Under the Patronage of the President of Kuwait University

4th Kuwait International Pharmacy Conference (KIPC)

4 - 6 FEBRUARY, 2013

ABSTRACT BOOK

جامعة الكويت

His Highness
Sheikh Sabah Al-Ahmad Al-Jaber Al-Sabah
Amir of the State of Kuwait

His Highness
Sheikh Nawaf Al-Ahmad Al-Jaber Al-Sabah
Crown Prince of the State of Kuwait

His Highness
Sheikh Jaber Mubarak Al-Hamad Al-Sabah
Prime Minister of the State of Kuwait

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General Information

Conference Date & Venue

4th to 6th February, 2013 at Maha Ballroom, The Regency Hotel, Kuwait

Conference Inaugural Ceremony

4th February, 2013 - 9.00 am by the Honourable President of Kuwait University

Plenary Lectures & Exhibitions

4th to 6th February, 2013 at Maha Ballroom, The Regency Hotel, Kuwait

Discussion Forum

5th February, 2013 from 18.45 to 19.45
6th February, 2013 from 18.30 to 19.30

Registration Desk

For registration and any enquiries or assistance, please proceed to the Registration Desk at the entrance area at Maha Ballroom, The Regency Hotel, Kuwait.

CME/CPD Credits

Registration Number:	**186/Ph0/Feb13**
Title of Activity:	4th Kuwait International Pharmacy Conference
Scheduling:	4th to 6th February, 2013
CME Provider:	Health Sciences Center, Faculty of Pharmacy
CME Organizer:	Dr. Mohammed Waheedi
CME/CPD Credits:	

Category 1:

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

Category 2:

Poster Viewing:	*2 credits*

MESSAGE

COMMITTEE'S MESSAGE

It is our great pleasure to invite you to attend the 4th Kuwait International Pharmacy Conference, to be held from 4th to 6th February 2013. This year's conference will include contemporary issues and developments from pharmacy practice to basic pharmaceutical science. There will be plenary sessions and proferred oral abstracts as well as posters related to advances in pharmacotherapy, medication adherence, drug delivery, neutraceuticals and pharmacogenomics. Invited lectures will be given by distinguished scholars from North America and Europe as well as locally from the Gulf region. Also included in the programme will be panel discussions on topical issues to elicit audience participation.

We hope that you will consider attending and submitting your research work to this bi-annual meeting and contribute to its success.

We look forward to seeing you.

With best wishes on behalf of the organizers.

Dr. Mohammad Waheedi
Chair of Organizing Committee

Prof . Yunus Luqmani
Chair of Scientific Committee

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Organizing Committee

Organizing Committee

Dr. Mohammed Waheedi (Chair)

Prof. Yunus Luqmani (Chair of Scientific Committee)

Dr. Maitham Khajah (Chair of Social Committee)

Dr. Abdelmoneim Awad

Dr. Ahmed El-Hashim

Dr. Mohsen Hedaya

Ph. Shaimaa Abdel-Meguid

Ms. Sanaa Akroof

Ms. Teena Sadan

Ms. Farah al-Aiadie (Services department-Khaldiya)

Dr. Omar El-said Omar (Ministry of Health)

Organizing Committee

Dr. Mohammed Waheedi
Chair of Organizing Committee

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Chair of Scientific Committee

Dr. Maitham Khajah
Chair of Social Committee

Dr. Abdelmoneim Awad

Dr. Ahmed El-Hashim

Dr. Mohsen Hedaya

Social Committee

Ms. Heba Kobah
Third year, Faculty of Pharmacy
Head of Media committee

Ms. Muneera Al Sardi
Fourth year, Faculty of Pharmacy
Head of Students Organizing committee

Ms. Sara Bouyabes
Fifth year, Faculty of Pharmacy
Head of Social Committee

A. Rami Ayoun Al Soud
Third year, Faculty of Pharmacy
Head of transportation committee

4th Kuwait International Pharmacy Conference (KIPC)

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Invited Speakers

Prof. Wendy Carolyn Duncan (Keynote Speaker)

St. Louis College of Pharmacy, USA

Prof. Fazlul H. Sarkar

Karmanos Cancer Center,
School of Medicine, Wayne University, USA

Prof. Hamid Ghandehari

Departments of Pharmaceutics & Pharmaceutical Chemistry and Bioengineering, Utah Center for Nanomedicine,
University of Utah, USA

Prof. Hind T Hatoum

Department of Pharmacy Administration
College of Pharmacy, University of Illinois at Chicago, USA

Prof. Jerome J Schentag

Pharmaceutical Sciences and of Pharmacy at the University at Buffalo (UB), State University of New York, USA

Dr. Mohamed E.H. El-Sayed

Pharmaceutical Sciences and of Pharmacy at the University at Buffalo (UB), State University of New York, USA

Prof. Wu, Xiao Yu

Leslie Dan, Faculty of Pharmacy, University of Toronto Canada

Dr. Laila C Abu Esba

King Faisal Hospital, Saudi Arabia

Program at a Glance

Monday 4th February, 2013	Tuesday 5th February, 2013	Wednesday 6th February, 2013
08:00 – 12.30 16.00 – 17.30	**Registration**	
09.00 am – 9.45 am **Opening Ceremony**	09.00 am – 10.30 am **Plenary Lectures**	09.00 am – 10.30 am **Plenary Lectures**
9.45 am – 10.45 am **Keynote Address**	10.30 am – 10.45 am **Coffee Break**	10.30 am – 10.45 am **Coffee Break**
10.45 am – 11.15 am **Break**	10.45 am – 11.45 am **Podium Presentations**	10.45 am – 11.30 am **Plenary Lecture**
11.15 am – 12.00 pm **Plenary Lecture**	11.45 am– 12.30 pm **Plenary Lecture**	11.30 am – 12.30 pm **Podium Presentations**
12.00 pm – 1.30 pm **Poster Presentations & Lunch**	12.30 pm – 1.30 pm **Poster Presentations & Lunch**	12.30 pm – 1.30 pm **Poster Presentations**
1.30 pm – 5.00 pm **Break**	12.30 pm – 5.00 pm **Break**	1.30 pm – 5.00 pm **Break**
5.00 pm – 6.30 pm **Plenary Lectures**	5.00 pm – 6.30 pm **Plenary Lectures**	5.00 pm – 6.30 pm **Plenary Lectures**
6.30 pm – 6.45 pm **Coffee Break**	6.30 pm – 6.45 pm **Coffee Break**	6.30 pm – 7.30 pm **Discussion Forum**
6.45 pm – 7.45 pm **Podium Presentations**	6.45 pm – 7.45 pm **Discussion Forum**	07.30 pm **Closing Ceremony and Farewell Dinner**

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Scientific Program

Scientific Program Day 1

4th February, 2013

Time	Topic	Speakers	Chair/Co-Chair
8.00 - 12.30 16.00 - 17.30	Registration		
9.00 – 9.45	**Opening Ceremony**		
9.45 – 10.45	Keynote address	**Prof W Duncan** Collaborating to educate tomorrow's leaders in patient-centred care	Dr M Waheedi Dr A Bassam
10.45 – 11.15	**Coffee Break**		
11.15 – 12.00	Plenary lecture-1	**Prof J Schentag** Diabetes and metabolic syndrome- a global problem with new solutions	
12.00 –1.30	**Poster presentation & Lunch**		
1.30 - 17.00	BREAK		
17.00 – 17.45	Plenary lecture-2	**Prof H Hatoum** Latest trends in patient-reported outcomes in type-2 diabetes and the role of the pharmacists in ensuring adherence to drug therapy	Dr A Awad Dr F Al Jeragh
17.45 – 18.30	Plenary lecture-3	**Dr LC Abu Esba** Drug information center: an experience from King Faisal Hospital, KSA	
18.30 – 18.45	**Coffee Break**		
18.45 – 19.05	Podium presentation 1	**Prof F Alali** A new paradigm for pharmacy practice and education	Prof M Abdel Hamid Dr I Khattab
19.05 – 19.25	Podium presentation 2	**Dr EB Raad** Is there any role for the clinical pharmacist in Lebanon?	
19.25 – 19.45	Podium presentation 3	**Dr D Malaeb** Pharmacist counseling versus leaflet education in improving awareness in vitamin D deficient Lebanese patients	

Scientific Program Day 2

5th February, 2013

Time	Topic	Speakers	Chair/Co-Chair
8.00 - 12.30 16.00 - 17.30	Registration		
9.00 – 9.45	Plenary lecture 5	**Prof H Ghandehari** Nanomedicine: polymeric systems for controlled drug delivery to tumours	Dr A Nada Dr M Hedaya
9.45 - 10.30	Plenary lecture 6	**Prof S Wu** Integrated drug delivery strategies for multidrug resistant and metastatic cancers	
10.30 – 10.45	**Coffee Break**		
10.45 – 11.05	Podium presentation 4	**Prof S Akhtar** Superfect polyamidoamine delivery system modulates EGFR signal transduction	
11.05 – 11.25	Podium presentation 5	**Prof AS Mustafa** Molecular techniques and bioinformatics identify next generation vaccine candidates against tuberculosis	Dr A Zaghloul Dr M Khajah
11.25 – 11.45	Podium presentation 6	**Dr A Zaghloul** Stability and bioavailability assessment of optimized self-emulsified drug delivery system of ibuprofen in human volunteers	
11.45 – 12.30	Plenary lecture 7	**Dr M El-Sayed** Development of “smart” vectors for enhanced cytoplasmic delivery of therapeutic nucleic acids	
12.30 – 13.30	**Poster presentation & Lunch**		
13.30 – 17.00	**BREAK**		
17.00 – 17.45	Plenary lecture 8	**Prof W Duncan** New health delivery models in relation to patient-centeredness and health teams	Prof S Kombian Dr F Al Saleh
17.45 – 18.30	Plenary lecture 9	**Prof H Hatoum** Risk of gastrointestinal bleeds in patients on aspirin for secondary prevention of cardiovascular events and the role that pharmacists can play	
18.30 – 18.45	**Coffee break**		
18.45 – 19.45	Discussion Forum	**Prof F Alali** Herb-drug interaction: a significant safety concern	

Scientific Program Day 3

6th February, 2013

Time	Topic	Speakers	Chair/Co-Chair
8.00 – 13.00	Registration		
9.00 – 9.45	Plenary lecture 10	**Prof F Sarkar** Development of targeted novel pharmaceuticals: focusing on cancer stem cell pharmacology and systems biology	Dr K Matar Prof JN Sharma
9.45 - 10.30	Plenary lecture 11	**Prof J Schentag** Tools for optimization of individualized chemotherapy: individualized antibiotic dosing based on PK/PD to maximize, efficacy and minimize bacterial resistance	
10.30 – 10.45	**Coffee Break**		
10.45 – 11.30	Plenary lecture 12	**Prof S Wu** Nanotechnology and smart polymer-enabled glucose-responsive insulin delivery for diabetes	
11.30 – 11.50	Podium presentation 7	**Ms LH Sharaf** Evaluation of novel oxazolidinones for monoamine oxidase inhibitory activity	Prof YA Luqmani Dr A El-Hashim
11.50 – 12.10	Podium presentation 8	**Dr K Orabi** Microbial metabolism of vulgarin	
12.10 – 12.30	Podium presentation 9	**Prof SB Kombian** Anticonvulsant screening of novel enaminones in the rat hippocampus in vitro.	
12.30 – 13.30	**Poster presentation**		
13.30 – 17.00	**BREAK**		
17.00 – 17.45	Plenary lecture 13	**Prof F Sarkar** Nutraceutical research: bench to clinic	Prof OA Phillips Dr K Orabi
17.45 – 18.30	Plenary lecture 14	**Prof H Ghandehari** Translating drug discovery to the market	
18.30 – 19.30	Discussion Forum	**Prof W Duncan** Pharmacy Education	
18.30 – 18.45	**Closing ceremony and farewell dinner**		

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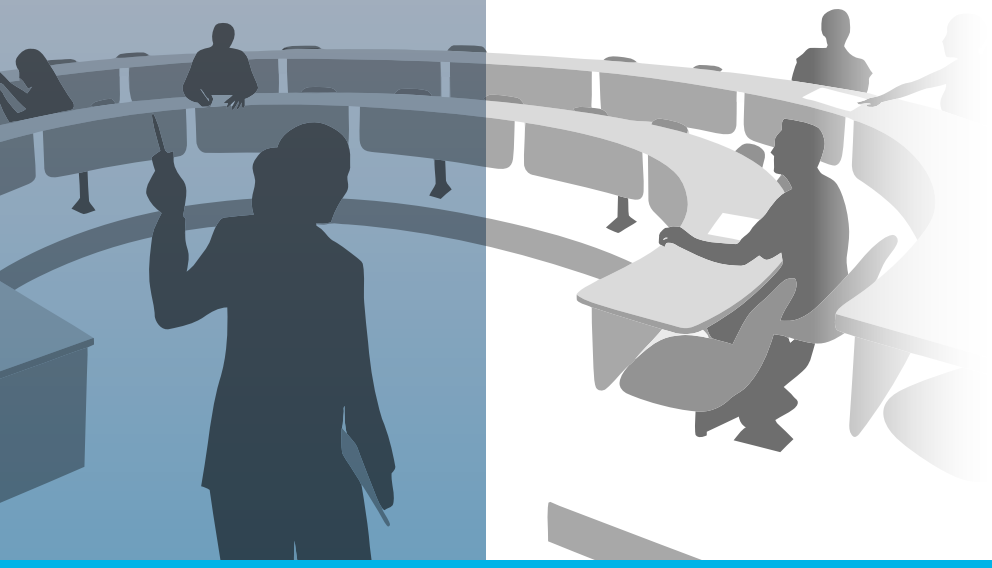

Abstracts - Plenary Lectures

Prof. Wendy Carolyn Duncan (Keynote Speaker)

St. Louis College of Pharmacy, USA

Collaborating to educate tomorrow's leaders in patient-centred care

Interprofessional collaboration is one of the cornerstones of patient-centered care, and as healthcare moves towards performance-based and health-oriented compensation, graduating health professionals must possess the requisite interprofessional knowledge, skills and attitudes if they are to be successful. However interprofessional education poses a significant problem for faculty who have been educated – and who practice on a fee for service basis – in the silos that exist today. It is likely that the responsibilities and identities of each health professional will need to change along with the systems of care provision, and this is a likely source of conflict. Experiential faculty development is a key first step and must enable faculty to uncover and resolve conflict, experiment with interprofessional practice models, evaluate and improve performance, develop competence in leadership and organizational change, and reflect on the co-evolution of their knowledge, identities, professional norms, and work. The presentation will provide participants with an overview of a conflict-oriented team building model, criteria for successful change management, and the characteristics of an authentic, patient-centered interprofessional practice.

Prof. Jerome J Schentag

Pharmaceutical Sciences and of Pharmacy at the University at Buffalo (UB), State University of New York, USA

Diabetes and metabolic syndrome - a global problem with new solutions

Because of safety concerns with many of the oral diabetes drugs, the focus of Diabetes Drug Development has been shifting away from simple Glucose control and towards the prevention of Cardiovascular complications. Metformin is ordinarily front line in T2D because it has no added CV risk, and is associated with modest lowering of HBA1c via the inhibition of hepatic gluconeogenesis. Metformin is considered weight neutral, but in practice most patients experience modest weight loss. Metformin does not have any lipid control properties, and it does not decrease insulin resistance or control hypertension. On the supply side model algorithm, metformin scores 2.2, as compared to the supply side value of 0.7 with weight gain associated T2D drugs such as sulfonylureas or long acting insulins(1). Cardiovascular complications are well known consequences of most metabolic syndromes, and it follows that new type 2 diabetes targets could come from an improved diabetes disease progression model with emphasis on cardiovascular endpoints. A score over 2.0 in the Supply Side Model is predictive of cardioprotection(2).

RYGB is the most cardioprotective measure ever discovered, and if we could understand why this surgical procedure cures diabetes and reverses cardiovascular damage from diabetes, and mimic the effect with an oral drug, that drug would be a true revolution in the treatment of type 2 diabetes worldwide. After RYGB surgery, T2D is controlled even before weight loss occurs, and even more surprisingly, it now seems clear that beneficial effects occur after RYGB even in patients without obesity. As an oral mimetic of RYGB surgery, Brake™ specifically targets the ileal Brake. When taken once daily, oral Brake™ treatment elicits the full range of hormonal mediator outputs and controls hyperglycemia, hyperlipidemia, and obesity. There was resolution of hepatic steatosis and NAFLD as added benefit. RYGB acts primarily by this pathway via a central satiety mechanism, rapidly reverses insulin resistance, and scores 4.0 on the Supply Side Model. Any oral mimetic of RYGB would be synergistic with Metformin, and the combination

of these two agents would demonstrate enhanced glucose control, lipid lowering, control of triglycerides, and weight loss of a greater magnitude than Metformin alone. We have recently developed an oral mimetic of RYGB called Brake™, named for its primary action as an ileal brake hormone releasing substance that reverses insulin resistance. The composition of Brake™ with metformin is called MetaBrake™.

MetaBrake™ is expected to control glucose, lipids and weight in T2D patients. Because RYGB is cardioprotective and reverses atherosclerosis, we anticipate a high degree of cardioprotection from MetaBrake™ in T2D patients. We are formulating Metformin and Brake™ into a combination product for testing in obese T2D patients with HBA1c >7.0 and hyperlipidemia.

The use of the Supply Side Model for Drug Design has therefore yielded a new approach to T2D therapeutics, as well as a means of describing the relative attributes of current diabetes targets with reference to CV risk potential. Underlying Metabolic Syndrome (MS) has many different manifestations such as Type 2 Diabetes, hyperlipidemia, obesity or NAFLD, but there is no means of tracking progression of MS in patient populations that may have any or all of these conditions to varying degree. It was our hypothesis that improved risk scoring could be accomplished via an index that considered a composite of MS system components.

The FS index (Fayad/Schentag) of MS considered the following: Fasting Blood Glucose, Fasting Insulin, HBA1c, BMI, AST, Triglycerides, Glucose Supply-Demand (S/D) index, and Proinsulin. Each parameter was mathematically arranged to increase as MS worsened, and weighted approximately equally in the prediction of MS progression and risk for CV events. The FS index was then applied to well-studied patient populations already in our databases, using a neural net model. The database included previously published 45 patients with T2D having AMIs, 45 precisely matched T2D controls without AMIs, 41 patients with RYGB surgery and reversal of MS, 300 patients with COPD and T2D, and 18 patients given Brake therapy for Hepatitis C, NAFLD, or prediabetes. FS index values were calculated from serial laboratory and clinical data over timeframes ranging 2-10 years. In these patient populations, a normal FS index value is 20-50. Patients with two or more manifestations of MS are above 200. Maximum values are above 500, typical when nearly every MS component is abnormal.

High FS index values predicted CV risk in this patient population, regardless of the specific components of MS that were abnormal. Abnormal and rising FS index values predicted AMI. Declines in FS index in patients with RYGB surgery were dramatic, taking scores of these patients from above 250 to values below 20 in most cases. Responses to oral Brake were similar to RYGB, even though Brake treated patients did not lose as much weight

Overall, the FS index, which is composed of mostly readily available laboratory and clinical measures, is a promising tool describing progression or amelioration of MS in routine practice.

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1. Monte SV, Schentag JJ, Adelman MH, Paladino JA. Glucose supply and insulin demand dynamics of antidiabetic agents. J Diabetes Sci Technol. 2010;4(2):365-81.
2. Monte SV, Schentag JJ, Adelman MH, Paladino JA. Characterization of cardiovascular outcomes in a type 2 diabetes glucose supply and insulin demand model. J Diabetes Sci Technol. 2010;4(2):382-90.

Prof. Hind T Hatoum

Department of Pharmacy Administration

College of Pharmacy, University of Illinois at Chicago, USA

Latest trends in patient-reported outcomes in type-2 diabetes and the role of the pharmacists in ensuring adherence to drug therapy

The complexity of healthcare needs of the population at large, coupled with the escalating costs and problems in ensuring optimal drug therapy practices begs for the involvement of the pharmacists in patient care processes. Pharmacists' involvement may lead to better adherence and that will in turn lead to better patients' outcome. Pharmacists in Kuwait can play a bigger role in helping patients with type-2 diabetes (T2-DM) towards optimal care for the diabetic population. T2-DM is not only a global epidemic, but also a significant health issue for Kuwait and the entire region. Pharmacists can use patient-reported-outcome (PRO) as the means to interact with the patients and as a mechanism to improve the process of diabetic care and consequently to improve patients outcome.

It is well acknowledged that T2DM is a long-term condition for which ongoing management rests mainly with the individual patient. As such, treatment acceptability and satisfaction may play an important role in adherence to long-term use of medications, and hopefully in achieving long-term clinical success. In addition, willingness to change life style and the psychological well-being of the patients before and after starting a treatment regimen that may influence this willingness to change, are instrumental in patients adhering and persisting on treatment. The presentation will focus on the following objectives:

1. Recent trends in the development of newer antidiabetic drug therapies whereby the central role that patients play in the management of their conditions is acknowledged and incorporated into clinical trials.
2. Describe some of the newer PROs used in diabetes.
3. How to use patient-reported-outcomes as means to inform clinical decisions?
4. Provide high level results on the impact of the newer therapies on PRO and most specifically patients' satisfaction with treatment.
5. Touch base on the impact of the frequency and severity of conventional treatment-related problems such as hypoglycemic episodes, weight gain, and fear of needle on patients' adherence to prescribed treatment regimens.
6. Propose some research agenda and incremental "baby" steps that could be taken by pharmacists in Kuwait to improve the process and outcomes of diabetic management.

Prof. Hamid Ghandehari

Departments of Pharmaceutics & Pharmaceutical Chemistry and Bio-engineering, Utah Center for Nanomedicine,
University of Utah, USA

Nanomedicine: polymeric systems for controlled drug delivery to tumours

A continuing challenge with the treatment of solid tumors is the dose – limiting toxicity of anticancer drugs. Polymeric carriers can be used to complex, conjugate or entrap drugs for systemic delivery [1]. Such delivery relies on, either passive targeting, taking advantage of the enhanced permeability and retention effect [2], or active targeting by using moieties recognizable by tumor cells or the surrounding vasculature. One way to deliver anticancer agents to solid tumors is by utilizing water-soluble polymers such as N-(2-hydroxypropyl) methacrylamide (HPMA) copolymers [3]. Despite progress made in this area, a challenge is limited delivery of the chemotherapeutic to the target site. Recent efforts in our lab involve co-delivery of heat with macromolecular systems to the tumor using gold nanorod-mediated plasmonic photothermal therapy (PPTT) [4-6]. We have shown that delivery of albumin as a model macromolecule to sarcoma tumors was enhanced using this technique. Further, accumulation of HPMA copolymers with pendent side chains terminated in glucose regulated protein 78 (GRP78) peptides was increased in the presence of PPTT in prostate tumor xenograft models. Finally, a synergistic effect has been observed with targeted delivery of docetaxel when combined with hyperthermia.

While small molecular weight anticancer drugs continue to have utility in cancer treatment, there is a need to develop gene therapy approaches for treatment of solid tumors. An intensive area of research is design and development of adenoviral gene therapy systems. Challenges with adenoviral delivery include increased uptake by the liver and spleen, and immune response. Recent work in our laboratory involves the design and development of recombinant silk-elastinlike hydrogels for localized matrix-mediated adenoviral gene delivery in the treatment of head and neck tumors [7]. We have shown that by precise engineering of the polymeric backbone, transfection efficiency and efficacy can be modulated. Ongoing work involves inclusion of matrix-metaloprotease responsive sequences for site-specific release. In this talk two examples, i.e., water-soluble polymers and hydrogels, will be discussed to illustrate the utility of polymeric systems in solid tumor therapy.

Acknowledgements: Efforts of laboratory members and collaborators some of whom cited in the references herein are acknowledged. Support was provided by the NIH (R01 EB007171, R01CA107621) and the Utah Science Technology and Research (USTAR) initiative.

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1) Polymer therapeutics as nanomedicines: new perspectives. Duncan R. Curr Opin Biotechnol. 22 (2011) 492-501.

2) Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review, Maeda H., Wu J., Sawa T., Matsumura Y., Hori K., J. Control. Release 65 (2000) 271–284.

3) HPMA copolymers: origins, early developments, present, and future. Kopeček J., Kopečková P., Adv Drug Del Rev. 62 (2010) 122-149.

4) Guided delivery of polymer therapeutics using plasmonic photothermal therapy, Gormley A. J., Larson N., Sadekar S., Robinson R., Ray A., Ghandehari H., Nano Today, 7 (2012) 158-167.

5) Gold nanorod mediated plasmonic photothermal therapy: a tool to enhance macromolecular delivery, Gormley A.J., Greish K., Ray A., Robinson R., Gustafson J. A., Ghandehari H., Int J Pharm, 415 (2011) 315-318.

6) Plasmonic photothermal therapy increases the tumor mass penetration of HPMA copolymers, Gormley A. J., Larson N., Banisadr A., Robinson R., Frazier N., Ray A., Ghandehari H., J Control Release (in press).

7) Silk-elastinlike protein polymers for matrix-mediated cancer gene therapy. Gustafson J. A., Ghandehari H., Adv Drug Deliv Rev., 62 (2010) 1509-1523.

Prof. Wu, Xiao Yu

Leslie Dan, Faculty of Pharmacy, University of Toronto
Canada

Integrated drug delivery strategies for treatment of multidrug resistant and metastatic cancers

According to the report of the World Health Organization, cancer is a leading cause of death worldwide. Despite advances in treatment modalities and new therapeutic agents, there were 7.6 million people died from cancer (around 13% of all deaths) in 2008, largely due to metastases. Chemotherapy has been applied alone or in combination with other modalities. However, multidrug resistance (MDR) of solid tumors and cancer cells is frequently encountered, which leads to failures in chemotherapy. Owing to multifactorial nature of MDR that involves various cellular and non-cellular mechanisms, drug resistance cannot be circumvented by a single approach such as the use of a specific efflux pump inhibitor or an inhibitor of a single pathway of disease progression. In addition, poor specificity and severe toxic side effects of anticancer drugs, and insufficient drug accumulation in tumor tissue further hinder the success of chemotherapy. Therefore, our laboratory has been exploring integrated drug delivery strategies to overcome multiple MDR mechanisms and to enhance chemotherapy. We have applied the knowledge of pharmaceutics, pharmacology, physiology, oncology, and nanotechnology for rational design of effective carrier systems and synergistic drug combination therapy, and for selection of appropriate drug delivery routes. We have demonstrated that synergistic dual agent-loaded polymer-lipid hybrid nanoparticles are able to overcome MDR in various membrane transporter-overexpressing breast cancer cells and to improve therapeutic efficacy while reducing toxic side effects in breast tumor models. Using the integrated approach, we have also developed a targeted drug delivery system that effectively inhibited lymphatic metastasis of lung cancer.

Dr. Mohamed E.H. El-Sayed

Biomedical Engineering

Cellular Engineering & Nano-Therapeutics Laboratory,

University of Michigan, USA

Development of "smart" vectors for enhanced cytoplasmic delivery of therapeutic nucleic acids

Plasmid DNA, antisense oligodeoxynucleotides, and silencing RNA molecules have displayed therapeutic activity against cancer, viral infection, cardiovascular diseases, and neurodegenerative disorders in preclinical models. However, development of these nucleic acids into clinically-viable treatments has been hampered by the lack of an efficient carrier that can deliver this DNA/RNA cargo selectively into the cytoplasm of the diseased cell without exhibiting non-specific toxicity to healthy tissues. In this talk, I will describe our efforts to design and synthesize a new family of star-shaped pH-sensitive polymers, which proved effective in condensing a large dose of silencing RNA (siRNA) molecules forming "smart" particles that efficiently shuttled their cargo into the cytoplasm of epithelial cancer cells to successfully suppress the expression of targeted genes.

Prof. Wendy Carolyn Duncan (Keynote Speaker)

St. Louis College of Pharmacy, USA

New health delivery models in relation to patient-centeredness and health teams

According to the report of the World Health Organization, cancer is a leading cause of death worldwide. Despite advances in treatment modalities and new therapeutic agents, there were 7.6 million people died from cancer (around 13% of all deaths) in 2008, mainly due to metastases. Chemotherapy has been applied alone or in combination with other modalities. However, multidrug resistance (MDR) of solid tumors and cancer cells is frequently encountered, which leads to failures in chemotherapy. Owing to multifactorial nature of MDR that involves various cellular and non-cellular mechanisms, drug resistance cannot be circumvented by a single approach such as the use of a specific efflux pump inhibitor or an inhibitor of a single pathway. In addition, poor specificity and severe toxic side effects of anticancer drugs, and insufficient drug accumulation in tumor tissue further hinder the success of chemotherapy. Therefore, our laboratory has been exploring integrated drug delivery strategies to overcome multiple MDR mechanisms and to enhance chemotherapy. We have applied the knowledge of pharmaceutics, pharmacology, physiology, oncology, and nanotechnology for rational design of effective carrier systems, synergistic drug combination therapy, and most appropriate drug delivery routes. We have demonstrated that synergistic dual agent-loaded polymer-lipid hybrid nanoparticles are able to overcome MDR in various membrane transporter-overexpressing breast cancer cells and to improve therapeutic efficacy while reducing toxic side effects in breast tumor models. Using the integrated approach, we have developed a targeted drug delivery system that effectively inhibited lymphatic metastasis of lung cancer.

Prof. Hind T Hatoum

Department of Pharmacy Administration

College of Pharmacy, University of Illinois at Chicago, USA

Risk of gastrointestinal bleeds in patients on aspirin for secondary prevention of cardiovascular events and the role that pharmacists can play

Background

- Aspirin use is the foundation of antiplatelet therapy for secondary CVD prevention.
- However, aspirin increases the risk of gastrointestinal (GI) adverse effects.
- In fact, low dose aspirin without the use of gastroprotective drugs (GPD) has been associated with a 2-fold increase in the risk of major GI bleeding.

Objectives

- A body of literature is devoted for the risk of GI complications in arthritic patients on non-steroidal-anti-inflammatory agents (NSAIDs).
- Less is known about the risk of GI complication in patients who are on aspirin for the prevention of secondary CVD.
- The likelihood of serious GI events associated with hospitalization or ER admission will be calculated for users of antiplatelet therapy for CVD prevention.
- Risk factors associated with GI events among patients using secondary CVD prevention will be discussed.

Methods

- Data source: 2001-2010 data from insurance claims submitted for payments.
- Inclusion criteria
    - Newly diagnosed patients (≥18 years, without warfarin use) with a CVD index event (hospital- or ER -associated stroke, acute myocardial infarction (AMI), coronary artery bypass grafting (CABG), or angiography).
    - Initiated on antiplatelet therapy within 7 days of the CVD event.

- Statistical analyses
  - o Univariate analyses
  - o Multiple regression: Logistic regression on risk of having a severe GI event, controlling for type of antiplatelet use, age, Charlson Comorbidity Index (CCI), gender, GI history, use of GP agent before the CVD index event, use of NSAID, and type of CVD (AMI or stroke) index event.

Results

- 54,215 new users of antiplatelet agents met the inclusion criteria.
- These included 376 aspirin, 1741 aspirin/dipyridamole, and 52,098 clopidogrel with or without adding aspirin users.
- Mean age: 59.22 (SD: 11.45).
- 70.56% were male patients.
- 335 (or 0.6%) had history of severe GI event.
- 20.1% patients had history of GPD use. 36.42% of the patients used GPD after the index date while on antiplatelet therapy.
- Overall, 86.8% GPD prescriptions were PPIs.
- 21.65% patients had history of NSAID use.
- Almost 1/4 (23.95%) of the patients used NSAID after the index date while on antiplatelet therapy.

Documented Study Outcome

- A total of 3.7% of patients incurred at least one severe GI event after the index date.
- The risk rate of severe GI event among the patients without GI history was 3.6% in 2 years, and 30.1% among those with history of severe GI event.
- Multiple regression results indicated that aspirin users, older age, females, higher co-exiting morbidities (CCI), GI history, use of GPD at baseline, and use of NSAIDs were associated with significantly higher risk of GI events.

Conclusions

- An average of 3.6% of patients without a history of GI events may be expected to develop a serious GI event within 2 years of antiplatelet use for secondary CVD prevention.
- In addition to antiplatelet therapy, roughly one quarter of patients was prescribed NSAIDs and one third was prescribed GP agents.
- Kuwaiti pharmacists can help monitor and hopefully minimize the risk of GI-complications in an already sick patients population by paying closer attention to patients already identified to have a higher than average risk for the experience of these complications. Namely a closer attention should be given to patients on aspirin, older patients, those who are already on gastro-protective drugs including PPI, and antacids, to patients on NSAIDs and in the sicker patient population.

Prof. Fazlul H. Sarkar

Karmanos Cancer Center,

School of Medicine, Wayne University, USA

Development of targeted novel pharmaceuticals: focusing on cancer stem cell pharmacology and systems biology

Last few decades have witnessed the discovery of several newer drugs (pharmaceuticals) for the treatment of human malignancies; however, almost all existing conventional cytotoxic agents or even targeted agents failed to meet the expectation toward cancer cure. Mounting evidence clearly suggesting the need for a paradigm shift in drug discovery especially based of emerging molecular knowledge of the complexities of human tumors, which demands newer approach for the development of better and targeted pharmaceuticals for realizing the dream of cancer cure. This presentation will discuss Tumor Microenvironment, Tumor Cell Heterogeneity, Molecular Features of Drug Resistance, Epithelial-to-Mesenchymal Transition (EMT), Cancer Stem Cells (CSCs) and the current Knowledge of Systems Biology. The presentation will be focused on the complexities of cancer cells especially what we know regarding cancer stem cell pharmacology and systems biology, and will further discuss how this knowledge will aid in the design and discovery of novel pharmaceuticals (targeted therapeutics) for the treatment of human malignancies. The knowledge gained from this presentation is expected to advance novel development of cancer-specific pharmaceuticals.

Prof. Jerome J Schentag

Pharmaceutical Sciences and of Pharmacy at the University at Buffalo (UB), State University of New York, USA

Tools for optimization of individualized chemotherapy: individualized antibiotic dosing based on PK/PD to maximize, efficacy and minimize bacterial resistance

Patients with serious infections like nosocomial pneumonia require bactericidal antimicrobial activity in precise regimens to succeed at organism eradication while minimizing the constant threat of acquired resistance. Defining a precise regimen requires understanding PK/PD because either too high a dose or two low can result in problems. Studies in our patient populations demonstrate that the minimum effective antimicrobial action is an area under the inhibitory titer (AUIC) of 125, where AUIC is calculated as the 24 hour serum AUC divided by the MIC of the pathogen. This target AUIC may be achieved with either a single antibiotic or it can be the sum of AUIC values of two or more antibiotics. There is considerable variability in the actual measured AUIC value for patients when antibiotics are given in their usually recommended dosages. Examples of this variance will be provided using aminoglycosides, fluoroquinolones, beta-lactams, and vancomycin. The achievement of minimally effective antibiotic action, consisting of an AUIC of at least 125, is associated with bacterial eradication in about 7 days for beta lactams and fluoroquinolones. When AUIC is increased to 250, the fluoroquinolones (which display in vivo concentration dependent bacterial killing) can eliminate the bacterial pathogen in 1-2 days(1). Beta lactams, even when dosed to an AUIC of 250, often require longer treatment duration to eliminate the bacterial pathogen, because the in vivo bacterial killing rate is slower with beta lactams than with the fluoroquinolones(2). This remains true even at AUIC values of 250 for both compounds, which is theoretically identical dosing.

Antibiotic activity indices such as AUIC allow clinicians to evaluate individualized patient regimens. Furthermore, antibiotic activity is a predictable clinical endpoint with predictable clinical outcome. This value is also highly predictive of the development of bacterial resistance(3). Antimicrobial regimens that do not achieve an AUIC of at least 125 cannot prevent the selective pressure that leads to overgrowth of resistant bacterial sub-populations. Presence of foreign bodies such as tubes and hardware and impaired host inflammatory response facilitate resistance, particularly when AUIC is below 100.

The use of PK/PD indices like AUIC can assist with patient management strategies in a prospective manner, and allow comparison of outcomes with different treatment regimens and dosing strategies. Our studies demonstrate that calculations of AUIC can be used to prospectively target regimens to improve the chances of cure with nosocomial pneumonia and other serious infections. A clinical intervention team has been organized to optimize antimicrobial regimens as early in therapy as possible, so as to lower the high cost events like failure and acquired bacterial resistance(4). We have recently developed mathematical progression models to correlate the PK/PD values achieved with indices of clinical response, and can thereby incorporate infection scoring and patient response into the PK/PD analyses used in patient care(5).

The PK/PD indices in vivo can allow comparison of antimicrobial outcomes with different treatment regimens and dosing strategies. Our studies demonstrate that calculations of AUIC can also be used to prospectively design antibiotic combination regimens to improve the chances of cure with nosocomial pneumonia and other serious infections. Resistance development can also be predicted, once the relationship between PK/PD and bacteriostatic action is identified in the human trials.

These calculations and measurements can be easily added to phase II and III dose-finding trials, and the reward is a measurable increase in the information value of the trials, arrival at the precise dose, and a good correlation between microbial effect and clinical outcome in the patients treated. Such parameters are useful to characterize either single agents or combination therapy, and in fact may be the only way to clinically demonstrate additivity and even synergy at the bedside where it is most important for the survival of our patients.

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Prof. Wu, Xiao Yu

Leslie Dan, Faculty of Pharmacy, University of Toronto
Canada

Nanotechnology and smart polymer-enabled glucose-responsive, closed-loop insulin delivery for diabetes

The total number of people with diabetes in the world is more than 371 million and 4.8 million people died due to diabetes in 2012 (IDF report). All Type 1 diabetic patients (~10%) administrate exogenous insulin by injection or infusion to sustain life and ~20% Type 2 diabetic patients manage their disease through insulin administration. Although the goal of insulin therapy is to achieve sustained normoglycemia, fluctuation in glycemia especially hypoglycemia occurs frequently as a side effect of intensive insulin therapy. The unsuccessful tight-control of blood glucose (BG) level with insulin therapy is largely due to lack of feedback mechanism of insulin delivery despite self-check of glucose levels by patients. Therefore, extensive efforts have been made in past few decades to develop closed-loop insulin delivery systems, so called artificial pancreas, to detect blood glucose levels in real time and control insulin release rate automatically. Various approaches have been attempted to achieve this goal including glucose sensor-coupled insulin pump, electromechanical devices, and chemically-driven systems such as glucose-responsive hydrogels. Our group has developed a glucose-responsive insulin delivery device based on nanocomposite and smart materials. This chemically-driven device integrated glucose-sensing and insulin releasing components in one unit, providing self-regulated insulin release with no need for electronic and mechanical parts. The device released insulin quickly in vitro and in vivo in response to changes in glucose concentration. The implanted device was able to control blood glucose levels in a diabetic rat model for an extended period of time. This presentation will first review the current progress and challenges in closed-loop insulin delivery and discuss how nanotechnology and smart polymers are utilized in the design of glucose-responsive insulin delivery device for diabetes treatment.

Prof. Fazlul H. Sarkar

Karmanos Cancer Center,

School of Medicine, Wayne University, USA

Nutraceutical research: bench to clinic

It is not readily realized that about 50% of current cancer therapeutics originated from the nature (natural compounds), and thus the role of nutraceuticals (natural agents) in human health especially the value of nutraceuticals for the prevention and/or treatment of human malignancies has not been fully appreciated. Since therapeutic resistance is one of the major challenge for the treatment of human malignancies especially solid tumors and since there are no avenues by which one could overcome therapeutic resistance, this presentation will provide some example on the role of natural agents in overcoming therapeutic resistance with special emphasis on emerging discoveries and knowledge of miRNAs, EMT and Cancer Stem-Like Cells (CSLCs). The presentation will also be focused on important signaling molecules such as Notch, NF-kB and Hedgehog signaling and will provide state of the art knowledge on the deregulation of miRNAs by natural agents (nutraceuticals). Specific examples will be given on the role of nutraceuticals such isoflavones, indoles and curcumin and will provide experimental evidence on the role of nutraceuticals for overcoming therapeutic resistance mediated via deregulation of miRNAs and their targets. Overall, the knowledge gained from this presentation is expected to advance novel development of cancer-specific pharmaceuticals from nutraceuticals. The expected educational objective of this presentation would be realized if it could generate newer dialogue on designing novel and tailored clinical trials for assessing the value of nutaraceuticals in achieving better treatment outcome of patients diagnosed with cancers.

Prof. Hamid Ghandehari

Departments of Pharmaceutics & Pharmaceutical Chemistry and Bioengineering, Utah Center for Nanomedicine, University of Utah, USA

Translating drug discovery to the market

In the United States, it takes an average of 12 years for a newly discovered drug to travel from the laboratory to the market place. Only 5 in 5,000 drugs that enter preclinical testing progress to human testing and only one of these 5 drugs that are tested in people is approved.

The process of drug approval is controlled in most countries by a governmental regulatory agency. In the United States the Food and Drug Administration (FDA) governs this process. To gain approval to market a new drug there are specific steps that it must go through in its 12 year journey from drug discovery to your medicine cabinet. These steps include securing intellectual property protection through patents and license agreements. In addition, in the United States, the FDA requires the following sequence of events before approving a drug.

Preclinical Testing: A pharmaceutical company conducts numerous studies before the future drug is ever given to a human being. Laboratory and animal studies must be done to demonstrate the biological activity of the drug against the targeted disease and to evaluate its safety.

Investigational New Drug Application (IND): The pharmaceutical company files an IND with the FDA to begin testing the drug in people.

Phase I Clinical Trials: Phase I studies are usually the first tests of a drug under development in healthy volunteers. The tests determine a drug's safety profile, including the safe dosage range, plus how the drug is absorbed, distributed, metabolized and excreted, and the duration of its action.

Phase II Clinical Trials: These are larger studies that are conducted in patients with the disease for which the drug is intended. This phase is usually designed to identify what are the minimum and maximum dosages. The trials generally involve 100 to 300 volunteer patients to assess the drug's effectiveness.

Phase III Clinical Trials: These are the definitive, large randomized trials that are submitted to the FDA in order to obtain approval of a drug. This phase examines the effectiveness as well as the safety (adverse events) of the new drug.

New Drug Application (NDA): Following the Phase III Clinical Trials, the drug manufacturer analyzes all the data from the studies and files an NDA with the FDA. The NDA contains all of the data gathered to date about the drug. (An NDA typically consists of at least 100,000 pages.) The median NDA review time for new drugs approved in 1999 was close to 12 months.

4th Kuwait International Pharmacy Conference (KIPC)

4 - 6 FEBRUARY, 2013

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Podium Presentations

Monday, 4th February, 2013

Prof. F Alali (18.45 – 19.05)
A new paradigm for pharmacy practice and education.

Dr. Eb Raad (19.05 – 19.25)
Is there any role for the clinical pharmacist in Lebanon.

Dr. D Malaeb (19.25 – 19.45)
Pharmacist counselling versus leaflet education in improving awareness in Vitamin D deficient Lebanese patients.

Tuesday, 5th February, 2013

Prof. S Akhtar (10.45 – 11.05)
Superfect polyamidoamine delivery system modulates EGFR signal transduction.

Prof. AS Mustafa (11.05 – 11.25)
Molecular techniques and bioinformatics identify next generation vaccine candidates against tuberculosis.

Dr. A Zagloul (11.25 – 11.45)
Stability and bioavailability assessment of optimized self-emulsified drug delivery system of ibuprofen in human volunteers.

Wednesday, 6th February, 2013

Ms. LH Sharaf (11.30 – 11.50)
Evaluation of novel oxazolidinones for monoamine oxidase inhibitory activity.

Dr. K Orabi (11.50 – 12.10)
Microbial metabolism of vulgarin.

Prof. S Kombian (12.10 – 12.30)
Anticonvulsant screening of novel enaminones in the rat hippocampus in vitro.

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4th Kuwait International Pharmacy Conference (KIPC)

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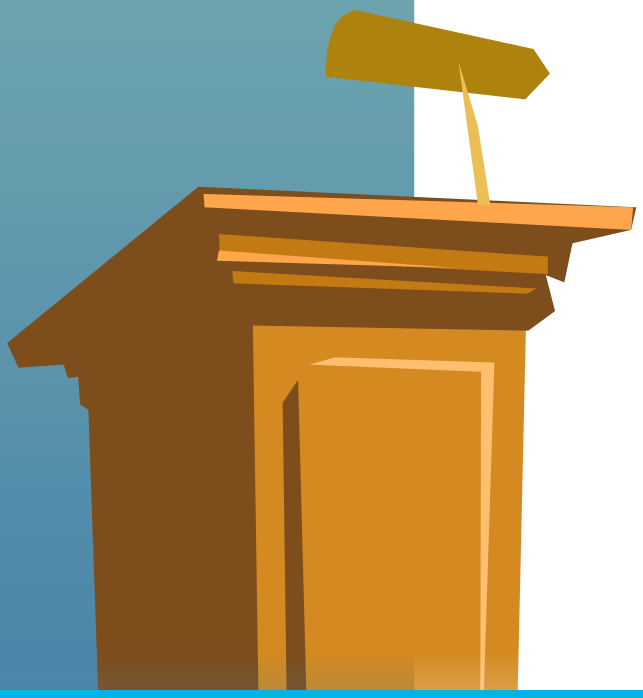

Abstracts - Podium Presentations

1: Oral

Superfect polyamidoamine delivery system modulates EGFR signal transduction

Akhtar S*[1], Chandrasekhar B[1], Attur S[1], El-Hashim AZ[2], Yousif MHM[1], Benter IF[1].
[1]Department of Pharmacology and Toxicology, Faculty of Medicine; [2]Department of Pharmacology and Therapeutics, Faculty of Pharmacy, Kuwait University, Kuwait.

Introduction:
Polyamidoamine (PAMAM) dendrimers are cationic branch-like macromolecules that are used as drug delivery systems for gene-based therapies. Ideally, they should only enhance drug delivery and exhibit no other adverse effects. However, little is known about their nanotoxicological profiles in terms of their proteomic interactions at the level of signal transduction pathways such as the epidermal growth factor receptor (EGFR). The EGFR is an important signaling cascade that regulates cell growth, differentiation, migration, survival and apoptosis. Here, we investigated the impact of Superfect (SF), a commercially available PAMAM dendrimer, on epidermal growth factor receptor (EGFR) tyrosine kinase signaling in human embryonic kidney (HEK-293) cells.

Methods:
SF was incubated alone or with the antioxidants, apocynin and catalase, in cultured HEK-293 cells for 4 or 24h. Cells were lysed and levels of total and phosphorylated EGFR were determined by Western blotting.

Results:
At concentrations routinely used for transfection, SF increased total and phosphorylated forms of EGFR at 4h and 24h following treatment. Dendrimer-induced changes in EGFR signaling could be attenuated by the antioxidants, apocynin and catalase.

Conclusions:
The SF PAMAM dendrimer delivery system stimulated EGFR expression and phosphorylation in HEK-293 cells via an oxidative stress-dependent pathway. These results suggest that dendrimers, aside from their ability to improve drug delivery, can modulate important cellular signal transduction pathways and thus, further understanding of their toxicology at the proteomic level will be important in their use clinically.

This research is funded by Kuwait University Grant Number MR05/09

Key Words: PAMAM; Dendrimer; EGFR

2: Oral

Is there any role for the clinical pharmacist in Lebanon?

Bou Raad E*[1,2], Malaeb D[2], Dekmak A[2], Awada F[2]
[1]Department of Pharmacy Practice, Pharmacy Faculty, Lebanese International University; Lebanon [2]Department of PharmD, Pharmacy Faculty, Lebanese International University; Lebanon

Introduction:
In Lebanon there is a lack of knowledge of the importance of the clinical pharmacist role in the hospitals, which contributes to the shortage of skilled personnel in this field. The increasing incidence of medication errors in different medical wards can be reduced through encouraging the role of the clinical pharmacist. The objective of the study was to determine the types of medications and hospital units that the clinical pharmacist can intervene in mostly and to evaluate the extent of the health-care members' cooperation with the clinical pharmacist by determining the percentages of the approved interventions.

Methods:
We conducted a prospective multicenter descriptive report in three Lebanese university hospitals during five months duration. We were interacting with the physicians and nurses for a period of one month on each floor through joining the daily rounds on patients. During this period, we screened inpatients' medical records. 297 interventions were collected from different hospital departments including cardiac care unit, intensive care unit, pediatrics, internal medicine, oncology and infectious departments. The primary outcome is to determine the types of medications and hospital units that the clinical pharmacist can intervene in mostly. The secondary outcome is to evaluate the extent of the health-care members' cooperation with the clinical pharmacist by determining the percentages of the approved interventions.

Results:
Two hundred and ninety seven interventions were done. The highest percentages of interventions were on non-adherence to guidelines (28.3%), dose adjustment (21.5%) and in the cardiac care unit (28%). Antibiotics had the highest percentage of interventions (24.9%) followed by proton pump inhibitors (10.8%),antithrombotics (9.4%),and fluids and electrolytes (8.1%) . The lowest interventions were on fibrates (0.3%).Out of 297, 122 interventions were approved (41.1%).The highest percentages of approved interventions were on non-adherence to guidelines (32.8%) and in cardiac care unit (33%). According to the medication classes, most approved interventions were on the antibiotic class (38.5%) followed by antithrombotics (14.8%) and fluids and electrolytes (4.1%). Interventions done on amiodarone were 3.7%, 8.1% of them were approved.

Conclusions:
The current findings showed that the introduction of a clinical pharmacist within the health- care team optimized the drug use on different hospital units. Unfortunately, the cooperation of the medical team was not as expected since more than half of the recommended interventions were not approved.

Key Words: Clinical Pharmacits Role in Lebanese Hospital; Medical Interventions

3: Oral

A new paradigm for pharmacy practice and education

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University of Science and Technology, Jordan

Introduction:
Pharmacy practice and education are currently undergoing a paradigm shift from a product-centered activity to a patient-centered system by which pharmacists are assuming new responsibilities, helping patients achieve healthy outcomes, and providing value. Pharmacy has struggled to receive full recognition as a profession this largely due to the responsibilities that pharmacists typically perform as part of their practices, that of fulfilling orders of physicians and other health professionals with prescribing privileges. I totally believe that the profession of pharmacy is uniquely positioned to provide the clinical expertise and administrative leadership necessary to assure the quality of drug therapy management through the delivery of pharmaceutical care. Pharmacy should looked at and be a primary health profession that aims to optimize medication management to produce positive health-outcomes.

Methods:
Pharmaceutical education needs to evolve to keep pace with changes in national and global health care systems. The key challenging question for the pharmacy educators is how this breadth and depth of knowledge can be applied in a meaningful way in the practice setting. Pharmacy schools should stress accreditation standards, quality assurance and audit system, curricular reforms, innovative educational techniques, and meeting market needs of qualified, competent and skillful pharmacist.

Results:
The pharmacy educational process should also change to a more problem-based, active and evidence-based learning. We should also assess the efficiency of traditional Bsc programs in meeting the demands of nowadays competitive and developing market place. When it comes to patient-centered pharmacy practice, Doctor of Pharmacy Degree should be highly encouraged.

Conclusions:
The challenge for schools of pharmacy will therefore be to provide education that will provide graduates with the knowledge, skills, and attitudes to move the profession forward, become leaders of change, maintain high standards of professional competence, and deliver pharmacy services that may be very different from those currently available.

Key Words: Pharmaceutical Education; Pharmacy Reforms; PharmD

4: Oral

Anticonvulsant screening of novel enaminones in the rat hippocampus in vitro.

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[1]Departments of Pharmacology and Therapeutics; [3]Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University, Kuwait;
[2]Department of Pharmaceutical Sciences, School of Pharmacy, Saint Joseph College, Hartford, CT, USA.

Introduction:
Enaminones are a novel group of compounds some of which have been shown to possess anticonvulsant activity. In this study, we screened different structural analogs for actions on hippocampal neuronal excitation to determine the optimal structures that can be further tested for anticonvulsant activity.

Methods:
We studied the effects of different halogen substituents on phenylamino moiety as well as varied substituents on the cyclohexenone ring that forms the backbone of enaminone structures on evoked population spikes (PS). We studied: ethyl 4-(2,4-dichlorophenylamino)-6-methyl-2-oxocyclohex-3-enecarboxylate (AK1); ethyl 4-(2,4-dibromophenylamino)-6-methyl-2-oxocyclohex-3-enecarboxylate (E249); ethyl 4-(2,4-diiodo-phenylamino)-6-phenyl-2-oxocyclohex-3-enecarboxylate (AK12); methyl 4-(2,4-dibromophenylamino)-2-oxo-6-phenylcyclohex-3-enecarboxylate (AK6); methyl 4-(2,4-diiodophenylamino)-2-oxo-6-phenylcyclohex-3-enecarboxylate (AK11); 3-(2,4-dibromophenylamino)cyclohex-2-enone (AK7); methyl 4-(2,4-dibromophenylamino)-2-oxo-6-methylcyclohex-3-enecarboxylate (FA1B); and 3-(2,4-dibromophenylamino)cyclopent-2-enone (FA5).

Results:
The effects of these compounds ranged from suppression of PS through no effect at all to enhancement in PS. The dichloro (AK1), and dibromo (AK6 and E249), derivatives having substitutes on the cyclohexenone ring, suppressed PS amplitude in a concentration-dependent manner. AK6 (6-phenyl, 1-CO_2Me) and E249 (6-methyl, 1-CO2Et) analogs had similar potencies, with EC50 values of 2.1 and 1.9 uM, respectively while AK1 (6-methyl, 1-CO2Et) was less potent with EC50 value of 10 uM. AK6 with a phenyl substituent on the cyclohexenone ring was more efficacious with a depression of 72% at 10 uM compared to 35% for E249 with methyl substituent. The rank order of efficacy (at 10 uM) for halogen substituents on the phenylamino group was dibromo-(AK6:- -72%) > dichloro-(AK1:- -25%) > diiodo-(AK11:- ≤5% -inactive). Removal of the phenyl or methyl substituent at position 6 of the cyclohexenone ring (FA2:- +35%) or replacement of the cyclohexenone ring with cyclopentenone (FA5:- +56%) resulted in proconvulsant compounds.

Conclusions:
Our data indicate that not all enaminones are anticonvulsant at comparable concentrations and that the cyclohexenone ring is necessary for anticonvulsant activity, with the dibromo substituents being the most potent and efficacious derivatives for anticonvulsant activity. Further screening and in vitro and in vivo testing should be performed on compounds with substituents at positions 5 and 6 on the cyclohexenone ring and dibromo on the phenylamino group.
Supported by Kuwait University Research Grant # PR01/08.

Key Words: Population spikes; Epilepsy; Drug discovery

5: Oral

Pharmacist counseling versus leaflet education in improving awareness in vitamin D deficient Lebanese patients

Malaeb D, BouRaad E, Jadid L, El-Masri R.
Lebanese International University

Introduction:
Patient education is the cornerstone of improving the quality of life and health in asymptomatic inadequate vitamin D patients. Pharmacists play an important role in providing essential information about improving the factors that affect vitamin D levels. The purpose of this study was to determine the role of the pharmacist counseling versus leaflet education in lifestyle adjustment of Vitamin D deficient patients.

Methods:
This is a prospective, interventional, multicenter study where patient's recruitment was done in two university settings. Patients above eighteen years of age with vitamin D level less than 30 ng/ml were enrolled. Patient screening took place from December 2011 till May 2012. Exclusion criteria: age above sixty five years, smokers, intake of either anticonvulsants or glucocorticoids, and with renal diseases. One peripheral blood sample was taken from each participant, serum 25 hydroxy vitaminD was measured using Elisa technique. The eligible patients then filled questionnaires that evaluated patient's knowledge about: food and recommended daily intake, sun exposure, drugs and/or diseases affecting vitamin D levels where a score was given for each factor. Patients were randomly counseled either by the pharmacist or the leaflet. After the two counseling interventions, the same questions were asked and scores were given. Each participant gave a written informed consent and the Institutional Review Board (IRB) approved the study design. The statistical test used was the paired sample students T-test and data was analyzed by the SPSS.

Results:
A total of 160 patients were screened and 107 were included. All baseline characteristics were similar between the two groups. The mean 25 hydroxyvitamin D was 20.89±5.02 ng/ml. Pharmacist counseling was more effective than leaflet intervention where the results were highly significant. The total mean of food and recommended daily intake of vitamin D of pharmacist counseling versus leaflet was 6.88 and 4.46, respectively [95 %, CI (1.801-3.052) P< 0.001], total mean of disease that affect vitamin D levels of pharmacist counseling versus leaflet were 2.79 and 1.66 [95 %, CI(0.457-1.810), P < 0.0001, total mean of sun exposure of pharmacist counseling versus leaflet were 2.47 and 1.09 [CI (0.972-1.787),P < 0.001], and total mean of drugs affecting vitamin D levels of pharmacist counseling versus leaflet were 3.19 and 1.97 [CI (0.430-1.999) ,P = to 0.003].

Conclusions:
The role of pharmacists is a continuous process that includes disease prevention and treatment. The pharmacist has a very important role in providing the education about factors that might affect the level of vitamin D and providing a good awareness about the importance of life style modifications more than leaflet education.

Key Words: Pharmacist counseling; Vitamin D patients

6: Oral

Molecular techniques and bioinformatics identify next generation vaccine candidates against tuberculosis

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Introduction:
Tuberculosis (TB), a major infectious disease, has been declared 'a global emergency' by the World Health Organization. The currently used vaccine against TB, i.e. BCG, has failed to have an impact on the morbidity and mortality due to TB. Therefore, next generation vaccines are urgently required to control the world-wide TB epidemic. The genomic studies have identified regions of differences (RDs) between M. tuberculosis and BCG. These RDs encode 89 M. tuberculosis-specific proteins. The aim of this study was to identify the RD proteins and peptides with potentials as next generation vaccines against TB.

Methods:
RD genes were cloned in plasmid vectors and expressed in E. coli. The peptides covering the RD protein sequences were synthesized and tested in cellular immune responses, i.e. protective T helper (Th)1, using cells from pulmonary TB patients and PPD+ healthy humans and M. bovis-infected cattle. The genes of immunodominant proteins were cloned and expressed in DNA vaccine vectors and mycobacterial hosts, and tested in animals for cellular immune responses. The bioinformatics analysis to identify immunodominant proteins and peptides of RDs was performed using web-based servers.

Results:
Recombinant protein expression technology could not yield all targeted proteins but synthetic peptides were obtained covering sequences of all proteins. When tested in humans and cattle, four RD proteins, i.e. PE35, PPE68, ESXA and ESXB were the best stimulators of Th1 cells. The bioinformatics analysis revealed that all of these proteins were promiscuous HLA-DR binders with several T-cell epitopes. Immunizations of mice and guinea-pigs with the recombinant constructs induced antigen-specific immune responses. Thus, both bioinformatics and experimental analyses confirmed the strong immunogenicity of the identified proteins.

Conclusions:
The study has identified several immunodominant proteins and peptides of M. tuberculosis RDs with potentials as new generation vaccine candidates against TB.
Supported by Kuwait University Research Administration grant MI02/12.

Key Words: Tuberculosis; RD genes; New Vaccine

7: Oral

Microbial metabolism of vulgarin

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Introduction:
The eudesmanolide vulgarin, a constituent of several *Artemisia* species, was found to be cytotoxic, hypoglycemic, cardiotonic and CNS stimulant. Metabolic profiles using microbial systems parallel those obtained from mammalian ones and, thus, are predictive. Previous attempts at microbial transformation of vulgarin were unsuccessful. This study would produce significant quantities of metabolites that would be difficult to obtain from animal systems.

Methods:
Preliminary screening was carried out using the standard two-stage protocol. Different cultures were screened for their abilities to metabolize vulgarin. Culture and substrate controls were prepared and used for comparison. After one and two weeks of incubation, test and controls were extracted and analyzed. Cultures with positive hits were selected for preparative scale fermentation. The produced metabolites were isolated using column chromatography, and identified using different spectral techniques. The identity of one metabolite was confirmed through chemical synthesis.

Results:
Seventy microorganisms were screened for their ability to metabolize vulgarin. Six of them showed definite metabolism. These cultures produced two more polar and one less polar metabolites, some of them were common among different cultures. *Beauvaria bassiana* almost completely metabolized vulgarin into the more polar metabolite 1-epi-tetrahydrovulgarin. *Hansenula anomala* partially converted vulgarin into a less polar metabolite, dihydrovulgarin, which was further metabolized into a more polar one, 3α-hydroxydihydrovulgarin. The identity of the last metabolite was further confirmed through chemical synthesis.

Conclusions:
This study showed microbes ability to serve as biocatalysts. The production of the 1S-isomer of 1-epi-tetrahydrovulgarin showed that reductase enzymes in *Beauvaria bassiana* are product-enantioselective. The production of 3α-hydroxydihydrovulgarin is believed to be done stepwise. The presence of the metabolite 1-epi-tetrahydrovulgarin in plants and microbial cultures suggested a similarity in enzymatic machinery between both.

Key Words: Vulgarin; Bioconversion; 1-epi-tetrahydrovulgarin

8: Oral

Evaluation of novel oxazolidinones for monoamine oxidase inhibitory activity

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Introduction:
Oxazolidinones are potent antibacterial agents plagued with unwanted side effects, which include inhibition of monoamine oxidases (MAO) due to structural similarity to the MAO inhibitor, toloxatone. The aim of this study was to investigate the MAO inhibitory activities of selected antibacterial oxazolidinones.

Methods:
Oxazolidinones were synthesized by previously described methods. In vitro MAO-A or -B inhibition was determined by a continuous peroxidase-linked spectrophotometric assay in 96 well microtiter plates. Chromogenic solutions containing vanillic acid (1mM), 4-aminoantipyrine (500µM), and peroxidase (4.7 units/10µl) in phosphate buffer (0.2M, pH7.6), test compounds (50 and 200µM) and pure commercial MAO-A or -B were incubated. Tyramine was used as a mixed substrate for MAO-A and -B. Blanks containing buffer instead of tyramine, and controls containing distilled water instead of test compounds, were run simultaneously with the samples. Total volume in each well was adjusted to 300µl with phosphate buffer (pH7.6). Reactions were followed in SunriseTM microplate absorbance reader. Absorbance measurements were taken at 498nm every minute for 10 minutes, then every 10 minutes for 20 minutes and every 20 minutes until 90 minutes.

Results:
A total of 22 oxazolidinone derivatives with antibacterial activity were tested. Results showed that some of the compounds evaluated demonstrated noticeable degree of inhibitory activity against MAO-A and -B. The morpholino desmethyltriazolyl oxazolidinone, PH27 with potent antibacterial activity showed significant MAO-A and -B inhibition; while the inhibitory activities of the piperazinyl triazolyloxazolidinones were dependent on the N4- piperazine substitutions.

Conclusions:
Inhibitory activities on pure MAO-A and -B are dependent on the substitution around the oxazolidinone pharmacophore. Further investigations are ongoing to determine the selectivity, potency and reversibility of MAO inhibition.

Supported by KURA Grant # PC01/09 (OAP), GS01/01 and GS03/01 (SAF)

Key Words: Monoamine oxidase; Oxazolidinones; Inhibitory activity

9: Oral

Stability and bioavailability assessment of optimized self-emulsified drug delivery system of ibuprofen in human volunteers

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Introduction:
To assess the stability and bioavailability of ibuprofen self-emulsified drug delivery system (IBSEDDS) developed in our lab and optimized for maximum in vitro drug release.

Methods:
The optimized formulation consisted of 50mg ibuprofen, 50% soybean oil (solvent), 40% Cremophore EL (surfactant) and 10% Capmul MCM-C8 (cosurfactant) and showed 100% in-vitro drug release in 60 min. The stability study was conducted at different storage temperatures viz 4^{o}C, room temperature and 37C for eight months. The stored formulations were examined visually for physical changes and assessed for dispersability in water, particle size, turbidity and in-vitro drug release at zero time and after 1, 2, 4, 6 and 8 months. Bioavailability was assessed after a single oral dose of two formulations, test (IBSEDDS) and reference (50 mg ibuprofen dissolved in soybean oil), with 7-days washout period using six healthy human volunteers. Venous blood samples of 5ml were collected immediately before dosing and after 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 8, and 10hr of dose administration. Plasma containing extracted drug was analyzed by HPLC.

Results:
The optimized formulation was physically stable without sedimentation, separation or color change. The changes in particle size, turbidity and dissolution rate after 8 months storage in refrigerator (4^{o}C) were smaller compared to those stored at room temperature or 37C. The pharmacokinetic parameters obtained for test/reference were: The Cmax was 0.892/0.468 ug/ml, the Tmax was 1/1.5hr, the AUC0-α was 3.956/1.986 mg.hr/ml and the relative bioavailability of the test against the reference was 199.114%.

Conclusions:
The optimized formulation stored at 4^{o}C were more stable compared to those at room temperature or 37^{o}C regarding the turbidity, particle size and in-vitro drug release. The test formulation showed higher rate and extent of drug absorption and bioavailability when compared to the oily drug solution.

Key Words: Ibuprofen Self-Emulsified Drug Delivery System; Stability; Bioavailability

4th Kuwait International Pharmacy Conference (KIPC)

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Abstracts - Poster Presentations

10: Poster

Evaluation of anti-oxidant potential of methanolic extract of Lipidium sativum L. seeds.

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Introduction:
Reacting active species induced oxidative damage of cellular tissue cause to many human diseases like cancer, cardiovascular disease, nephropathy and aging. Naturally occurring antioxidant supplements from plants are vital to counter the oxidative damage in cells. Recently, attention has focused on phytochemicals as new sources of natural antioxidants. Therefore, the main objective of the present study was to investigate the in-vitro antioxidant potential of methanolic extract of Lepidium sativum L seeds (Fam.: Brassicaceae).

Methods:
The methanolic extract was used study their phytochemical composition, in vitro antioxidant activity including 1,1-Diphenyl-2-picrylhydrazyl (DPPH) radical scavenging, Hydrogen peroxide scavenging and Reducing power scavenging.

Results:
The methanolic extracts produced more or less similar DPPH anion scavenging power (62µg/ml) at 100µg/ml concentration and 38µg/ml for Ascorbic acid. In this study depicted DPPH anion scavenging power of extracts. Discoloration of violet DPPH to Yellow clearly demonstrated the effect of extracts as an antioxidant. The methanolic extract of Lepidium sativum exhibited concentration dependent scavenging activity against hydroxyl radical generated in a Fenton reaction system. Comparison of the antioxidant activity of the extract and ascorbic acid were observed. The IC50 value of methanolic extract Lepidium sativum was found to be 5.24µg/ml,. The IC50 value of the extract was found to be comparable to reference standard ascorbic acid (IC50 2.50µg/ml).

Conclusions:
Finally it was concluded that the methanolic extract of Lepidium sativum (62µg/ml) is found to more effective as comparison accordingly to DPPH method in comparison to std. ascorbic acid (38µg/ml) while Lepidium sativum also contains good antioxidant activity in comparison Ascorbic acid by Hydrogen peroxide method and Power Reducing method found is more active.

Key Words: Antioxidant activity; Lepidium sativum; DPPH

11: Poster

Hepatoprotective activity of lantana camara extract against thioacertamide-induced liver cirrhosis in rats

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Introduction:
Liver cirrhosis is considered as an irreversible process. The main mechanisms of fibrotic or cirrhotic initiation and progression have been elucidated in the past two decades. The present study was undertaken to investigate the hepatoprotective activity of the ethanolic extract of leaves of L. camara against thioacetamide-induced hepatotoxicity in rats.

Methods:
Male Wistar rats received intraperitoneal (i.p.) injections of thioacetamide (TAA) 200 mg/kg thrice weekly for 8 weeks. Daily treatments with 100 mg/kg, 200 mg/kg ethanol leaf extract and Silymarin (50mg/kg) were administered orally for 8 weeks. At the end of the study, hepatic damage was evaluated by analysis of liver function tests in serum (biochemical parameters) and histopathological studies.

Results:
Ethanol leaf extract was found to be effectively hepatoprotective, as evidenced by biochemical parameters and histopathological investigations. The hepatoprotective effect of ethanolic extract was comparable to that of silymarin as a standard hepatoprotective agent. Pre-treatment with L. camara ethanol extract, or silymarin significantly reduced the impact of thioacetamide toxicity on plasma protein and urea levels as well as on plasma aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase and gamma-glutamyl transpeptidase activities compared with thioacetamide-treated animals (cirrhosis control). Hepatic histopathology results revealed that ethanol leaf extract of L. camara, and silymarin treatments decreased the mean score of fibrosis in TAA-treated rats.

Conclusions:
It can be concluded that ethanol leaf extract of L. camara slowed down liver fibrosis progression. According to these data, L. camara might be a promising antihepatotoxic activity, suggesting the need to isolate the chemical principles responsible for this activity and to study this activity in a model of thioacetamide-induced cirrhosis.

Key Words: Lantana Camara extract; Hepatoprotective activity; Liver cirrhosis

12: Poster

Awareness and adherence to insulin therapy among patients with diabetes: an exploratory study

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Introduction:
Diabetes is considered as one of the most challenging health problems in the 21st century. Its prevalence in Kuwait has doubled in the last 15 years, reaching 21.2% in 2011. Poor adherence to the diabetes pharmacotherapy is widely acknowledged as a potential cause of poor glycaemic control. Improved blood glucose control in patients with diabetes reduces the risk of long-term complications. This study was designed to determine patients' adherence to insulin therapy and their awareness about insulin storage conditions and 'use by' date.

Methods:
A descriptive cross-sectional study, which included sixty randomly selected diabetic patients from the out-patient pharmacy department in AlAdan hospital was performed using structured face to face interview for data collection. Data were analysed using SPSS version 17.

Results:
The mean (±SD) age of the patients is 23.3 (19.4) years, and 40 (66.7%) are between 4-17 years. Thirty two (53.3%) respondents have been administering their own insulin doses, and 18 (56.3%) of these are aged between 4-17 years. Twenty eight (46.7%) of the patients are administered insulin doses by caregivers, and 22 (78.6%) of these are ≤ 17 years old. Forty nine (81.7%; 95% CI: 69.6-90.5%) patients/caregivers adhered to the prescribed insulin doses. Non-adherence is non-significantly common among the self-administered group (25%) compared to those by caregivers (10.7%), and the younger age group ≤ 17 years (22.5%) compared to the older age group (10.0%) [$p > 0.05$]. Suitable storage conditions of insulin were reported by 96.7% (95% CI:88.5-99.6%) of patients/caregivers. Forty three (71.7%; 95% CI: 58.6-82.6%) respondents indicated their awareness about the 'use by' date for the insulin vials/cartridges after being opened, which is different from the expiry date.

Conclusions:
The present findings highlight the need for more patient education to improve awareness and adherence to insulin therapy in order to achieve good glycaemic control. Further research with a representative sample size and validated assessment tool is required to provide more valid results

References:

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Key Words: Insulin therapy; Diabetes pharmacotherapy

13: Poster

Evaluation of outpatient-pharmacies' counseling behavior and content at a teaching hospital in Jordan

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Introduction:
Lack of patients' knowledge about their medication can lead to serious problems that can be avoided by appropriate patient education. Therefore, pharmacists do have a unique opportunity to maintain good health, to avoid ill health and to make the best use of medicines.[1] This study aimed to characterize and evaluate the counseling behavior and content by pharmacists and pharmacy assistants in a sample of outpatient pharmacies at a teaching hospital in Jordan.

Methods:
The study included 6 outpatient pharmacies at the recruited hospital; Endocrinology, Cardiology, Respiratory, Pediatrics, Family Medicine and Emergency staff. The study consisted of observing 60 patient-pharmacist/assistant interactions behaviors and counseling content (if exists) in 6 different outpatient pharmacies. Observations were conducted by a trained researcher using a pre-validated and piloted data collection form. Categorical data were coded and entered into the SPSS version 17. The qualitative part of the data was analyzed using the Content-Analysis method. Content Analysis involved a structured examination of the text by identifying any grouping themes and coding, classifying and developing categories.[2]

Results:
Out of the 60 observed interactions, only 18 interactions involved patient counseling, the type of which was both verbal and written. The initiator of counseling in 44.4% of the cases was the patient. More than two-third (70.0 %) of provided information to patients in all interactions was conducted using written labels only. There was a significant relationship ($p < 0.05$) between the different pharmacies and the method of interaction with patients.

Conclusions:
The overall observed rate of counseling at the participating outpatient pharmacies is low. Pharmacists and assistants mainly tended to give out basic written information including mainly the dose and frequency. Pharmacist's communication and counseling style needs to be further developed into a more patient centered approach.

References:

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Key Words: Counseling; Jordan; Outpatient pharmacy

14: Poster

Effects of garlic and ginger compared to aspirin on indicators of oxidative stress and nephropathy in STZ-induced diabetic rats

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Introduction:
Diabetes mellitus (DM) affects over 165 million people and is responsible for about 7% of all deaths annually. Chronic hyperglycemia in DM leads to microvascular disease that can result in diabetic nephropathy leading to end-stage renal disease and death. Thus, the use of drugs and natural products to alleviated hyperglycemia and nephropathy is under active investigation worldwide.

Methods:
The current study was conducted to determine the biochemical and histological efficacies of garlic and ginger in comparison to aspirin in streptozotocin-induced diabetic rats. Diabetes was induced by IP injection of streptozotocin (STZ) and a fasting blood sugar >300 mg/dl indicated diabetes. Diabetic rats were divided into 4 groups: control, garlic-treated, ginger-treated and aspirin-treated. Garlic and ginger extracts were administered daily for 8 weeks. Kidney catalase (CAT), malondialdehyde (MDA), lactate dehydrogenase (LDH), protein and total antioxidants were measured.

Results:
The results showed that kidney MDA levels of untreated diabetic rats (2.54 ± 0.45 mmole/g tissue) were significantly increased compared to both the normal controls (1.25 ± 0.31 mmole/g tissue) and the garlic-, ginger- and aspirin-treated animals (1.40 ± 0.27, 1.45 ± 0.11 and 0.79 ± 0.19 mmole/g tissue, respectively). Similarly, kidney LDH activity of untreated diabetic rats (0.49 ± 0.01 U/mg protein) were significantly increased as compared to both the normal controls (0.20 ± 0.01 U/mg) and the garlic- and ginger-treated animals (0.34 ± 0.02 and 0.37 ± 0.01 U/mg, respectively). The kidney LDH activity of aspirin-treated diabetic rats was not significantly different from diabetic controls. Total kidney antioxidant levels of untreated diabetic rats (0.049 ± 0.008 mmole/g tissue) were significantly lower than those of both the normal controls (0.135 ± 0.008 mmole/g tissue) and the three treated groups (0.096 ± 0.008 - 0.120 ± 0.011 mmole/g tissue). Kidney CAT and protein levels of untreated diabetic rats (0.238 ± 0.011 U/mg protein and 17.64 ± 2.22 mg/g tissue) were significantly decreased as compared to the normal controls (0.395 ± 0.072 U/mg protein and 37.53 ± 1.34 mg/g tissue) and the garlic- (0.310 ± 0.070 U/mg protein and 25.73 ± 1.02 mg/g tissue) and ginger-treated (0.334 ± 0.074 U/mg protein and 27.79 ± 1.02 mg/g tissue) groups. Aspirin-treated rats were not statistically different from the diabetic non-treated rats in regard to CAT and protein and from the garlic- and ginger-treated rats with respect to MDA and total antioxidants. Diabetic renal corpuscles showed general distortion,in particular deterioration in capsular membrane and reduction in capsular space. All treatments attenuated the renal corpuscle modulation with garlic and ginger being more potent. by.

Conclusions:
Our results suggest that the hypoglycemic effects of garlic and ginger can help in ameliorating diabetic nephrology, and it is concluded that these two herbs can be administered as a supplementary precaution against diabetes.

This work was supported by the College of Graduate Studies, Kuwait University and KFAS grant #2007-1302-04 and KU grant #SL 06/08.

Key Words: Asprin; Garlic; Ginger

15: Poster

Medication safety practice models in psychiatric hospital, Saudi Arabia managing high-alert medication (Clozapine)

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Introduction:
Routine monitoring is a pre-requisite of clozapine use because of the risk of neutropenia and agranulocytosis and other risky side effects. Prescribers are therefore required to ensure that effective ongoing monitoring is maintained throughout clozapine therapy. The aim of this study was to provide a safe system for monitoring clozapine therapy for patients by establishing a"Clozapine Clinic" run by pharmacists.

Methods:
All psychiatric patients on clozapine attending outpatient clinic in Alamal hospital will be referred by psychiatrist to the clozapine clinic for monitoring patients safety, pharmacist will check all the lab result of patient (CBC, FBG, lipid profile, LFT, and side effects by using clozapine a side effect checklist). Pharmacist will order new urgent CBC (WBC-ANC) investigation for the patient and according to the blood results patients will be classified to :

1. Green (WBC>3500-ANC>2000) schedule monitoring every 4 weeks.
2. Amber (3500>WBC>3000-2000>ANC>1500) change in the monitoring frequency every 2 weeks
3. Red (WBC<3000-ANC<1500) leukopenia and/or neutropenia; pharmacist must stop clozapine immediately.

In this study we included all patients who attended the clinic from 1st March 2012 to the end of August 2012, and evaluated the impact of clozapine clinic on patient safety. Data analyses was performed using SPSS version 12.0

Results:
One hundred and eighty patients visited the clozapine clinic (27% male, 73 % female), 80% in green area, 10% amber area and 8% red. All pharmacist interventions related to patients in red area were accepted by the physician. During clinic visit, pharmacist handled side effects such as hyper-salivation (16%), tachycardia (12%), constipation (6%), and involuntary jerky movement (4%).

Conclusions:
Implementation of new Clozapine Clinic run by pharmacists, ensured close monitoring of WBC count and ANC according to monitoring schedule and other side effects prior to delivery of the next supply of medication. This led to better safety outcomes.

Key Words: Routine monitoring; Neutropenia; Agranulocytosis

16: Poster

Pharmacovigilance: trends and barriers for psychotropic medication in Saudi Arabia

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Introduction:
Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and preventing of adverse effects and all other problems related to medicine. Although the reporting of adverse event (AE) is the keystone of PV, we in Saudi Arabia are still under-reporting capacity and quality in both general practice and in psychiatric practice In psychiatric hospitals the rate of ADEs was 10 per 1000 patient-days and 10.2 per 100 admissions including (13%) that were preventable and (87%) that were classified as non-preventable. The severity of harm for most ADEs was significant (66%) with fewer being serious (31%) and life-threatening (2%) events.

Methods:
A postal questionnaire survey of 6 psychiatric hospitals randomly selected was conducted. 180 health professionals were randomly selected during November 2011. The questionnaire was modified after piloting on 10 randomly selected Health professionals of whom 10 (100%) responded. The Questionnaire has 23 questions; 10 questions about knowledge and practice, (12) to masseur attitude and barriers. At the end of the questionnaire there is one open question asking about the other factors that may affecting reporting practice.

Results:
180 health professionals participate in this study. The majority were pharmacists (49%), the remaining were physician (35 %) and nurses 16%. 86% of health care provider reported limited knowledge of the important of spontaneous reporting ADRs as a barrier. Good attitude toward reporting ADRs was noted in 88% of the sample as they willing to practice pharmacovigilance if they have enough knowledge of the reporting mechanism. 50 % reported that time was a reason for under-reporting.

Conclusions:
The healthcare professionals at the psychiatric hospitals in Saudi Arabia had a relatively good attitude but limited knowledge towards pharmacovigilance and ADRs. The majority of the healthcare professionals felt that ADR monitoring is important, but only a few had ever reported an ADR to the pharmacovigilance centers. Reasons for under-reporting were either they unaware of the existence of a pharmacovigilance system or the important of spontaneous reporting. The findings of the study suggest that there is a need for a continuous education and awareness for the doctors, nurses and the pharmacists.

Key Words: Psychotropic Medication; Pharmacovigilance

17: Poster

Medication reconciliation experience in psychiatric hospitals, Saudi Arabia

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Introduction:
In 2006, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) started the new year with a mandate for accredited organizations to implement an innovative initiative: Medication Reconciliation. The mandate attempted to address the 1.3 million iatrogenic adverse events that occur annually, many of which are related to medication. Medication reconciliation is an effective process to reduce errors and harm associated with loss of medication information, as patients transfer in service (handoffs). It may prevent up to 70% of all potential errors and 15% of all adverse drug events. In general, few studies have investigated medication reconciliation in psychiatric hospitals worldwide, in fact information on medication reconciliation in psychiatric hospitals in Saudi Arabia is lacking. The aim of this study was to gain insight into the medication reconciliation practice at psychiatry hospital and barriers.

Methods:
We developed and administered a survey to pharmacy directors at all psychiatry hospitals in Saudi Arabia (20 hospitals).The survey included scales measuring (1) pharmacists attitudes towards medication reconciliation, (2) pharmacists knowledge towards medication reconciliation and (3) the current practice in Saudi Psychiatry hospitals.Statistical analyses were performed using SPSS.

Results:
Ninety percent of pharmacy directors in psychiatric hospitals in Saudi Arabia returned the survey, 70% indicated that they were familiar with the concept of medication reconciliation and believed that medication reconciliation represented an important safety intervention. Only 25 % of pharmacy directors have initiated the medication reconciliation practice, although 40 % did not believe that they had the necessary resources to manage discrepancies. Pharmacy directors reported several implementation barriers, 67 % reported that lack of time and pharmacy staff. On other hand 60 % reported that limited knowledge and information about the importance of medication reconciliation.

Conclusions:
We identified a wide range of barriers and attitude of pharmacy directors influence the implementation of medication reconciliation. Medication reconciliation can be implemented if these barriers are adequately addressed. There is a need to develop a strategy for implementation of medication reconciliation in psychiatric hospitals in Saudi Arabia

Key Words: Medication Reconciliation; Saudi Psychiatry Hospitals

18: Poster

In silico search culminating in identification of β-Secretase

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Introduction:
Alzheimer's (AD) is a degenerative disease of the brain and the most common form of dementia. A variety of therapeutic strategies for modulating the progression or prevention of AD are currently being investigated. The etiology of the disease is characterized by aggregates of amyloid plaques, largely composed of amyloid-beta peptide formed from the amyloid precursor protein cleaved by β-secretase. β-secretase is a membrane-bound aspartic protease, which has become known as an important but difficult protein target.

Methods:
Molecular docking study using Ligand Fit Docking and Scoring as well as LibDock Docking functions was performed as a preliminary *in-silico* screening test using binding pocket of BACE (PDB code: 2IQG) resolution:1.7 Amstrom. This was followed by *in vitro* enzyme inhibition assay for National Cancer Institute (NCI) database. NCI compounds in their un-ionized forms were docked into the binding site; high-ranking docked conformers and poses were scored using seven scoring functions. The validation for our docking–scoring procedure was performed through employing the same conditions to dock a well-known BACE inhibitor F2I. High ranking compounds were evaluated in vitro using BACE fluorescence resonance energy transfer (FRET) assay.

Results:
The docking simulation resulted in a close model to the crystallographic structure. Five of the important interactions are shared between the co-crystallized ligand and *in silico* hits. Virtual screening identified low micromolar inhibitory leads from the NCI list of compounds. The most potent hit exhibited BACE IC50 values of 11.1 micM in BACE enzymatic assay.

Conclusions:
We have identified a low micro-molar BACE inhibitor with IC50 of 11.1 micM. Our results suggest that *in silico* high-throughput screening approach can serve as useful means to identify new hits which can be used as lead candidates for synthetic modification in order to develop more potent enzyme inhibitors.

Key Words: Alzheimer's disease; Beta-secretase inhibitors; Docking, in silico search

19: Poster

Investigation of basal activity of the incretin receptors

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Introduction:
The incretin effect is mediated by two gut hormones; glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). GLP-1 and GIP both potentiate insulin secretion in a glucose dependent manner by binding to their respective receptors on pancreatic beta-cells. The GIP and GLP-1 receptors (GIPR and GLP-1R) are Family B (Secretin) G Protein-Coupled Receptors (GPCRs) and couple positively to adenylate cyclase via Gs. In type 2 diabetes mellitus (T2DM) an insensitivity to GIP develops so the focus has been on targeting GLP-1R to treat T2DM. The aim of this study was to investigate basal signaling via these two receptors in order to shed light on why type 2 diabetics remain responsive to GLP-1 but not GIP.

Methods:
GIPR and GLP-1R were transiently expressed in HEK-293 cells and receptor activity was assessed using a cAMP-responsive luciferase reporter gene assay. Dose-response curves were normalised to maximum forskolin response. Arrestin recruitment to either GLP-1R or GIPR was measured using enzyme fragment complementation and visualized on a confocal microscope using YFP-labelled arrestin.

Results:
GLP-1 and GIP stimulated cAMP-responsive luciferase activity with a pEC50 value of 10.3 (±0.05) and 10.7 (+/-0.15) respectively (n=3). Basal GIPR activity was significantly ($P>0.005$) higher than that of GLP-1R (77% compared to 28%). GLP-1 and GIP stimulated arrestin recruitment to their receptors with a pEC50 value of 8.2 (±0.14) and 8.1 (±0.27) respectively (n=3). Basal arrestin binding to GIPR was significantly higher ($P<0.05$) than GLP1R (75% compared to 39%) and YFP-labelled arrestin displayed a robust translocation to agonist stimulated GLP-1R but not to GIPR.

Conclusions:
GIPR displays significantly higher basal activity and significantly higher basal arrestin binding than GLP 1R. This apparent constitutive activity may contribute to the loss of function of GIP in T2DM.

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Key Words: Constitutive-Activity; GLP-1; GIP

20: Poster

Impact of using insulin pumps in the management of type 1diabetes mellitus: subjective experience of children/young people and their parents

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Introduction:
Insulin pumps were introduced in the UK since the 1970s to manage people with type 1 diabetes mellitus (T1DM). Advances in medical technology and research documenting clinical effectiveness have led to their worldwide growth. The use of insulin pumps in the UK children is limited and there is little evidence regarding their impact on patients' lives. Therefore, the purpose of this study was to investigate domains of life impacted on initiating insulin pumps and to assess their impact from the perspectives of children/young people and their parents.

Methods:
Face-to-face semi-structured interviews were conducted with children and young people with T1DM (aged 5-17 years; n = 34,) and their parents (n=38), receiving insulin pump therapy and attending pediatric diabetes outpatients clinics at a major university teaching hospital, London. Measures of glycated haemoglobin A1c (HbA1c) values from 6 months prior to, and after pump therapy were obtained from medical records. Qualitative and quantitative approaches were undertaken for data analysis.

Results:
Both parents and the children/young people reported that they found it easier to maintain glycaemic control within their target range with insulin pumps compared to injections. This was supported by HbA1c measures and the reported frequency and severity of hypoglycaemic episodes. Whilst participants generally found the device itself easy to use and more acceptable than injections, use of insulin pumps was associated with continuous, hard work (e.g., frequent blood glucose monitoring, changing infusion set and complexity of dose adjustments). Parents and children reported an overall increase in flexibility in lifestyle and their ability to participate in daily activities.

Conclusions:
Use of insulin pump impacted patients and their families on different aspects of their lives. Parents and children found it easier to lead normal lives which is a central goal of health policy for children and young people in the UK.

Key Words: Insulin pumps; Type 1 diabetes mellitus; Children and young people

21: Poster

Importance of activation energy in drug stability: determination of activation energy of p-nitrophenyle acetate

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Introduction:
Drug decomposition or degradation occurs during storage because of chemical changes of the active ingredients or additives. Therefore, drug stability studies may be conducted advantageously for patient assurance for economical reasons and as legal requirements for drug control administration. A comprehensive USP protocol prescribes the criteria for acceptable levels of stability. Several factors affect the reaction rates including the effect of temperature.which are quantitatively described by the activation energy using Arrhenius equation. Several studies describe the hydrolysis of p-nirophenyl acetate at different pH range. In this study the hydrolysis of p-nitrophenyl acetate in Tris buffer was investigated to determine the activation energy as this is one of the main limitations for accelerated stability studies which should be ranged between 15-30 Kcal/molk.

Methods:
A spectrophotometric assay method used was fully validated. The percentage of the drug decomposed was measured at different time intervals at different temperatures using a thermostatic water baths. The slope of the data which is equal to the rate of decomposition was determined for each temperature. The energy of activation was determined graphically by plotting natural logarithm of k against reciprocal of temperature in Kelvin to determine the energy of activation using the equation. Ink=InA-(Ea/R).(1/T) Where: (Ea/R) = slope; Ea energy of activation KJ/mo; R gas Constant = 8.31 J/molK, 1.879 Cal /mol K

Results:
A first-order reaction rate constant of p-nitrophenyl acetate at temperatures 25^{o}C, and 30^{o}C was observed. Although the data appeared to be widely scattered at higher temperature 40^{o}C an overall pseudo first first-order rate constant was observed.

Conclusions:
The study gives an activation energy of 22.10 Kilo J/molK and O.55 KiloCalries/molK, which are quite common for many reactions and the hydrolysis of p-nitrophenyl acetate in tris buffer conforms to Michaelis-Menten kinetics.

Key Words: Chemical kinetic; Activation energy; Drug stability

22: Poster

Economic burden of diabetic tuberculosis patients

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Introduction:
Tuberculosis (TB) is a bacterial infectious disease caused by Mycobacterium tuberculosis. Coexistence of diabetes mellitus (DM) and TB is well documented, but data surrounding its economic burden is lacking. In this study, we sought to assess the impact of DM on the cost of the TB treatment.

Methods:
Study patients were placed in the TB only, DM only, or DM-TB groups, with each group including 200 patients. Information related to demographics, chronic disease comorbidity, duration of hypertension (HTN) and DM, and economic variables were obtained from the patients' medical files both at the beginning and end of the study period. The economic burden of DM-TB patients was assessed from hospitalization periods, frequency of clinic visits, and diagnostic requests. Data were processed using SPSS, version 11.5, and statistical significance was achieved when $p \leq 0.05$.

Results:
Durations of DM and HTN were 9.2 and 5.6 years, respectively, for the DM only group compared to 5.3 and 1.1 years, respectively, for DM-TB subjects ($P<0.001$). For both diabetic groups, diabetes preceded HTN, with onset of HTN occurring approximately 4 years after patients were diagnosed diabetic. Approximately 86% of DM only subjects suffered additional comorbidity, and 44.5% had three or more coexisting chronic diseases compared to 56% and 11.4%, respectively, in the DM-TB group ($P<0.001$). The hospitalization period was 10.2 days for the DM-TB group compared to 7 and 4 days for the TB only ($P> 0.05$) and DM only groups ($P < 0.001$), respectively; however, 43% of TB only subjects needed surgical intervention compared to 17% in the DM-TB group. The total cost was RM4530 for the DM-TB group compared to RM6945.26 and RM 3082.8 for the DM only and TB only groups, respectively.

Conclusions:
DM antedated HTN in our patients. Durations of both DM and HTN were longer for the DM only group. The number of diagnosed chronic diseases and overall treatment cost was higher in the DM-TB group compared to TB only group, but lower compared to the DM only group. The TB only group required the most surgical intervention.

Key Words: Tuberculosis; Disease Precedence; Mortality

23: Poster

Assessment of the co-relationship of diabetes mellitus and co-morbid tuberculosis on leukocyte and platelet counts

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Introduction:
Although coexistence of diabetes and TB is well known, there is scarcity in the studies assessing hematology and glucose levels of TB and DM patients. The aim of this study was to assess and compare leukocyte and platelet counts among the patients with TB alone and co-morbid with DM.

Methods:
This was a preliminary study conducted at the respiratory clinic at public hospital, Pulau Pinang, Malaysia. Four groups were defined retrospectively i.e patients with DM (118 patients), patients with TB (115 patients), DM-TB (76 patients) and control subjects (118 patients). Laboratory values like; leukocyte count, platelets, and blood glucose levels of these groups were retrieved from the medical records and then were compares to see the possible association. Data was processed using SPSS, version 11.5. One Way ANOVA and multiple Post Hoc comparison were used for data analysis. Statistical significance was achieved when $p \leq 0.05$.

Results:
DM patients showed quantitatively higher lymphocyte and neutrophil count ($P < 0.001$) than patients with TB only. Higher thrombocytosis was observed among TB only patients compared with DM ($P < 0.05$) only and control ($P < 0.01$) groups.

Conclusions:
Findings demonstrated that lymphocyte and neutrophils levels were higher among diabetic patients than those with TB alone. However, thrombocytes levels were higher among the patient with TB alone and with diabetes mellitus.

Key Words: Diabetes mellitus; Neutrophilia

24: Poster

Evaluation of spray dried gliclazide PVP K 30 solid dispersions

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Introduction:
Transformation of hydrophobic drugs into more soluble high energy amorphous form is one of the methods used for improving the dissolution rate of such compounds. The objective of the present study was to enhance the aqueous solubility and dissolution rate of a hydrophobic anti-diabetic drug i.e. gliclazide (GLC) by the spray drying technique, using polyvinylpyrrolidone (PVP) K 30 as the dispersion matrix.

Methods:
Phase solubility study with increasing PVP K 30 concentrations was performed to analyze its influence on solubility of GLC. Solid dispersions (SD) of GLC and PVP K 30 in different w/w ratios (1:1, 1:2 and 1:3) were prepared by spray drying technique. The spray dried products were compared with plain GLC as well as physical mixtures (PM) for in-vitro dissolution and saturation solubility. DSC and FTIR studies were performed to identify the physicochemical interaction between the drug and the carrier.

Results:
GLC solubility increased linearly with increasing PVP K 30 concentration depicting an AL type of phase solubility curve. Intrinsic solubility of GLC in water was found to be only 6.144 µg/ml. The dissolution properties of the drug increased with increase in polymer concentration. SD (1:3w/w ratio) showed 100% drug release whereas plain GLC showed only 14.8% release at the end of 60 minutes. Results of DSC and FTIR studies confirmed that enhanced dissolution of GLC from the spray dried dispersions could be due to the amorphous nature of dispersed GLC and physical interaction between the drug and polymer.

Conclusions:
This study shows the potential of formulating GLC:PVP K 30 spray dried solid dispersions with improved aqueous solubility and dissolution rate as compared to the free drug.

Key Words: Gliclazide; PVP K 30; Spray drying

25: Poster

Patient perspectives and willingness to pay for medication review services in the Middle East: Jordan, Emirates and Iraq

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Introduction:
Worldwide, the expansion of clinical services includes different models of Medication Review (MR) services. The aim of this study was to explore patient perspectives of the role of the pharmacist and willingness to pay for MR services in the Middle Eastern countries.

Methods:
This was a single phased observational study conducted in three Middle Eastern countries: Jordan, Emirates and Iraq, in 2010. A questionnaire was designed and validated, then completed by patients walking into community pharmacies. The source of advice regarding patient's medication use, medical management (Specialist, General Practitioner, Pharmacist, Pharmacist assistant, Nurse, Herbalist) and patients' perceived counseling needs from the pharmacist were investigated. Participants' responses were analyzed using Statistical Package for the Social Sciences (SPSS, version 17, Chicago, IL, US). Descriptive analysis and Chi square test was used to identify significant differences between the three countries.

Results:
Patients visiting community pharmacies from Jordan (n=1000), Emirates (n=1000) and Iraq (n= 968) were recruited into the study (mean age 35.9±13.1, 50.6% males). More patients chose the pharmacist to be their primary source of advice on medication use vs. the specialist from Jordan (50.8% vs. 37.3%) and Iraq (41.9% vs. 36.7%) compared to Emirates (38.0% vs. 40.1%), $P<0.001$, Chi-square test. More patients returned to the specialist for review of their chronic condition in the Emirates (68.1%) and Jordan (65.0%) compared to Iraq (9.4%) ($P<0.001$). Majority of patients from Jordan, Emirates and Iraq admitted their need to receive counseling services from the pharmacist (53.6% vs 57.1% vs 63.6%, respectively); while only some agreed to paying for MR services (19.5% vs 24.7% vs 2.3%, respectively).

Conclusions:
This study is important for all future social pharmacy research in the Middle East. Current situation resulting in the lower socioeconomic status in Iraq seems to lead to patients' higher reliance on the pharmacist, compared to Jordan and Emirates. Although more patients from Jordan and Emirates are happy to pay for the MR service compared to Iraq, in the Middle East in general, majority are not willing to pay. This finding calls onto the health care policy makers in the area to highlight the importance of the MR service in the country and allocate resources for future remuneration.

Key Words: Medication Reviews; Pharmacist role; Patient perspectives

26: Poster

The efficacy of angiotensin-receptor blockade versus converting–enzyme inhibition in delaying progression of macroalbuminuria in type two diabetes mellitus; a retrospective multicenter descriptive trial

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Introduction:
Angiotensin II–receptor Blockers (ARB) and angiotensin-converting–enzyme (ACE) inhibitors have been used for the treatment of patients with micro- or macroalbuminuria in type two diabetes. However, only few studies have compared the effects of ARB and ACE inhibitors in delaying the progression of nephropathy in persons with type two diabetes. The purpose of this study was to compare the effects of ARB and ACE inhibitors in slowing the decline in creatinine clearance in patients with macroalbuminuria.

Methods:
The institutional review board approved this retrospective, multicenter, and descriptive study. We followed 100 subjects with type 2 diabetes, hypertension and macroalbuminuria (>300 mg/day) receiving either angiotensin II–receptor blocker (51 subjects) or the ACE inhibitor (49 subjects) over 24 months. The primary endpoint was the change in creatinine clearance between the baseline value and after 24 months treatment with ARB or ACE inhibitor. The secondary endpoint was the change in urinary albumin excretion rate.

Results:
The mean CrCl at baseline was 69.27 ml/min and 72.80 ml/min in the ARB and ACE inhibitor group, respectively. After 24 months the change in CrCl was -35.24 ml/min in the ARB group, compared to -35.13 ml/min in the ACE inhibitor group (P=0.471). This indicates that there was no statistically significant difference between ACEI and ARB in delaying the progression of diabetic nephropathy, measured as the decline in CrCl over a 24 months period. Urinary albumin excretion ratio was 1.60 in the ARB group compared to 2.22 in the ACE inhibitor group, (P=0.162). The urinary albumin excretion rate (UAER) was 6.6% in the ARB group compared to 9.1% in the ACEI group. UAER was slower in the ARB group, although it was not statistically significant.

Conclusions:
There were no differences between ARB and ACE inhibitor in delaying the progression of diabetic nephropathy and in the urinary albumin excretion rate.

Key Words: Angiotensin II–receptor Blockers (ARB); Angiotensin-converting–enzyme

27: Poster

Enhancement of haloperidol permeation through human skin using ultrasound and hydroxypropyl-beta-cyclodextrin

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Introduction:
Transdermal drug delivery offers several advantages over traditional delivery routes. Transdermal delivery route can't be applicable to all drugs due to low skin permeability. Several methods, were employed to enhance the permeation of drugs, which include chemical enhancers, cyclodextrins application of ultrasound. Cyclodextrins are carbohydrates capable of forming readily dissociated inclusion complexes with many drugs. The purpose of this study was to investigate the effect of low frequency ultrasound and hydroxypropyl β-cyclodextrin (HPβ cyclodextrin) on the enhancement of percutaneous absorption of haloperidol through human cadaver skin.

Methods:
An in vitro transdrmal study was conducted to assess the transdermal delivery of haloperidol from gel and and cyclodextrin solution. each formulation was applied to six human cadaver skin mounted onto Franz Diffusion Cells. Following a 5mg dose, receptor solutions were collected over 24 hours for both formulations. The steady state flux was determined using a validated HPLC method. lag time, and the permeability constant were also calculated. low frequency ultrasound of 3 MHz and intensity of 3 Watt/cm^2 was applied for 5 minutes to the haloperidol/ gel formulation. Phase solubility diagram of Haloperidol in HPβ cyclodextrin aqueous solution (.005% - .01%) at 25^oC was constructed. Differences between two related parameters were considered statistically significant for $p < 0.05$ using one-way analysis of variance.

Results:
The phase solubility diagram obtained is of Higuchi's Type and formation of 1:1 complex. Permeation rate of haloperidol through human skin were constructed. The maximum flux from cyclodextrin and ultrasound were found to be 3.9 and 6.4 µgcm-2/hour which were approximately 2 and 4 times higher than that of the control (1.90 μgcm^{-2}/hour) respectively, while the values of lag time were not significantly changed ranged between 4-4.6 hours. Furthermore, higher permeation rates with higher permeation constants of 0.17 for cyclodextrins, 0.34 ultrasound compared to 0.14 for the control were observed.

Conclusions:
The application of ultrasound of a suitable frequency and HPβ cyclodextrin significantly enhances the transdermal transport haloperidol across human skin.

Key Words: Transdermal delivery; Cyclodextrin; Ultrasound

28: Poster

In-cell fluorescence activation and labeling of proteins mediated by FRET- quenched split inteins

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Introduction:
Techniques to visualize, track, and modify proteins in living cells are central for understanding the spatial and temporal underpinnings of life inside cells. Although fluorescent proteins have proven to be extremely useful for in vivo studies of protein function, their utility is inherently limited because their spectral and structural characteristics are interdependent. These limitations have spurred the creation of alternative approaches for the chemical labeling of proteins.

Methods:
Fluorescence resonance emission transfer (FRET)-quenched DnaE split inteins technique for site-specific labeling and concomitant fluorescence activation of proteins in living cells was applied. This approach was successfully employed for the site-specific in-cell labeling of the DNA binding domain (DBD) of the transcription factor YY1 using several human cell lines. We initially used the well characterized Syncechocystis sp. strain PCC6803 (Ssp) DnaE split intein in combination with fluorescein and dabcyl as fluorescence donor and FRETquencher, respectively. The fluorescein group was introduced at the C-terminus of the first four residues (Cys-Phe-Asn-Lys) of the C-extein, which are required for efficient trans-splicing. Then, the dabcyl group was introduced as quencher at the N-terminus of the IC polypeptide.

Results:
The chemical introduction of a fluorescence quencher on specific locations of the Ic polypeptide showed quenching, in a reversible fashion, the fluorescence of a suitable fluorogenic probe located in the C-extein fragment, thus rendering any unreacted Ic virtually nonfluorescent. Hence, only after the trans-splicing reaction has occurred and the C-extein fragment has been transferred to the acceptor protein, the fluorescence of the probe was activated resulting in the concomitant fluorescence activation and labeling of the protein of interest. Furthermore, the simultaneous introduction of a nuclear localization signal (NLS) and a fluorescent label into the C-terminus of DBD YY1 allowed the localization and visual tracking of the resulting protein into the nucleus.

Conclusions:
This study has shown that this approach can be used for modifying proteins to control their cellular localization and potentially alter their biological activity. This new strategy allows the use of protein trans-splicing for the site-specific labeling of proteins with fluorophores.

Key Words: FRET; Intein; YY1

29: Poster

Emulsion and rectal formulations of myrrh total oil for better patient compliance

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Introduction:
Myrrh have been used for its circulatory, disinfectant, analgesic, antirheumatic, antidiabetic, and schistosomicidal properties.

Methods:
Myrrh total oil (MTO) was extracted from the oleo-gum resin of Commiphora molmol and formulated into emulsions and suppositories to mask/avoid the bitter taste. Three oil-in-water emulsions (E1-E3) were formulated and taste was evaluated by 10 volunteers. Particle size distribution was measured and correlated to the excipients and preparation method. Physical and chemical stability testing was carried out for the optimum formulation (E2). Seven suppository formulations were investigated (F1-F7). Suppocire-AML (F1) and Suppocire-CM (F2) were chosen as fatty bases, and polyethylene glycol (PEG) 1500 (F3), PEG 4000 (F4), and PEGs blend (50% PEG 6000+30% PEG 1500+20% PEG 400) (F5) as water soluble bases. A blend of PEG 1500 and Suppocire-CM was also used (F7). Camphor (5%) was added to PEG 1500 (F6). Disintegration time, release rate, DSC, fracture points, and weight uniformity were evaluated.

Results:
The overall average bitterness for formulations E1, E2, and E3 was 6.44, 4.15, and 3.45, respectively. Suppositories containing Suppocire-AML showed the least disintegration time (1.5 min) with dissolution efficiency (DE) of 56.8%. PEG 1500-containing F3 showed a fast disintegration time of 2.5 min. and maximum DE of 93.5%. PEGs blend produced a favorable release: (DE = 90.9%). Mixed fatty and water soluble base (F7) showed a disintegration time of 5 min and low DE (33.4%).

Conclusions:
Stable MTO emulsion with acceptable taste was formulated to improve patient's acceptability and compliance. F3-suppositories gave satisfactory results, while formulations containing fat-soluble bases exhibited poor release.

Key Words: Myrrh total oil; Emulsions; Suppositories

30: Poster

Study on adverse reaction to drugs and its monitoring at a private corporate hospital

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Introduction:
A prospective-observational "Study on Adverse Reaction to drugs and its monitoring at a private corporate hospital" was conducted in the Department of General Medicine of a 640 bedded multi-specialty hospital over a period of 10 months from June 2011 to March 2012 through daily ward visit by the pharmacist. The aim of the study was to detect, document, assess and report the suspected Adverse Drug Reactions.

Methods:
A total of 53 ADRs were identified in 3247 general medicine ward admissions during the study period. Severity of the suspected ADRs assessed using Modified Hartwig and Siegel Scale, revealed that 5 suspected ADRs were severe, 19 ADRs were moderate and 28 ADRs were mild in severity. Causality assessment was done by using Naranjo scale, which showed that 31 ADRs were possibly drug-related, whereas16 were classified as probable and 6 were definite. Nine patients were admitted due to an Adverse Drug Reaction compared to 44 who were affected by ADR after hospital admission.

Results:
The majority (47%) of patients who suffered from ADRs were in the age range between 30-59 years. The organ systems most commonly affected were central nervous system (25 patients, dermatological in 11 patients, and gastro intestinal in 3 patients). The drug class mostly associated with ADR was Antibiotics followed by NSAIDs. About 42 patients recovered, while in 10 cases the ADRs decreased. One fatal case was reported. Preventability of suspected ADRs were assessed by using Modified Schumock and Thornton scale, revealed that 44 ADRs were definitely preventable while 4 ADRs were probably preventable.

Conclusions:
Our study documented that almost 83% of reactions were preventable. Intervention was required in all ADRs as it indirectly contributed to affect the patient's Quality of Life. Our ability to anticipate and prevent such ADRs can be facilitated by the establishment of standardized approaches and active reporting of suspected ADRs.

Key Words: Adverse drug reaction; Suspected untoward events; Antibiotics

31: Poster

Local and systemic distribution of CPZEN-45 after administration by different routes

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Introduction:
CPZEN-45 (CPZEN) is a novel anti-TB drug considered for MDR-TB treatment. This study evaluated the local and systemic drug concentrations achieved after CPZEN administration by
different routes.

Methods:
CPZEN was administered to guinea pigs (GP) as solutions (IV and SC) or as inhalable powder by the pulmonary route (insufflation and passive inhalation). Blood samples were collected at predetermined time points and bronchoalveolar lavage (BAL) was conducted at the end of the study to sample drug concentration in the GP's airways and lung tissue to determine the drug absorbed. CPZEN concentrations were analyzed by HPLC after extraction.

Results:
The plasma concentration versus time profile after pulmonary administration of CPZEN by insufflation was statistically not different from that after IV administration indicating an efficient delivery of the dose and a rapid absorption by the pulmonary route. However, when the same nominal dose was delivered by passive inhalation, CPZEN plasma levels were lower, even though drug was absorbed rapidly as indicated by the peak concentration at the first time point. Locally, CPZEN concentrations in the airways and lung tissue at the end of the study were influenced favorably by the route of administration.

Conclusions:
Drug concentrations in the lungs, the primary site of infection, support the potential of the pulmonary route for administration of CPZEN.

Key Words: Tuberculosis; Bronchoalveolar lavage; CPZEN-45, pulmonary route

32: Poster

In vitro and *In vivo* evaluation of capsules containing coated isoniazid-rifampicin combination

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Introduction:
This study was conducted to evaluate if enteric coating of isoniazid can prevent its interaction with rifampicin in anti-tuberculosis FDC containing both drugs.

Methods:
Investigations with different polymers at different ratios showed that isoniazid coated with Eudragit L100 (1:2) has the lowest dissolution rate in acidic medium and the highest dissolution rate in alkaline medium. Capsules filled with rifampicin alone, rifampicin-isoniazid physical mixture and rifampicin-coated isoniazid were used for stability testing, and for determination of rifampicin dissolution rate and percentage dissolved at pH 1, 3, and 7.4, and rifampicin relative bioavailability after single administration in 12 healthy human volunteers.

Results:
Accelerated stability study at 40±2°C/75% RH±5% RH for 3 months and long-term stability for 12 months showed less than 3% degradation indicating minimal interaction between rifampicin and isoniazid in the dosage form. Rifampicin percent dissolved in 120 minute from capsules containing rifampicin alone, rifampicin-isoniazid physical mixture, and rifampicin-coated isoniazid were 98.01±1.77, 64.20±7.34, and 95.69±9.31 at pH 1, 25.09±4.68, 15.06±5.85, and 39.71±1.78 at pH 3.0, and 26.47±0.65, 27.74±1.41, and 30.53±9.02 at pH 7.4. These suggest that isoniazid coating may prevent isoniazid-rifampicin interaction in the acidic medium of the stomach. Rifampicin bioavailability determined for rifampicin-isoniazid physical mixture and rifampicin-coated isoniazid mixture relative to rifampicin alone were 65.3%±6.56 and 97.3%±4.92, respectively as determined from rifampicin AUC calculated after single oral dose. This indicates that coating of isoniazid prevented its interaction with rifampicin in vivo.

Conclusions:
Isoniazid coating before mixing can be a useful strategy for preparing fixed-dose combinations containing rifampicin and isoniazid.

Key Words: Rifampicin isoniazid interaction; Enteric coating; Anti-TB FDC

33: Poster

The combined anticancer effect of ascorbic acid and docetaxel

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Introduction:
Docetaxel is widely used for cancer chemotherapy; however it has problems such as drug resistance and adverse effects. Ascorbic acid is an important antioxidant, which is required for tissue repair and protection. In many studies, ascorbic acid has shown anticancer activity against various cancer cell types at high concentrations. Our aim was to study the effect of combining these two agents, on the proliferation of MCF7 breast cancer cells. Furthermore, toxicity of ascorbic acid to normal cells was also assessed

Methods:
The anticancer effect for ascorbic acid was studied at 0.2mM, 1mM, 2mM and 4mM on MCF7 cells with and without 2.5ng/ml docetaxel. The cell viability was measured using MTT assay. MCF7 were seeded in flasks with no treatment, 2mM ascorbic acid, 2.5ng/ml docetaxel, or a combination of the two for flow cytometry. Toxicity of ascorbic acid on normal breast cells (HBL-100) was assessed at 0.2mM to 20mM using MTT assay.

Results:
The MTT assay showed that the cell viability decreased to 71.5% with 0.2mM and 27.9% with 4mM ascorbic acid. When docetaxel was combined with ascorbic acid, the cell viability was 45.1% at 0.2mM and 18.4% at 4mM. Flow cytometry data showed that ascorbic acid at 2mM and docetaxel at 2.5ng/ml caused 17.6% and 45.56% respectively of the cells to undergo apoptosis and 67.6% when combined. Furthermore, the cell viability did not change significantly in HBL-100 cells at all ascorbic acid concentrations tested.

Conclusions:
Our results show that both agents when combined give an anticancer action greater than either one alone and this is through increased apoptosis. However, 2mM ascorbic acid induced less apoptosis than the reduction in cell viability observed in the MTT assay, suggesting that ascorbic acid slows cancer cell proliferation. Interestingly, ascorbic acid showed no toxicity on HBL-100 cells indicating a possible cancer selective effect. Results from other studies have also suggested that ascorbic acid can protect normal cells from chemotherapy.

Key Words: Anticancer; Ascorbic acid; Docetaxel

34: Poster

Fatigue of synaptic vesicle exocytosis is prevented by fluoxetine

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Introduction:
The therapeutic mechanism of antidepressants comprises short-term and long-term effects to unfold its benefit in depressed patients. In this study, we addressed short-term effects of the selective serotonin uptake inhibitor (SSRI) fluoxetine on stimulation-dependent exocytosis at hippocampal nerve terminals.

Methods:
Exocytosis was triggered by electric field stimulation and imaged by fluorescence microscopy. Synaptic vesicles were fluorescently labeled and destained with FM 1-43 in two consecutive cycles and several kinetic parameters from both trials were compared.

Results:
In control preparations, the second staining-destaining cycle caused a significant reduction of relative fluorescence loss, number of active synapses and fluorescence half-decay time. These fatigue effects were largely prevented by short-term administration of 1 µM fluoxetine, which was present before and during the second stimulation cycle. Fluoxetine concentrations above 10 µM inhibited exocytosis almost completely but showed no other toxic effects on neurons. Stressed neurons, grown under hyperosmotic conditions, were even more fatigue-protected by fluoxetine.

Conclusions:
These observations support the idea that therapeutic concentrations of fluoxetine enhance the recovery of neurotransmission and this effect might contribute to the abuse of fluoxetine (Prozac) as psychostimulant.

Key Words: Fluoxetine; Hippocampal synapses; FM 1-43

35: Poster

Prevalence and severity of asthma, rhinitis and eczema in UAE children: a baseline pharmaceutical intervention

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Introduction:
The prevalence and severity of symptoms of asthma, allergic rhinitis and eczema in children differs from country to country. In the UAE only few studies were done related to the trends in the prevalence of these symptoms. The aim of this project was to study further the trends in the prevalence and severity of symptoms of asthma, allergic rhinitis and eczema in children in three cities within United Arab Emirates(U.A.E). The cities were Dubai, Sharjah and Ajman. We also investigated some of the factors that might contribute to severity of the disease including breast-feeding, passive smoking and pet ownership.

Methods:
The international study of asthma and allergies in children (ISAAC) standard questionnaire was used in children of age 4-19 years. The result were computed and analyzed using the Statistical Package for Social Sciences version 20.0 (SPSS 20.0). Independent t-test was used to compare the mean age, height and weight of children. The significance of frequencies for the prevalence of symptoms was analyzed using Chi-square and univariate analysis of variance method. Values were significant when determined $p < 0.05$ %, highly significant when $p < 0.01$ and very highly significant when $p < 0.001$.

Results:
The prevalence of symptoms of life long wheezing, current wheezes, wheeze after or during exercise and cough was 15.6, 9.5, 6.6, and 12.7% respectively. There was significant difference in these symptoms in boys, 18.8, 18.5, 8.4 and 15.2% compared to girls, 13.3, 7.4, 5.3 and 11.0% respectively

Conclusions:
A high prevalence of asthma and rhinitis symptoms were found in boys compared to girls but in case of eczema the girls was higher. Breastfeeding for 12 or more months was found to be protective against asthma and rhinitis but not for eczema.

Key Words: Asthma in children; Rhinitis; Eczema

36: Poster

Nigella sativa (Blackseed) possesses potent immunosuppressive and anti-tumor activities

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Introduction:
The search for natural immunosuppressive drugs holds a great hope for discovering effective remedies for preventing and treating a wide range of medical conditions. In this study, the potential immunomodulatory effects of Nigella sativa are investigated in light of splenocyte proliferation, macrophage function, and NK anti-tumor activity using BLAB/c and C57/BL6 primary cells.

Methods:
Splenocyte proliferation was assessed by [3H]-thymidine incorporation. ELISA was performed to assess cytokine secretion by splenocytes and macrophages, and Griess assay was performed to evaluate NO production by macrophages. Using YAC-1 lymphoma cells, the potential of Nigella sativa extract to promote the cytotoxic activity of NK cells was also examined by JAM assay.

Results:
Our findings reveal that the aqueous extract of Nigella sativa significantly enhances splenocyte proliferation in a dose-responsive manner. In addition, the aqueous extract of Nigella sativa favors the secretion of Th2, versus Th1, cytokines by splenocytes. The secretion of IL-6, TNFα, and NO; key pro-inflammatory mediators, by primary macrophages is significantly suppressed by the aqueous extract of Nigella sativa, indicating that Nigella sativa exerts anti-inflammatory effects in vitro. Finally, experimental evidence indicates that the aqueous extract of Nigella sativa significantly enhances NK cytotoxic activity against YAC-1 tumor cells, suggesting that the documented anti-tumor effects of Nigella sativa may be, at least in part, attributed to its ability to serve as a stimulant of NK anti-tumor activity.

Conclusions:
Our data present Nigella sativa as a traditionally used herb with potent immunomodulatory, anti-inflammatory, and anti-tumor properties. We anticipate that Nigella sativa ingredients may be employed as effective therapeutic agents in the regulation of diverse immune reactions implicated in various conditions and diseases such as cancer.

Key Words: Herbal Medicine; Immunosuppression; Anti-Tumor

37: Poster

Molecular and clinical aspects in the diagnosis of patients with chronic hepatitis B in Ramadi, west of Iraq

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Introduction:
Hepatitis B virus causes a highly complex chronic infection that impacts a significant proportion of the world's population. Hepatitis B quantitative DNA analysis by PCR can be used in conjunction with clinical presentation and other laboratory markers of disease status as an aid in managing individuals infected with HBV. This study has been undertaken to assess quantitative viral DNA load by RT-PCR in the diagnosis of chronic hepatitis B infection.

Methods:
The study included one hundred and thirty six patients who attended the Department of Internal Medicine of Ramadi Teaching Hospital, Ramadi and outpatients in Private Clinics during the period from February to October, 2012. They were diagnosed by an expert clinician as chronic hepatitis B infection. Preliminary screening for hepatitis B liver function tests and viral HBV-DNA load by real time PCR were performed. The study cases were divided into four groups of chronic hepatitis B: immune tolerance, immune clearance, inactive HBsAg carrier and HBe-Ag negative chronic hepatitis B.

Results:
RT-PCR detected synthetic HBV DNA in the range of 101 to 108 copies/reaction with each primer and probe set. A linear relationship was obtained between the Ct and the number of copies of standard HBV DNA. Our study revealed that HBe-Ag negative chronic hepatitis B were the most common (47; 34.5%) followed by immune tolerance group (11; 8.1%), immune clearance (10; 7.4%) and inactive HBsAg carrier (68; 50%).

Conclusions:
We conclude that RT-PCR assay for HBV DNA is superior to other methods. This assay may be especially useful in cases of spontaneous reactivation of HBV carriers and acute exacerbation, in predicting chronicity following acute infection and in monitoring the therapeutic effect of antiviral treatments.

Key Words: Chronic hepatitis B; Viral load; Real time-PCR

38: Poster

The potential of TH-9, a theophylline derivative, as a memory enhancer in dementia

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Introduction:
Dementia is a general term referring to cognitive deficit, including memory impairment. Alzheimer's disease (AD), the most common form of dementia is one of the most disabling and burdensome health conditions worldwide. Memory loss, the main and initial complaint in AD, is associated with defects in synaptic transmission and plasticity in the hippocampus and other brain areas. Since AD is largely an age-dependent disease and its prevalence continues to rise due to increasing human life expectancy, there is an urgent need for novel drugs that can cure AD. This study investigates the effect of TH-9 on synaptic transmission, long-term potentiation (LTP) and long-term depression in young and old rats.

Methods:
350-microm coronal hippocampal slices were generated from brains of male Sprague-Dawley rats aged 1 and 20 months. Evoked, field excitatory postsynaptic potentials (fEPSPs) were recorded from the dendritic layer of area CA1 of the hippocampus by stimulating appropriate afferents. LTP was induced using high-frequency stimulation (HFS; 100 Hz for 1 second) while LTD was elicited using low-frequency stimulation (LFS; 1 Hz for 5 minutes).

Results:
TH-9 (10 μM) increased the slopes of fEPSPs by 34.9±7.3% ($p<0.05$) and 38.9±18.7% ($p<0.05$) in young and old rats respectively. LTP induction resulted in an increase of 59.9±11.0% ($p<0.05$) and 47.4±16.5% ($p<0.05$) in fEPSP slopes in slices from young and old rats, respectively. Induction of LTP in the presence of TH-9 resulted in a greater total increase in fEPSP slopes in old rats compared to young rats (58.3±10.1% and 89.1±27.8%, respectively). LFS depressed fEPSP slopes by 24.7±3.4% ($p<0.05$) and 26.7±3.9% ($p<0.05$) in young and old rats respectively. However, pre-treatment with TH-9 abolished LTD responses in old but not young rats.

Conclusions:
TH-9 enhances LTP in hippocampal slices of both young and old rats while preventing LTD maintenance only in older rats. This action of TH-9 is consistent with a potential to be used for dementia.

Key Words: Learning and memory; Synaptic plasticity; Hippocampus

39: Poster

Mitochondria-targeting properties and photosensitizing activity of Zn(II) N-alkylpyridylporphyrin-based photosensitizers

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Introduction:
Photodynamic therapy (PDT) is emerging as a promising medical treatment for both neoplastic and non-neoplastic disorders. In PDT, cell destruction is achieved by a combination of visible light and light-sensitive compounds called photosensitizers (PSs), which upon illumination produce cytotoxic reactive species. Since mitochondria play a key role in regulating apoptotic cell death, they are considered to be a promising PDT target. The aim of this study was to investigate how the structure of specially designed Zn (II) N-alkylpyridylporphyrins (ZnPs) would affect their PDT efficacy, mitochondrial accumulation and damage to mitochondrial targets.

Methods:
A homologous series of ZnPs with increasing length of alkyl chains were synthesized. Their effect on LS174T cells viability was tested by the MTT assay. Effect on mitochondria was determined by measuring respiration, inactivation of a specific mitochondrial marker enzymes (cytochrome c oxidase - Cox), photo-oxidation of cytochrome c and cross-linking of mitochondrial structural proteins.

Results:
ZnPs were found to be potent photocytotoxic agents. The amphiphilic longer chain hexyl derivatives were the most efficient in killing cancer cells than the shorter chain derivatives, and were the most efficient in inhibiting respiration. This coincided with inactivation of Cox and also rapid photo-oxidation of ferro-cytochrome c (cyt c-Fe2+) to ferri cytochrome c (cyt c-Fe3+). Electrophoretic analysis of photo-treated mitochondria demonstrated extensive protein cross-linking and Western blot analyses demonstrated photo-induced alterations in mitofilin (key structural protein of the inner mitochondrial membrane) after photo-treatment with the hexyl analog.

Conclusions:
The increase of the length of the chains attached at the periphery of the porphyrin ring of ZnPs increased not only their cellular uptake and the ability to reach mitochondria, but also their selectivity in photo-damaging specific mitochondrial components. The combination of positive charges and lipophilicity provides the driving force for efficient uptake and mitochondrial targeting of the hexyl derivatives.

Key Words: Photodynamic therapy; Singlet oxygen; Photosensitizer

40: Poster

Assessment of knowledge on adverse drug reactions among health care professionals

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Introduction:
Under reporting of adverse drug reactions (ADRs) is a cause of concern, the reasons for which may be due to lack of trained staff and lack of awareness about detection, communication and spontaneous monitoring of ADRs. As many physicians are not aware of the importance of monitoring and reporting of ADRs, they may be under reported. The objectives of this study were to determine the level of awareness of Health Care Professionals (HCP) about ADR reporting and extent of their involvement in pharmacovigilance activities.

Methods:
This was a questionnaire-based study involving HCP who were surveyed with a questionnaire at a 700 bed multi-specialty hospital. The first four questions were designed to evaluate the basic knowledge of ADR. The remaining questions were designed to reveal the information regarding their knowledge about pharmacovigilance, ADR reporting, and possible reasons for non-reporting of an encountered ADR.

Results:
A questionnaire containing 19 questions was distributed to 30 faculties, 20 physicians, 30 nurses and 30 students. Only 20 faculty, 8 physicians, 20 nurses and 22 students completed and returned the questionnaire, giving the response rate of 66.66%, 40%, 66.66% and 73.33% respectively. Out of these, as per the WHO definitions, only 8 (40%) faculty, 6 (27.27 %) students, 3 (37.5%) prescribers and 1 (5%) nurses could correctly define an ADR. Spontaneous reporting system was well known to 7 (31.81%) students, 7 (87.52%) prescribers, 14 (70%) faculty and 11 (55%) nurses. The majority of the participants said that ADR should be reported if it causes both inconvenience and death to the patients while 8 (36.36%) students, 11 (55%) faculty and 10 (50%) nurses were not reporting the ADR because they are not aware of correct reporting center, but 5 (62.5%) prescribers having better knowledge about reporting centers than other groups. The majority of reasons for underreporting of ADR were lack of knowledge about the reporting center in 16 (72.72%) students, 6 (75%) prescribers, 12 (60%) faculty and 18 (90%) nurses, and uncertainity of the drug causing ADR in 17 (77.27%) students, 4 (50%) prescribers, 17 (85%) faculty and 16 (80%) nurses.

Conclusions:
Despite of good observation and knowledge of ADR among HCP the rate of reporting to ADR centers is very low.

Key Words: Adverse drug reactions,; Knowledge; Spontaneous reporting

41: Poster

Evaluation of toxicological profile (acute and sub-acute) of cremophor in dacarbazine formulation in rodents

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Introduction:
Cremophor is widely used as a solvent in many cancer formulations, however, there are no complete toxicity studies done for its use as a solvent in dacarbazine formulation. The present investigation was conducted to determine the safety of cremophor as a solvent in dacarbazine formulation by determining its potential toxicity after acute and sub-acute study in rodents.

Methods:
In the acute study, mice were divided into three groups of six animals each and each group received a single 100, 500, 1000 mg/kg dose of the formulation by the intravenous route. .In the sub-acute study, the first group of rats served as the control receiving standard dacarbazine while the second group was given vehicle and the other three groups were given solvent containing formulation at doses of 25, 50 and 100mg/kg, respectively via the intravenous route every 5 days up to 28 days . Behavioral changes, and body weight were determined. Biochemistry and haematology analysis were done for sub-acute toxicity study. Histopathological examination of rat kidney, liver and brain were carried out after 28 days.

Results:
The IV LD50 for the formulation was found to be 466mg/kg. Sub-acute toxicity showed no significant changes in biochemical and haematological parameters. No pathological changes were observed in rat liver, kidney and brain. The biochemical, haematological and histopathological parameters did not show any abnormality due to the use of cremophor as a solvent in dacarbazine formulations.

Conclusions:
Based on the observed findings, the cremophor in dacarbazine formulation was fairly nontoxic at the IV dose tested, as it did not cause any death or adverse behavioral changes and Cremophor can be incorporated in dacarbazine formulation.

Key Words: Cremophor; Dacarbazine; Acute and Sub-acute toxicity;

42: Poster

Synthesis of oxoquinoline derivatives coupled to different amino acid esters and studying their biological activity as cytotoxic agents

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Introduction:
Quinolines are an important group of organic compounds since several compounds containing a quinoline residue are known to possess useful biological activity and are used as antibacterial, antifungal and antitumor agents. These pharmacological properties of quinolines aroused our interest in synthesizing several new compounds featuring heterocyclic rings of the quinoline derivatives linked to amino acid ester side chains with the aim of obtaining a pharmacologically active compounds

Methods:
Quinoline was N-alkylated by the bromoacetic acid and then oxidized with an alkaline potassium ferricyanide solution to get N-alkylated quinolone. Conventional solution method for peptide synthesis used as a coupling method between the carboxy-protected amino acids with the acetic acid side chain of quinolone. The DCC/ HOBt coupling reagents used for the peptide bond formation.

Results:
The proposed analogues were successfully synthesized and their structural formulas were consistent with the proposed structures as they were characterized and proved by thin layer chromatography (TLC), melting point, infrared spectroscopy (IR) and elemental microanalysis.

Conclusions:
All tested analogues showed cytotoxic activity on the HEp-2 cell line (tumor of larynx) with inhibitory concentration percent (IC %) of 49.01 % - 77.67%. These are promising data for the discovery of new anticancer agents in the future.

Key Words: Quinolones; Quinoline anticancer; Quinolines biological activity

43: Poster

An ethno-pharmacological study of Egyptian bedouin women's herbal medicine

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Introduction:
Herbal medicine is still the main source for health care within the bedouins in Egypt. Bedouin women are heavily involved in all aspects of medicinal plant utilization. The traditional medical skills held by women with respect to reproductive health, are generally valued. Female reproductive health within these communities is an intimate and private affair that traditionally is only dealt with by women, especially when there is limited access to modern medical facilities and professional female practitioners. Therefore, the aim was to document and record their knowledge for the treatment of their reproductive health problems such as dysmenorrhoea, perinatal problems and urinary tract infections.

Methods:
An ethnopharmacological survey was undertaken within bedouin women in Egypt. Phytochemical and pharmacological investigations of plant material were carried out with the aim of identifying active compounds.

Results:
Data collected showed that the bedouin women commonly use more than 45 different plant species. Four plant species were chosen for phytochemical and pharmacological investigations and the isolated compounds:

- significantly inhibited the TNF-α production in LPS-stimulated cells In vitro studies.
- showed antimicrobial and antioxidant activity.
- inhibited the spontaneously contracting muscle preparations from mouse uterus. The inhibitory effect was attributable to the activation of beta-adrenoceptor agonists.

Conclusions:
Studying herbal medicine use by bedouin in Egypt can serve as a starting point in future drug development aimed at the production of new safe, effective and bio-accessible therapeutic agents. Some of this work justified the use of these plants within the bedouin communities for the treatment of menstrual pain, genital infection and perinatal problems and provide a scientific correlation between traditional medicinal plant use among the bedouin and the pharmacological basis for their administration.

Key Words: Bedouin women; Medicinal plants; Anti-microbial and anti-inflammatory

44: Poster

Contraceptive vaginal suppository containing nonoxynol-9 and zinc acetate salt in a clinical trial

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Introduction:
Nonoxynol-9 (N-9) is the most common active ingredient of spermicides. Spermicides containing N-9 are available in many forms, such as jelly, films, suppositories and foams.. The two major problems reported on using N-9 spermicide were high failure and high irritation rates which were the main causes of its withdrawal from markets. We tried to modify N-9 products in a new formula which is safe, and effective. The new preparation based on the addition of low concentrations of zinc acetate salt (Zn (OAC)2) to N-9 that reduce the irritation of mucous membranes on frequent use and increase the efficacy of N-9. The new preparation made in the form of vaginal foaming suppository. It was tested *in vitro* and *in vivo*. The *in vitro* results show a significant increase in efficacy of the combination (Zn (OAC)2 & N-9) than N-9 alone. Additionally, the *in vivo* results indicated a significant decrease in failure and irritation rates in the combination than (N-9 alone) market suppository.

Methods:
The study recruited 78 participants referred for using spermicide suppository formulated of N-9 (market or compounded) for conception purpose at family planning unite at General Abo-Korkase hospital during the period from July 2010 to August 2011. The study was carried out to achieve two purposes, which were to decrease failure and irritation rates. All participants were instructed on how to use the test products. Participants were followed through at least 12 menstrual cycles (approximately 13 months) and had 8 study visits and two study phonecalls. Notes were taken about pregnancy if it occurred, vaginal irritation, coital problems, cycle irregularities, secretions and other compliances after use.

Results:
The results were observed on the positive side as vaginal irritation decrease with a high significant difference (P=0.02) when zinc acetate salt added to N-9. Irritation in this context may be evidenced by redness or other changes in coloration, inflammation or swelling, hypersensitivity, the occurrence of burning, itching or other painful stimuli. The results show increasing spermicidal efficacy of Zinc acetate, N-9 combination more than N-9 alone. Failure rate of N-9 was decreased significantly ($p = 0.03$).

Conclusions:
Our results recommend addition of zinc acetate to N-9 spermicidal formula to achieve the best properties of spermicidal contraceptive.

Key Words: Contraceptive; Nonoxynol-9; Zinc acetate

45: Poster

Isolation of bioactive sesquiterpene lactones from *Centaureaaegyptiaca* ethanol extract

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Introduction:
In a previous work, the ethanol extract of *Centaurea aegyptiaca* had shown potential cytotoxic activity against liver and larynx carcinoma cell lines. The aim of this study was to continue the isolation of the compound(s) that may be responsible for the potent biological activity of *Centaurea aegyptiaca* extract.

Methods:
The shade-dried aerial parts of *Centaurea aegyptiaca* were coarsely powdered and extracted with ethanol (96%). The ethanol extract was subjected to chromatographic separation on a flash silica gel column gradually eluted with an increasing strength of acetone in toluene. Two compounds were isolated and analyzed using different spectroscopic methods. Moreover, the cytotoxic activity of these compounds were evaluated against liver and larynx carcinoma cell lines using Skehan et al. protocol. IC_{50} (micromolar) of the two compounds were determined using doxorubicin as a positive control.

Results:
Two guaianolide sesquiterpene lactones, linichlorin A (1) and sinaicin (2) were isolated and characterized from the ethanol extract of *Centaurea aegyptiaca*. Compounds 1 and 2 exhibited potential cytotoxic activity against larynx carcinoma cell line with IC_{50} values of 48.43 and 38.89 micromolar, respectively. However, the most potent cytotoxic activity was against liver carcinoma cell line with IC_{50} values of 10.42 and 21.83 micromolar, respectively.

Conclusions:
Chemical investigation of *Centaurea aegyptiaca* ethanol extract led to the isolation and identification of two sesquiterpene lactones. Moreover, these compounds may be responsible for the cytotoxic activity shown by *Centaurea aegyptiaca* ethanol extract against liver and larynx carcinoma cell lines.

Acknowledgements:
Spectral analyses were done at Kuwait University, Faculty of Science, Science Analytical Facilities, (SAF) supported by Grant numbers GS01/01, GS01/03.

Key Words: Centaurea aegyptiaca; Cytotoxicity; Sesquiterpenes

46: Poster

The diabetic obese chronic obstructive pulmonary disease patients in pulmonary rehabilitation programme: new challenges and opportunities for pharmacists

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Introduction:
The prevalence rate of chronic obstructive pulmonary disease (COPD) and obesity are increasing. The morbidity and mortality from COPD and obesity are also increasing. Obesity frequently coexists with COPD, since both conditions are common. This may be attributed to people with COPD leading more sedentary lifestyles, which is why implementing an exercise programme is important. Thus, obese patients with COPD benefited from pulmonary rehabilitation (PR)

Methods:
We have reviewed relevant publications on COPD, obesity and PR.

Results:
Standardized outpatient PR programme for COPD patients, diabetes as a comorbidity in PR, smoking as a risk factor for diabetes, causes of COPD exacerbations and the pathophysiological basis of lung disease in diabetes will be discussed. We will illustrate the combined effects of PR on these conditions, bronchial hygiene, breathing retraining, physical reconditioning, individualized pharmacologic therapy, smoking and diabetes. We will explore and address the following questions: does diabetes alter lung function?, does therapy for COPD exacerbate diabetes?, does exercise benefit glycemic control? and does exercise reduce inflammation in chronic disease?.

Conclusions:
Conclusions will be based on the pathophysiologic basis for diabetic lung, drugs used for COPD patients and exacerbation of diabetes, glycemic control during PR, the effect of exercise on systemic inflammation. The roles of pharmacist in the management of the diabetic obese COPD patients participating in PR and the new challenges and opportunities for pharmacists will be explored.

Key Words: COPD; Pulmonary Rehabilitation; Obesity

47: Poster

Clinical spirometry: how clinical pharmacists can interpret spirometry results

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Introduction:
In the diagnosis of chronic obstructive pulmonary disease COPD, pulmonary function tests (PFTs) are performed to assess lung function and determine the degree of damage to the lungs. PFTs have become important for clinical pharmacists in the evaluation of respiratory health. PFTs are used for the following reasons: screening for the existence of lung diseases, determining the patient's condition prior to surgery to assess the risk of respiratory complications after surgery, assessing the progression of lung disease and the effectiveness of treatment, and clinical trials.

Methods:
Spirometry and PFTs will be demonstrated and r interpreted. Clinical spirometry using pulmonary function tests are used in the diagnosis of COPD and can be differentiated from asthma.

Results:
We will focus onr VC-Vital Capacity - The amount of air that can be forcibly exhaled from the lungs after a full inhalation, FVC-Forced Vital Capacity - the amount of air which can be forcibly exhaled from the lungs after taking the deepest breath possible, FEV1-Forced Expiratory Volume in one second - the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, FEV1/FVC-FEV1-percent (FEV1%) - The ratio of FEV1 to FVC, PEFR Peak Expiratory Flow Rate- measures if treatment is effective in improving airway diseases such as COPD, FEF-Forced Expiratory Flow - A measure of how much air can be exhaled from the lungs, it is an indicator of large airway obstruction, and MVV-Maximal Voluntary Ventilation.

Conclusions:
Obstructive pattern: due to conditions in which the airways are obstructed e.g: asthma or COPD; the FEV1 and FVC are reduced disproportionately. Restrictive pattern: due to conditions in which the lung volume is reduced, e.g: fibrosing alveolitis; the FEV1 and FVC are reduced proportionately.

Key Words: Spirometry; Lung function tests; Obstructive lung disease

48: Poster

Knowledge and attitude of school children in Amman/Jordan towards the appropriate use of medicines: A cross-sectional study.

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Introduction:
The prevalence of medicine use in children, both prescribed and over-the-counter (OTC) is reported to be high.[1] Previous research supported the use of direct, developmentally appropriate, child-centered health care education, which in turn is hoped to improve both medicine use and treatment adherence. The aim of this study is to examine the knowledge, practice, and attitude towards medications of different primary school children at age group (7-9) years.

Methods:
This cross sectional study adopted the form of structured interviewing technique using a validated and pre-piloted questionnaire. The questionnaire consisted of a mixture of multiple choice and open-ended questions, 15 USP pictograms and 6 dosage form demos. A randomized stratified target sample of 200 students (n=100 of each gender), of the first, second and third grades from the four Amman Education Directorates was recruited. School children were interviewed regarding their knowledge, attitude and the way they think medicines should be used. All data was coded and entered stepwise into SPSS® database for windows version 16, then SAS® database for statistical analysis. Both ANOVA and Chi-square tests were used to test for any significant differences among variables (P-value <0.05).

Results:
The mean score value achieved by children in all the knowledge questions was 23.26±0.25 out of 32, which was considered as satisfactory knowledge by the research team. The most significant factors affecting children's knowledge (including: multiple choice questions, pictograms and dosage forms) were: age, school/area of residency, and the presence of a first-degree relative working in a medical job. The majority of participants (79%) stated that the taste of the medication was the main factor to prevent them from taking their medication.

Conclusions:
In general, school children in our sample have satisfactory knowledge and a generally positive attitude towards medicines. However, school curricula in Jordan should include more education regarding the effective and safe use of medicines.

References:
1. Kogan, M. Pappas, G. and Kotelchuck, M, 1994. Over-the-counter medication use among US preschool-age children. Health Educ.13, 1025-30.

Key Words: Attitude; Children; Jordan

49: Poster

Role of diabetes in the prognosis and therapeutic outcome of Tuberculosis

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Introduction:
Increased susceptibility of diabetic mellitus (DM) patients to infection, including tuberculosis (TB), is well documented. The prevalence of DM in Malaysia is reaching epidemic proportions. In this study, we sought to assess risk factors for TB and the impact of DM on the outcome of TB treatment.

Methods:
TB patients, diabetic patients, and diabetic patients with TB were divided into three groups of 200 subjects each. Data were obtained from patients' medical files at the beginning and end of the study period. Prevalence rates of DM and HIV among TB patients were assessed. Prognosis, TB-related complications, anatomical site of infection, and duration of infection and diabetes were also examined. Data was processed using SPSS version 11.5. Statistical significance was achieved when $p \leq 0.05$.

Results:
The prevalence rates of HIV and DM amongst TB patients were 7.7 and 30%, respectively. The diabetic TB patient group contained more males (72%; $P < 0.01$) and smokers (45.5%; $P < 0.01$) compared to the non-diabetic group (58.3% and 33.5%, respectively.). Approximately 74% of diabetic patients were Mycobacterium sputum positive compared to only 51% of non-diabetic patients ($P < 0.01$). Diabetic patients were also more likely to develop pulmonary TB (87%) compared to non-diabetic TB patients (59%; $P < 0.01$). Diabetic TB patients had significantly poor treatment outcome and higher mortality rate (7.5%) compared to the TB only and DM only groups (1 and 2%, respectively.). The duration of TB symptoms was longer in non-diabetic TB patients compared to diabetic TB patients (4.5 versus 2.6 months, respectively.). Diabetes antedated TB by a mean time of 4 years.

Conclusions:
We found a higher number of sputum-smear-positive cases and pulmonary TB cases as well as a greater number of males and higher mortality rate in diabetic patients compared to non-diabetic patients.

Key Words: Tuberculosis; Mortality

50: Poster

An HPLC method for determination of 15 pharmaceutical compounds in anti-cold products.

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Introduction:
A validated HPLC method was developed for determination of paracetamol, phenylephrine hydrochloride, pseudoephedrine hydrochloride, salicylamide, guaifenesin hydrochloride, sodium benzoate, methylparaben, chlorpheniramine maleate, triprolidine hydrochloride, dextromethorphan hydrobromide, diphenhydramine hydrochloride, promethazine hydrochloride, propylparaben and both of para aminophenol and 4-chloroacetanilide as related compounds for paracetamol in different pharmaceutical dosage forms of anti-cold products such as tablet, syrup, suspension

Methods:
The performed measurements were done by using symmetry C18 column at 25°C with UV detection at 215 nm. A linear gradient elution was employed starting with 92% mobile phase A and 8% mobile phase B for 6 min to reach 73% mobile phase A and 27% mobile phase B at 20 min then 60% mobile phase A and 40% mobile phase B at 35 min. The total run time is 40 min using solution of 30 mM sodium dihydrogen phosphate containing 3 mM hexanesulphonic acid sodium salt and adjusted to apparent pH 3.0 with phosphoric acid as mobile phase A and acetonitrile as mobile phase B.

Results:
For simultaneous determination of the fifteen compounds, it is necessary to make adjustments of the HPLC system to avoid overlapping and provide optimum separation of the peaks. Due to the variation of uv absorbance for the analyzed compounds the wavelength used for detection should be selected to give good response for all the tested compounds. The gradient system and the organic ratio of the mobile phase should be adjusted to give good separation for the tested compounds with less baseline noise. The experimental variables were optimized to give a simple, sensitive and accurate HPLC method.

Conclusions:
The developed HPLC method provides simple, accurate, sensitive, specific, precise and direct quantitative analysis for the simultaneous determination of the above mentioned 15 compounds in pharmaceutical products. The advantages of the developed method include low limit of detection and quantitation, good precision (standard deviation less than 1%) with symmetric, pure and perfect homogeneity for the studied compound peaks. The specificity of the method was evaluated by studying the peak purity index values for the studied compounds.

Key Words: HPLC; Anti-cold products; Related substances

51: Poster

Taking medication history: no short cuts allowed

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CASE REPORT

Background:
Isotretinoin [the most common brands are Roaccutane (Hoffman-La Roche, known as Accutane in the United States before July 2009), Amnesteem (Mylan), Claravis (Barr), Isotroin (Cipla) or Sotret (Ranbaxy)] is a medicine taken by mouth to treat the most severe form of acne (nodular acne) that cannot be cleared up by any other acne treatments. Accutane can cause serious side effects and accordingly, the U.S. Food and Drug Administration (FDA) required patients and their doctors and pharmacists to register and use a web site in order to receive this acne drug. Ophthalmologists are seeing increasingly more younger patients with dry eyes, Blepheritis, contact lens intolerability and other ocular presentations which necessitate paying more attention to patients' and doctors' education about potential side effects of this widely used medication in Kuwait.

Case summary:
A total of 36 female medical students from Kuwait University completed a self-reporting questionnaire. The ages ranged from 17-24 years (majority Kuwaiti); 47% reported suffering from acne and 9 of them were on medication. Three participants were currently on Roaccutane, 1 on oral antibiotics, 2 on topical medication and 3 did not know the medication they were currently taking. One of the participants on Roaccutane reported having dry eyes and one gave history of viral conjunctivitis. Interestingly, two participants were currently using non-medically prescribed contact colored lenses (one of which is monthly wear) and both were using sun glasses without added UV protection filter.

Conclusion:
While no registry exists in Kuwait for patients taking Roaccutane as advised by the FDA, it is vital to take the medication history from all patients presenting with ocular signs and symptoms. Ethically, no short cuts should be accepted in this vital step of the doctor-patient encounter.

Key Words: Roaccutane; Acne; Ethics

52: Poster

Antibacterial activities of novel N-substitutedglycinyl 1H-1,2,3-triazolyl oxazolidinones

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[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University; [2]Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
The introduction of "Spacers" containing hydrogen bond donor and / or acceptor groups on the terminal substituent moiety at the C-4 position of the phenyloxazolidinone pharmacophore yielded potent antibacterial activity due to enhanced interactions at the bacterial 50S ribosomal binding sites. In this study we investigated the influence of varied N-substituted glycinyl on the antibacterial activity of piperazinyl-5-(4-methyl-1,2,3-triazolyl) oxazolidinones.

Methods:
Novel substituted-glycinyl oxazolidinones were synthesized and evaluated against clinical and reference strains of Staphylococcus aureus, coagulase-negative staphylococci, enterococci, Streptococcus pneumoniae and Moraxella catarrhalis. Minimum inhibitory concentrations (MIC's, ug/ml) was determined by agar dilution method on Mueller Hinton agar containing dilutions of antibacterial agents ranging from 0.06 - 64 ug/ml, with and without 50% human plasma.

Results:
Against all Gram-positive bacteria strains tested, derivatives with aroyl substitution on the N-glycine were more potent (MIC: 0.06-4 ug/ml) than the substituted-acyl (MIC: 2-8 ug/ml) derivatives. Nitro substitution on aryl and heteroaryl rings significantly enhanced activity against Gram-positive bacteria, as noted with the 5-nitrofuran-2-carbonyl and 3,5-dinitrobenzoyl derivatives with MIC ranges of 0.06-0.5 and 0.25-0.5 ug/ml, respectively. The 3,5-dinitrobenzoyl and 5-nitrofuran-2-carbonyl derivatives showed extended activity against M. catarrhalis with MIC ranges of 0.25-1 ug/ml, compared to linezolid (MIC: 8ug/ml).

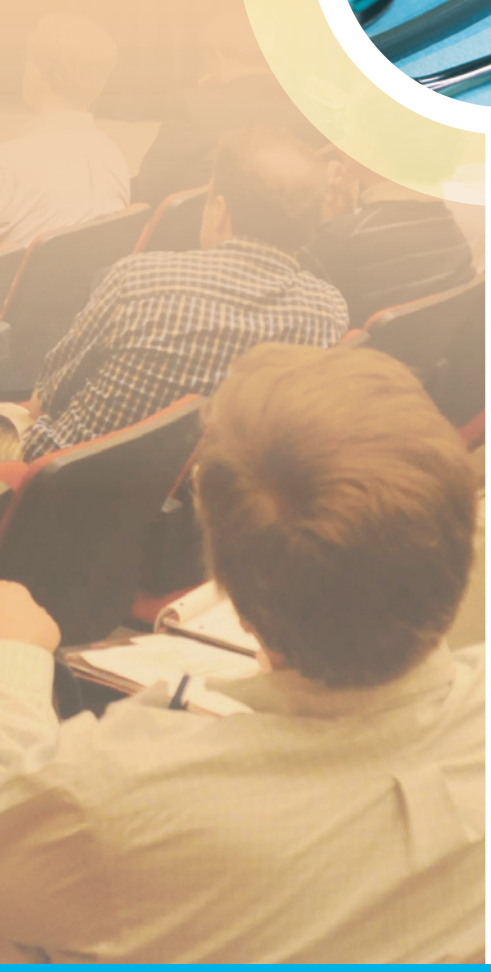
Conclusions:
The newly synthesized compounds exhibited moderate to strong antibacterial activity against all Gram-positive cocci tested with extension against M. catarrhalis. Further structural modifications around the amino acid substituent is warranted.

Supported by KURA Grant # PC01/05 (OAP) and GS01/01, GS01/03 and GS01/05 awarded to Science Analytical Facilities (SAF).

Key Words: Antibacterial activities; N-Glycinyl spacer substitution; Triazolyl

4th Kuwait International Pharmacy Conference (KIPC)

4 - 6 FEBRUARY, 2013



Discussion Forum

5th February, 2013 - 18.45 - 19.45

Herb-drug interaction: a significant safety concern

Prof. F Alali

6th February, 2013 - 18.30 - 19.30

Pharmacy Education

Prof. W Duncan

5th February, 2013 - 18.45 - 19.45

Discussion Forum: Herb-drug interaction: a significant safety concern

Moderator: Prof. Feras Alali, Ph.D

Dept of Medicinal Chemistry and Pharmacognosy , Faculty of Pharmacy, Jordan

Co-Moderator: Dr Khaled Orabi

Dept of Pharmaceutical Chemistry, Faculty of Pharmacy, KU

Many consumers believe that herbal medicines are natural and therefore safe, but this is a dangerous oversimplification. The concomitant use of herbal medicines and pharmacotherapy is widespread. Some herbal medicines are associated with adverse effects, which include interactions with prescribed drugs. Drug–herb interaction may cause adverse reactions that may be minor, moderate, life threatening or lethal. The interaction of drugs with herbal medicines is a significant safety concern, especially for drugs with narrow therapeutic indices (e.g. warfarin and digoxin) or with drugs administered for serious chronic diseases.

There are increased numbers of reports on herb-drug interactions, although many of them are case reports, case series and limited clinical observations. Herb-drug interactions may be significantly under- reported and underestimated, and occur more frequently than drug-drug interactions. Most patients do not reveal their herbal use, adding to the lack of comprehensive surveillance system for monitoring the adverse effects.
There are other reasons for concern: herbs have been used on a traditional basis, and rigorous preclinical and clinical assessments are not required by regulatory authorities. In addition, most clinical trials of herbs have limited value, because of poor design, small sample size and, above all, use of poorly defined products of uncertain composition and consistency because of the lack of good quality control.
Herbal products contain several chemicals that are metabolized by phase I and phase II pathways and also serve as substrates for certain transporters. Due to their interaction with these enzymes and transporters there is a potential for alteration in the activity of drug metabolizing enzymes and transporters in the presence of herbal components. Inhibition and induction of drug-metabolizing enzymes (e.g. cytochrome P450 3A4) and drug transporters (e.g. P-glycoprotein) are the major mechanism underlying many pharmacokinetic drug–herb interactions.

6th February, 2013 - 18.30 - 19.30

Discussion Forum: Pharmacy Education

Moderator: Prof. Wendy Carolyn Duncan

St. Louis College of Pharmacy, USA

Co- Moderators: Prof. David Biggs

Prof. Samuel Kombian

Dept of Pharmacology & Therapeutics, Faculty of Pharmacy, KU

This session will discuss general topics related to aspects of pharmacy education. We would like to aim for an interactive debate between the Panel and the audience, to call on our collective experience in addressing such issues as:

- What should undergraduate students of pharmacy be learning – should this be a purely vocational degree or should it also include general aspects of medical education ?
- Should there be one set of international standards of educational/professional outcomes for pharmacy graduates worldwide, or should these be subject to local needs and take into account socio-economic differences ?
- What role, if any, does scientific research in pharmacy have in undergraduate teaching, and how important is it?
- What role should be adopted by Faculty members in the student learning process; are lectures the best way to impart information and ideas ?
- What can be done to increase motivation and interest of pharmacy students in Kuwait?

4th Kuwait International Pharmacy Conference (KIPC)

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2. Awarding grants and prizes to enhance the intellectual development in the State of Kuwait and other Arab countries, and to reward excellence in the field of science in particular.

3. Contributing to the Arabic language library with specialized references and studies in various fields of knowledge, as well as reviving Arabic language as a medium for the study of science.

4. Disseminating and developing scientific culture in the society, as well as encouraging and nurturing in it the appropriate scientific and technical skills.


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