness that require additional improvements were seen in the dimensions of 'Teamwork Across Units', 'Hands-off and Transition' and 'Supervisor/Manager Expectations and Actions Promoting Patient Safety', which scored 68.2%, 63.6% and 59.8% respectively.

Conclusions:
Improving patient safety culture is pivotal if hospitals want to improve quality and safety of patient care. In spite of having several areas of weaknesses, secondary government hospitals in Kuwait were found to have numerous areas of strengths. Results from this study may elaborate on strategies to further improve the system leading to patient safety practices.

Key Words: Safety Culture; Hospital Survey on Patient Safety Culture; Survey;

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Physicians' attitudes towards physician-pharmacist collaborative practice in Kuwait hospitals.

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Introduction:

Healthcare collaboration is multiple health team workers from different professional backgrounds collaboratively working to deliver comprehensive services with maximum quality of care. The pharmacist's role was shifted from preparing and dispensing of medicines to evaluating and managing patients' drug related needs. Different studies have explored physicians-pharmacists collaborative relationships in practice, which showed that effective collaboration has a positive impact on overall patients' health outcomes and reduce medication errors. Due to the lack of studies in the area of physicians-pharmacists relationship in Kuwait, this study was conducted to fill the gap in the literature. Aims: -Explore the attitudes of physicians working at Kuwaiti governmental hospitals towards physician-pharmacist collaboration practice. -Assess their opinions about the barriers affecting their collaboration in practice.

Methods:

The research was conducted via an online self-administered questionnaire consisted of three sections assessing physicians attitudes and the barriers affecting the collaborative practice in Kuwait. The survey was distributed through social media platforms. The study targeted physicians working at Kuwaiti general and specialised hospitals including primary care centres. Physicians working at private sectors and as administrative role were excluded from the study. Questionnaire was piloted and ethical approval was obtained from the Human Ethical Committee, Ministry Of Health, Kuwait, as well as University of Hertfordshire Human Ethical Committee. Data was entered into the SPSS system and Microsoft Excel 2017. Mann-Whitney and Kruskal–Wallis test for Independent-sample were used to complete descriptive interpretations of the results.

Results:

A total number of 174 physicians participated in this survey. Female represents 67% of total participants, while male were 32%. Majority of the participants showed positive attitudes towards the role of pharmacists, 97% of them agreed that physicians and pharmacists should be educated to establish collaborative relationships. Most of the participants indicated that pharmacists being physically separated from patient care areas and lack of pharmacists' access to the patient's medical information records are the main barriers towards effective collaborative practice.

Conclusions:

Physicians revealed a positive attitude towards physicians-pharmacist collaborative practice and identified the possible barriers in the practice. Efforts are needed to improve inter-professional healthcare collaboration, and to minimise obstacles in the implementation of proper collaboration to foster a team approach to patient care.

Key Words: Physician-pharmacist, inter-professional collabora; Healthcare team practice;

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Development of Institutional Guideline for Post Operative Venous Thromboembolism Prophylaxis in Bariatric Surgery in Kuwait

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CASE REPORT

Background: With 80% of its population overweight and 47.5% obese, Kuwait has a serious obesity problem which lead to widespread practice of bariatric surgery. The country has the highest numbers of operations performed as a percentage of national population. While different bariatric surgery procedures are effective in achieving weight loss, they have potential risks and complications. Venous thromboembolism (VTE) events, which include deep vein thrombosis and pulmonary embolism (PE), are an important source of postoperative morbidity and mortality among bariatric surgery patients.

Case Summary: Through a qualitative expert interview, we identified that clinicians are faced with the question of how bariatric surgery affects the absorption, pharmacokinetics, bioavailability, efficacy and safety of oral anticoagulant agents especially with the limited dedicated studies of oral anticoagulation. The optimal approach of post operative VTE prophylaxis in these patients is unclear, with multiple open questions. In this case report we present the local professional experience of one of the active bariatric surgical units in a secondary care hospital in Kuwait introducing an institutional guideline regarding postoperative VTE prophylaxis. This newly introduced guideline specified that: “If the Body Mass Index (BMI) of a patient is < 35 with comorbidities or if it is between 40 and 50, to start the patient on subcutaneous ENOXAPARIN SODIUM (Clexane)-a low molecular weight Heparin- 40mg once a day for 2 weeks. If the BMI is >50, to start the patient on Clexane 60 mg once a day for 2 weeks”.

Conclusion: There was a clinical need to introduce an institutional guideline regarding the use of anticoagulant prophylaxis in post bariatric surgery. Until more evidence-based data are available, institutional quality improvement efforts should focus on an ethical and interdisciplinary approach to develop such clinical guidelines.

Key Words: Bariatric Surgery; Anticoagulation Prophylaxis; Development of Clinical Guidelines

15

Impact of a Pharmacy Led-Medication Reconciliation Service at an Ambulatory Care Setting: Dialysis Patients

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Introduction:
Maintaining an accurate medication list in dialysis patients is challenging due to polypharmacy and multiple prescribing. Therefore, it is important to implement medication reconciliation (MedRec) as a standard of care to prevent drug therapy problems (DTPs). A MedRec service was provided by trained pharmacist to hemodialysis patients at the dialysis centre. The aim of the study was to evaluate the impact of the service and describe identified medication discrepancies.

Methods:
Completed best possible medication history (BPMH) and reconciliation forms were collected from the patients' file from January to June 2018. The primary outcome was the number and types of identified discrepancies and DTPs. The secondary outcome was the difference between home medications and documented action taken when discrepancies were identified. Continues variables were reported as median ± interquartile range or percentages as appropriate. Difference between home mediations and documented action was compared by Mann Whitney test with significance level of $P<0.05$.

Results:
In total, 51 forms were completed. At least two sources of information were used in 51%, while three and four sources were used in 41 and 8% respectively. The main source was the patient or family, followed by medical file (80%), medication list (41%), and medication containers (35%). The total number of medications identified was 571 with a median of 11±3, which was reduced to 400 with a median of 8±5 ($P<0.05$) following MedRec. Discrepancies identified accounted for 53, were mostly frequency related (23%) while the most identified DTP was medication with no indication (60%).

Conclusions:
This study demonstrates that ambulatory MedRec is an effective safety tool to prevent adverse drug events in dialysis patients. The results suggested that pharmacists' involvement could improve the process. However, a systematic approach has to be implemented and followed for all patients, which emphasizes the need for continuous training and education.

Key Words: Medication Reconciliation; Medication discrepancy; Hemodialysis;

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Factors Affecting the Healthcare System Experiences in the Medication Management of Patients with Dementia, Systematic Review and Meta-Synthesis

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Introduction:
Background: Dementia is a neurodegenerative syndrome and it's a leading cause of disability, needs and death among older adults. It affects more than 800,000 individuals in the UK. In chronic diseases medications are the most common type of healthcare intervention, and their management is challenging for patients with dementia. Aim: Explore the medication management experiences of patients with dementia from the perspective of individuals in the healthcare system and identify the factors that affect these experiences.

Methods:
A systematic review was conducted using different databases including: Scopus, CINHAL, PsycExtra, and PsycINFO. Qualitative studies or studies with mixed methods considering healthcare medication management in patients with dementia were included. The selected studies were transferred to Mendeley and then data was processed using NVivo 11. A meta-ethnographic approach and a comparative thematic analysis were adopted in the synthesis. The relationship between the concepts from the studies was identified and a line of argument synthesis was undertaken.

Results:
Twenty studies were selected based on the inclusion criteria. The initial synthesis resulted in four major themes and nine subthemes. Major themes included: the daily practice; perceptions and attitudes, identified needs and recommendations. The line of argument synthesis identified financial and human resourses, knowledge, attitudes and communication as factors affecting the healthcare experiences.

Conclusions:
Dementia is a progressive disorder with a complex medication management process. Although the healthcare system is a vital element in this process, guidelines based their recommendations for improving this system mainly through the feedback experience of patients and their families. The findings in this research highlighted the factors affecting individuals in the healthcare system. Future interventions should support the healthcare system by targeting these factors.

Key Words: Dementia; Medication management; Healthcare

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Comparing glycaemic control: Super Attenders vs. Poor Attenders; A 5-year retrospective study in young patients with type 1 diabetes.

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Introduction:
Aims / hypothesis: Type 1 Diabetes Mellitus (T1DM) is a potentially life-threatening condition, affecting people across the world, with the majority of sufferers being children. The standard treatment for this disease depends mainly on administering insulin, usually through injections. However, professionals have also recognised the importance of managing the condition, often through a multidisciplinary care team, but also by the patient taking a degree of responsibility and commitment to the care plan. This includes adherence to medication, changes in lifestyle, and also attending appointments with the care team, who can then more effectively monitor the condition and treatment. The aim of this study is to examine the often-held but unconfirmed hypothesis that better clinic attendance correlates with improved management and outcomes.

Methods:
To select a sample for the study, Brighton's Royal Alexander Children's Hospital's database was used. Records of patients going back to 2009 were examined, but final selection was limited to patients with a full six-year record from the start of 2011 to the end of 2016. The first year of this period was then discounted, to remove any possibility of a "honeymoon period" (where the child may still have traces of natural insulin in the body), leaving a sample of 54 children, with full five-year records. All the children had Type 1 diabetes. Their HbA1c records were also provided, along with attendance records, which additionally showed the type of visit. All the samples were anonymised.

Results:
Firstly, there was a general statistical correlation between non-attendance and poor glycaemic control, with high HbA1c levels, and a corresponding relationship between good attenders and better control. Secondly, poor attendance was generally linked with a longer duration before any improvement in HbA1c levels was recorded, whereas the opposite was true for regular attenders. More significantly, between the super attenders and poor attenders there was an average difference, over the five years, of 1.1% in their HbA1c levels. Furthermore, there were no instances of excellent levels of glycaemic control among the poor attenders, while nearly 25% of super attenders achieved this. Finally, the minimum average number of annual visits by any of the super attenders was 3.4, while the maximum number in the other group was 3, suggesting that the minimum number of visits to aim for annually should be 4.

Conclusions:
From the results, it can be seen that clinic attendance positively affects the management of Type 1 diabetes in children, whereas non-attendance tends to lead to less satisfactory levels of glycaemic control. Therefore, attendance needs to be encouraged and this important feature should be emphasised to both the patient and their care provider. Considering most T1DM patients are children, their parents or guardians also need to be informed and helped to work toward a better attendance level.

Key Words: Diabetes; Non-attendance - Clinical appointments; Glycaemic control - bA1c

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Self-medication practice among patients in Saudi Arabia

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Introduction:
The practice of self-medication becomes widespread in Saudi Arabia. Self-medication practice has some advantages but is also can be cause serious unwanted effect to the patients. Several published reviews evaluate self-medication worldwide. However, all these reviews did not include the studies conducted in Saudi Arabia Objectives: To review published studies exploring the self-medication practice in Saudi Arabia and associations factors that influencing self-medication practice.

Methods:
Electronic databases including PubMed, Cochrane Library, EMBASE, CINAHL, ProQuest, Scopus, and Google Scholar were searched for articles published without a time limit from inception to June 2017. Inclusion criteria were: studies published in English or Arabic, and conducted in Saudi Arabia.

Results:
Key findings: sixteen studies of 67 published studies met the inclusion criteria which conducted in Saudi Arabia. Observational cross-national was the manly methods used to investigate self-medication practice in the selected studies. Seven of these Studies were conducted in Riyad. Non-steroidal anti-inflammatory drugs, antibiotic, vitamins are the most common medicines that involved in the self-medication practice in Saudi.

Conclusions:
Self-medication practice is common among patients in Saudi Arabia. Special attention should be given to educating the public and health care providers on which illnesses for which they can seek self-medication without the advice of a healthcare provider, and responsible governmental and nongovernmental organizations should work hard to ensure the rational use of medication

Key Words: Self-medication; Over the counter; Pharmacy

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Formulation and stability study of Atrovaststin cocrystals containing tablets

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Introduction:
Tablets by direct compression (DC) can improve the stability and drug integrity. The aim was to prepare atorvastatin tablets containing cocrystals of glucosamine and nicotinamide as coformers and to study their stability under different storage conditions.

Methods:
The powder flow properties, Hausenr's ratio (H), and Carr's compressibility index (C) were estimated. The formulated tablets (F2 and F4) were evaluated for hardness, thickness, friability, uniformity of weight, disintegration time, content uniformity, and dissolution rate (DR). The tablets were stored at 40 ± 2degreeC/75 ± 5% RH and at room temperature (RT), evaluated for drug content after 1,2, 3, 12 months and after 3 and 12 months for DR.

Results:
The cocrystals improved the flow properties of ATC, where (H) decreased from 1.31 to 1.26 in both F2 and F4 and (C) was reduced from 23.75% to 20.41% (F2) and 20.83% (F4). All post-compression parameters of the prepared tablets met the BP-2015 requirements. More than 91% of drug was released from F4 tablets and more than 82% from F2 tablets after 20 min. No significant changes were observed in ATC content after 12 months of storage at both storage conditions. When DR results of all freshly prepared tablets and after 3 and 12 months' storage were compared, the freshly prepared tablets and the aged tablets at RT exhibited higher and differ significantly from those at 40degreeC after 3 &12 months.

Conclusions:
AT cocrystals were successfully compressed by DC and the tablets revealed excellent stability at RT and at 40°C after 3 months without any significant change in drug content and absence of any degradation products. These tablets also maintained high DR throughout stability study. However, after 3 months at 40°C, DR was reduced due to partial dissociation of the prepared cocrystals.

Key Words: Atorvastatin; Cocrstals; Sability;

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National Rates of Emergency Department Visits Associated With Diabetes in Saudi Arabia- 2011-2015

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Introduction:
Despite the fact that diabetes is an important component of the burden of disease on the individual and on the national healthcare systems in the Kingdom of Saudi Arabia (KSA), knowledge on the volume of emergency Background: department (ED) visits for diabetes is unclear. To address this lack of information, this study examines the changes in ED visit rates associated with diabetes that occurred from 2011 through 2015 in the KSA.

Methods:
Publicly available books of health statistics published annually by the Saudi Ministry of Health from 2011 through 2015 were used to extract ED visits related to diabetes. ED visits associated with diabetes were compared over time and by gender. We calculated diabetes-specific rates per 10,000 persons for each sex category by dividing the total number of diabetes-associated ED visits in that category by the sex-specific population. We used ED visit rates for the years 2011 and 2015 of the study years and calculated the rate difference (RD) between the two years with 95% CIs for the RD.

Results:
From 2011 to 2015, a total of 102.2 million visits were made to EDs in the Ministry of Health (MOH) hospitals in the KSA. Total annual visits to the ED for management of diabetes increased from 617,683 cases in 2011 to 748,605 in 2015. The annual number of ED visits associated with diabetes increased by 21% over the study period and 20% and 23% for males and females, respectively. Compared to males, female individuals exhibited a larger increase in visit rates from 240.5 to 249.8 visits per 10,000 women over the study years (RD, 9.6; 95% CI, -16.4 to 26.6; P=.01).

Conclusions:
In conclusion, This study of recent trends of ED visits associated with diabetes in the KSA population revealed that the rate of ED visits for diabetic patients remained relatively stable after 2012 to the end of the study period. However, because of the compelling evidence that the prevalence of diabetes among the Saudi population will continue to rise in the future. Development and implementation of new and more effective preventive national programs are crucial to improve health outcomes among individuals with diabetes and consequently prevent ED use.

Key Words: Emergency department (ED); Rate difference (RD); Ministry of Health (MOH);

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Exploratory Study of Antibiotics' Prescription by Primary Care Physicians in Kuwait: Evidence-Based Clinical Guidelines and Educational Interventions Are Needed

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Introduction:
Inappropriate use of antibiotics is a global public health problem. In Kuwait, a 2009 report indicated that 40% of prescriptions at 50 primary healthcare centers involved an antibiotic.(1) Studies have provided strong evidence of an association between prescribing antibiotics in primary care and antimicrobial resistance worldwide. (2,3,4) With high tendency to prescribe antibiotics and the rising antibiotics resistance worldwide; efforts need to focus on studying knowledge, attitude, perception and practice of antibiotics prescription among healthcare professionals in our community.

Methods:
Data were collected utilizing a validated self-reporting questionnaire from a convenience sample of physicians from 28 primary healthcare centers in Kuwait. The results of the first 100 responses are reported.

Results:
Around 70% of participants were <45 years old, 63% females, 58% registrars, 48% Kuwaiti, and 67% graduated from a medical school abroad. Nearly 78% prescribed antibiotics to □10 patients monthly. Only 11% were highly confident about their knowledge and prescription practice. Moreover, 58% were unaware of the antimicrobial resistance rates and patterns in their own clinics. Inappropriate use of antibiotics was attributed by 49% to lack of effective policies, and 25% to overworked physicians. Although 96% did not agree with "anyone should be able to buy antibiotics without a prescription", 8% believed that "it is always better to overprescribe than under prescribe". A total of 65% reported that "physician education on appropriate antimicrobial therapy would help in controlling antimicrobial resistance". Alarmingly, only 1% reported that they will consider clinical pharmacists as a source for antibiotics prescription advice.

Conclusions:
Interdisciplinary professional efforts are needed to address the results of this study. It is necessary to generate evidence-based policies and guidelines for clinical practice and to design effective educational interventions. Additionally, recognition of clinical pharmacists' role in primary care need more attention.

Key Words: Antibiotics; Primary Care; Professional Education;

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National audit of antidote stocking in hospitals that provide emergency care in Kuwait

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Introduction:
Antidote stocking represents a major challenge to hospitals all over the world, including Kuwait. This study aimed to evaluate antidote stocking and availability in public and private hospitals that provide emergency care in Kuwait.

Methods:
A cross-sectional study using a pre-tested, validated questionnaire was conducted from January-December 2018. The questionnaire was designed to assess immediate and non-immediate availability of 41 antidotes in all six public and 13 private hospitals in Kuwait that provided emergency care. The pharmacists and pharmacist directors in these hospitals were provided the questionnaire to report availability of antidotes. Reasons for non-availability of antidotes were also noted. Descriptive statistics were used to report demographical data, and independent t-test analysis was used to analyze continuous variables. Statistical analysis was done using SPSS 25.0.

Results:
All six public hospitals in Kuwait, and eight private hospitals returned completed questionnaires. Among the 14 hospitals surveyed, none had complete stock of all essential antidotes. The mean (SD) availability of immediate antidotes in public hospitals was 79.7% (32.6) compared to 52.1% (44.4) in private hospitals. Moreover, the mean availability of non-immediate antidotes was 64.5% (37.7) in public hospitals compared to 14.6% (22.8) in private hospitals.

Conclusions:
Public and private hospitals in Kuwait have suboptimal stocks of essential antidotes. There is an urgent need to develop expert consensus guidelines to assist hospitals, to reduce costs and improve patient care, by adequate stocking of essential antidotes.

Key Words: Antidotes; Pharmacy; Emergency;

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Whole Exome Sequencing Identifies Novel Genes Associated with Hereditary Spastic Paraplegias among Saudi Patients

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Introduction:
Hereditary Spastic Paraplegias (HSP) are diverse group of neurodegenerative disorders characterized by progressive dysfunction in the lower extremity and spasticity. In this study we aimed to identify disease causing mutations in Saudi HSP patients.

Methods:
Two consanguineous families with three affected individuals sharing the classical symptoms of HSP were included in the study at King Faisal Specialist Hospital & Research Centre. Peripheral blood samples were collected from the patients and family members. DNA was isolated and used for a comprehensive genetic analyses that included targeted gene panel screening, whole exome sequencing (WES), confirmatory Sanger sequencing for family segregation and comprehensive in silico bioinformatics analyses.

Results:
The DNA was screened using a comprehensive neuropanel that included previously reported HSP genes and mutations. The screening did not yield any positive results in the patients. Then, we performed autozygosity mapping based on the genome-wide screening of loss of heterozygosity in the affected individuals using a comprehensive SNP genechip array. Concurrently, we run WES in the DNA from the index cases in each family. Our comprehensive filtering of WES coupled with autozygome and in silico bioinformatics analyses resulted in a few putative pathogenic variants in genes that were not previously linked to HSP. Segregation analyses using Sanger sequencing confirmed the likely involvement of the variants. In the family 1, a missense variant (c.2324 C>T, p.P775L) was identified in KIAA1024 whereas in the family 2, another missense variant was found in QSTM1 (c.571 G>A, p.G191R) that has been previously linked to ataxia but not to HSP.

Conclusions:
We discovered likely disease-causing novel genes and variants that were not previously associated with HSP. Our work will create opportunities for genetic testing for diagnostic screenings for HSP in Saudi Arabia and may also facilitate acceleration for gene therapies and drug development for HSP in the future.

Key Words: Novel; Genes; Consanguineous;

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Pharmacists Related Interventions to Prevent Prescribing Errors among Hospitalized Patients in Acute Care Setting at a Tertiary Teaching Hospital in Saudi Arabia

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Introduction:
Prescribing errors (PEs) are common in practice and can cause morbidity and mortality. The pharmacist has an identified role in minimizing and preventing PEs; however, additional evidence is required to understand the nature of pharmacist's related interventions (PRIs) regarding preventing PEs. Objective: To explore the different interventions conducted by pharmacists to prevent or minimize PEs among hospital admitted patients.

Methods:
Design and Setting: A retrospective analysis of PRIs to prevent or minimize PEs recorded between 1st April and 30th September 2017 in the electronic medical system of a tertiary teaching hospital in Riyadh were collected. Data were entered in a purposefully designed Excel sheet for this study. Collected data comprised patient demographic data, medication information, and related interventions by the pharmacist. An appropriate descriptive analysis was done for all variables and presented as frequencies and percentages. The study was ethically reviewed and approved by the hospital IRB committee [E-18-3251].

Results:
A total of 2,564 PEs and PRIs including 1,565 patients with average age (±SD) of (42.77±27.2) years were recorded. Wrong dose (54.3%), unauthorized prescription (21.9%) and prescribing of duplicated therapy (10.9%) were the most commonly encountered PEs. Anti-infectives for systemic use (49.2%) and alimentary tract and metabolism (18.2%) were the most common involved medications with PEs where parenteral medications had the highest rate of PEs (58.4%). PEs in intensive care unit (23.9%) followed by medical wards (23.2%) then surgical wards (15.2%) were the highest encounters. Most reported PRIs were dose adjustment (44.0%) followed by restricted medications approval (21.9%) and therapeutic duplications (11%).

Conclusions:
Pharmacists play major role in preventing PEs consequences especially through dose adjustments. Prescribers can benefit the most from pharmacist's interventions; therefore, enhancing medication safety among patients.

Key Words: Prescribing errors; Pharmacists Interventions; Hospitlized Patients

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Hetero-dimerization of the Incretin Receptors

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Introduction:
The incretin hormones; glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) are important regulators of many aspects of metabolism including insulin secretion. Their receptors (GIPR and GLP-1R) belong to the secretin class of G protein coupled receptors, which recently have been shown to form dimers. Since both GIPR and GLP-1R are expressed on pancreatic beta-cells there is a possibility that they could form hetero-dimers. Our objective is to investigate whether these receptors can form hetero-dimers in vitro and to investigate the impact of receptor activation on dimer formation.

Methods:
Receptor dimerization was investigated using a bioluminescence resonance energy transfer (BRET) saturation assay. GLP-1R was labelled at the C-terminus with a nano-luciferase (Nluc) and stably expressed in Flip-In HEK-293 cells. These cells were then transiently transfected with increasing concentrations of GIPR labelled at the C-terminus with a variant of yellow fluorescent protein (SYFP2). BRET saturation curves were generated following incubation in the absence of agonist to monitor constitutive dimerization or in the presence of either 1 micro M GIP or GLP-1.

Results:
BRET saturation curves were plotted as a ratio of SYFP2 fluorescence to Nluc luminescence. In the absence of agonist an exponential curve was generated, increasing and then reaching an asymptote, consistent with a saturable BRET signal. Treatment with GLP-1 resulted in a significant ($P<0.05$) increase in maximum BRET signal whereas treatment with GIP resulted in a non-significant decrease compared to non-stimulated, n=3.

Conclusions:
The results support the hypothesis that GIPR and GLP-1R form hetero dimers. The increase in BRET signal observed with GLP-1 treatment can be interpreted as either an increase in the number of dimers formed or a change in receptor conformation. Future experiments will investigate the impact of receptor dimerization on cells signaling.

Key Words: GIP; GLP-1; Dimerization;

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A detailed analysis of the signaling properties of a dual incretin receptor agonist.

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Introduction:
Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like pepide-1 (GLP-1) are important regulators of glucose homeostasis, making their receptors (GIPR and GLP-1R) attractive targets in the treatment of type 2 diabetes mellitus. While GLP-1R agonists are used clinically to treat diabetes and obesity, the use of GIPR agonists remains controversial. Recent studies however suggest that simultaneous activation of GIPR and GLP-1R with a single peptide may provide superior glycemic and weight control than activation of GLP-1R alone. Our aim in this study was to investigate the signaling properties of a recently reported 'dual incretin' receptor agonist (P18).

Methods:
GIPR, GLP-1R or the closely related glucagon receptor (GlucR) were transiently expressed in HEK 293 cells. Activation of adenylate cyclase via Gs was monitored using a highly sensitive reporter gene assay (CRE-Luc). G protein-independent signaling was monitored using a bioluminescence resonance energy transfer (BRET) arrestin assay.

Results:
The native peptides; GIP, GLP-1 and glucagon displayed exquisite selectivity for their receptors in the CRE-Luc assay. The dual incretin P18 was able to activate both GIPR and GLP-1R with significantly higher potency ($P<0.05$) than the endogenous peptides. In contrast P18 was only able to activate GlucR at concentration above 1 µM. Furthermore, P18 did not act as an antagonist at GlucR. Interestingly P18 was significantly ($P<0.0001$) less potent than GLP-1 at recruiting arrestin to GLP-1R.

Conclusions:
P18 activates both GIPR and GLP-1R with higher potency than the native peptides but has little activity at GlucR in a CRE-Luc assay. In terms of arrestin recruitment P18 was significantly less potent than GLP-1 at GLP-1R, suggesting that as well as being a dual incretin receptor agonist P18 is also a biased agonist.

Key Words: Incretins; Type 2 diabetes Mellitus; Receptor

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Assessment of Disaster Medicine Knowledge, Attitude, and Readiness to Practice among Healthcare Profession Students in Qatar University

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Introduction:
Natural disasters and manmade disasters like wars and blockades, impair healthcare systems. Healthcare professionals and students should be well-prepared for disasters. Knowledge (K), attitude (A), and readiness to practice (rP) are the key components of disaster medicine preparedness. Although Qatar is subjected to different types of manmade disasters, there is a lack of studies evaluating the level of disaster medicines preparedness. This study aims at assessing the knowledge, attitude, and readiness to practice regarding disaster medicine among healthcare students in Qatar.

Methods:
A cross-sectional survey-based study was performed among 104 students from the colleges of medicine, pharmacy, and health-sciences at Qatar University. A survey tool to measure KArP was developed by adapting the Disaster Preparedness Evaluation Tool (DEPT). Responses were scored and categorized as high (75th quartile), moderate (75th-25th quartiles), low (25th quartile). KArP scores were compared between different genders and colleges using independent t-test, and one-way ANOVA, respectively. Pearson-correlation was used to investigate relation between KArP parameters. Regression analysis was performed to investigate the effect of K and A on rP. Alpha level used was 0.05.

Results:
The average level of disaster knowledge was 9.54± 3.03(moderate), attitude:48.99±10.35 (moderate), readiness-to-practice: 33.78±.20(moderate). There was no significant difference in KArP parameters neither between genders nor colleges ($p>0.05$). However, there was a statistically significant direct moderate correlation between K and A($r=0.505$; $p<0.001$), and between K and rP($r=0.613$; $p<0.001$), and between A and rP($r=0.560$; $p<0.001$). Moreover, K and A levels have a direct moderate effect on rP ($R2=0.452$; $p<0.001$).

Conclusions:
Health colleges students at Qatar University have moderate disaster preparedness. They would benefit from structured education about disaster medicine preparedness.

Key Words: Disaster; Knowledge, attitude, readiness; Health-related students;

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Patient Understanding and Satisfaction with the Use of Patients Knows Best application (PKB)

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Introduction:
Recent development in technology has produced new ways to promote wellbeing and deliver patients' education. Following organ transplants, patients require complicated treatment regimens and most importantly are the immunosuppressant drugs, failure to adhere to their medications results in poor clinical outcomes and increased rate of graft rejection. Hence,
increasing cardiothoracic transplant medicine knowledge is vital to avoid allograft rejection. The main objectives of the study is to explore users satisfaction and evaluates knowledge level pre- and post- the Patients Know Best® (PKB) application, among patients receiving treatment following cardiothoracic transplantation.

Methods:
The quantitative service evaluation was conducted at Harefield Hospital (London). A service evaluation of a recently launched application by the hospital Royal Brompton and Harefield called Patients Knows Best®. A total of 30 patients were recruited with a follow up of 2 weeks. Knowledge evaluation was assessed by a pre- and post-usage of the PKB app quiz. A Satisfaction survey was carried out to assess the patient satisfaction rate with the PKB app. Ethical approval was received from UCL School of Pharmacy.

Results:
Fifteen patients were included in the final analysis, while only 5 have completed the both pre- and post-knowledge quiz. Baseline knowledge score demonstrated good understanding of steroids and tacrolimus while the other drugs had an average score below 50%, thus requiring further education. Overall patients rated the app as useful and average knowledge score improved by 10% between pre and post score (p=0.188).

Conclusions:
Embedding patient education into PKB® application was promising and satisfying to patients as it enhanced patient medicine knowledge. Further and longer research targeting transplant population involving patient centered use of telehealth application to assess level of knowledge and other health care parameters are necessary to understand the impact of such technologies on high risk population such as Cardiothoracic transplant and to strengthen the results.

Key Words: Patient education; Heart and lung Transplant; Mobile Application;

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Rapid discrimination and quality evaluation of Cinnamomum species powders using Near-IR diffuse reflectance spectroscopy and multivariate analyses

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Introduction:
Objectives: Alongside the steadily increasing global interest in alternative medical practices, high measures of adulterated pharmaceuticals have bein reported to invade the global market and therefore detection of such commercialized items is becoming inevitable. This article aims to uncover the adulteration of Cinnamomum verum (zeylanicum) with Cinnamomum cassia and exhausted C. verum. A speedy and non-destructive near infrared (NIR) method in conjunction with the multivariate statistical tools of chemometrics was used to distinguish authentic cinnamon from its commonly incorporated adulterants.

Methods:
The unsupervised pattern recognition techniques; Principal Component Analysis (PCA) and hierarchical clustering analysis (HCA) were first implementedon all the samples. Depending on the PCA loadings outputs, the most significant variables in the 5200–5900 cm-1 region were utilized to build a recognition pattern, a supervised one, O2PLS-DA model to discriminate unadulterated samples from adulterated ones. Finally, partial least squares (PLSR) regression was used to build the correlation for adulterated samples regarding their cassia and exhausted cinnamon content.

Results:
The O2PLS-DA model could successfully predicet and judge the quality of C.verum powder without any false prediction. For PLSR regression, the R2 of calibration and validation were all higher than 0.9, while the root mean square errors (RMSE) were all lower than 0.05, indicating that the established models were successful.

Conclusions:
Overall, NIR-diffuse reflectance spectroscopy using pattern recognition was proven to have significant potential as a time saving and accurate method for the identification of true cinnamon powder, which can help to maintain the quality of the herbal drug by avoiding its adulteration and could be implemented as a routine screening in its quality control with no need for any sample preparation. Presenting a novel implementation of near- IR diffuse reflectance spectroscopy in conjunction with chemometry for the purpose of quality control and adulteration detection of such a herbal drug.

Key Words: NIR diffuse reflectance spectroscopy; Cinnamon adulteration; Chemometrics

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The Readiness of Hospital Pharmacists in Kuwait to Practice Evidence-Based Medicine: A cross-Sectional study

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Introduction:
The evolving role of pharmacists in providing pharmaceutical care, as part of the healthcare team, challenges them to acquire up-to-date knowledge of medicines to make the best clinical decisions. The volume of medical literature is on the increase, and it is important to utilize these resources to optimise patients' therapeutic outcomes. This study aimed at assessing the readiness of government hospital pharmacists in practising evidence-based medicine (EBM) in Kuwait in regards to their attitude, knowledge and skills, as well as the perceived barriers and facilitators.

Methods:
This descriptive cross-sectional study used pre-tested self-reported questionnaires to collect information from pharmacists working at government hospitals in Kuwait. In addition, one-to-one, face-to-face semi-structured interviews were conducted with the chief pharmacists of all health regions in Kuwait to discuss and identify the barriers and facilitators of implementing EBM in the hospitals. Quantitative and qualitative analytical measures were undertaken for the data acquired from the questionnaires and interviews, respectively.

Results:
A total of 176 pharmacists (of 445) working in secondary and tertiary government hospitals in Kuwait agreed to take part in the study, giving a response rate of 40%. Over half of the study sample (n?=?94, 53.4%) were confident in performing online database searches. Approximately 50% of the pharmacists were familiar with searching the Internet for medical resources, asking answerable clinical questions and retrieving research evidence. However, 67% of the pharmacists (n=118) were neither able to apply research evidence to patient care nor capable of identifying knowledge gaps in practice. Barriers to EBM practice were identified, which included limited access to EBM resources (75%), a lack of time and patient overload (71.6%). The interview results confirmed the willingness of hospital pharmacists to adopt EBM in their practice if necessary resources such as computers and internet connection were provided.

Conclusions:
Hospital pharmacists in Kuwait showed good attitude and willingness towards EBM, however, they need to acquire adequate knowledge and skills for applying it in 'real life' practice. Using the current results, clinical implications were recommended to demonstrate how to overcome the barriers, wherein hospital pharmacists could be ready to practice EBM.

Key Words: Pharmacy Practice; Evidence-Based Medicine; Readiness of Hospital

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The attitudes of pharmacists towards pharmacist-physician collaboration in Kuwaiti hospitals

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Introduction:
After the milestone report 'To Err is human' has shed light on the incidents of medical errors, international health organisations called for the need of interprofessional collaboration. Moreover, a single healthcare provider cannot provide an inclusive patient care as the complexity of patients' conditions and needs are increasing. Interprofessional collaborative practice involves combing knowledge and skills to work on mutual goals and to enhance the quality of care (Bridges et al., 2011). Furthermore, there are many reports in the literature about the effect of pharmacist-physician collaboration on patients' safety. Also, the impact of interprofessional collaboration is not solely for patients, but it also increases healthcare providers' job satisfaction. This study aims to explore pharmacists' perception toward pharmacist-physicians collaboration in Kuwaiti hospitals. In addition, to identify pharmacists' apprehended barriers to effective collaborative practice in Kuwait.

Methods:
A self-administered questionnaire was distributed to pharmacists who works in Kuwait Hospitals. Results were analyzed through SPSS, and descriptive and comparative analyses were done. The statistical significance was accepted at $p<0.05$.

Results:
The participants (n=154) had an overall positive attitude towards pharmacist-physician collaboration. The three most rated barriers to collaborative practice were: the assumption that physicians are totally responsible in clinical decisions, lack of interprofessional collaboration training and education for pharmacists and physicians, and organizational obstacles, such as the unsupportive administration.

Conclusions:
Pharmacists in Kuwait governmental hospitals has a positive attitude towards collaborative practice with physicians however, several barriers were recognized, and they hinder the implementations of such practice. A directed effort between the MOH in Kuwait and health educational organizations are needed to resolve the barriers and change the pharmacy practice into a collaborative one.

Key Words: Interprofessional collaboration; pharmacist-physician; Kuwait, attitudes

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Curriculum Mapping and Perspectives of Pharmacy Students on the Development and Implementation of Pharmacist Prescribing in Qatar

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Introduction:
The scope of pharmacy practice has undergone considerable transformation in recent years. In this regard, pharmacists in many developed countries have been granted prescribing privileges, under what is known as non-medical prescribing. However, such prescribing privileges are not available in many developing countries. The objectives of this study were: (1) to evaluate the existing BSc (Pharm) curriculum at Qatar University College of Pharmacy (QUCPH), for addressing international prescribing competencies, and; (2) to determine the perspectives of pharmacy students and recent graduates on pharmacist prescribing and its potential implementation in Qatar.

Methods:
This study involved: (1) curriculum mapping process to assess the QUCPH BSc (Pharm) curriculum, for addressing international prescribing competencies, and; (2) a cross-sectional survey involving current pharmacy students and recent graduates using a validated questionnaire.

Results:
The majority of the prescribing competencies addressed in the Australian National Prescribing Service (NPS) Prescribing Competencies Framework were covered in the CPH BSc (Pharm) curriculum. However, gaps were identified in the content related to the use of electronic system for prescribing purposes, concepts related to physical examinations and preparing patients for investigations, and policies and procedures for appropriate use of medicines. The survey results showed that the majority of the respondents (94.4%) were aware of the prescribing competency related to considering treatment options. Furthermore, the majority (92.4%) believed that pharmacists should have prescribing training and accreditation or certification before being legally allowed to prescribe. The most perceived barrier to prescribing by respondents was lack of legal rights to prescribe medicines by pharmacists (65.3%), while interprofessional collaboration was the most perceived facilitator to pharmacist prescribing (63.6%).

Conclusions:
The curriculum mapping provided evidence that the existing pharmacy curriculum at QUCPH prepares the students to achieve prescribing competencies. Furthermore, the majority of the pharmacy students were in favor of pharmacist prescribing being implemented in Qatar. However, special training program was deemed necessary to qualify pharmacists to prescribe safely.

Key Words: Pharmacist prescribing; Curriculum mapping; Qatar;

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Educational Strategies for Improving Stigma and Perspectives of Mental Health Disorders

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Introduction:
The National Mental Health Strategy (NMHS) of Qatar has set forth several goals to improve mental healthcare, including changing negative perceptions of mental health so that people seek help without fear of stigma.

Methods:
The aim of this study is to compare the effectiveness of two different educational interventions aimed to reduce mental health stigma among university students. A sample of Qatar University students were randomized into three groups. Group 1 participated in a one-hour face-to-face workshop; Group 2 participated in an online-module that had the same content of the workshop; Group 3 did not receive any educational intervention (control group). All three groups completed a survey assessing the effectiveness of the different educational strategies by measuring outcomes before-and-after the intervention. The survey consisted of a set of validated questionnaires were modified, translated and assessed for reliability. The survey was divided into items that explored beliefs and attitudes towards mental health, and help-seeking behaviours.

Results:
Results were obtained from 137 participants. Of these, more than 85% were females, more than 90% were single and the vast majority were aged between 18 to 24 years old. After the educational intervention, the proportion of people who believed mental illnesses are due to chemical imbalances improved [workshop (66.3% to 90.91%); online-module (55.81% to 75%) groups]. There was an improvement in participants perception in regard to working or studying with a mentally-ill person [workshop (78.3% to 93.7%); online-module (67.4% to 73.6%)], as well as an increase in the percentage of participants who would seek psychological help if they feel depressed for a long-time [workshop (30.3% to 50%); online-module (30.9% to 35.2%)].

Conclusions:
Beliefs, attitudes and help-seeking behaviours improved after the interventions. The interactive workshop group had the most promising results compared to the independently done online module.

Key Words: Mental illness stigma; Social behaviour; Educational intervention;

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Medication Related Factors Influencing Medicine Refusals among Patients with Dementia

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Introduction:
Dementia is one of the major causes of disability and dependency worldwide. It is a syndrome that affects behaviour and cognitive function which may impact on patients' willingness to take medication. The refusal of medications among this patient group is an on-going issue with various medical, social and economic implications. Objectives: To determine the rate of medication refusals in patients diagnosed with dementia and to determine the medication factors associated with them. Setting: An aged care facility in Perth, Western Australia.

Methods:
Data from 100 residents were accessed by the primary researcher via the facility's electronic iCare system. Residents' medication refusals for the period from April 2017 to May 2017 were recorded on a spreadsheet.

Results:
The number and rate of medication refusals, and the odds of refusals based on factors: patient age, medical history, drug category, formulation, and dosing interval. Results: A total of 70 patients were included in the study. Twenty-four patients refused 348 doses out of a total of 7800 doses with a mean number of 14.5 refusals per patient. Age did not appear to influence refusal of medications, however, female patients refused more than males. The number of medical conditions did not influence the odds of a medication refusal. Additionally, psychiatric, ear and eye disorders which may hinder medication administration did not influence the odds of a refusal. The odds of a refusal were lower in patients with dementia and the chance of a refusal decreased as the number of regular medications per patient increased. The most commonly refused drug group was pain relief medications followed by supplements and ophthalmic medications. Solid dosage forms were the most commonly refused formulations. Most refusals occurred in the morning and late afternoon-evening sessions, when most medications were prescribed to be taken.

Conclusions:
Medications are frequently refused by patients suffering from dementia. Most refusals occurred in the times of day when the sundowning effect may have been the cause. Individual patient factors with comprehensive reasons for refusals should be further explored to provide an individualised care approach. Medication management by a clinical pharmacist in aged care facilities should be considered to optimise treatment. Impact on practice: Medication refusals may have serious clinical consequences including hospitalisation, increased morbidity and mortality, and unmet therapeutic outcomes. Medication refusals may have resource implications on the healthcare system and the public purse. Medications commonly refused by patients diagnosed with dementia in aged care should be identified to allow for individualised medication management.

Key Words: Dementia; Geriatric; Medication;

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Dual stimuli-responsive polypyrrole nanoparticles for anticancer drug delivery

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Introduction:
The development of dual stimuli-responsive nanoparticles with potential for anticancer therapy is a new emerging field to combat this serious and fatal disease.

Methods:
The nanoparticles are composed of a conjugated polymer (polypyrrole, PPY) loaded with an anticancer drug (allicin), and were characterized by a variety of physicochemical techniques. The dual stimuli-responsive nature of the PPY nanoparticles was validated in vitro: the PPY nanoparticles delivered an anticancer drug (allicin) in response to exposure to an electric field in vitro as demonstrated with UV–vis spectroscopy.

Results:
The PPY nanoparticles exhibited photothermal activity upon irradiation with near infrared light which resulted in resulted in toxicity towards HEP G2 cells in vitro.

Conclusions:
We believe that such nanoparticles have long term potential for application in cancer therapy in a variety of tissue niches (e.g. breast cancer, liver cancer, lung cancer, skin cancer).

Key Words: Photothermal; Nanoparticles; Polypyrrole;

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Gelatinized-core liposomes: One step further for the successful formulation of hydrophilic molecules

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Introduction:
Liposomes offer many advantages as a drug delivery system, however, they have several limitations that need to be overcome, including stability issues, low entrapment of hydrophilic drugs, and difficulty in controlling the release of such hydrophilic drugs. The current work introduces a novel approach to overcome the aforementioned problems; liposomes with a gelatinized core which are prepared using the GRAS biocompatible material gelatin.

Methods:
A full-factorial experimental design was used to compare the gelatinized-core liposomes relative to the conventional liposomes with respect to the loaded amount of a model hydrophilic molecule; Na salicylate. Artificial neural networks modeling was utilized to evaluate the effects of gelatin and cholesterol incorporation in the liposomal formulation on the entrapment efficiency.

Results:
The results showed the successful preparation of the novel gelatinized-core liposomes, which had better entrapment efficiencies (52.6% - 91.7%, formulated with cholesterol) compared to conventional liposomes (25.8% - 30.7%, formulated with cholesterol). Three model molecules; Na salicylate, sesamol, and doxycycline were used to evaluate drug release, and the presence of both gelatin and cholesterol in the formulation resulted in a significant reduction in the percentage of drug release. The liposomal formulation with 33 mg cholestrol and 80 mg gelatin resulted in superior stability (retained 99.1% of loaded drug) after storage at 5 °C for 2 months compared to the conventional liposomes.

Conclusions:
These novel liposomes have the potential as a successful drug delivery system for hydrophilic drugs.

Key Words: Liposomes; Gelatin; Stability;

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Simulation for developing clinical skills: A mixed-method study exploring pharmacists' experiences and perspectives in Kuwait

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Introduction:
Simulation has been integrated in pharmacy education in many developed countries to prepare students for pharmacy practice. Most of the evidence about simulation-based education comes from Western educational systems. This study aimed to explore pharmacists' experiences and perceptions about simulation use for learning clinical skills in Kuwait.

Methods:
This was an exploratory descriptive study of pharmacists' perceptions about simulation. A mixed-method research was employed whereby pharmacists participated in focus groups and completed self-administered survey. Focus groups were audio-recorded, transcribed verbatim and qualitative data were analysed using framework analysis. Descriptive statistics were used to describe characteristics of study participants and survey findings. Data were analysed using SPSS, version 22.

Results:
A total of 110 pharmacists participated in the focus groups, of whom 88 completed the survey. Survey showed that many pharmacists (26.1%) had no prior experience in simulation use. Some graduates from Kuwait (20.5%), and other countries (13.6%) reported simulation use during undergraduate education. Focus groups revealed that pharmacists had different experiences in relation to simulation use for learning. They identified many benefits of simulation such as allowing learners practice and rehearse skills in safe environments. Participants suggested that simulation can be used to train pharmacists on pharmacy practice and teamwork skills. Most participants expressed positive attitudes towards simulation and welcomed its integration in pharmacists' education and training.

Conclusions:
Pharmacists in Kuwait have diverse educational experiences regarding simulation use for learning. Collaborative efforts between educational institutions and healthcare authorities are needed to standardize and expand simulation use in training pharmacy students, trainees and practitioners to equip them with the clinical skills essential for safe practice.

Key Words: Simulation; Clinical skills; Pharmacists;

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Decreased Urocortin 3 expression in diabetic overweight humans and its modulation with physical exercise

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Introduction:
Type 2 diabetes (T2D) are characterized by disturbed insulin secretion and insulin resistance due to reduced insulin action in target tissues such as adipose tissue. Urocortin3 (Ucn3) is a novel insulin secretion regulator and a molecular marker for mature pancreatic beta-cells. However, it's circulating levels as well as its expression by adipose tissue in the context of diabetes is still not well investigated. The aim of this study was to assess (i) the effects of diabetes on circulating UCN3 and its expression in adipose tissue and (ii) if these levels are affected by physical exercise.

Methods:
Adult male and female human subjects consisting of 205 overweight (25<=BMI<40 kg/m2, 107 non-diabetic and 98 diabetic) were enrolled in the study followed by a 3-month moderate exercise program. Subcutaneous adipose tissue (SAT) biopsies and venous peripheral blood were collected before and after exercise along with anthropometric measurements and blood biochemistry analysis. Metabolic markers were measured using Bioplex-200 system.3T3-L1 mouse preadipocytes cells were differentiated with co-culture of RAW macrophages to mimic conditions of diabetes. The expression and circulating levels of Ucn3 were assessed using ELISA, RT-PCR, western blot and confocal microscopy.

Results:
Plasma UCN3 levels were significantly increased in diabetic compared to non-diabetic overweight. On the contrary, SAT Ucn3 expression decreased with diabetes. In preadipocyte cell lines, following co-cultured differentiation, a similar decrease in Ucn3 gene and protein expression was observed. Our 3-month supervised physical exercise protocol, increased the levels of circulating UCN3 in non-diabetic but not in the diabetic group. Furthermore, a significant reduction in Ucn3 levels was observed in the SAT of both groups following physical activity.

Conclusions:
Circulating and SAT Expression of Ucn3, representing the feedback loop linking insulin secretion and glucose levels, is disrupted in established diabetic subjects. Hence, Ucn3 might be a key player in the pathophysiology of diabetes and further studies are warranted to investigate its role in the onset and progression of diabetes.

Key Words: Urocortin 3; Diabetes; Physical exercise;

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Increased expression levels of soluble epoxide hydrolase 2 in obese and its modulation by physical exercise.

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Introduction:
Soluble epoxide hydrolase (sEH) is an emerging therapeutic target in several chronic states that have inflammation as a common underlying cause such as immunometabolic diseases. Indeed, sEH is known to play a pro-inflammatory role by metabolizing anti-inflammatory, epoxyeicosatrienoic acids (EETs) to pro-inflammatory diols. Recently, it was shown sEH to be linked to diet and microbiota interaction in rat models of obesity. Nevertheless, the functional contribution of sEH and its anti-inflammatory substrates EETs in obesity remain poorly understood.

Methods:
Using RT-PCR, western blot and immunofluorescence confocal microscopy We compared the expression pattern of sEH along with ER stress and inflammation markers in subcutaneous adipose tissue (SAT) and peripheral blood mononuclear cells (PBMCs) of lean and obese nondiabetic human subjects before and after 3-months supervised physical training. 3T3-L1 murine preadipocytes were used as model to investigate this pathway invitro using homocysteine and other ER stress inducers.

Results:
We show here that the level of sEH mRNA and protein to be significantly increased in obese subjects with concomitant increase in ER stress components (GRP78 and ATF6α) and inflammatory markers (TNF-α, IL-6) when compared to lean controls. Moreover, we report for the first time that 3-months supervised physical exercise significantly attenuated the expression of sEH in both the SAT and PBMCs, with a parallel decrease in the expression of ER stress markers along with attenuated inflammatory response. Expression of she correlated positively with adiposity markers, arterial pressure and GRP78 but negatively with VO2, max. In vitro, homocysteine treatments increased sEH levels along with ER stress markers in 3T3-L1 cells.

Conclusions:
Collectively, our data suggest that sEH upregulation is strongly linked to ER stress in adiposity and that physical exercise modulates its expression. This gives further evidence that exercise might be useful as a strategy for managing obesity and preventing its associated complications.

Key Words: Soluble epoxide hydrolase 2; Obesity; Physical exercise;

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Differential cell death of human gastrointestinal malignancies treated with Sorafenib and natural phenolic compounds.

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Introduction:
Sorafenib (Sora), a multi-kinase inhibitor drug approved by the FDA, has a compelling antiangiogenic and anticancer activities. Efficient strategies are needed to lessen the side-effects and augment Sora efficacy. In this study, we aimed to investigate the effects of combining Sora with natural phenolic compounds (NPC), on both human colorectal cancer (CC) and hepatocellular carcinoma (HCC) cell growth and intracellular signalling pathways involved in cell cycle and apoptosis.

Methods:
MTT assay was used to monitor the cytotoxicity of Sora, NPC and their combinations on CC (SW1116 and SW837) and HCC (Hep3b and HepG2) cell lines using different treatment regimens; sequential, reverse sequential and simultaneous. Flowcytometry was used to analyze cell cycle. apoptosis was examined by Annexin V/PI double staining and mitochondrial membrane potential (MMP). Finally, western blot analysis was used to monitor the expression of proteins related to apoptosis and cell cycle regulation.

Results:
Four NPCs; curcumin (Cur), quercetin (Que), kaempferol (Kmf) and resveratrol (Rsv) were tested in combinations with Sora, against CC and HCC cells. These combinations showed a potent cytotoxicity on both CC (SW1116, Cur simultaneous treatment, Sensitization ratio, SR= 14, P </=0.048; Que SR= 8 and SW837 sequential treatment, Cur SR=24, , Kmf SR= 9.0) and HCC with simultaneous treatment for both cell lines (Hep3b, Cur SR=27, Kmf SR=17; HepG2; Cur SR= 10, Kmf SR=4) in a dose- and schedule- dependent manner. Combination treatments arrested CC and HCC cells growth at S and G2/M phases and induced extensive mitochondrial membrane damage and apoptotic cell death. Finally, protein expression of cell cycle (p27, cyclin A2, B, D1 and pRB) and apoptosis (Bax, Bcl-xL, cleaved caspase 3, 9) is altered in both CC and HCC by combination treatments in a dose-dependent manner.

Conclusions:
Our results indicate a significant improvement of Sora efficacy on CC and HCC cells. Further in in-vivo studies of Sora and NPCs combinations are need to test their potential as a novel therapeutic strategy for CC, HCC and other types of cancer.

Key Words: Colorectal cancer and hepatocellular carcinoma; Natural phenolic compounds;

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Exendin-4, a GLP-1 analogue, protects pancreatic BTC-6 cells against cellular stress induced by palmitic acid

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Introduction:
Lipotoxicity is an important factor in the pathogenesis of type 2 diabetes resulting in defective beta-cell proliferation and increased apoptosis. Increase in glucagon-like peptide-1 (GLP-1) activity has recently emerged for the treatment of type 2 diabetes (T2D) by enhancing the glycemic control and helping in decreasing body weight of most patients. Recent studies have suggested beneficial effects of these peptides on insulin-responsive tissues such as adipose tissue, muscles and liver aside with pancreatic beta-cells. We investigated here the potential beneficial effects of a GLP-1 mimetic on mouse pancreatic cells under stressing levels of palmitic acid (PA).

Methods:
Using mouse pancreatic cell line (BTC-6), we investigated the impact of GLP1 mimetic (Exendin-4) on MAPKs in the presence of stressing amounts of PA (400uM) using RT-PCR and Western blot. Differential protein expression pattern was investigated using Mass Spectrometry approaches (LC-MS/MS Orbitrap system and label-free quantification). Cell viability assay and Oil Red O staining was also performed.

Results:
We showed that ERK MAP-Kinase phosphorylation was highly increased by Exendin-4 both in presence and absence of PA. Furthermore, cell viability assays have shown that exendin-4 significantly alleviated the PA-induced cell death. This was further confirmed with proteomics analysis where various cellular functions were improved in presence of Exendin-4, including cell growth, cellular assembly and organisation. Moreover, proteomics analysis highlighted a panel of interconnected heat shock proteins (HSP) that have been modulated by Exendin-4. This was further confirmed by Western blot where the heat-shock inducible HSP72 was significantly increased by PA and attenuated in presence exendin-4.

Conclusions:
Our results suggest that GLP-1 mimetics alleviate the lipotoxicity-related cellular stress in pancreatic cells and enhance heat shock response thus restoring normal cellular homeostasis.

Key Words: GLP-1, GLP-1 analogues; Proteomic profiling; Heat shock, HSP, MAPKs

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Factors influencing provision of palliative care in advanced dementia: a systematic review

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Introduction:
Dementia is a progressive neurodegenerative life-limiting disease. The international literature indicates that patients with advanced dementia may benefit from palliative care provided during the end of life phase. However, evidence indicates that many fail to access such provision at this time despite the increased recognition of their palliative needs. Aim: To investigate the factors influencing provision of palliative care services for people with advanced dementia.

Methods:
A mixed studies systematic review of empirical articles, written in English was undertaken. 11 electronic databases were searched such as Embase, Medline, PubMed, CINHAL and Scopus from 2008 to 2018. Narrative synthesis and content analysis were used to analyse and synthesise the data.

Results:
In total, 34 studies were included. 25 studies providing qualitative data, 6 providing quantitative data and 3 mixed methods studies. The review identified barriers and facilitators of the provision of palliative care for people with advanced dementia across different care settings from the perspective of various stakeholders. The most commonly reported barriers are lack of skills and training opportunities of the staff specific to palliative care in dementia, lack of awareness that dementia is a terminal illness and a palliative condition, pain and symptoms assessment/management difficulties, discontinuity of care for patients with dementia and lack of co-ordination across care settings, difficulty communicating with the patient and the lack of advance care planning.

Conclusions:
Even though the provision of palliative care was empirically recognised as a care step in the management of dementia, there are barriers that hinder access of dementia patients to appropriate facilities. With dementia prevalence rising and no cure on the horizon, it is crucial that health and social care regulatory bodies integrate a palliative approach into their care using the identified facilitators to achieve optimal and effective palliative care in this population.

Key Words: Advanced Dementia; Palliative Care; Barriers, Facilitators

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Green synthesis of silver nanoparticles using Omani Pomegranate peel extract and two polyphenolic natural products and evaluation of their antimicrobial, cytotoxic and antioxidant properties: A comparative study.

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Introduction:
Green synthesis of silver nanoparticles (AgNPs) has gained popularity due to the more economical and eco-friendly approach associated with it. The study aimed to compare the antioxidant, antimicrobial and cytotoxic activities of AgNPs synthesized using pomegranate peel extract (P), quercetin (Q) and gallic acid (GA).

Methods:
AgNPs were synthesized by reduction of 2 mM AgNO3 by Omani pomegranate peel extract, quercetin and gallic acid as per optimized procedure. The formation of AgNPs was confirmed using UV-Vis Spectrophotometer and XRD analysis. The zeta potential and the average size distribution of the AgNPs were measured using Zeta Analyzer and ZetaSizer. TEM and SEM were used to study surface morphology and shape of the nanoparticles. Various in vitro assay methods were used to investigate biological activities such as anti-oxidant activity by DPPH, cytotoxic activity by using Brine shrimps lethality bioassay and anti-microbial activity against E. coli, P. vulgaris, S. aureus and B. subtilis bacteria by agar well diffusion method.

Results:
A color change to brown, a sharp peak in a UV spectrum at 425 nm, 421 nm and 413 nm were observed for Q-AgNPs, P-AgNPs and GA-AgNPs, respectively. Peaks in XRD (20:38.38, 44.62, 64.72 and 82.06) correspond to reference silver crystal. SEM and TEM analysis showed particles to be predominantly spherical with few aggregates. Average size distribution was found to be 43.6 nm for Q-AgNPs, 31.6 nm for P-AgNPs and 21.7 nm for GA-AgNPs with a surface charge of -18.01 mV, -21.5 mV and -27.9 mV respectively. P-AgNPs showed the excellent antioxidant activity (77.33-89.16%). P-AgNPs and GA-AgNPs exhibited good antimicrobial activity against four bacterial strains comparable to cefuroxime but Q-AgNPs failed to inhibit the growth of P. vulgaris. AgNPs were found to be moderately cytotoxic.

Conclusions:
Omani pomegranate peel extract content appears to be potential and suitable source for the simple synthesis of antimicrobial and anti-oxidant AgNPs.

Key Words: Silver nanoparticles; Anti-oxidant; Cytotoxic;

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Use of Trans-Resveratrol and Hesperetin to Prevent Methylglyoxal-Induced Cardiac Insulin Resistance

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Introduction:
Type 2 Diabetes mellitus is characterized by hyperglycemia and insulin resistance. Methylglyoxal (MG), a highly reactive dicarbonyl compound that is also increased in diabetes. MG has been shown to have deleterious effects on cardiovascular cells and impair insulin signaling. Moreover, MG is detoxified by the enzyme glyoxalase-1 (Glo-1) using reduced glutathione (GSH) as a co-factor. Cardiac insulin resistance is associated with diabetic cardiomyopathy. Trans-Resveratrol (tRES) and Hesperetin (HES) combination has been shown to induce Glo-1 and improve insulin signaling in obese patients. This study investigates whether tRES-HES combination prevents MG-induced insulin resistance in cardiomyocytes in culture and the underlying mechanisms.

Methods:
H9C2 rat cardiomyocytes were treated with MG (0-200 µM) for 24 hours with and without tRES-HES (10 µM each). Protein expression of Glo-1, P-Akt and P-GSK3b was determined using Western blot. In some experiments, cells were stimulated with insulin (100 nM) for 10 minutes to test insulin sensitivity. The experiments were repeated 4-5 times.

Results:
MG reduced Glo-1 expression significantly ($P<0.05$) in a dose-dependent manner and Glo-1 expression was restored by tRES-HES combination. Insulin induced phosphorylation of Akt and GSK3b (a marker of insulin sensitivity) was blunted in cells treated with MG compared to control cells (without MG) by ALMOST=50%. This effect was prevented by tRES-HES ($P<0.05$).

Conclusions:
tRES-HES combination prevented MG-induced cardiac insulin resistance that was associated with an increase in Glo-1 expression. This study has implications for prevention and treatment of cardiovascular complications of diabetes such as diabetic cardiomyopathy.

Key Words: Methylglyoxal; Glyoxalase; Trans-resveratrol and hesperetin;

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Immunization with Mycobacterium tuberculosis-specific antigen Rv3619c effectively alleviates allergic asthma in mice.

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Introduction:
Asthma is a complex syndrome characterized by the inflammation and narrowing of the airways with significant eosinophil and lymphocyte infiltration and airway hyper-responsiveness, which affects 5-16% of people worldwide. Inhaled corticosteroids are currently the most important therapy for controlling airway inflammation, but their long-term usage can result in side effects. In asthma, antigen-specific Th2 cells and their cytokines are primary mediators of the pathological consequences. Whole cell mycobacteria have been shown to suppress asthmatic responses in mice by preventing the development of asthma with altered Th1/Th2 cytokines ratios. In this study, we evaluated the efficacy of immunization with M. tuberculosis-specific antigen Rv3619c, utilizing a Th1 delivery system, in modulating the allergic airway inflammation in a Th2 driven model of asthma.

Methods:
The rv3619c gene was cloned and expressed in E. coli, and purified to homogeneity using affinity chromatography. Mice were immunized with the recombinant proteins emulsified in Freund's Incomplete Adjuvant (IFA) and challenged with ovalbumin (OVA). Mice were sacrificed and 1) total and differential cell counts from BAL fluid, 2) histological changes and airway remodeling of lung tissue, 3) Th2 cytokine (IL-5) secretion from spleenocytes, 4) OVA-specific IgE from sera, and 5) pERK1/2 signaling from lung tissue, were assessed.

Results:
Rv3619c was successfully cloned, expressed and purified from E. coli. In OVA-challenged mice, immunization with Rv3619c/IFA effectively inhibited the OVA-induced total cell counts, eosinophil airway cell infiltration in BAL fluid, perivascular and peribronchial inflammation and fibrosis, and goblet cell hyper/metaplasia in the lung, elevated IL-5 levels in spleenocytes, OVA-specific IgE levels in sera, and up-regulation of pERK1/2 in the lung.

Conclusions:
The study is a "proof of concept" that Rv3619c/IFA may be an effective vaccine for the prevention of asthma.

Key Words: Asthma; Rv3619c; Vaccine;

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The Potential Role of Costus speciosus in Inducing Apoptosis in Breast Cancer Cell: Possible Involvement of MAPK Pathway

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Introduction:
Background, Objective: Medicinal plants play important roles in the folkloric medicine and the modern one, as well. Costus speciosus rhizomes extract is reported to demonstrate in vitro inhibition of cell proliferation and induction of apoptosis in different cancer cell lines. The main mechanism by which it exerts this action is not yet known. One of the major pathways involved in breast cancer is mitogen activated protein kinase (MAPK) that consists of ERK, P36, and c-Jun N-terminal Kinase (JNK), which is involved in cell differentiation and apoptosis. This study aims at investigating the possible involvement of MAPKs and other possible signaling cascades in the apoptosis induced by C. speciosus extract in MDA-MB-231and MCF-7 breast cancer cells.

Methods:
C. speciosus rhizomes were extracted in 80% methanol and the dried extract was fractionated, using vacuum liquid chromatography, into eleven fractions with different polarities. C. speciosus extract activity was evaluated on MDA-MB-231 and MCF7 breast cancer cells, using MTT assay, Western blotting and ELISA.

Results:
C. speciosus extract significantly induced cytotoxicity and reduced the viability of MDA-MB-231 (22% ± 9.2) and MCF-7 (31.7% ± 6.4) breast cancer cells in a time- and dose-dependent manner when compared to controls. Additionally, the extract induced apoptosis and promoted proteolytic cleavage of PARP (31.3% ± 8 and 3.55 ± 1.54) and caspase-3 (17.6% ± 4 and 21.7% ± 4), which correlated with an increase in the cytoplasmic Bcl-xl (0.2% ± 0.02 and 0.13% ± 0.11) and Bax (0.7% ± 0.13 and 0.38% ± 0.14) protein degradation in both cell lines, respectively. More importantly, the extract specifically activated JNK in a time- and dose-dependent manner. These effects were significantly inhibited by the JNK selective inhibitor, SP60025. Moreover, C. speciosus extract synergized the cytotoxic effect of doxorubicin.

Conclusions:
C. speciosus can be a potential lead in cancer treatment. It showed synergism with doxorubicin that can culminate into dose reduction and, consequently, fewer side effects.

Key Words: Costus speciosus; MAPK; Breast cancer;

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Pharmacists' Attitudes toward Continuing Education in Kuwait

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Introduction:

Objective: To determine pharmacists' attitudes toward continuing education in Kuwait. Settings and Design: This study was a descriptive cross-sectional survey study of pharmacists working in Kuwait private and public sectors. Sample: A sample of community pharmacies, polyclinic pharmacies and hospital pharmacies in both the public and the private sectors were selected and visited by the pharmacy student who was responsible for the whole data collection process. All pharmacists in the selected pharmacies were invited to participate in the study. Those who consented to participate were provided with a 14-item validated questionnaire (range 1-4) to complete and returned to the pharmacy student. The data collection process started in January 2017 and was completed in April 2017.

Methods:

Data collection: The Jefferson Scale of Physician Lifelong Learning (JeffSPLL) was adapted, by the pharmacy student and reviewed by an academic, for the administration to pharmacists in Kuwait. Analysis: The items were grouped together to generate an aggregate score for each participant to measure their attitude toward continuing education. A score of 43 to 56 indicates good to excellent attitude, 29 to 42 indicates fair attitude and 14 to 28 indicates poor attitude toward CE. An ethical approval for this study was obtained from the ''Human Ethical Committee, Health Sciences Center, Kuwait University'

Results:

A total of 409 with a response rate of 82%, completed the questionnaire. The median age of the sample population was 34 years (range: 22-63); 51% of which were female. Participants had a median score of 44 (good to excellent attitude), with a minimum of 22 and a maximum score of 56. Pharmacists with a post graduate qualification had a higher score (p < 0.05, spearman). Almost 70% of the participants had attended CE activity within a year. The most common type of CE activity was attending a seminar. The main barriers to continuing education were heavy workload (66%), conferences not being regularly organized (38%), lack of scientific databases (25%), and lack of time (21%).

Conclusions:

Participants had good to excellent attitude toward CE. The most common type of CE activity was attending a seminar. The main barrier identified for CE was heavy workload. The results of this study might be used to explore more engaging programs that overcome the identified barriers and provide more relevant CE to pharmacists in Kuwait.

Key Words: Continuing education; Attitude; Pharmacist;

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Hypomagnesemia in Diabetes Patients: Comparison of Serum and Intracellular Measurment of Responses to Magnesium Supplementation and its Role in Inflammation

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Introduction:
Background, Objectives: Hypomagnesemia contributes to the pathophysiology of diabetes and metabolic syndrome. Magnesium (Mg) supplementation in diabetes patients with hypomagnesemia was shown to diminish inflammatory parameters. However, serum magnesium level only represent less than 1% of total magnesium; whereas cellular Mg deficiency is a more reliable parameter for assessing magnesium. In most diabetes patients; where hypomagnesemia occurs, the important depletion of cellular Mg levels is usually not measures. In this clinical trial, we assessed the efficacy of magnesium (Mg) supplementation in hypomagnesemic type 2 diabetes patients in restoring serum and intracellular Mg levels. The study had two co-primary end points: the change in serum and intracellular Mg level between baseline and after 3 months of supplementation. We compared the efficacy with regard to lowering hemoglobin A1c (HbA1c), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), and 8-isoprostane as secondary end points.

Methods:
In an open-label trial, 47 hypomagnesemic type 2 diabetes patients were administered 336 mg Mg daily. At baseline and after 3 months, serum, cellular Mg, and inflammation biomarkers were measured. For intracellular Mg levels, sublingual epithelial cells were analyzed by analytical scanning electron microscopy using computerized elemental X-ray analysis. Blood samples were analyzed for Mg, HbA1c, and CRP. Systemic inflammatory markers including TNF-α, and the oxidative stress marker 8-isoprostane were determined using enzyme-linked immunosorbent assay.

Results:
Mg supplementation significantly increased the intracellular and serum levels. Statistically clinical improvement in HbA1c and CRP levels was not observed, but significant decreases in TNF-α as well as in 8-isoprostane were found.

Conclusions:
A feasible clinical method for the assessment of intracellular Mg was demonstrated in tissue samples obtained noninvasively, providing evidence for potential clinical translation of this method to routinely determine intracellular Mg concentration.

Key Words: Hypomagnesemia; Type 2 diabetes; Intracellular magnesium;

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Exploring Mental Health Stigma among Qatar University Students

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Introduction:
Background: Research has shown increased psychological burden among university students with poor help-seeking attitudes. Lack of awareness and stigmatizing mental health disorders may be a contributing factor.

Methods:
This study aims to understand the extent of awareness of mental health disorders and associated stigma amongst university students in the middle east region in order to develop appropriate strategies to improve mental health literacy. A 10-minute survey consisting of questions extracted from previously validated questionnaires was administered to a cohort of university students enrolled in non-health-related disciplines. The survey covered participants' demographics, their perceptions towards general mental health issues and more specifically about depression, as well as their help-seeking attitudes.

Results:
A total of 123 students participated. Twenty-two percent of the participants were males and 18.9% were nationals. Most participants (96.8%) were between the ages of 18 to 24 and enrolled in programs from the College of Arts and Sciences (39.3%). A minor proportion of students were scholarship holders (28.7%), but more than 70% of their fathers and 60% of their mothers were holders of university degrees or had post-graduate education. Results indicated low awareness of general mental health issues. Only 14.7% of the students thought depression affects a person's life in a significant way, while 46.6% thought that people with depression can "snap-out" of their condition at will. Social stigma was also evident as 33.8% indicated to be unwilling to marry someone with a mental illness, and 27.7% affirmed that they would not tell anyone if they had depression. Moreover, 37.1% thought that medications used to treat mental disorders are addictive.

Conclusions:
Intensive interventional strategies are necessary to improve middle eastern university students' perceptions of mental health disorders.

Key Words: Mental illness stigma; Social behaviour; Mental health awaremess;

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Introduction and Background

Kuwait Foundation for the Advancement of Sciences (KFAS) has a 40 year history of supporting the advancement of science and technology in Kuwait. In 1976, a visionary call by the late Amir of Kuwait, Sheikh Jaber Al- Ahmad Al-Jaber Al-Sabah, then Crown Prince and Prime Minister of Kuwait, was favourably embraced by the Chamber of Commerce and leaders of the economic sector in the country. It resulted in the establishment of the Kuwait Foundation for the Advancement of Sciences by an Amiri Decree on 12th December 1976; stating its mandate as a private non-profit organization devoted to supporting scientific research today. The Foundation's work is overseen by a Board of Directors, chaired by H.H. the Amir, Sheikh Sabah Al-Ahmad Al-Jaber Al-Sabah. It is financially supported by Kuwaiti private sector companies who have made generous contributions throughout the years, the contribution is currently set at 1% of their net annual profit.

One of the foremost goals of KFAS is to promote scientific development in the State of Kuwait by supporting scientific projects, the scientific community, and the country's scientific infrastructure.

While much has been accomplished by KFAS and related scientific institutions in Kuwait, there is much still to be sought after. The State of Kuwait has grown rapidly in terms of population and economy, the latter as a result of steadily increasing oil revenues. Today, the public sector accounts for more than 70% of the GDP and employs more than 85% of the national workforce. The consensus among the majority of stakeholders is that this growth is not structurally sustainable in the long run and that alternative national development strategies, based on building a complimentary, efficient and competitive private sector economy, are urgently needed.

Recognizing this need, H.H. the Amir of Kuwait, Sheikh Sabah Al-Ahmad Al Jaber Al-Sabah, commissioned in 2007 a "blue-ribbon panel"; the Kuwait Research Review Panel (KRRP), which was tasked to review the organization and the performance of Research and Development and make recommendations for restructuring and advancing Science, Technology and Innovation (STI) in Kuwait.

The panel presented a number of recommendations aimed at strengthening the overall STI system and culture throughout Kuwait, i.e. improving the capabilities and in some cases redirecting the activities of several STI institutions including KFAS, Kuwait University (KU), Kuwait Institute for Scientific Research (KISR), Public Authority for Applied Education and Training (PAAET), National Technology Enterprises Company (NTEC), and the Kuwait Science Club (KSC).

Recognizing its unique role within the national STI system in Kuwait and responding to the recommendations in the panel's report, KFAS conducted an extensive assessment of its historical performance by benchmarking itself against similar institutions in the region and on a global level. KFAS consulted with representatives from its key stakeholders and worked closely with recognized leading international and domestic experts in Research and Development (R&D), policy, and STI evaluation to support this assessment.

Based on the KRRP's recommendations and external assessment and findings in 2009, KFAS management embarked on developing a new strategic plan that would help meet the future needs of Kuwait's STI system. The preparatory steps were carefully designed.

The first step was the evaluation of current situation (status quo), followed by numerous steps like the determination of the basic requisites, identification of the targeted sectors, revision of vision and mission,

defining the primary goals of the strategy and the expected results. An examination of the on-going and proposed programs and activities were then made.

Problem and solution trees for each program were carefully prepared and analysed, and the institutional requirements and arrangements to achieve the goals of the strategic plan were identified. The last step was to come up with a set of key performance indicators to measure the degree of success over the years at all levels.

KFAS Strategy (2012 – 2016)

The strategy is a result of intensive consultation through numerous meetings lead by the management team at KFAS and its centers. It reflects the latest thinking on the STI needs of Kuwait, the proper role of KFAS and its centers in meeting part of those needs, and a more systematic approach to formulating and selecting programs for KFAS funding.

KFAS programs in the strategy are directed towards contributing tangibly to the development of an effective STI system and culture in Kuwait.

In addition to supporting R&D capacity and activities in priority fields, such as water, energy, the environment, and the development and the dissemination of STI culture, the plan puts further emphasis on STI capacity building of the private sector and strengthening of innovation system.

Vision:

"An Effective Science, Technology and Innovation System and Culture, to which KFAS has contributed, that underpins the sustainable development of the State of Kuwait"

This vision statement reflects several important concepts based on the Foundation's past experience and current philosophy. It is nationally-focused and draws on valuable resources to successfully position Kuwait to compete in a knowledge-based economy in the future.

Mission:

Stimulate, support, and invest in initiatives and human resources that contribute to the building of a strong STI system and culture and fostering an enabling environment. The initiatives include improving public understanding of science; strengthening innovation and research capacity and enhancing the enabling cultural environment; supporting the gifted and talented; translating knowledge into innovation; and encouraging private technology capabilities.

This mission statement defines KFAS' role and ambitions driving the strategy outlined below. It primarily redefines KFAS as a funding institution. Given its modest annual resources, when compared to the overall STI funding by public institutions at the national level; KFAS will need to effectively leverage its targeted investments and efficiently execute its role as a catalyst to achieve its goals.

Strategic Thrust Areas

In developing the strategy, four thrust areas were identified. They address the development and human resource needs of the Science, Technology and Innovation System by leveraging the resources of KFAS and other stakeholders. Distribution of KFAS' available resources was given great consideration to ensure maximum impact.

Strategic Thrust 1 – Advocacy of Scientific Culture:

Contribute to the development of a strong advocacy for science including science education, support the gifted and talented, and to help advance scientific culture and the enabling environment in Kuwait

Strategic Thrust 2 – Scientific Research:

Enhance and integrate Research and Development capacity in and among Kuwaiti Scientific Institutions to address national development priorities

Strategic Thrust 3 – Innovation in Science and Technology:

Support innovation and assist in developing the required links to commercialization within a framework of an integrated Science, Technology and Innovation (STI) system

Strategic Thrust 4 – Innovation and Enterprise:

Supporting the development of the Private Sector's scientific and technological capacities and participate in building a knowledge economy

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