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Future of Pharmaceutical Sciences

Al-Zaytoonah University of Jordan
November 6-7, 2019

Conference Proceedings

كلية الصيدلة - جامعة الزيتونة الأردنية
Faculty of Pharmacy
Al-Zaytoonah University of Jordan

COLLEGE OF PHARMACY AND PHARMACEUTICAL SCIENCES
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In submitting Conference Proceedings to this special issue of Journal of Pharmacy & Pharmacognosy Research (JPPRes), we certify to the Publisher that we adhere to the Editorial Policy of JPPRes in order to safeguard a good scientific practice in publishing.

Moreover, we manifest that all articles have been subject to peer review administered by the proceeding's editors. Also, reviewers have been conducted by expert referees, who have been requested to provide unbiased and constructive comments aimed, whenever possible, at improving the work. Proceeding's editors have taken all reasonable steps to ensure the quality of the materials they publish and their decision to accept or reject a paper for publication has been based only on the merits of the work and the relevance to the journal.

Proceeding's editors:

Prof. Tariq Al-Qirim
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PREFACE

Al-Zaytoonah University of Jordan and The University of Toledo would like to take this opportunity to welcome all of you to the 7th International Pharmaceutical Conference 2019, which will be held during November 6-7th, 2019 in Amman, Jordan. Through our theme "Future of Pharmaceutical Sciences", the conference will analyze the recent advancements and challenges in pharmaceutical sciences and research.

The main objective of the conference is to link up Pharmacists, Academicians, Scientists, Researchers, Graduate students to discuss the future of pharmaceutical sciences. More than 90 participants from different universities and research centers will represent the results of their latest researches in the area of pharmacy and public health, those participants come from different countries including the United States of America, United Kingdom, Germany, Pakistan, Malaysia, Saudi Arabia, Iraq, Cyprus, United Arab Emirates, Palestine, Libya and Jordan. This conference is a great opportunity to share knowledge and build bridges between different researchers that will create opportunities for new research cooperation

We welcome everybody to the beautiful city of Amman and thank you for your participation.

Organizing Committee

PROGRAM

Wednesday, November 6th, 2019

9:30 - 10:30: Registration.

11:00 - 11:30: Opening ceremony.

Main Theatre of the Al-Zaytoonah University of Jordan.

- Opening remarks:
  - Chairman of the conference: Professor Tariq Al-Qirim. Dean, Faculty of Pharmacy, Al-Zaytoonah University of Jordan.
  - Professor Muhammad Al-Majali. President of Al-Zaytoonah University of Jordan.
  - His Excellency Dr. Saad Fayez Jaber. Minister of Health.

11:30 - 12:00: Coffee Break.

Session (1):

Main Theatre

Moderators: Prof. Abla Albsoul & Prof. Reema Abu Khalaf.

Time	Speaker	Title
12:00-12:40	Prof. Patrick Lam *Drexel University College of Medicine, United States of America.*	Discovery of Eliquis /Apixaban, a novel factor Xa anticoagulant and Chan-Lam coupling reaction.
12:40-13:00	Prof. Jonathan Ling *Sunderland University, United Kingdom.*	A review of strategies for reducing air pollution in urban areas.
13:00-13:20	Prof. Frederick Williams *University of Toledo, United States of America.*	The use of Casper zebrafish to study behavior and identify psychostimulant targets related methamphetamine.
13:20-13:35	Dr. Taqwa Ahmad Maqatef *JFDA, Jordan.*	Clinical studies in Jordan (current status, regulations, and responsibilities).

13:40-15:00: Lunch.

Session (2):

Moderators:

Dr. Imad Al Doghim & Dr. AbdelQader Albawab. Dr. Taqwa Ahmad & Dr. Ala Alhusban.

Time	Main Engineering Hall	Library Hall
15:00-15:15	Prof. Waleed Sweileh *An- Najah National University, Palestine.* *Acinetobacter baumannii* infections: a 3–year hospital-based retrospective study.	Prof. Wolfgang Weigand *Friedrich-Schiller-Universität Jena, Germany.* DAZA-based ^{68}Ga complexes or PET liver imaging in ovo.
15:15-15:30	Dr. Farida Hanim Islahudin *Universiti Kebangsaan, Malaysia.* Assessing individual medications in chronic kidney disease.	Prof. Muhammed Alzweiri *University of Jordan, Jordan.* Designed fumigaclavine analogues as neuroprotective agents.
15:30-15:45	Dr. Abdul Qader Qawasmeh *Hebron University, Palestine.* Smoking secession in Palestine: Pharmacists' awareness and attitude.	Dr. Abdulaziz Amro *Taibah University, Kingdom of Saudi Arabia.* Voltammetric method development for itopride assay in a pharmaceutical formulation.
15:45-16:00	Dr. Iman Elmahdi Ali *Benghazi University, Libya.* Vitamin D status in patients with type 1 and type 2 diabetes in Benghazi.	Dr. Belal Rahhal *An- Najah National University, Palestine.* Phytochemical investigation and diuretic activity of the Palestinian *Crataegus aronia* in mice using an aqueous extract.

Thursday November 7th, 2019

Session (1):

Moderators:

Prof. Rana Obaidat & Dr. Ola Tarawneh — Prof. Frederick Williams & Dr. Luay Alessa

Time	Main Engineering Hall	Library Hall
9:00-9:15	Dr. Naser Shraim *An- Najah National University, Palestine.* Investigation of the influence of food on the oral absorption of clarithromycin from immediate release tablet using physiological modeling.	Prof. Rozita Rosli *Universiti Putra, Malaysia.* Breast cancer recurrence: Targeting aldehyde dehydrogenase+ cells with citral.
9:15-9:30	Dr. Muhammad Akhtar *The Islamia University of Bahawalpur, Pakistan.* Multiparticulate pH triggered delayed-release chronotherapeutic drug delivery of celecoxib-β-cyclodextrin inclusion complexes by using Box-Behnken design.	Prof. Nancy Hakooz *University of Jordan, Jordan.* Genetic variants of vascular endothelial growth factor-634 and vascular endothelial growth factor-936 in circassians and chechen subpopulations in Jordan.
9:30-9:45	Dr. Einas Abu Arrah *Universiti Sains Malaysia, Malaysia.* Formulation of omeprazole nanosuspension using evaporative precipitation-ultrasonication technique.	Prof. Yousef Sari *University of Toledo, United States of America.* Astrocytic glial glutamate transporters in the brain: Therapeutic targets for the treatment of drugs of abuse.
9:45-10:00	Dr. Sharif Abdel Ghany *University of Jordan, Jordan.* Comparative study of alginate modified PLGA nanoparticles *vs* non-modified PLGA nanoparticles encapsulating two antibiotics for the treatment of tuberculosis.	Dr. Ramzi Shawahna *An- Najah National University, Palestine.* Optimizing the hCMEC/D3 cell line as a powerful tool in predicting drug disposition to the human brain: a focus on drug transporters and metabolizing enzymes.
10:00-10:15	Dr. Ahmad Eid *An- Najah National University, Palestine.* Fusidic acid and sodium fusidate nanoemulgel development and antimicrobial activity evaluation.	Dr. Mohammad Dweib *Hebron University, Palestine.* Antibiotic resistance and microbiological profile of urinary tract infections in Palestine.

Session (1) *(continued…)*:

Moderators:

Prof. Rana Obaidat & Dr. Ola Tarawneh

Prof. Frederick Williams & Dr. Luay Alessa

Time	Main Engineering Hall	Library Hall
10:15-10:30	Dr. Omar Abu Abed *Hebron University, Palestine.* Development and characterization of novel polymeric-based nanocapsules for oral delivery of insulin.	Prof. Naser Idkaidek *University of Petra, Jordan.* The use of saliva as a surrogate in drug BA/BE and TDM studies in humans.
10:30-10:45	Dr. Suhair Sunoqrot *Al-Zaytoonah University, Jordan.* Green synthesis of versatile nanoparticles from plant polyphenols: Case example of quercetin.	Dr. Abdulfattah Madi *Pharmacy Association, Libya.* Assessment of expired medicine in some healthcare and medical supply organization in Benghazi.
10:45-11:00		Dr. Rima Hajjo *Al-Zaytoonah University, Jordan.* Integrative informatics for drug discovery and biomarker prioritization.

11:00-12:30: Coffee Break & **Poster session*** (Hall 143).

Session (2):

Moderators:

Prof. Waleed Sweileh & Dr. Alaa Hammad Prof. Yusuf Al-Hiari & Dr. Ali Ibrahim

Time	Main Engineering Hall	Library Hall
12:30-12:45	Dr. Hatem Hejaz *Hebron University, Palestine.* Prevalence of depression among Palestinian adults with diabetes mellitus: A cross sectional study.	Prof. Reema Abu Khalaf *Al-Zaytoonah University, Jordan.* Antidiabetic sulfonamides: Synthesis, QPLD studies and biological evaluation.
12:45-13:00	Dr. Abdulla Naser *Isra University, Jordan.* Prevalence of chronic kidney diseases in patients with diabetes mellitus in the Middle East: A systematic review and meta-analysis.	Dr. Alaa' Al-Dajani *University of Petra, Jordan.* The antiemetic, domperidone, as an acrab-tolc inhibitor in multi-drug resistant *Escherichia coli.*
13:00-13:15	Dr. Iyad Ali *An- Najah National University, Palestine.* Drug–drug interaction in ICU patients: A retrospective study.	Dr. Waleed Zalloum *American University of Madaba, Jordan.* Interaction of zinc-bound tetrahedral gem-diolate trapoxin A with histone deacetylase 8: Conventional molecular dynamics simulation and umbrella sampling.
13:15-13:30	Dr. Saed Zyoud *An- Najah National University, Palestine.* Management of acute poisoning cases in emergency departments among various types of hospitals in Palestine.	Dr. Samar Thiab *Applied Science Private University, Jordan.* The development of analytical procedures for analysis and speciation of trace metals in pharmaceutical formulations.
13:30-13:45	Dr. Waleed Abu Rayyan *University of Petra, Jordan.* Effects of smoking and obesity on the serum levels of vitamin D3 in the central region of Jordan.	Dr. Murad Abualhasan *An- Najah National University, Palestine.* Evaluation of heavy metals and microbiological contamination of selected herbals from Palestine.
13:45-14:00	Dr. Walid Al-Qerem *Al-Zaytoonah University, Jordan.* Applicability of spirometry equations formulated in the Middle East and North Africa regions to a sample of Jordanian school aged children.	Dr. Dima Sabbah *Al-Zaytoonah University, Jordan.* N-substituted-4-hydroxy-8-methoxy-2-quinolone-3-carboxamides: Design, synthesis, and biological evaluation as PI3Kα inhibitors.

Session (2) (*continued…*):

Moderators:

Prof. Waleed Sweileh & Dr. Alaa Hammad Prof. Yusuf Al-Hiari & Dr. Ali Ibrahim

Time	Main Engineering Hall	Library Hall
14:00-14:15	Dr. Suhaib Hattab *An- Najah National University, Palestine.* Prescription trends and rate of interactions between psychotropic drugs in Palestine.	Dr. Muna Barakat *Applied Science Private University, Jordan.* Immunostimulatory effects of atmospheric pressure non-thermal plasma exposure on murine macrophages.
14:15-14:30		Dr. Adham Abu Taha *An- Najah National University, Palestine.* Prevalence and risk factors for extended spectrum beta-lactamase-producing uropathgens among patients in the governmental hospitals of North West Bank: A cross-sectional study.

14:30-16:00: Lunch.

*****Please display your poster in the hall 143 between 9:00-10:00 am, and remove your poster at 14:30-15:30, as we will not be responsible for any posters remaining in the hall after the poster session.

Index

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Conference Proceedings
The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan

A review of strategies for reducing air pollution in urban areas

Jonathan Ling, Nicola Hall, Monica Price, Stephanie Wilkie

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Background: Air pollution has a significant impact on health, especially in cities. There is strong evidence supporting the potential for the reduction of PM2.5, PM10, and NO2 to produce improvements in both circulatory and respiratory disease mortality and morbidity as well as a range of significant economic benefits. All three have an impact on circulatory diseases while NO2 has a more substantial impact on respiratory disease. This impact extends to other health outcomes including reduced all-cause mortality, fewer restricted activity days, and improved quality of life.

Aim: In this study, we review current evidence for proposed strategies to reduce these pollutants.

Methods: Findings were based on 52 review and primary studies published between 2015 and 2018.

Results and Conclusion: The results were broadly categorized into the impact on circulatory/respiratory disease of improved air quality through reduced PM2.5, PM10, and NO2 concentrations, the effectiveness of traffic management strategies to reduce these pollutants, and the effectiveness of interventions to change individual behaviors related to the production of or exposure to air pollution, as well as active transportation. The strongest potential was for air quality or information alerts to produce desired changes to behavior. We make several recommendations based on this review for the improvement of air quality in cities, which will improve circulatory and respiratory health, and deliver economic benefits.

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Conference Proceedings
The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan

The use of Casper zebrafish to study behavior and identify psychostimulant targets related methamphetamine

Frederick E. Williams[1], Alexander Wisner[2], Austin Horton[1], Ethel Tackie-Yarboi[1], Katelyn Hagood[1], Tue Chau[1], Frank Scott Hall[2], Isaac T. Schiefer[1]

[1]Department of Medicinal and Biological Chemistry, College of Pharmacy and Pharmaceutical Sciences, University of Toledo, Toledo, Ohio, 43614, United States of America.
[2]Department of Pharmacology and Experimental Therapeutics, College of Pharmacy and Pharmaceutical Sciences, University of Toledo, Toledo, Ohio, 43614, United States of America.

Background: Psychostimulatory drug abuse has happened in many cultures throughout history. Advances in chemical synthesis has led to a growing variety of synthetics based on common drugs of abuse like methamphetamine and 3,4 methylenedioxymethamphetamine (MA and MDMA, respectively). The current rate of creation of novel agents of abuse has far outpaced pharmacological evaluation and detection using current animal models. The zebrafish has become a widely known animal model for neurobehavioral research due to high throughput capabilities combined with a robust behavioral repertoire and advancing genetics.

Objectives: We used synthetic probes of methamphetamine and Casper zebrafish to assess behavioral effects of the probe and methamphetamine while attempting to identify targets by photo-affinity labelling using modern techniques in chemical biology.

Methods: Adult fish were exposed to equimolar concentrations of MA (5-65 mg/L) or a methamphetamine photo-reactive probe (MAP, 6-83 mg/L). Fish were transferred to a novel tank following exposure and behavior tracked followed by UV light induced labeling of binding partners. Afterwards, the brain was excised and preserved for analysis.

Results: A dose response relationship for MA and MAP was shown in the Casper line with respect to behavioral analysis with MAP and MA eliciting similar changes behaviorally in the novel tank test. In addition, gels of photo-affinity labeled proteins show concentration dependent increases in protein modification.

Conclusions: The results support the use of this model for *in vivo* target identification in neurobehavioral pharmacological research.

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Conference Proceedings
The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan

Acinetobacter baumannii infections: a 3–year hospital-based retrospective study

Sonia Sabra, Hadeel Abu Ghannam, Adham Abu Taha, Waleed Sweileh*

An-Najah National University, Nablus, Palestine.

Aims: The aim of this study was to investigate the clinical profile of ICU patients with *Acinetobacter baumannii* infection and to assess susceptibility profile of *A. baumanni*i to various tested antibiotics.

Method: Retrospective analysis of electronic data of patients admitted to An-Najah National University hospital during the study period from 2015 to 2017. All information regarding culture and sensitivity tests were extracted from the electronic data of the ICU unit.

Results: In total, 99 cases of positive *A. baumannii* cultures were identified during the study period. The mean ± SD age of the identified cases was 59.9 ± 18.8 (range: 15 – 87 years). The majority of cases were males (58; 58.6%). Out of 99 cases, 46 (46.5%) died. Approximately 75% of the cases had the infection during their stay in the hospital (nosocomial infections). Twenty-one different anti-microbial agents were tested against *A. baumannii.* Colistin was the most effective with 98.9% sensitivity. Tigecyline also showed high efficacy (75.9%) against *A. baumannii* but lesser than that recorded for Colistin. Other less effective antimicrobial agents included rifampin, minocycline, and co-trimoxazole. There was no significant association between sensitivity profile for the anti-microbial agents and the following variables: gender, age, health status, and number of comorbid diseases. However, there was significant association between sensitivity profile and time factor as well as source of infection.

Conclusion: Strict infection control policy and rational use of antibiotics are needed to control *A. baumannii* infections and reduce development of future resistance in *A. baumannii.*

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ISSN 0719-425

Conference Proceedings
The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan

Assessing individual medications in chronic kidney disease

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Background: Chronic kidney disease (CKD) is a major non-communicable disease and a leading cause of mortality. In CKD patients, the risk of multiple comorbidities and the wide range of debilitating symptoms affect the patient's quality of life. Pharmacological management is key in slowing disease progression, however due to the high pill burden, adherence becomes a problem. Unfortunately, most work assesses overall adherence to medication with the assumption that all medicines are taken similarly.

Aim: To compare between both overall adherence and adherence of individual medications in CKD patients.

Method: CKD patients were recruited from 10 hospitals across Malaysia. Overall adherence was assessed using a set of statements based on a one-month period of medication-taking, similar to normal practice (adherence score category: adherent if score $\geq$75%, non-adherent if score <75%). When assessed individually, patients were asked how often they forget to take each medication within a one-month period (adherence score category: adherent if score $\geq$ 80%, non-adherent if score <80%). In individual medication assessment, patients were then categorized as adherent, if they were adherent to all medications.

Results: A total of 491 patients were recruited. The average number of medications prescribed was found to be 7.0 ± 2.4, ranging from 1 to 14 medicines. Overall medication adherence was reported in 404 (82.3%) patients. When assessing individual medication adherence, a total of 135 patients (27.5%) were considered adherent to their medications. The number of patients that were adherent to medications was significantly lower when using individual assessments compared to an overall assessment (χ^2=40.1, df(1), p<0.01). Patients were mostly adherent to ACE inhibitors (n= 77, 89.5%), and least adherent to statins (n=120, 37.4%). The most common reason for non-adherence to ACE inhibitors was that the patient felt better (n=5, 55.6%), whilst for statins was because they forgot (n=100, 82.6%).

Conclusion: Current work suggests that adherence is probably lower than suggested in previous work, if individual medications are assessed. Pharmacists should identify new methods in determining adherence of medication to ensure effectiveness of pharmacological management.

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The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan

Designed fumigaclavine analogues as neuroprotective agents

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Background: Alzheimer disease (AD) is a neurodegeneration disease, anticipated to be the second cause of mortality by 2040. AD is demonstrated by recognition loss and dementia. In addition to the deficiency of acetylcholine release in neuronsynapse, there are other theories explain etiology of the disease. The most agreeable one is associated with accumulation of damaged proteins outside and inside neurocytes; β-amyloid Aβ and hyperphosphorylated tau, respectively. These protein aggregates may induce inflammatory responses leads to degenerations of neuronal tissue. Fumigaclavine is a marine fungus alkaloid acquires anticancer and a strong anti-inflammatory effect. Moreover, its structure has the requirements of acetylcholine esterase inhibition.

Methods: Seventeen analogues, derived from fumigaclavine structure, were synthesized. Basically, Heck and Mannich reactions were implemented to 4-bromo indole nucleus to generate a group of potentially active fumigaclavine analogues. The others were subsequently cyclized by utilizing nitromethane and zinc reduction procedures.

Results and Conclusion: Some of these compounds represented neuroprotective, neuronal anti-inflammatory and apoptotic activity against microglia, stronger than donepezil, which is the currently used anti-Alzheimer drug. They have also a noticeable acetylcholinesterase inhibitory activity. More than twelve molecular targets, attributed with AD etiology, were tested versus the synthesized compounds by *in silico* modeling. Docking scores of modeling were plotted against *in vivo* activity of the compounds. The one gave rise the strongest positive correlation was ULK-1, which has a significant role in neurocyte autophagy.

Optimization of the synthesized structures according to the poses of *in silico* modeling and *in vitro* results will be accomplished. *In vivo* testing is going to be carried out if promising candidates are obtained from *in vitro* testing against ULK-1.

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The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan

Vitamin D status in patients with type 1 and type 2 diabetes in Benghazi

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Background: Evidences from both animal and human study have reported that there is a relation between vitamin D deficiency and diabetes incidence. Furthermore, studies have shown that vitamin D has a role in beta cell activation and insulin sensitivity.

Aim: This research aimed to find out if there a relation between vitamin D and type 1 and 2 diabetes patients in Benghazi.

Methodology: A pilot study has been conducted at Benghazi Diabetes Center. Data were collected through structured questionnaires during the period (19 Nov 2017 to 1 March 2019). Questionnaires were filled by 192 patients. It includes age, gender, type of diabetes, vitamin D level, having another disease, and treatment. The collected data were analyzed by using Microsoft excel 2013.

Results: The total number of participants was 192 (96 type 1 and 96 type 2 diabetes). Most of patients were female 76 type 1 (T1D) and 60 type 2 (T2D). The majority of participants of both types of diabetes was at age over 60 years except males with T1D (51-60 years old). Regarding vitamin D level, all cases of both gender and type of diabetes have vitamin D level less than the target (31 ng/mL). Most of the cases have vitamin D level between 21-30 ng/mL. Females with T1D (13%) and T2D (17%) have serum vitamin D level < 5 ng/mL. Also, most of patients with T1D were prescribed vitamin D supplement. However, nearly 51% of females with T1D and T2D have cardiovascular diseases beside diabetes whereas 75% of males T1D have diabetes only. The percentage of hyperthyroidism cases was higher in T1D 25% of males and 12% females. Females of both types of diabetes have higher percentage of hyperlipidemia 11% T1D and 17% T2D then males.

Conclusion: The results have shown there might be an association between vitamin D level and diabetes especially in diabetic patients with cardiovascular disease and/or hyperlipidemia.

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Phytochemical investigation and diuretic activity of the Palestinian *Crataegus aronia* in mice using an aqueous extract

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Division of Physiology, Pharmacology and Toxicology, Faculty of Medicine and Health Sciences, An- Najah National University, Nablus, Palestine.

Background: Throughout history, various natural materials were used as remedies for treatment of various diseases, and recently a vastly growing and renewed interest in herbal medicine is witnessed globally. In Palestinian folk medicine, *Crataegus aronia* is used as a diuretic and for treatment of hypertension.

Aim: To assess the preliminary phytochemical properties and the diuretic effect of the aqueous extracts of this plant in mice after its intraperitoneal administration.

Methods: It is an experimental trial applied on mice [n=8, Male, CD-1, weight range: (25-30 g)], which are divided into two groups (4 in each). The first group administered with the plant extract (500 mg/kg), and the second with normal saline as negative control group. Then urine output and electrolyte contents were quantified up to 6 hours for the three groups and then compared to the control one.

Results: Preliminary phytochemical screening reveals the presence of tannins, alkaloids and flavonoids as major phytoconstituents in aqueous extract. Significant diuresis was noted in those received the aqueous extract of *Crataegus aronia* ($p<0.05$) compared to controls. Moreover, aqueous extract had an acidic pH and a mild increase in the electrolyte excretion (Na, K).

Conclusions: Our results revealed that *Crataegus aronia* aqueous extract has a potential diuretic effect. Further studies are needed to evaluate this diuretic effect in the relief of diseases characterized by volume overload.

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Multiparticulate pH triggered delayed-release chronotherapeutic drug delivery of celecoxib-β-cyclodextrin inclusion complexes by using Box-Behnken design

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Aim: The present study was aimed to develop novel colon targeted microparticles of celecoxib-β-cyclodextrin (CXB-β-CD) loaded Eudragit S 100 (ES100) microparticles for chronotherapy of rheumatoid arthritis (RA).

Methods: β-cyclodextrin was used to enhance the aqueous solubility of celecoxib (CXB) and ES100 was used as pH dependent polymer. CXB-β-CD loaded ES100 microparticles were fabricated by oil-in-oil emulsion solvent evaporation method. A three-factor three-level Box-Behnken design was used to optimize formulation variables. CXB was complexed with β-cyclodextrin by kneading method and analyzed by using saturation solubility studies. CXB-β-CD microparticles were characterized with respect to morphology, particle size, encapsulation efficiency and *in vitro* drug release studies. FTIR and XRD studies were performed to determine the interaction between the formulation components. DSC studies were also done to analyze the thermal stability of drug, polymers and formulation containing CXB-β-CD complex.

Results: SEM imaging revealed smooth, uniform and spherical shape microparticles. There was 5.73, 5- and 7.3-folds' increase in saturation solubility of CXB-β-CD inclusion complex in distilled water, phosphate buffer pH 1.2 and phosphate buffer pH 7.4, respectively. Particle size was in the range of 50.42 µm to 238.38 µm with entrapment efficiency in the range of 68.47% to 91.65%. Biphasic drug release pattern was found i.e. initially delayed release in stomach and small intestine followed by fast release at colonic pH with first order release kinetics and non-Fickian diffusion pattern.

Conclusions: This study concluded that CXB-β-CD loaded ES100 microparticles can be successfully fabricated with enhanced solubility for the chronotherapy of rheumatoid arthritis.

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Astrocytic glial glutamate transporters in the brain: Therapeutic targets for the treatment of drugs of abuse

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Ample evidence demonstrated the implication of glutamatergic system in drugs of abuse. Chronic exposure to several drugs of abuse can cause elevation in extracellular glutamate levels in several reward brain regions, including nucleus accumbens (NAc) and prefrontal cortex (PFC). Indeed, study from our laboratory showed that chronic alcohol exposure increased extracellular glutamate level in the NAc. Extracellular glutamate is regulated mainly by the astrocytic glutamate transporter 1 (GLT-1) as well as cystine/glutamate antiporter (xCT). Our laboratory showed that chronic exposure to alcohol, methamphetamine, cocaine, and nicotine downregulated the expression of GLT-1 and xCT in the NAc, PFC, amygdala, and hippocampus in rat models. Importantly, we reported that treatment with selected medications upregulated GLT-1 and xCT expression in several central reward brain regions and attenuated dependence to alcohol as well as relapse to alcohol-seeking behavior. These effects were associated with normalization of extracellular glutamate level in the brain. In addition, we reported that upregulation of GLT-1 and xCT expression attenuated reinstatement to cocaine seeking behavior. We further tested the upregulatory effects of these astrocytic transporters in other drugs of abuse. We demonstrated that upregulation of GLT-1 and xCT expression attenuated reinstatement to hydrocodone (opioid drug), cannabinoid receptor agonist (CP 55,940) and methamphetamine using conditioned place preference paradigm. Furthermore, we revealed that upregulation of the expression of GLT-1 and xCT attenuated the effects of exposure to higher doses of methamphetamine in the brain. This involved the attenuation of neurotoxicity that might be associated with excess of glutamate in the synaptic cleft of the brain. These studies from our laboratory and others demonstrated clearly that astrocytic glutamate transporters are considered major therapeutic targets for the treatment of addiction to drugs of abuse as well as treatment of neurotoxicity to certain drugs of abuse.

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Fusidic acid and sodium fusidate nanoemulgel development and antimicrobial activity evaluation

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Background: Fusidic acid (FA), sodium fusidate (SF) have problems in their skin penetration and stability resulting in reduction in their potency.

Aim: To developed FA and SF nanoemulgels to improve their antimicrobial activity.

Methods: FA and SF nanoemulgel formulations were prepared by incorporation of FA and SF nanoemulsions with Carbopol hydrogel. First the drugs were screen for their solubility in different oils and surfactants to choose the suitable oil and surfactants for the drugs, and then drugs nanoemulsion formulations were prepared by self-nanoemulsifying technique using Tween 80, Span 20 and pine oil. Drugs nanoemulgel were evaluated for their particle size, polydispersibility index PDI, rheological behavior, drug release and anti-microbial activity.

Results: Based on the solubility test pine oil, Tween 80 and Span 20 showed the highest solubilizing ability for both drugs. The optimum self-nanoemulsifying formulations showed particle size for FA and SF 140.58 nm and 151.86 nm respectively and both showed low PDI below 0.3. After incorporating both drug SNEDDS formulations with Carbopol at different concentration, the results of the drugs particle size and PDI showed no significant difference. Zeta potential results for both drugs nanoemulgel showed negative potential with more than 30 mV. All nanoemulgel formulations showed pseudo-plastic behavior with the highest release pattern at 0.4% Carbopol. The antibacterial activity of both drugs nanoemulgel formulations showed superiority over the market product.

Conclusion: Nanoemulgel is promising delivery system for FA and SF that helps in improving their stability and antimicrobial activities.

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Antibiotic resistance and microbiological profile of urinary tract infections in Palestine

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Aim: The aim of this study was to describe the frequency, microbiological profile, bacterial resistance, and the sensitivity to antibiotics of microorganisms causing urinary tract infection in six hospitals in Palestine.

Methods: A total of 2000 culture samples processed at the microbiology laboratories between 2005 and 2018, were analyzed for presence of bacteria and sensitivity to antibiotics. A sensitivity score was created by dividing the number of times antibiotics affected bacterial growth (bacteria was sensitive) over the total number of antibiotics tried for every culture.

Results: A total of 2000 samples for urine cultures (UC) were analyzed, of which 1581 were taken in women (79.05%) and 419 in men (20.95%), the age of the patients was between 1 day and 99 years. The major etiological agent was *Escherichia coli*, representing 56.22% followed by *Klebsiella* with 10.15%. The most frequently tested antibiotic was cefuroxime (1603 times) followed by amoxicillin/clavulanate (1588 times). Resistance to cefuroxime increased from 32% in 2005 to 46.4% in 2018, while resistance to amoxicillin/clavulanate increased from 16.9% to 45.6% between the same two years. Highest antimicrobial resistance was found for ampicillin (69.8%) and cloxacillin (65.4%). The sensitivity score decreased from 68.4% in 2005 to 66.8% in 2018.

Conclusions: Bacterial UTI persists as one of the most common infections affecting all age groups and both genders. As in other countries, *E. coli* was the major causative agent in Palestine with 56.22% of total cases. In general, resistance to most tested antibiotics increased over the study time period.

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Green synthesis of versatile nanoparticles from plant polyphenols: Case example of quercetin

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Background: Plant polyphenols have received considerable attention in recent years due to their ability to undergo oxidation-triggered self-polymerization, forming biocompatible coatings and templated nanoparticles (NPs) that could be leveraged for a variety of biomedical applications. Here we show that untemplated NPs can be green synthesized from the abundant plant polyphenol quercetin (QCT) as promising nanocarriers for drug delivery, imaging, and cosmetics.

Methods: NPs were synthesized by oxidation-triggered self-polymerization of QCT by simple mixing with oxidizing agents or under basic conditions. NPs were characterized by UV-Vis, FT-IR, ^{1}H-NMR, and X-ray photoelectron spectroscopy (XPS), and by dynamic light scattering (DLS) and transmission electron microscopy (TEM) to understand their physicochemical properties. Antioxidant and cell viability assays were also conducted to demonstrate the NPs' free-radical scavenging activity and biocompatibility. Tumor targeting potential of drug-loaded NPs was evaluated by *in vivo* imaging and flow cytometry.

Results: NP size was highly dependent on the synthetic conditions and the incorporated cargo. QCT NPs could accommodate hydrophobic and hydrophilic drug molecules as well as surface ligands such as poly(ethylene glycol) (PEG). PEGylation was confirmed by DLS and XPS. Antioxidant activity and biocompatibility support the use of the NPs as dermal UV protective agents. Drug-loaded NPs were readily internalized by cancer cells *in vitro* and demonstrated sustained drug release and potent cytotoxicity. Moreover, *in vivo* imaging of tumor-bearing mice and ex vivo analysis of tumor homogenates following tail vein injection of labeled NPs showed significant tumor accumulation of the NPs up to 24 h.

Conclusion: Our findings present a promising new application for naturally occurring polyphenols as a renewable source of versatile nanocarriers that can be synthesized at low cost with minimal equipment.

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Integrative informatics for drug discovery and biomarker prioritization

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Background: Informatics approaches allow the exploration of big drug discovery data resulting from large-scale gene or protein expression or metabolite profiling to identify networks of genes (or proteins) that may collectively define a disease phenotype, and aid in the drug and biomarker prioritization.

Aim: Herein, we developed and applied a novel integrative informatics workflow to predict clinically relevant biomarkers and drugs targets for Alzheimer's disease.

Methods: Our workflow included several *in silico* approaches that integrate 'omics' data mining from NCBI's Gene Expression Omnibus, the prioritization of disease gene signatures, and the analysis of disease pathways and networks.

Results: Preliminary results led to the prioritization of tens of promising Alzheimer's-tracking biomarkers and drug targets that were significantly up- or down- regulated in Alzheimer's disease patients. Unbiased enrichment analyses highlighted several kinases and chemokine receptors. Biased knowledge-based analyses focusin on neurological disorders reduced the initial hit list into 10 higher confidence, clinically relevant, biomarkers and drugs targets (including LRRK2, BDNF and CXCR4).

Conclusion: These final hits should serve as computational hypotheses awaiting their experimental validation.

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Antidiabetic sulfonamides: Synthesis, QPLD studies and biological evaluation

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Background and Aim: Diabetes mellitus is considered a great worldwide health problem that presently affect 425 million people and expected to affect more than 690 million people by 2045. Dipeptidyl peptidase-IV (DPP-IV) inhibitors are new hypoglycemic agents boosting incretin hormones activity, which encourage insulin secretion from beta cells of pancreas.

Methods: In the current work, synthesis of seven piperazine sulfonamides **3a-3g** was carried out. The synthesized compounds were characterized using ^{13}C-NMR, ^{1}H-NMR and IR. *In vitro* biological study displayed similar inhibitory activities against DPP-IV enzyme ranging from 19%-30% at 100 µM concentration. Moreover, *in vivo* hypoglycemic activity of compound **3d** was assessed using streptozotocin-induced diabetic mice.

Results: It was observed that **3d** significantly decreased blood glucose level when compared to saxagliptin. QPLD studies found that the synthesized compounds fit the binding site of DPP-IV and form H-bonding with R125, E205, E206, K554, W629, Y631, Y662, R669, and Y752.

Conclusion: Piperazine derivatives were found to be a successful new scaffold for DPP-IV inhibition.

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Prevalence of chronic kidney diseases in patients with diabetes mellitus in the Middle East: A systematic review and meta-analysis

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Background: Diabetes mellitus is a major risk factor for chronic kidney diseases (CKDs). Chronic kidney diseases increase the risk of morbidity and mortality as a result of cardiovascular complications and may progress to end-stage renal diseases. The prevalence of CKDs in patients with diabetes mellitus in the Middle East region is unclear.

Aim: To review the existing literature on the prevalence of CKDs in patients with diabetes mellitus in the Middle East region.

Methods: PubMed, EMBASE and Cochrane Review databases were searched for relevant studies up to January 2019. The search strategy was conducted using both keywords and MeSH terms. Following PRISMA guidelines, two reviewers independently screened articles, extracted data and assessed the quality of the included studies. Randomized controlled trials (RCTs) and observational studies including patients from all age groups, and any study design related to the prevalence of CKDs in patients with diabetes mellitus were included in the review. Pooled estimate for the prevalence of CKDs in patients with diabetes were calculated using random effect models with 95% confidence intervals (CI).

Results: A total of 489 citations were identified of which only 3 studies matched our inclusion criteria and were included in this review. The three studies were of an observational study design (two retrospective and one prospective study), covering a total of 57,122 patients with type 2 diabetes mellitus aged 25 years and above. The pooled estimate of the prevalence of CKDs in patients with diabetes mellitus was 25.4% (95% CI, 8.1 – 42.8).

Conclusions: The findings of this review highlighted that there is a lack of studies on the prevalence of CKDs in patients with diabetes mellitus in the Middle East region. Further epidemiological studies are required to investigate the prevalence of CKDs among patients with diabetes mellitus.

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The antiemetic, domperidone, as an AcrAB-TolC inhibitor in multi-drug resistant *Escherichia coli*

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Background: Antibiotics attack bacteria and inhibit their growth by different mechanisms. The majority of antibiotics target molecules inside the bacterial cell, therefore their permeability to reach these targets is essential for their actions. However, bacteria are defending themselves against antibiotics by different techniques, one of these mechanisms is the over expression of efflux pumps, which usually results in multi-drug resistant (MDR) strains of bacteria.

Aim: In this work, we focused on countering the MDR effect of the over expressed AcrAB-TolC pump, an RND efflux pump, in *Escherichia coli* (*E. coli*).

Methods: Ligand docking, and virtual high-throughput were used in search for safe and effective AcrAB-TolC inhibitor.

Results: Domperidone, a known and safe antiemetic drug, showed highly promising *in silico* results. Microbiological testing was performed in AcrAB-TolC over expressing *E. coli* strains. The use of domperidone was found to improve the susceptibility of the MDR bacteria to the antibiotics, levofloxacin and ciprofloxacin.

Conclusion: This result is promising to promote the use of antibiotic-domperidone combination clinically to treat MDR infections.

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Drug-drug interaction in ICU patients: A retrospective study

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Aim: The purpose of this study was to determine the frequency, severity of drug combinations involved in DDIs during hospitalization at ICU. Moreover, making the medical staff more aware of the potential effects of DDIs, which will increase the patient's safety and decrease overall morbidity and mortality.

Methods: This study was conducted retrospectively in three hospitals, including governmental and nongovernmental hospitals in Nablus city, Palestine. The duration of the study was 6 months, started in Jan 2018 up to June 2018. The sample size included 232 ICU patients and the collected data was used to assess the type of severity and the frequency of drug-drug interactions using drug.com android application.

Results: The number of patients that had potential drug-drug interactions was 167 (72%). Whereas, the total number of potential drug-drug interactions in the study was 442. Out of the total potential drug-drug interactions identified, we recorded 9.5% (40) of DDI were major drug-drug interactions, 66.6% (283) were moderate drug-drug interactions and 23.9% (101) were minor drug-drug interactions.

Conclusions: It has been found that the ICUs in the Palestinian hospitals do not pay enough attention to identifying all possible drug-drug interactions. None of the hospitals has the computerized software, which are easily accessible, for assessing DDIs. Therefore, it is recommended to start using application for assessing DDIs and train medical staff to use such applications.

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Interaction of zinc-bound tetrahedral gem-diolate trapoxin A with histone deacetylase 8: Conventional molecular dynamics simulation and umbrella sampling

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Background: Targeting the genetic material without its destruction is a priority to develop safe anticancer drugs. One of the recent drug targets is epigenetic enzymes which control the transcription of genes, where they could be targeted without interfering with the gene itself. Histone deacetylase 8 enzyme (HDAC8), which is proved to be involved in carcinogenesis, is one of the enzymes associated with the chromatin for post-translational deacetylation of lysine residue.

Methods: In this study, HDAC8 co-crystallized with the intermediate state tetrapeptide trapoxin A (TA) inhibitor and the holoenzyme are utilized to find their conformational ensembles. Also, the co-crystallized intermediate gem-diolate trapoxin A was used to find optimum interaction with the active site by conventional molecular dynamics simulation and umbrella sampling.

Results: This research showed that HDAC8 is flexible and exists in conformational ensembles in its holoenzyme state. Binding of the intermediate state of the inhibitor stabilizes it. Furthermore, umbrella sampling showed the optimum binding of the intermediate of trapoxin A inhibitor to HDAC8 with a distorted octahedral geometry.

Conclusion: Results of this study will be used to design inhibitors mimicking the intermediate state of the inhibitor for improved selectivity and potency.

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Effects of smoking and obesity on the serum levels of vitamin D3 in the central region of Jordan

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Aim: The aim of this study is to determine the levels of vitamin D3 in the province of Russeifa-Jordan and to clarify the effect of demographic variables on vitamin D3 concentration.

Method: A cross-sectional study was conducted in the period of April 2016 up to August 2018 in Al-Russeifa, Jordan. Two hundred and seventy-eight subjects were enrolled in this study; 211 females and 67 males, among them 168 nonsmokers and 110 smokers.

Results: Vitamin D3 levels ranged from 2 to 36 ng/mL with a mean of 17.37 ± 7.23 ng/mL. Ages ranged from one year to 80 years with a mean of 36.3 ± 12.7. Vitamin D3 levels were higher in males than females 19.11 ± 7.399 and 16.82 ± 7.110 ng/mL, respectively. 75% of the study population suffered from insufficiency, 20% were obeying sever deficiency levels and only 5% showed sufficient levels of vitamin D3. Negative correlation was demonstrated between smoking, BMI and vitamin D3 serum levels ($r= -0.324$, $p<0.01$) ($r= -0.229$ $p<0.001$), respectively.

Conclusion: Smoking, age, and BMI are inversely associated with low levels of vitamin D3 in the Jordanian population.

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Evaluation of heavy metals and microbiological contamination of selected herbals from Palestine

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Background and Aim: Herbal medicine is widely used for prevention and treatment of diseases worldwide including Palestine and may require long term usage. The level of some heavy metals and microbial contaminants in some of these medicinal plants consumed by Palestinians were studied in order to evaluate their quality.

Methodology: The level of metals like zinc, cadmium, lead and copper were quantified by atomic absorption spectrophotometry. Moreover, the bacterial and fungal contamination was determined for the dried powdered of the selected plants. All of our procedures are done under USP technique.

Result: The result of the heavy metals showed that copper and cadmium were above the allowable limits in all the tested plant. And zinc metal was above the allowable limit in 78.9% of the tested samples. The microbiological results of the tested plants revealed that 63.2% of it was contaminated by bacteria, and 89.5% contaminated by yeast.

Conclusion: Herbal used in the Palestinian markets doesn't meet the international requirement of heavy metal and microbiological limits. Thus, an urgent action has to be taken by the responsible such as implementing importation and registration requirements and performing regular quality check of sold and imported herbal.

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Applicability of spirometry equations formulated in the Middle East and North Africa regions to a sample of Jordanian school aged children

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Background: Choosing the right spirometry reference equations is essential to accurately interoperate the spirometry results.

Aim: To evaluate the most suitable regional equation for a sample of Jordanian children.

Methods: spirometry was conducted for 582 (311 boys) healthy 6-13 years old Jordanian children. z-scores, predicted values, percent predicted values and frequency of records below lower limit than normal (LLN) were calculated for each child using the studied equations.

Results: None of the studied equation produced a perfect representation of the study data.

Conclusion: There is an urgent need to generate Jordanian specific spirometry reference values to improve respiratory care among Jordanian children.

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N-substituted-4-hydroxy-8-methoxy-2-quinolone-3-carboxamides: Design, synthesis, and biological evaluation as PI3Kα inhibitors

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Background: Phosphoinositide-3-kinase α (PI3Kα) has been intensively investigated as a promising target for anticancer drug design and development.

Aim: Target compounds were designed to investigate the effect of introducing a methoxy moiety on quinolone-3-carboxamide scaffold to elucidate their structure-activity relationship (SAR) and improve their biological activity as anticancer compounds.

Methods: Chemical synthesis of the targeted compounds, biological evaluation tests against human colon adenocarcinoma (HCT-116) and human epithelial colorectal adenocarcinoma (Caco-2) cell lines, as well as Glide docking studies.

Results: A series of *N*-substituted-4-hydroxy-8-methoxy-2-quinolone-3-carboxamides (6a-h) was synthesized and characterized by FT-IR and NMR (^{1}H and ^{13}C). The prospective compounds inhibited the proliferation of human colon carcinoma (HCT-116) cell line. Compound functionalized with *p*-OH (6f) (IC_{50} = 218 μM) showed promising activity implying that H-bond acceptor and/or donor mediates ligand/PI3Kα complex formation. Compounds tailored with *o*- (6c) (IC_{50} = 231 μM) and *p*-F (6e) (IC_{50} = 238 μM) exerted higher activity interrogating H-bond acceptor drives ligand/PI3Kα interaction. The induced-fit docking (IFD) against PI3Kα demonstrates that the series accommodates PI3Kα kinase binding pocket and form H-bonds with key binding residues.

Conclusion: The series exerted a potential PI3Kα inhibitory activity in human carcinoma cell lines expressing PI3Kα.

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Prescription trends and rate of interactions between psychotropic drugs in Palestine

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Background and Aim: The aim of the study was to identify the pattern of prescribing psychotropic drugs for the treatment of five major psychiatric diseases in a governmental public psychiatric clinic in Palestine. In addition, we ought to investigate the rate of potential drug interactions within prescriptions made.

Methods: This was a retrospective; cross-sectional study. We targeted a cohort of all prescription orders made by the governmental psychiatric clinic in Nablus, West Bank, Palestine over the period from October 2018 to January 2019. The prescriptions which were issued for patients diagnosed with five major psychiatric disorders namely schizophrenia, depression, anxiety, bipolar and schizoaffective disorders were included in the study. These prescriptions were analyzed for the groups of medications ordered and checked for the presence and grade of potential drug interactions by entering the drugs listed in the prescriptions to "Medscape drug interactions checker".

Results: A total of 1079 prescriptions for psychotropic drugs were issued. The mean age of the patients was 47 years (SD= 13.6) and two-thirds of the patients were males (693 males vs. 386 females). Fifty-two percent of the patients were diagnosed with schizophrenia while 16% were diagnosed with depression. The later third was diagnosed with bipolar, schizoaffective and anxiety disorders (15%, 11% and 5% respectively). We found that 900 patients (83%) were prescribed more than one drug, and drug-drug interactions (DDIs) were identified in 842 (78%) prescriptions. These DDIs were classified as minor [4 (0.4%)], significant [437 (52%)] and serious [401 (47.6%)].

Conclusions: This study found that psychotropic drugs are not well prescribed and the potential for harmful DDIs is high. These results highlight the need for the implementation of pharmaco-vigilance units in psychiatric clinics in Palestine.

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Immunostimulatory effects of atmospheric pressure non-thermal plasma exposure on murine macrophages

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Background: Atmospheric pressure non-thermal plasmas (APNTP) exhibit marked biological effects and potentially widespread applications. One emerging application of APNTP is immune modulation, which has mainly been described as a potential adjunct to cancer therapy.

Aim: To examine the ability of APNTP to stimulate RAW264.7 murine macrophages and their phagocytosis of foreign bodies.

Methods: RAW 264.7 cells were exposed to a kHz-driven plasma jet in culture medium (indirect treatment) for different exposure times. Pro-inflammatory cytokine (TNF-α, IL-6) concentrations were measured in plasma treated cell supernatants using ELISA. Plasma-induced phagocytosis was examined using flow cytometric analysis and fluorescent imaging following incubation of the plasma exposed macrophages with fluorescent latex-carboxylate modified polystyrene beads (diameter 0.5 μm) and pHrodo™ red bioparticles®.

Results: The ELISA results revealed a significant stimulatory effect, as measure by a significant increase in expression of both TNF-alpha and IL-6, evident after 15 s of macrophage exposure to plasma. However, the optimum stimulatory activity was observed following 60 sec of plasma treatment. Flow cytometric data demonstrated plasma-induced enhancement of macrophage phagocytosis of both types of beads, following 15 second and up to 60 seconds of plasma exposure time.

Conclusion: APNTP elicited a promising stimulatory effect in immune cells, which could be used in future for management of bacterial infection.

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Antidiabetic therapy de-intensification from a physician perspective and factors affecting their prescribing: A cross-sectional study

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Background: There are limited guidelines that address antidiabetic therapy de-intensification in order to decrease the burden of its associated hypoglycemic events. The high prevalence of inappropriate intensive antidiabetic therapy has increased the importance of investigating physicians' perspectives towards this approach, including their decision to individualize their treatment goal, de-intensify antidiabetic therapy, and factors which affect their prescribing.

Aim: This study aims to understand the physicians' perspective regarding antidiabetic therapy de-intensification and factors that affect their prescribing for patients with type 2 diabetes mellitus (DM).

Methods: A cross-sectional survey study was conducted using a self-administrated questionnaire from January 2018 to January 2019 in Saudi Arabia. Two previously validated questionnaires, one developed by Genere and the other by Grant, were adopted and used in this study. Univariate/multivariate logistic regression was used to assess the relationship between physicians' demographic and practice characteristics and their awareness of, agreement with and practice of HbA1c individualization and their practice of antidiabetic therapy deintensification.

Results: A total of 205 physicians have participated in the study. The findings of this study showed that the majority of the physicians reported that they were familiar with the principle of antidiabetic therapy de-intensification (89.3%, n =183), and agreed with it (68.2%, n = 118). However, only 78.6% of them reported that they were applying it frequently. In addition, this study highlighted factors considered while prescribing antidiabetic medications and showed that physicians reported giving more importance to patients' medical profiles such as comorbidity, last measured HbA1c level, and physician's assessment of patient's health status rather than other variables like patients adherence, preference to delay or avoid therapy, or specific requests with regards to their therapy.

Conclusions: It is suggested that healthcare professionals should pay more attention to other non-clinical factors as they are associated with better adherence and disease control.

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Longitudinal pharmacodynamic effect of gliclazide on glycated hemoglobin in patients with type 2 diabetes

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Background: Diabetes is a global health issue that affects more than 425 million people and is expected to affect over 690 million people by 2045.

Aims: 1) To quantify longitudinal glycemic response to gliclazide (GLC) therapy in type 2 diabetic patients using population pharmacodynamic modeling. 2) To identify patients, characterize associated with glycemic response to GLC.

Methods: We conducted a population pharmacodynamic analysis with covariate screening analysis. Nonlinear mixed effects modeling approach was implemented. First, we described the longitudinal change in hemoglobin A1C (HbA1c) and Fasting Plasma Glucose (FPG) without including patients' characteristics as covariates. This was followed by multiple linear regression between individual Emax values and various covariates. Finally, significant covariates identified with multiple linear regression were included in the final pharmacodynamic model using backward deletion approach.

We quantified longitudinal change in HbA1c and FPG levels in response to GLC therapy in type 2 diabetic patients using population pharmacodynamic modeling. We also identified patient characteristics associated with glycemic response to GLC. Baseline FPG and lymphocyte count were identified as significant covariates that affect glycemic response to GLC.

Results: Longitudinal change in HbA1c and FPG following GLC therapy was described using a mechanistic pharmacodynamic model. Having a higher baseline FPG was associated with increased magnitude of reduction in HbA1c overtime resulting from GLC therapy. Having a higher baseline lymphocyte was associated with smaller reduction in HbA1c.

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Attitudes and perceptions towards hypoglycemia in patients with diabetes mellitus: A multinational cross-sectional study

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Background: Patients' knowledge and attitude towards their disease plays an important role in the success of diabetes management and prevention of disease development and complications.

Aims: To explore hypoglycemia problem-solving ability of patients who have diabetes mellitus and factors, which determine their attitudes and perceptions towards their previous events.

Methods: A cross-sectional study was conducted in three Arab countries (Jordan, Saudi Arabia, and Kuwait) in patients with diabetes mellitus, who were prescribed antidiabetic therapy and had experienced hypoglycemic events in the past six months, for the duration between October 2017 and May 2018. The hypoglycemia ProblemSolving questionnaire was used in this study. This questionnaire contains two subscales; problem orientation (6-questions) and problem-solving skills (18-questions), using 5-point Likert scale (range 0 – 4). Multiple linear regression analysis was used to identify predictors of hypoglycemia problem-solving abilities.

Results: A total of 895 patients have participated in this study from the three countries (300 from Jordan, 302 from Saudi Arabia, and 293 from Kuwait). The mean patient age was 53.5 (SD= 13.7) years, of which 52.4% (n= 469) were males. Around 10.4% (n= 93) of the patients had a previous history of severe hypoglycemia that lead to admission during the past 6 months. Patients had moderate overall problem-solving ability with a median score of 63.00 (IQR = 13.00). Patients had better problem-solving skills score, 68.1% compared to problem-orientation skills score, 58.3%. The highest sub-scale scores were for detection control, setting problem-solving goals, and evaluating strategies, 75.0%. The lowest sub-scale score was for problem-solving perception and immediate management, 50.0%. Older age, being educated, married, having T2DM, prescribed insulin therapy, and not admitted to hospital for hypoglycemia were important predictors of patients problem-solving ability ($p<0.05$).

Conclusions: Healthcare professionals advised to educate patients more on how to selfmanage their hypoglycemic events; specifically, they should focus on the overall problem-solving perception of hypoglycemia, and its immediate management.

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The cost of hospitalization and length of stay due to hypoglycemia in patients with diabetes mellitus: A cross-sectional study

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Background: hypoglycemia in patients with diabetes mellitus (DM) is a frequent and costly adverse drug event. There have been no studies in the Middle East countries that estimate the hospitalization cost and length of stay due to hypoglycemia in patients with DM.

Aims: To estimate hospitalization cost and length of stay due to hypoglycemia, and to identify determinants of variation in hospitalization cost and length of stay among patients with diabetes mellitus.

Methods: a cross-sectional study was conducted in Jordan using inpatients records of two private hospitals for patients with diabetes mellitus, who have been hospitalized due to hypoglycemia between January 2009 and May 2017. All hospitalization costs were inflated to costs in 2017. Hospitalization cost was estimated from patient's perspective in Jordanian dinars patient's multiple linear regression analysis was used to identify predictors of hypoglycemia hospitalization cost and length of stay.

Results: A total of 126 patients with diabetes mellitus were hospitalized due to hypoglycemia. The mean patients age was 64.2 (SD = 19.6) years old, of which half were male. The median length of hospital stay was two days (IQR = 2 days). The median cost of hospitalization for hypoglycemia was 163.2 JOD ($230.1) (IQR = 216.3 JOD, $305.0). Patients who had a family history of diabetes mellitus had higher hospitalization cost and longer length of stay (0.306 and 0.275, $p<0.05$). Male patients and patients who were without smoking history had longer length of stay (0.394 and 0.456, $p<0.01$).

Conclusions: Hospitalization due to hypoglycemia among patients with diabetes mellitus represents a substantial economic burden within hospital settings. Healthcare professionals should give more attention to this adverse drug event to decrease the burden of its associated cost.

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Effect of SAMe-TT2R2 score on predicting the quality of anticoagulation control in Qatari patients treated with warfarin

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Background: Warfarin is the most commonly used oral anticoagulant for the treatment and prevention of thromboembolic disorders. SAMe-TT_2R_2 score is a simple clinical-derived score developed to aid decision-making on whether to start the patient on warfarin or direct oral anticoagulant and whether or not a patient is likely to achieve good anticoagulation control on warfarin.

Aim: To identify the ability of SAMe-TT_2R_2 to predict the level of INR control by measuring time in therapeutic range (TTR) at the maintenance phase (post first month of treatment) in a cohort of Qatari patients.

Methods: An observational case-control study. The SAMe-TT_2R_2 score was studied on cohort Qatari patients treated with warfarin at Hamad Medical Corporation related. TTR using Rosendaal method was measured to assess the level of anticoagulation control. 148 patients were included in the study who attended the clinic from 01/01/2017 to 31/12/2017.

Results: None of the factors in the SAMe-TT_2R_2 score had a significant effect on the TTR except for the female gender where TTR was significantly lower in females (n=89) compared to male (n=59) (59.6 ± 21% vs. 67.2 ± 20%, p = 0.03). Furthermore, patients with SAMe-TT_2R_2 score (0,1) had significantly better TTR compared to those with higher score (76.5 ± 17% vs. 61.8 ± 21%, p=0.04).

Conclusion: The SAMe-TT_2R_2 was modestly associated with TTR in a cohort of Qatari patients. SAMe-TT_2R_2 score ≥ 2 was consistent with poorer TTR. Anticoagulation with warfarin is more likely to be less effective, and, thus, the use of direct oral anticoagulants should be considered in patients with SAMe-TT_2R_2 score ≥ 2.

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Structure-based design: synthesis and biological evaluation of n-substituted-4-hydroxy-6-methoxy-2-quinolone-3-carboxamide derivatives as PI3Kα inhibitors

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Background: Phosphatidylinositol 3-kinase α (PI3Kα) has been highlighted as a hot target for anticancer drug design.

Aim: Target compounds were designed to probe the effect of bearing a methoxy moiety on quinolone-3- carboxamide scaffold to elaborate their structure-activity relationship (SAR) and improve their biological activity as anticancer compounds.

Methods: Chemical synthesis of the targeted compounds, biological evaluation tests against human colon adenocarcinoma (HCT-116) and human epithelial colorectal adenocarcinoma (Caco-2) cell lines, as well as induced-fit docking (IFD) studies.

Results: A series of *N*-substituted-4-hydroxy-6-methoxy-2-quinolone-3-carboxamides was designed and synthesized as potential PI3Kα inhibitors employing structure-based drug design and molecular docking approach. The synthesized compounds were characterized using FT-IR and (^{1}H and ^{13}C) NMR analysis technique. Biological studies in human colon carcinoma (HCT116) cell line showed that the analogues **5**, **7-12** exhibited antiproliferative activity against PI3Kα. Compound tailored with *p*-OH (**10**) exerted promising activity interrogating that H-bond acceptor and/or donor mediates ligand/PI3Kα complex formation. Extension of the carboxamide linkage with one carbon (**11**) enhanced the activity implying that **11** orientated deeply in the binding pocket.

The induced-fit docking studies against PI3Kα demonstrated that the derivatives accommodate PI3Kα kinase catalytic domain and form H-bonding with the key binding residues. Our results suggest that further optimization of this series would be beneficial for colon cancer treatment.

Conclusion: The series exhibited a potential PI3Kα inhibitory activity in human carcinoma cell lines encoding PI3Kα.

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Penetration of gold nanoparticles through blood brain barrier and their accumulation into the brain: Effect of nanoparticles' shape and surface chemistry

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Background: Blood brain barrier (BBB) is a very selective barrier that protects the brain and the central nervous system (CNS) from the entry of harmful substances and help regulate the exchange of different molecules and nutrients from and into the brain and the CNS. This selectivity makes delivering therapeutic and diagnostic materials across the BBB very challenging.

Aim and Methods: In this study, different shapes and sizes of gold nanoparticles (GNPs) were synthesized and functionalized with five different thiolated ligands to acquire GNPs with various surface chemistry. GNPs of different sizes, shapes and surface modifications were injected intraperitoneally (IP) into laboratory mice.

Results and Conclusion: Gold nanorods (GNRs) functionalized with 4-mercaptophenol showed the highest penetration ability across the BBB with no significant toxic effect on brain tissue. However, slight toxic features were observed upon histology examination of spleen and liver tissues. The size and shape of GNPs have detrimental effect on the penetration ability of GNPs across the BBB. Gold nanospheres demonstrated high deposition percentages into different organs compared to the rod counterparts. Large GNRs revealed less accumulation into the brain, however their accumulation into the liver and spleen was maximized. GNPs could be a promising candidate for enhancing brain delivery across the BBB.

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Synthesis of antioxidant nanoparticles from coffee bean extracts

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Background: Plant polyphenols have attracted attention in recent years due to their ability to undergo oxidation-triggered self-polymerization, enabled by the presence of multiple oxidizable hydroxyl groups, forming biocompatible nanoparticles (NPs) for various biomedical applications.

Aim: To investigate whether the polyphenol-rich coffee bean extracts could also serve as a natural source of raw materials for NP synthesis.

Methods: Ground Arabica beans (green/unroasted, medium-roasted, and dark-roasted) were obtained from a local shop. Extracts were prepared by heating the ground beans in water at 50 °C with or without the addition of different oxidizing agents followed by filtration. The extracts were characterized by measuring their total phenol content and antioxidant activity. Characterization was also performed by UV-Vis and FT-IR spectroscopy, dynamic light scattering (DLS), and transmission electron microscopy (TEM).

Results: All coffee bean extracts were found to contain similar polyphenol content ranging from 3.5 – 4.4 mg gallic acid equivalents/g. They also exhibited comparable antioxidant activity. Importantly, particle size measurements by DLS and TEM revealed that all extracts spontaneously formed spherical NPs even without the addition of an oxidizing agent. Adding the oxidizing agent caused a significant change in NP size and size distribution, which also varied according to the degree of roasting. Although some antioxidant activity was lost after synthesis, the NPs still maintained significant antioxidant activity.

Conclusions: Our findings provide important insights into the versatility of polyphenols found in coffee beans as a novel source of nanoscale carriers that can be synthesized from readily available resources.

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Effect of warfarin indication on SAME-TT2R2 score prediction ability and quality of anticoagulation control in Qatari patients

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Background: Warfarin therapy is fundamental for the prevention of thromboembolic events in atrial fibrillation (AF) patients. Limited studies globally have shown the ability of SAMe-TT_2R_2 to predict INR control in AF patients. However, it is not well known if this score can still predict INR control in other indications.

Aim: To assess the ability of SAMe-TT_2R_2 risk score at predicting the control of warfarin in AF patients compared to other population on warfarin. We also aim to compare the quality of INR control in AF versus other warfarin indications

Method: In a retrospective observational case-control study, 149 Qatari patients on warfarin were enrolled. Patients were classified as AF vs. other indication. Quality of warfarin control was assessed as the percentage time to the therapeutic range (TTR) as well as percentage visits in range, over a follow-up of 1 year. P-value of 0.05 was considered statistically significant. Ethical approval was approved from QU-IRB and HMC.

Results: Among the 149 patients, 96 (64.4%) had AF while 53 (35.6%) had other indications including DVT, PE and valve replacement. SAMe-TT_2R_2 did not have an impact on TTR in neither AF (68 ± 19 in those scoring <2 vs. 64 ± 21 in those scoring higher, p=0.6 or the other indications (60 ± 23 in those scoring <2 vs. 57 ± 20 in those scoring higher, p=0.3). While TTR was not different across AF and other indication, % visits in range were higher in AF vs other indications (62.5 ± 18 vs. 53 ± 17, p=0.003) SAMe-TT_2R_2 score was 1.75 in AF population vs.1.96 for the other indication.

Conclusion: SAMe-TT_2R_2 score did not predict the quality of INR control in neither AF nor other indications in a cohort of Qatari population. Quality of INR control was better in AF compared to other indications. Indications other than AF may require more rigorous follow up during their course of warfarin anticoagulation.

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Development and optimization of a polymeric nanoparticle formulation for thymoquinone

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Background: Nanotechnology has provided promising solutions to address the pharmaceutical challenges of poorly water-soluble drug molecules.

Aim: To develop a novel nanoscale formulation for thymoquinone (TQ), a water insoluble natural compound isolated from *Nigella sativa* that has demonstrated promising chemopreventive and chemotherapeutic activity.

Methods: TQ-encapsulated nanoparticles (NPs) were prepared by nanoprecipitation using poly(ethylene glycol)-b-poly(ε-caprolactone) (PEG-PCL) copolymer with varying PCL chain lengths. NPs were in the form of nanospheres (NS; matrix-like NPs) or castor oil-filled nanocapsules (NC; core/shell NPs). The formulations were characterized by Dynamic Light Scattering (DLS) and High-Performance Liquid Chromatography (HPLC) to evaluate their particle size, polydispersity, and drug loading efficiency.

Results: TQ-NC formulations exhibited significantly higher particle size (163 – 167 nm) compared to TQ-NS formulations (92 – 94 nm) due to the presence of the oil-filled core, regardless of the PCL chain length. NC formulations were also associated with greater homogeneity, achieving polydispersity indices (PDI) between 0.14 – 0.16, compared to NS formulations with PDI between 0.21 – 0.25. Notably, drug loading capacity measured by HPLC was significantly improved in TQ-NC formulations, reaching 58.7 – 60.1% encapsulation efficiency, compared to only 24.0 – 26.3% encapsulation efficiency for TQ-NS formulations.

Conclusions: Our results indicate that oil-filled NC is a more suitable nanoformulation for TQ to carry out future *in vitro* release and biological assays.

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Development of a polymeric nanoformulation for cirsiliol isolated from Jordanian *Teucrium polium* L.

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Background: Cirsiliol (CIR) is an abundant bioactive plant flavonoid, which has been shown to exhibit inhibitory activity against phosphatidylinositol-3-kinase (PI3K), an enzyme implicated in many cancer types.

Aim: To develop a novel polymeric nanoscale platform for CIR extracted from Jordanian *Teucrium polium* L. to enhance its biopharmaceutical properties.

Methods: CIR-loaded nanoparticles were prepared by nanoprecipitation in the form of core-shell nanocapsules (NC) using poly(ethylene glycol)-b-poly(ε-caprolactone) (PEG-PCL) as the polymer shell and castor oil in the core. The formulation was characterized by Dynamic Light Scattering (DLS), FT-IR and UV spectroscopy, and *in vitro* release. Antioxidant and anticancer assays were also conducted to evaluate the formulation's bioactivity.

Results: Highly monodisperse CIR-encapsulated NC (CIR-NC) were produced with a mean diameter of 158.1 nm and an almost neutral surface charge. CIR-NC contained on average 53.7 µg CIR/mg polymer at an encapsulation efficiency of 53.5%. The NC formulation exhibited remarkable stability with no significant increase in particle size up to 6 months at 4°C or in the presence of serum. Lyophilization of the formulation in the presence of mannitol as lyoprotectant maintained its colloidal stability. The formulation also demonstrated sustained drug release in PBS (pH 7.4), with 41% of CIR released after 4 days. An antioxidant assay showed that the free radical scavenging activity of CIR was maintained after encapsulation. Cytotoxicity assays in MCF-7 breast cancer cells showed dose-dependent cytotoxicity of CIR-NC, with an IC_{50} of 53 µM, which was comparable to free CIR.

Conclusion: Our findings present a promising nanoformulation for a naturally occurring potent anticancer compound with the potential to improve its delivery challenges.

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Method development and validation of UV-spectrophotometric method for the assay of acetyl salicylic acid tablet in different matrices for testing the dissolution rate

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Background: A validated method of UV-spectrophotometric determination of acetyl salicylic acid (ASA) has been developed in different matrices at different pH's (6.8 and 4.9) to study their effect on the maximum wavelength (λ) and absorptivity (ε).

Aim: The effect of physiological conditions on dissolution rate of ASA were investigated and compared against compendial tests using two commercial brands for ASA to confirm the results.

Methods: All parameters of the analysis were chosen according ICH guideline and validated statistically.

Results and Conclusion: The results showed definite effect of selecting solvent to detect λ and ε. When ethanol (EOH) was used to dissolve ASA as co-solvent, ε was found to be 3.15 while it was 18.50 when NaOH was employed. Regarding the dissolution tests, the results showed that after 4 h during dissolution test, the release of ASA didn't reach 20% when the absorptivity is 18.50, while it was 95% at 3.15 concerning same time. Furthermore, the effect of fed and fasted pH was not significant on dissolution rate where both brands met the compendial requirement.

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Synthesis and characterization of green silver nanoparticles

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Background: A novel, non-toxic, eco-friendly biological material; *Bellevalia flexuosa Boiss (Asparagaceae)* was used to biosynthesize silver nanoparticles (AgNPs).

Methods: The plant was milled and soaked in chloroform. The resulted solvent was reconstituted in methanolic mixtures and evaporated several times to yield the dried methanolic extract. Silver nanoparticles were prepared and studied by changing the reaction conditions with respect to the concentrations of silver nitrate ($AgNO_3$), *Bellevalia* extract and ammonia solutions, pH and temperature. The green nanoparticles were studied using UV–visible spectra and zeta sizer. The zeta sizer was used to determine the mean particle size, polydispersity index and zeta potential of the nanoparticles and to study their stability. In addition, X-ray diffraction analysis (XRD) and infra-red spectroscopy (FTIR) were used to characterize the nanoparticles. The morphologies of AgNPs were investigated using (SEM). Energy Dispersive X-Ray Analysis (EDAX) was used to identify the elemental composition of AgNPs. Finally, the antimicrobial activity of the formed AgNPs was displayed.

Conclusion: AgNPs can be produced using economic and eco-friendly method for their antimicrobial applications.

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Preparation and characterization of chitosan-tobramycin nanoparticles in combination with zinc oxide nanoparticles

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Background and Aim: Herein we describe the preparation, characterization and the antibacterial effect of tobramycin loaded in chitosan nanoparticles in combination with metallic (zinc oxide) nanoparticles.

Methods: Chitosan-tobramycin nanoparticles were prepared by the ionic gelation method using TPP as a cross-linker. The NPs size, zeta potential, polydispersity, entrapment efficacy, morphology, antibacterial activity and the drug release *in vitro* were investigated. Zinc oxide nanoparticles were physically mixed with chitosan-tobramycin nanoparticles and the combination was analyzed by X-ray powder diffraction (XRD), Fourier transform infrared spectrometer (FTIR). The antibacterial activity of the Zinc oxide nanoparticles, chitosan-tobramycin nanoparticles and their mixture against *P. aureginosa* was studied. Results and Conclusion: It was showed that the chitosan nanoparticles controlled the release of the antibiotic and had good antibacterial activity. Zinc oxide nanoparticles had no antibacterial activity and the addition of zinc oxide nanoparticles had no effect on the antibactericidal effect as chitosan-tobramycin nanoparticles.

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Identification and separation of the degradation products of vildagliptin tablets using LC-MS, NMR, and then exploration of the corresponding degradation pathways

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Background and Aim: A gradient high-performance liquid chromatography (HPLC) method has been development for the qualitative and quantitative analyses of vildagliptin related substances.

Methods: This method is based on using of RP-C18 column (250 × 4.6 mm) and a mixture of phosphate buffer and methanol as mobile phase. Various forced degradation studies were conducted to establish an impurity profile for vildagliptin raw material and in the tablet formula.

Results: Three degradation products were produced upon exposing vildagliptin to different degradation conditions (acidic, basic, oxidative, photolytic, aqueous and thermal); their structures were characterized using LC-MS and NMR (^{1}H NMR, ^{13}C NMR and DEPT) techniques.

Conclusions: Excipient components, examined in this study, have no effect towards producing any extra new degradation products.

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Neurotoxic effect of paracetamol on female rats: Role of vitamin E

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Background: Paracetamol (acetaminophen) is the most common nonprescription analgesic and antipyretic drug used. It can be found in different pharmaceutical dosage forms such as syrup, capsule, suppositories and intravenous (I.V) infusion solution. Paracetamol is commonly taken by pregnant women. The intake frequency and the dose of paracetamol usually varied during pregnancy with a tendency toward higher doses in the last trimester. The effect of paracetamol overdose was extensively studied on hepatocyte and nephrocyte of laboratory animals. However, the effect of paracetamol dose on the brain toxicity is the least studied after paracetamol overdose.

Aim: This study is to focus on the effect of paracetamol overdose on neurotoxicity (within hippocampus, cerebellum, and olfactory bulbs) of paracetamol in the last trimester of pregnant rats.

Methods: This study was done through studying oxidative stress markers, the biochemical and antioxidant tests that indicate the presence of hepatotoxicity and nephrotoxicity, along with the protective effect of vitamin E as antioxidant in pre- and post-single toxic dose administration]H1[. Twenty females pregnant Wistar rats (average weight 200 ± 10 g) at gestational day 18 (GD_{18}) were used. The pregnant rats were divided into four groups; the first (control) group received a 0.5 mL p.o of corn oil. The second group (paracetamol) group received a 3000 mg/kg p.o paracetamol dissolved in corn oil. The third (E + paracetamol) group received a 3000 mg/kg paracetamol one hour after 300 mg/kg p.o vitamin E. The fourth (paracetamol + E) group received a 3000 mg/kg paracetamol one hour before 300 mg/kg p.o vitamin E dissolved in corn oil. Twenty-four hours after paracetamol administration the rats were euthanized and the brain, the liver, the kidney, and the blood were collected. Various biochemical tests were performed to show the effect of paracetamol overdose on liver including alanine aminotransferase (ALT), aspartate aminotransferase (AST). Additionally, the effect of paracetamol on blood urea nitrogen (BUN) and creatinine levels were determined to detect nephrotoxicity.

Results: The results showed significant elevation within the paracetamol treated group (148.7, 451.89, 287.7, 170.8% increase respectively) and levels were restored to the normal levels with vitamin E treated groups (58.9, 83.3, 70.4 and 63.9% reduction for pre-treatment and 57.6, 82.7, 63.0 and 56.3% reduction for post-treatment). Uric acid (UA) and superoxide dismutase (SOD) were used to detect the oxidative stress within the liver, the kidney, the hippocampus, the cerebellum, and the olfactory bulbs. Results showed significant depletion in both uric acid (UA) (23.8, 26.3, 10.3, 8.1 and 22.3% reduction) and superoxide dismutase SOD (69.5, 72.6, 61.4, 68.6 and 70.8% depletion) in paracetamol treated group. On the other hand, vitamin E treated group showed significant restoration to their normal levels (29.1,

34.4, 6.0, 6.0 and 20.9% elevation for pre-treatment and 34.4, 38.7, 4.0, 6.0 and 27.4% elevation in post-treatment for UA, and 242.0, 96.5, 172.7, 224.8 and 236% increase for pre-treatment and 239.7, 93.9, 156.1, 159.6 and 234.5% improvement for post-treatment).

Conclusion: Results showed that paracetamol overdose in late pregnancy can cause oxidative stress in liver, kidney and various brain regions. Pre- and post-vitamin E treatment restores the damage caused by oxidative stress within those organs. These results suggest the effectiveness of using vitamin E for prevention and treatment as antioxidant in paracetamol overdose.

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Design and synthesis of phosphoinositide-3-kinase (PI3Kα) inhibitors

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Background: Phosphatidylinositol 3-kinase (PI3Kα) has been emerged as a therapeutic target for anticancer drug design.

Aims: Design and synthesize of novel PI3Kα scaffolds that fit PI3Kα inhibitors pharmacophore model.

Methods: Ligand-and structure-based drug design tactics, synthesis of the targeted core nucleus, crystallography, and full biological evaluation tests against human cancer cell lines expressing PI3Kα.

Results: New core structures have been synthesized and characterized using FT-IR, NMR (^{1}H and ^{13}C), HRMS and elemental analysis, namely: *N*-substituted- 4-hydroxy-2-quinolone-3-carboxamides, *N*-substituted-4-hydroxy-substituted-2-quinolone-3-carb oxamides, 2-oxo-1,2-diphenyl ethyl-substituted-benzoate, 2-(substituted-phenylimino) -1,2-diphenylethanol, 1,2-bis(4-methoxyphenyl)-2-oxoethyl 4-nitrobenzoate, and *N*'-(diphenylmethylene)-2-nitro benzenesulfonohydrazide.

In addition, the identity of a core nucleus was successfully characterized with the aid of X-ray crystallography. Biological activity of prepared compounds was investigated *in vitro* against human cancer cell lines. Results revealed that these compounds inhibit cell proliferation and induce apoptosis through an increase in caspase-3 activity and a decrease in DNA cellular content. Molecular docking studies against PI3Kα showed that analogues accommodate PI3Kα kinase catalytic domain and form H-bonding with key binding residues.

Conclusion: The scaffolds exhibited a potential PI3Kα inhibitory activity in HCT-116 cell line.

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Effect of physiological conditions on candesartan cilexetil release

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Background: Quality control (QC) tests are set of routine analysis tests to guarantee the release of finished products. QC tests are designed by experienced professional teams. Typically, minor details were not clarified completely.

Aim and Methods: Herein, the effect of physiological conditions on dissolution rate of candesartan cilexetil (CC) were investigated and compared against compendial tests.

Results: Two commercial brands were used in order to confirm the results. Dissolution was affected by viscosity, surface tension and pH. All physiological conditions showed significant slower dissolution rate in than official USP conditions.

Conclusion: The obtained results recommend that all specifications should be mentioned in order to compute accurately the required parameters. Furthermore, there has to be correlation between *in vitro* dissolution and variable *in vivo* conditions that may affect absorption to ensure patient safety when following pharmacists' consultation.

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Evaluation of knowledge, attitude and practice of pharmacovigilance among healthcare professionals at Benghazi hospitals

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Background**:** Physicians and pharmacists play a critical role in pharmacovigilance. The main essence of pharmacovigilance is the reporting of drug adverse effects. The healthcare professionals have to follow a certain technique for reporting adverse drug reactions (ADRs) in order to improve the effectiveness of patient care and drug safety.

Aims: This research aimed to test and evaluate the knowledge, attitude and practice of pharmacovigilance by the healthcare professionals in Benghazi.

Methodology: A structured questionnaire from a study at Pakistan by Nisa et al. (2018) was used. One hundred questionnaires were distributed in August 2019 and filled by physicians and pharmacists worked in different hospitals in Benghazi, Libya including Benghazi Medical Center. 26 of them were rejected because they were not filly completed.

Results: The participants were 57% physicians and 43% pharmacists. The majority (57%) was at age 31-40 years old. 47% had correctly defined pharmacovigilance while only 19% know what is meant by ADRs. On the other hand, 47% of them did not have any information about any drug that has been drawn from the Libyan markets because of its serious side effect. Moreover, 61% of participants did not share any information about raising ADRs in some patients with other healthcare professionals. 82% of participants were not aware about any formal ADRs reporting system in other countries. Also, 49% of participants have answered that renal failure is commonly with the incidence of ADRs. 35% of healthcare professionals did not know about ADRs reporting system in Libya. Whereas, 42% of participants have strongly agreed that reporting of ADRs is essential. 41% and 45% of participants have strongly believed that reporting of ADRs is not time consuming and it increases patient safety, respectively.

Conclusion: According to pervious data, educational programs and training courses about the importance of pharmacovigilance in Benghazi are needed. In addition, healthcare professionals in Benghazi should be informed that Libya is an associated member at global pharmacovigilance network.

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Smoking secession in Palestine: Pharmacists' awareness and attitude

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Background: Smoking is a major risk factor for many diseases that may causes death. Pharmacists are uniquely positioned to promote smoking cessation as that are a key interface between patients and the health-care community.

Aims: To assess Palestinian pharmacists' awareness and attitudes regarding smoking cessation and determine the barriers preventing pharmacists performing their role in smoking cessation.

Methods: A simple, self-administered surveys was distributed to practicing community pharmacists in Palestine (west bank), the survey consisted of 42 questions serve the purpose of research. Data was analyzed using Statistical Package of Social Sciences (SPSS®) version 23.

Results: Preliminary results involving, 90 pharmacists working in community pharmacies showed that pharmacists had a good knowledge regarding smoking and their role in smoking cessation. A 20% of the pharmacists reported that they 'always' or 'most of the time' asked their patients about their smoking status. Once patients' smoking status was identified, a 40% of the pharmacists provide advices regarding smoking cessation and only 25% assess smokers' readiness to quit. Almost 33% of the recruited pharmacists 'always' and 'most of the time' assisted smokers in quitting by advising the use of nicotine replacement therapy (NRT). Only 39, 10, and 9% of the pharmacies expressed the availability of smoking cessation treatments such as NRT, bupropion, and champix, respectively. Only 38% of the pharmacist 'strongly agreed' and 'agreed' that the smokers appreciate their advice about quitting.

Conclusion: Palestinian community pharmacists have good awareness and positive attitude about smoking cessation counseling. Most pharmacies do not provide smoking cessation counseling due to the lack of proper communication skills, population demand and treatments.

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Prevalence of depression among Palestinian adults with diabetes mellitus: A cross sectional study

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Background: Diabetes mellitus (DM) is one of the most psychologically demanding chronic medical illness in adult. Comorbidity between diabetes and depression is quite common, but most studies were based on developed country sample. Depression affects DM patient's treatment goals negatively.

Aims: To determine the prevalence of depression and identify its socio-demographic or clinical correlates in patients with established diabetes mellitus attending an out-patient clinical health care in Ramallah.

Methods: This was a cross-sectional study at Ramallah primary healthcare clinic, Ramallah, Palestine. About two hundred patients with established DM were evaluated for depression using Patient Health Questionnaire the nine-item PHQ-9 (Arabic version). Patients data were also collected including age, sex, marital status, Body Mass Index (BMI), level of education, smoking status, physical activity, duration of diabetes mellitus, use of insulin, presence of additional illnesses, glycosylated hemoglobin (HbA1c) levels and medications. In order to achieve the objectives of the study, we used descriptive and analytical approach for representing the results.

Results: Patients with DM (n=196) were evaluated [82 (41.8%) male and 114 (58.2%) female]. Age < 30 years (11, 5.6%), 31-40 (17, 8.7%), 41-50 (38, 19.4), 51-60 (65, 33.2%) and > 60 (65, 33.2%). The majority of the study patients have their sources of information about how to use the medications are from physician (94.9%), then from pharmacist (3.6%). The majority of the study patients have duration of diabetes (5-9.99 years, 34.2%). 25% of patients do not suffer from other disease but others have more than one disease and about 28.1% suffer also from hypertension. Majority of patients used two drugs (132, 67.3%) and (64, 32.7%) uses insulin for treatment of DM. Majority of them (132, 67.3%) have family history of diabetes. HbA1c was found 7 or higher in 105 patients (53.6%) and 91 patients (46.4%) their HbA1c was less than 7. The blood glucose levels during fasting were found in these patients and the majority 118 patients 60.2% was found above 140. The BMI for 95 patients (48.5%) was between 25-29 (overweight) and for 62 patients (31.6%) were found above 30 (obese). The Number of prescribed medication administration per day was relatively high and varied from 1-10 medications. Of the study patients, 139 (71%) met the criteria for major depression, 43 (21.9%) for moderate depression and the remaining 14 (7.1%) had no clinically significant depression. Among these 139 patients diagnosed major depression, 84 patients (42.9%) suffered from major depression, mild severity, 45 patients (23%) suffered from major depression, moderate severity and 10 patients (5.1%) diagnosed major depression, severe severity. Of the study43 patients (21.9%) suffers from minimal depressive symptoms. When the patients asked if these problems in the questionnaire

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Conference Proceedings
The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan

(PHQ-9) made any difficulties to do their work, take care of things at home, or get along with other people, the majority; 120 patients (61.2%) answered not difficult at all, 69 patents (35.2%) answered somewhat difficult and 7 patients (3.6%) very difficult.

Conclusion: This study showed high prevalence of depression in patients with DM. The risk factors for depression were age, obesity, diabetic complications, diseases and increased of medications. However, the likelihood of depression was not significant with duration of diabetes and insulin use. Major depression was highly prevalent among people with DM and none were being treated with anti-depressants. Psychosocial assessment should be part of routine clinical evaluation of these patients at primary healthcare clinics and possible treatment for depression in order to improve quality of life and decrease adverse outcomes among diabetic patients.

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N-substituted-4-hydroxy-6-fluoro-2-quinolone-3-carboxamides: Design, synthesis, and biological evaluation as PI3Kα inhibitors

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Background: The oncogenic potential of phosphoinositide-3-kinase α (PI3Kα) has been rated as a promising target for anticancer drug design and development.

Aim: Target compounds were designed to investigate the effect of introducing a fluoro moiety on quinolone-3-carboxamide scaffold to understand their structure-activity relationship (SAR) and optimize their biological activity as anticancer compounds.

Methods: Chemical synthesis of the targeted compounds, biological evaluation tests against human colon adenocarcinoma (HCT-116) and human epithelial colorectal adenocarcinoma (Caco-2) cell lines, as well as Glide docking studies.

Results: A series of *N*-substituted- 6-fluoro-4-hydroxy-2-quinolone-3-carboxamides (**6a-f**) was synthesized and characterized by FT-IR and NMR (^{1}H and ^{13}C). The derivatives exhibited an inhibitory activity against human colon carcinoma (HCT-116) cell line.

Compound tailored with *o*-F (**6d**) (IC_{50}= 76.74 μM) showed higher inhibitory activity suggesting that H-bond interaction mediates ligand/ PI3Kα on *o*-position. Attaching *m*-F (**6e**) (IC_{50}= 169.8±5 μM) or *p*-F (**6f**) (IC_{50}= 338.6 μM) moiety on the aromatic side decreased the potency deducing that *o*-H-Bond acceptor moderated ligand/PI3Kα interaction. Unsubstituted aromatic motif enhanced the activity referring that aromatic nucleus orientates the ligand properly in the kinase domain. Elongating the carboxamide linkage with one carbon placed the ligand deeply in the binding domain. Introducing *p*-OCH_3 (**6c**) (IC_{50}= 238.5 μM) decreased the activity suggesting that steric effect impedes the proper orientation in the binding domain.

Glide docking studies against PI3Kα displays that the derivatives fit PI3Kα kinase pocket and form H-bond with key binding residues.

Conclusion: The series exerted a potential PI3Kα inhibitory activity in human carcinoma cell lines encoding PI3Kα.

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Immunomodulatory and anti-cancer activities of wheat bran consumed in Jordan

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Background: Wheat bran has been widely tested for its health promoting effect. Many studies proved the biological activities of various components extracted from wheat bran. However, no previous studies were conducted to evaluate the anti-cancer and immune-modulatory activities of wheat bran consumed in Jordan.

Aim: Herein, we evaluate the anti-cancer and immune-modulatory effect s of different extracts prepared from wheat bran available in Jordanian market.

Methods: Wheat bran was obtained from the Hashemite mill in Amman, and four different solvent extracts (ethanol, methanol, chloroform and water) were prepared. The anti-cancer effect had been tested for these extracts against three breast cancer cell-lines (EMT6/p, MCF-7, T47D). The effect of each extract on the immune system was evaluated by conducting mitogen proliferating assay, pinocytosis and phagocytosis in splenocytes treated with different extracts. In addition to testing the wheat bran's prophylaxis effect when applied in 3 different ratios (20, 30 and 40%) against tumor size and prevalence in four (Balb/c) mice groups inoculated with EMT6/p cell-line subcutaneously, serum samples were collected to evaluate the effect on cytokines (IL-10, IL-4, IL-2 and INF-ɣ).

Results: An inhibitory effect on three different breast cancer cell types was observed after treatment with different extracts, furthermore, immune system stimulatory effect was witnessed when tested on splenocytes and macrophages, in addition to reduction in tumor size and prevalence in-vivo.

Conclusion: Wheat bran is a promising source of anti-cancer and immunomodulatory agents. However, further studies are needed to fully understand its mechanism of action.

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Behavioral alterations induced by chronic exposure to silicon dioxide nanoparticles

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Background: Silicon dioxide nanoparticles (SiO_2 NPs) are widely invested in different sectors of medicine, industry, agriculture and consuming products. However, these nanomaterials may reveal a high potential risk for human health and the ecosystem with little, if any; information is available about their behavioral toxicity.

Aim: To investigate the behavioral alterations that might be induced by chronic exposure to 10 nm SiO_2 NPs.

Methods: Balb/c mice were subjected to 36 injections of SiO_2 NPs (2 mg/kg bw). The control animals and the treated ones were subjected to the following neurobehavioral tests: Elevated plus-maze test, elevated zero-maze test, multi-radial maze test, open field test, hole-board test, light-dark box test, forced swimming test, tail-suspension test, Y-maze test, Morris water maze test and multiple T–maze test.

Results: In comparison with the control animals, the mice exposed to SiO_2 NPs demonstrated that silica NPs are anxiogenic and could aggravate the depressive phenotype with effect on learning and memory. In addition, exposure to these nanomaterials could lower the overall activity and reduce the exploratory behavior.

Conclusion: The results of the present study may suggest that silica nanomaterials could induce potential oxidative stress in the body leading to neurobehavioral alterations with possible changes on the central nervous system.

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Comparative behavioral alterations induced by three different nanoparticles

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Background: Gold nanoparticles (NPs), silicon dioxide NPs and zinc oxide NPs are widely invested in different sectors of medicine, industry, agriculture and consuming products. However, these nanomaterials may reveal a high potential risk for human health with little, if any; information is available about their behavioral toxicity.

Aims: To investigate alterations in the behavioral activity induced by chronic exposure to three different nanomaterials: gold NPs, silicon dioxide NPs and zinc oxide NPs.

Methods: Four groups of Balb/c mice were subjected to 21 injections of normal saline solution, gold NPs, silicon oxide NPs and zinc oxide NPs respectively. The control mice and the treated ones were subjected to the following neurobehavioral assays: marble burying test, sucrose preference test, balance beam maze test, tube dominance test, burrowing tube test and nest construction test.

Results: In comparison with the control mice, the animals subjected to nanomaterials induced variable alterations in their behavior concerning burrowing, nesting, social dominancy activities, marbles burying, sensorineural balance and coordination that might be related to anxiety and neophobia. In addition, subjection to these nanomaterials could induce anhedonia that might be related to depression.

Conclusion: The finding of the current work may suggest that the invested NPs could induce deterioration in the ability of exposed subjects to perform daily life activities. More work is needed to correlate the induced neurobehavioral alterations with possible histological and ultrastructural alterations in the nervous system.

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N-substituted-4-hydroxy-6-nitro-2-quinolone-3-carboxamides: Design, synthesis, and biological evaluation as PI3Kα inhibitors

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Background: Phosphatidylinositol 3-kinase alpha (PI3Kα) has emerged as a hot target for anticancer drug design.

Aim: Target compounds were designed to investigate the effect of introducing a nitro moiety on quinolone-3- carboxamide scaffold to elucidate their structure-activity relationship (SAR) and improve their biological activity as anticancer compounds.

Methods: Chemical synthesis of the targeted compounds, biological evaluation tests against human colon adenocarcinoma (HCT-116) and human epithelial colorectal adenocarcinoma (Caco-2) cell lines, as well as Glide docking studies.

Results: A series of *N*-substituted-4-hydroxy-6-nitro-2-quinolone-3-carboxamides were designed and synthesized as PI3Kα inhibitors employing structure-based drug design and molecular docking. The identity of core nucleus of this series as well as the synthesized derivatives were characterized using (^{1}H and ^{13}C) NMR analysis technique.

Biological studies in human colon carcinoma (HCT116) cell line showed that the analogues (**5**, **6 a-g**) inhibited cell proliferation. Promising PI3Kα inhibitory activity was exhibited for analogues bearing H-bond acceptor and small hydrophobic moieties on *p*-position (**6b**) (IC_{50} = 0.704 mM). Derivatives tailored with *p*-H-bond donor and/or acceptor (**6e**) and small hydrophobic moiety (**6f**) were inactive. Elongation the carboxamide motif by –CH_2 (**6c**) (IC_{50} = 5.89 mM) and NH (**6d**) (IC_{50} = 0.734 mM) potentiates the inhibitory activity implying that a steric factor pushes the compound deeply into the binding cleft. The activity of **6d** suggests that H-bond acceptor drives ligand/PI3Kα complex formation. The activity of **6g** (IC_{50} = 4.95 mM) infers that bulky *m*-substituent impedes the proper orientation of ligand in the kinase domain. Glide docking studies against PI3Kα demonstrated that the derivatives accommodate PI3Kα kinase catalytic domain and form H-bonding with the key binding residues. Our results suggest that further optimization of this series would be beneficial for colon cancer treatment.

Conclusion: The series exerted a potential PI3Kα inhibitory activity in human carcinoma cell lines encoding PI3Kα.

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Investigation of different binder compressibility effect on metformin HCl

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Background and Aim: The aim of the present study is to use different binders to understand the compressibility of poorly compressible metformin HCl using Direct Compression (DC) method. Compaction simulator aids in giving real time compression data, which is used in evaluating the compressibility of powder formulation.

Methods: Metformin HCl is used as our model drug; particular attention was applied while choosing the suitable excipients for formulations. Three different binders were used at two concentrations (2% and 5%), HPMC Pharmacoat®, LHPC LH-21, and Kollidon® VA 64F. As disintegrant we used Starch®1500. Primojel® as superdisintegrant and magnesium stearate as lubricant. Tablets were pressed with flat faced Euro B punch of 15mm diameter at two different forces (20 kN and 30 kN) using Stylcam R200 compaction simulator. Due to poor compressibility of Metformin HCl itself, Avicel®102 as filler, was set at constant ratio 1:0.75 (API:Filler), used for all formulations.

Results: Functional excipients versus physicochemical behavior of tablets has been investigated and it was found that, in relation with binder concentration, Kollidon® VA 64F at 2% showed optimum tensile strength 1.27 MPa and 2.07 MPa at 20 kN and 30 kN respectively. HPMC and LHPC had no significant effect in compressibility of Metformin HCl. Compressibility was analyzed by applying Heckle equation and yield pressure (Py) was calculated. Results derived indicated that Metformin HCl shows greater brittle fragmentation.

Conclusion: Kollidon® VA 64F as DC binder has superior binding characteristics and excellent results with different compaction forces on tablet tensile strength, disintegration time and friability tests.

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The Protective Role of Metformin against Oxandrolone-Induced Mood Depression and Infertility

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Background: Oxandrolone is a synthetic testosterone analogue that preserves or restores muscle mass and is widely used among bodybuilders and athletes. Oxandrolone is associated with many different side effects such as hepatic impairment, sexual dysfunction and mood depression. In the other hand, the antidiabetic metformin is known to reduce the infertility in diabetic patients.

Aim: To investigate the protective role of metformin against oxandrolone induced mood depression and infertility.

Method: Twenty-eight rats were divided into four groups and each group contained seven rats. The first group received the vehicle dimethyl sulfoxide, second received 10 mg/kg oxandrolone, third was administrated 10 mg/kg oxandrolone plus 70 mg/kg metformin, and the last group received 70 mg/kg metformin. The administration was continually for 14 day in doses equivalent to the doses used clinically. During drug administration, the alterations in the mood were examined using sucrose intolerance and swimming force test. After animal scarification, testes and livers were isolated from the rats for analysis of the morphological, histological and biochemical changes.

Result: It was found that oxandrolone significantly ($p<0.05$) reduced the relative weights of livers and testes, while metformin attenuated significantly this reduction in the relative weights. The sperm count was decreased significantly ($p<0.05$) in in rats treated with oxandrolone by 82%, while metformin normalized the sperm count to reach to reach 51% of the sperm count of the control group. In addition, metformin prevented the sharp decline in serum testosterone levels induced by oxandrolone. Regarding the mood alterations, the results of the swimming force test showed that oxandrolone significantly ($p<0.05$) reduced the immobility time (0.6 min), but the time was significantly longer (4 min) in rats treated oxandrolone plus metformin. In sucrose test, our results showed that rats treated with only oxandrolone consumed only 2% of the total volume of sucrose solution and metformin co-administration with oxandrolone increased significantly ($p<0.05$) the sucrose consumption to 29.5%.

Conclusion: The present study concluded that metformin has a protective influence against oxandrolone induced mood depression and infertility.

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Nanomaterial loaded into methacrylate hydrogel: cytotoxicity and antibacterial activity

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Background: Nanomaterials loaded into hydrogels have attracted a lot of attention due to their potent wound healing effect.

Aim: In this project, we prepared gold nanospheres decorated with polyethylene glycol (PEG) and sodium 3-mercapto-1-propanesulfonate (MPS) and cross-linked with methacrylate in order to obtained nanomaterial dressing film.

Methods: The prepared gold nanospheres coupled with PEG or MPS were characterized by optical spectra, zeta potential and hydrodynamic size. In addition, the obtained nanomaterial film was characterized in terms of release profile, viscosity and water absorptivity.

The cytotoxicity of gold nanospheres cross-linked with methacrylate was investigated *in vitro* against human dermal fibroblasts. Furthermore, the wound healing ability of the nano-film was investigated against the human dermal fibroblast using cell migration test. The antimicrobial activity of the prepared film was studied using flask shaking method against the most common pathogens encountered in skin wounds such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Results and Conclusion: The preliminary results indicate that gold nanospheres cross-linked with methacrylate was not toxic to the human dermal fibroblasts and could be promising as a wound healing dressing material.

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Investigating the toxicity of gold nanorods of different surface chemistries loaded into polymeric hydrogel upon application onto intact rat skin

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Background and Aim: Herein, the toxicity of nanomaterial preparations containing gold nanorods (GNR) modified with two different polymers; poly-ethylene glycol (PEG) and poly allylamine hydrochloride (PAH) was investigated upon application onto intact rat skin.

Methods: The gold nanomaterial was prepared using a mixture of CTAB surfactant and oleic acid and the surface of GNR was modified with polymers by using layer by layer technique. The obtained modified GNR; PEG-GNR and PAH-GNR were loaded into poloxamer hydrogel and were characterized by optical spectroscopy, zeta potential and hydrodynamic size. GNR of different surface chemistries were applied onto the skin surface of rats (6 rats for each group), and the signs of topical toxicity such as redness and swelling were followed over 14 days of treatment and were compared to control group. The penetration and accumulation of GNR of different surface chemistries into different body organs through intact skin was investigated too.

Results: After 14 days of treatment, main body organs (heart, brain, spleen, lungs and liver) were obtained after scarifying the rats and the amount of gold accumulated into these organs was analyzed by using inductively coupled plasma-optical emission spectroscopy (ICP-OES) analysis technique. Furthermore, histology examination of the organs tissues was carried out to investigate any sings of cytotoxicity.

Conclusion: The preliminary results revealed that no signs of toxicity were observed upon applying gold nanorods onto intact rat skin, which support their biomedical applications as topical nanomaterials.

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Anti-*Helicobacter pylori* activity of selected bioactive compounds: *In silico* and *in vitro*

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Background: *Helicobacter pylori* is one of the most prevalent pathogens that infects about 50% of population leading to dyspepsia, peptic ulcer disease, atrophic gastritis, gastric adenocarcinoma and MALT. *H. pylori* treatment stands for proton pump inhibitor with two or three antibiotics (amoxicillin, metronidazole with or without clarithromycin). The increase of antimicrobial resistance levels showed an emergence need to look for alternative therapy.

Aim: To check the possible inhibitory effect of some bioactive compounds of plant origin on *H. pylori* urease.

Methods: The bioactive compounds (thujone, terpineol, limonene, pinene and β-sitosterol) where screened for their effect on urease enzyme of *H. pylori* by docking. *In vitro* screening for their inhibitory effect against *H. pylori* using standard agar diffusion method was followed by minimal inhibitory concentration (MIC) assay for each tested bioactive compound using agar dilution method. The best inhibitors were combined with metronidazole to check for their possible synergistic effect using checkerboard method.

Results: Among the tested bioactive compounds thujone (25%) and terpineol (12.5%) reported the best MIC against *H. pylori*. β-sitosterol showed inferior activity against *H. pylori* with MIC of 100% (w/v)

Conclusion: In the light of the recent study results some bioactive compounds reported remarkable inhibitory effect against *H. pylori*. Thus, those compounds could be alternative options for *H. pylori* treatment.

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Impact of genetic polymorphisms on the sulfation of 4-hydroxytamoxifen and endoxifen by human cytosolic sulfotransferase SULT1A1

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Background: Human sulfotransferase 1A1 (SULT1A1) catalyzes the sulfation of a wide variety of substances including 4-hydroxytamoxifen (4-HT) and endoxifen, the active metabolites of tamoxifen. Polymorphisms were reported in *SULT1A1* gene. A functional single nucleotide polymorphism (SNP) in the *SULT1A1* gene (R213H) showed lower catalytic activity and thermal enzyme stability. Previous data have suggested that this particular genotype may account for a portion of individual variation in responding to tamoxifen therapy.

Aims: To investigate the effects of SNPs of human *SULT1A1* genes on the enzymatic characteristics of the sulfation of 4-HT and endoxifen by SULT1A1 allozymes.

Methods: Online databases were searched for *SULT1A1* nonsynonymous coding SNPs. Nine SULT1A1 allozymes coded by missense SNPs were selected based on the predicted importance of the amino acid variations, were generated, bacterially expressed and purified by glutathione-sepharose affinity chromatography. Purified SULT1A1 allozymes were analyzed for sulfating activity using an established assay procedure.

Results: Specific activity obtained showed the differential sulfating activities of SULT1A1 allozymes toward both antiestrogenic compounds.

Conclusion: The activity data obtained for the SULT1A1 allozymes analyzed indicated the importance of the amino acid residues in the proper functioning of the SULT1A1 enzyme, which may affirm the variability in the metabolism of tamoxifen that could affect its efficacy in individuals with different *SULT1A1* genotypes.

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Heterozygous dopamine transporter knockout mice as an animal model of ADHD: effects of amphetamine and the serotonin 1B receptor antagonist SB224289

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Background: Dopamine is a neurotransmitter that plays a major role in attention, working memory, reward, motivation, and motor activity. Perturbations in dopamine signaling have been implicated in several developmental psychological disorders, including attention deficit/hyperactivity disorder (ADHD), schizophrenia, and obsessive-compulsive disorder. The dopamine transporter (DAT) is a critical regulator of dopamine release dynamics. Developmentally, dopamine activity influences prefrontal cortex maturation, with consequent effects on response inhibition ability and decision making. It has been suggested that DAT KO mice may model aspects of ADHD. DAT +/-mice do not show many behavioral effects observed in homozygous DAT KO (DAT -/-) mice, but they have not been well-studied in tests of attention and cognitive function.

Aims: Therefore, DAT +/-mice were examined in the 5-choice continuous performance (5-CCPT) task to assess attention and impulsivity, as well as the effects of amphetamine and the 5-HT1B antagonist SB 224289.

Methods: Male DAT +/-and DAT wildtype (DAT +/+) mice were examined in the 5-CCPT. A modified short version of 5-CCPT was used. After stable performance was attained mice were tested in challenge sessions after being injected with different doses of amphetamine (0, 0.3, 0.66, and 1.5 mg/kg IP). After a 10-day wash-out period with continued baseline testing, mice were tested with the serotonin 1B receptor antagonist SB 224289 (0, 10, 20 mg/kg, IP).

Results: In the 5-CCPT DAT +/-mice made more premature errors and had a higher percentage of incorrect responses that DAT +/+ mice. These impairments were reduced by amphetamine administration. The high dose of amphetamine also increased the sensitivity index in DAT +/-mice. DAT +/-mice also showed fewer premature errors after administration of SB 224289.

Conclusions: In the present study, DAT +/-mice showed evidence of motor impulsivity and impaired attention in the 5-CCPT. Amphetamine reduced this impulsivity in a dose dependent manner. One of the current goals of preclinical ADHD research is to identify non-stimulant approaches to the treatment of ADHD. The 5-HT1B antagonist SB 224289 also reduced impulsivity in the 5-CCPT. This data suggests that DAT +/-mice may model key aspects of ADHD and may provide a useful approach to identifying new treatments for ADHD.

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Hyperthyroidism and memory change, association with vitamin B12 deficiency among type 2 diabetic patients – Cross sectional study

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Background: Metformin usage can lead to Vitamin B12 deficiency, which can have an impact on neuropathy and lead to further complications.

Aims: To address the prevalence of low serum vitamin B12 level among type 2 diabetic patients in Ramallah district and to determine the factors associated with it.

Methods: The study comprised a total sample size of 400 patients and all the participants gave their informed consent. Relevant medical history and laboratory data were obtained from the medical records of the patients. A questionnaire was taken from the participants directly by the researcher. Statistical analysis was done by Statistical Package for Social Science (SPSS, version 11.5).

Results: The results show that (60.5%) of the diabetic patients were obese. The majority of patients (62.8 %) had dyslipidaemia, (59.8%) hypertension and (12%) hyperthyroidism. (36.5%) complained of numbness, (13.8%) memory changes, and (6.5%) of mood changes. Only (21.5 %) had diabetic retinopathy, (5.3%) had diabetic nephropathy and nearly (10.3%) had diabetic neuropathy. It was observed that (39.5%) had a low serum Vitamin B12 level and no significant effect was observed ($p>0.05$) on the prevalence of low serum vitamin B12 level among patients of T2DM who encountered different diabetic complications.

Conclusions: There was a negative significance between low serum level of vitamin B12 and metformin treatment while a significant correlation was observed with Insulin usage. A negative significant effect was observed on the prevalence of low serum vitamin B12 level among patients who encountered different diabetic complications.

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N-Substituted-4-hydroxy-6-methyl-2-quinolone-3-carboxamides: Design, synthesis, and biological evaluation as PI3Kα inhibitors

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Background: Phosphatidylinositol 3-kinase alpha (PI3Kα) has been highlighted as a hot target for anticancer drug design.

Aim: Target compounds were designed to investigate the effect of introducing a nethyl moiety on quinolone-3-carboxamide scaffold to understand their structure-activity relationship (SAR) and optimize their biological activity as anticancer compounds.

Methods: Chemical synthesis of the targeted compounds, biological evaluation tests against human colon adenocarcinoma (HCT-116) and human epithelial colorectal adenocarcinoma (Caco-2) cell lines, as well as induced-fit docking studies.

Results: A series of *N*-substituted-4-hydroxy-6-methyl-2-quinolone-3-carboxamides was designed and synthesized as possible PI3Kα inhibitors recruiting structure-based drug design and molecular docking. The identity of the core nucleus and synthesized derivatives was characterized using (^{1}H and ^{13}C) NMR analysis technique. Biological studies in human colon carcinoma (HCT116) cell line showed that the analogues **5**, **6a-g** exhibited distinct antiproliferative activity against PI3Kα. Compound tailored with hydrazide motif (**6d**) exhibited higher inhibitory activity (IC_{50} = 0.323 mM) suggesting that H-bond interaction improves the binding affinity. Compound tailored with *o*-COOH and *p*-CH_3 (**6g**) showed high activity (IC_{50} = 0.567 mM) implying that H-bond and hydrophobic interaction on the *o*-and *p*-positions elicit the activity. Compounds **6a** and **6c** displayed comparable antiproliferative activity (IC_{50} = 0.849 and 0.811 mM) inferring that similar binding conformation is generated in the kinase domain. The loss of activity of compounds **6e** and **6f** indicates that *p*-H-bond acceptor and/or donor doesn't mediate ligand/PI3Kα complex formation. Conversely, the activity of **6b** (IC_{50} = 1.54 mM) suggests that *p*-OCH_3 accommodates a tight hydrophobic cleft and confirms the absence of H-bond acceptor on *p*-position. The Induced-fit docking studies against PI3Kα demonstrated that the derivatives accommodate PI3Kα kinase catalytic domain and form H-bonding with the key binding residues. Our results suggest that further optimization of this series would be beneficial for colon cancer treatment.

Conclusion: The series exerted a potential PI3Kα inhibitory activity in human carcinoma cell lines encoding PI3Kα.

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Weight management services to reduce the risk of non-communicable diseases offered in Palestinian community pharmacies: a cross-sectional study

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Background: Obesity is listed among the top five preventable risk factors for non-communicable diseases. Health authorities around the world periodically publish evidence-based weight management recommendations to guide healthcare providers. Community pharmacies are increasingly offering weight management products and programs.

Aim: To explore weight management services being offered in community pharmacies in Palestine and adherence of pharmacists to authorities' recommendations.

Methods: The study was conducted in a cross-sectional observational design using a validated and reliable questionnaire. The sociodemographic and practice characteristics of the pharmacists were collected. The pharmacists replied to 60 items related to services offered, adherence to guidelines, training required, and best methods to promote weight management.

Results: The study tool was completed by 350 community pharmacists, of whom 89.7% offered weight management services, 53.2% had experience of more than 10 years, 45.1% had training on weight management, 49.1% counseled more than 5 patients per week on weight management, 56.9% thought the information available to them were adequate. Pharmacists were more likely to adhere to regulatory guidelines and offer more services when they had had training on weight management (χ^2 = 9.282, p-value = 0.003), had more than 10 years of practice experience (χ^2 = 4.606, p-value = 0.040), and when they counseled more than 5 patients per week (χ^2 = 4.454, p-value = 0.013).

Conclusions: Community pharmacists are in key position to promote weight management and reduce risk of non-communicable diseases. Further training might improve services and adherence to guidelines.

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Shortcuts in bioequivalence testing

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Aim: To review the availability of *in vitro* testing and simulation methods that can be adopted to predict *in vivo* performances of generic products and aid in the development of drug formulations.

Methods: Pubmed and Google Scholar databases were used to review published literature over the past 10. The terms that used were "simulation AND bioequivalence" and "modelling AND bioequivalence" in the title of the published manuscripts to be eligible for reviewing.

Results: A total of 44 research papers were reviewed. Computer simulation using software such as GastroPlus™, PK Sim® and SimCyp® find applications for drug modelling into compartmental, non-compartmental and physiologically based pharmacokinetics (PBPK) models. This allows the input of data from *in vitro* or *in vivo* results of drug concentrations and comparison with the available data in literature for a reference product. The benefits of this include the strategic decision making and saving time and cost for formulation development. For immediate release drug products belonging to the Biopharmaceutics Classification System I (BCS I) difference factor (f_1) and similarity factor (f_2) can be used from the *in vitro* dissolution data of drug formulations to claim biowaiver and therefore save time, however, this method can be more discriminatory and might not be reflected by *in vivo* bioequivalence testing.

Conclusions: Computer simulations can be an important tool to show the possibility of bioequivalence for equivalent drug products even when dissolution profiles are different.

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Tamoxifen induced resistance in breast cancer: Correlating metabolic and molecular biomarkers changes in MCF-7 cell line

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Cancer is considered as the second major cause of mortality and morbidity in Jordan and accounts for 16.5% of annual deaths, according to latest national mortality data in 2014. Breast cancer is the most common cancer among Jordanians females, which accounts for 39.4% of cases diagnosed in 2015. Around two thirds of patients diagnosed with breast cancer are Estrogen Receptor alpha (ERα)-positive and are treated with tamoxifen. However, not all patients respond to initial tamoxifen treatment, and resistance has been reported to be acquired over time. Therefore, identification of molecular pathway and metabolic biomarkers would be of great benefit to patients to determine the potential response to tamoxifen treatment. MCF-7 cell line represents estrogen receptors-positive (ER+) and progesterone receptors-positive (PR+) breast cancer. Consequently, in this study the investigation of mechanisms of genetic and epigenetic variations in these cells have been conducted, and these changes will be correlated with metabolic biomarkers level changes such as lactate, pyruvate and glutamine that are produced and/or consumed by cells in the supernatant media through cell line resistance induction using gradual treatment with tamoxifen (starting from 0.1 μM up to 42 μM) by applying a selective and sensitive analytical method to accurately quantify their concentrations and correlate their changes with cells count.

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Design, synthesis, and biological evaluation of N-substituted-4-hydroxy-8-methyl-2-quinolone-3-carboxamide derivatives as PI3Kα inhibitors

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Background: Phosphoinositide-3-kinase α (PI3Kα) has emerged as a potential target for anticancer drug design and development.

Aim: Target compounds were designed to probe the effect of bearing a methyl moiety on quinolone-3- carboxamide scaffold to elaborate their structure-activity relationship (SAR) and improve their biological activity as anticancer compounds.

Methods: Chemical synthesis of the targeted compounds, biological evaluation tests against human colon adenocarcinoma (HCT-116) and human epithelial colorectal adenocarcinoma (Caco-2) cell lines, as well as induced-fit docking (IFD) studies.

Results: A series of *N*-substituted-4-hydroxy-8-methyl-2-quinolone-3-carboxamides (**6a-h**) was synthesized and characterized by FT-IR and NMR (^{1}H and ^{13}C). The derivatives inhibited the proliferation of human colon carcinoma (HCT-116) cell line. Analogues functionalized with *m*-CF_3 (**6c**) (IC_{50} = 118 µM) and *p*-CF_3 (**6d**) (IC_{50} = 89 µM) showed promising activity implying that hydrophobic interaction guides ligand/PI3Kα complex formation. The induced-fit docking (IFD) against PI3Kα demonstrates that the series occupies PI3Kα kinase and H-bond with key binding residue.

Conclusion: The series exhibited a potential PI3Kα inhibitory activity in human carcinoma cell lines encoding PI3Kα.

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Validating an Arabic tool, the quality of life of diabetics in Jordan

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Background: Diabetes quality of life (DQOL) instrument has been broadly used to evaluate quality of life among diabetics.

Aim: To develop a revised validated Arabic version of DQOL questionnaire in diabetic patients in Jordan.

Methods: Patients were enrolled in this cross-sectional study from 1st, January through April/2019 at several public health clinics in Jordan. The original DQOL questionnaire was translated to Arabic and then back translated by a different translator, then the two versions were compared. Prior to circulating the final version of the questionnaire cognitive validity test were applied to ensure that all the questions were clear. Then a questionnaire that included demographical and other health related questions in addition to the final Arabic version of the DQOL was circulated to the participants. The data of the questionnaire were analyzed using exploratory factor analysis and confirmatory factor analysis after excluding duplicated questions and questions that included more than 10% missing data, also Cronbach alpha was conducted to confirm internal consistency.

Results: The final revised Arabic version of DQOL included 29 item divided into three factors :"Satisfaction", "Impact", and "worries".

Conclusion: This study developed a validated Arabic version of DQOL that can measure quality of life of diabetics in the Arabic speaking world.

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Predicting milk to plasma ratio based on simple physiochemical characteristics: Milk excretion classification system (MECS)

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Aim: The study aimed to propose a Milk Excretion Classification System (MECS) for prediction of the milk to plasma (M/P) concentration ratio based on drug physicochemical characteristics.

Methods: A data set of 221 drug compounds, with experimentally derived M/P values were compiled from the literature. Similarly, physiochemical characteristics and plasma protein binding data were compiled for the same drugs. Data analysis was conducted in order to predict which parameters predict milk transfer that ultimately revealed a milk excretion classification system (MECS).

Results: Based on physicochemical properties, one can propose milk excretion classification system, where drugs can be classified into 5 classes. For acidic and zwitterionic compounds milk transfer is expected to be low (Class 1, M/P <1) and 94% of compounds are correctly predicted. Similarly, ~85% of neutral drugs (Class 2) are correctly predicted to have low milk to plasma ratio (M/P <1). On the other hand, ~90% of basic drugs with low protein binding (<90%) and MW <400 Da (Class 3A), showed milk accumulation with higher concentration in milk than in the plasma (M/P ≥1). Also, (74%) of bases with low protein binding (<90%) and MW ≥400 Da or high protein binding (≥90%) with MW<400 Da (Class 3B) are correctly predicted with low milk to plasma ratio (M/P <1). Likewise, 94.1% of bases with high protein binding and MW ≥400 Da (Class 3C), drug concentrations in human milk are low compared with maternal plasma (M/P <1).

Conclusion: Milk excretion of basic drugs is significantly affected by molecular weight and protein binding ($p<0.000$). While accumulation of Class 1 (acidic and zwitterionic) and Class 2 (neutral) compounds into maternal milk are not significantly affected by drugs molecular weight or protein binding. MECS provides a framework for predicting the extent of the xenobiotic transport into human breast milk based on simple drug characteristics.

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The manufacture and characterization of microbicide medical platforms for oral infections

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Background: Oral infectious diseases are dominantly common and affect 35% of the adult population worldwide. The poor adhesion and rapid disintegration of gels and pastes necessitate the need to develop microbicide impregnated adhesive dried films with the ability of eluting an antimicrobial agent over the period of treatment of different oral infections.

Methods: The dried films contained a combination of nystatin, metronidazole and were loaded in mixture of polyvinyl pyrrolidone (PVP) and hydroxyethyl cellulose (HEC) using casting method. Characterization involved thermal analysis of differential scanning calorimetry (DSC) and dynamic mechanical thermal analysis (DMTA) in order to detect the crystalline/amorphous state growth and glass transition temperature (Tg). Fourier transmission infra-red (FTIR) study was performed to obtain the conformational stretching and bending vibrations of the films. Mechanical properties were conducted to compare the strength and flexibility between the films. A microbial evaluation was also conducted on *Candida albicans* to assure the films ability to eradicate microbes.

Results: DSC showed appearance of amorphous drugs. Tg was highest with increasing the load of HEC. Also, the tensile strength and Yong's modulus increased. FTIR showed wide peak in the OH moiety indicating interaction between the polymers and the drugs. Furthermore, the films showed capability of eradicating the microbes for periods greater than 72 hours.

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The impact of genetic polymorphism on predicting the quality of anticoagulation control in Qatari patients treated with warfarin

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Background: Numerous studies have discussed the importance of pharmacogenetics at the time of warfarin initiation as a potential predictor for the maintenance dose of warfarin. Previously, variants of *CYP2C9 (coding for cytochrome P-450), VKORC1 (coding for vitamin K epoxide reductase),* and *CYP2F4* were investigated for their association with warfarin dose predictions. However, evidence does not exist relating to the role of pharmacogenetics on the quality of INR control after the initiation phase and on the maintenance of stable INR on the long term as measured by the time in therapeutic range (TTR).

Aim: To investigate the impact of genetic variants in *CYP2C9, VKORC1,* and *CYP2F4* on the level of INR control (by measuring TTR) at the maintenance phase (post first month of treatment).

Methods: This is an observational nested case-control study. This study was conducted on a cohort of Qatari patients treated with warfarin at Hamad Medical Corporation (HMC) with previously identified genotype for *CYP2C9, VKORC1,* and *CYP2F4.* The sample size of the cohort is 148 patients.

Results: The mean TTR was 62.8 ± 21%. TTR was not significantly different among carriers of the *CYP2C9*2,*3* compared to their non-carriers alleles (66.9 ± 20% vs. 60.8 ± 20%, p=0.108). Similarly, *VKORC1(-1639G>A G>A)* and *CYP4F2*3* did not have a significant effect on TTR (63.4 ± 20% in *VKORC1 A* carriers vs. 60.4 ± 22% in non-carriers p=0.45) (64.5 ± 21% in *CYP4F2*3* carriers vs. 59.1 ± 21% in non-carriers p=0.145) .

Conclusion: Genetic variants have no contribution to the quality of INR control in a cohort of Qatari patients treated with warfarin.

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Knowledge, attitude and awareness of practice regarding hepatitis B of pregnant females in Jordan

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Aims: The study aimed to assess the awareness of pregnant females towards hepatitis B during their pregnancy. As well as to assess gynecologists' practice regarding hepatitis B from patients' perspectives.

Method: A cross-sectional questionnaire was completed by a convenience sample of pregnant females in Amman, Irbid and Al Zarqa. The pregnant females were approached while waiting to be seen in the gynecologists' clinics in public hospitals. The questionnaire included Likert scale questions that measured their basic knowledge, attitudes regarding hepatitis B.

Results: The survey was completed anonymously by 330 pregnant females in Amman (n=152), Irbid (n=80) and Al Zarqa (n=98). They were aged 17-46 years (mean 28.7 ± 6.5). The majority 63.2% were in the third trimester of pregnancy. Most of the respondent females were below secondary education (70.9%). The results represented a significant difference between level of education and patient's knowledge about HBV, as only 31.2% (p=0.002) were aware of the risk of transmission from mother to fetus. Minority 35.6% knew about HBV vaccine. More than 90% of the patients agreed on not being counseled nor asked to do the HBV tests on their first perinatal visit. As for attitude questions, 95% of the patients are willing to be screened for HBV, 91% are willing to take antiviral drugs in case of HBV infection and 90% would let their baby receive HBV vaccine.

Conclusion: Our results suggest that there should be some awareness programs for pregnant females to improve their knowledge about hepatitis B infection. Efforts should be gathered from different healthcare professionals and patients to halt the spreading of this major global health problem, reducing the risk of vertical transmission of hepatitis B.

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Conference Proceedings
The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan

Author Index

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ISSN 0719-425

Conference Proceedings
The 7th International Pharmaceutical Conference 2019 (ZTIPC 2019), Amman, Jordan