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Sulfonamides, macrolides, torasemide, fumagillin and chloramphenicol were simultaneously analyzed in surface water samples by using solid-phase extraction (SPE) and reversed-phase (RP) liquid chromatography-electrospray tandem mass spectrometry (LC-ESI-MS/MS). In the pre-concentration and clean-up process, the pH value of samples and volume of the solvent for extraction of analytes from cartridge were optimized. Extraction recoveries were high with values in the range from 62 to 115%. Limits of quantification (LoQ) were in the range from 0.02 µg L\(^{-1}\)–0.2 µg L\(^{-1}\). Repeatability of the method was evaluated at LoQ and expressed as relative standard deviation (RSD). Calculated RSDs were low with values in the range from 2.4 to 14.5%. The method was successfully applied for analysis of the real samples of surface waters. Samples were collected along the rivers in Croatia on 19 sampling sites in Danube and Adriatic catchment areas in 2013, and another 20 places in 2014. Altogether, 20 target compounds were analyzed in 362 water samples and detected in 24 samples in the range, 0.02–5.3 µg L\(^{-1}\) or in 6.6% of samples. The most frequent and highest concentrations were detected for macrolide antibiotics. This is the first attempt of monitoring of antibiotics in surface waters in Croatia.

Biography
Irena Žuntar is working as a Full Professor and Specialist of Toxicology at University of Zagreb, Faculty of Pharmacy and Biochemistry, Croatia. She is Course and Unit Leader of Toxicology. Also, she considerably designed postgraduate specialist university program of Toxicology for health professionals and others interested or working in the field. She participated as Expert in scientific and professional opinions for Ministry of Health and Croatian Food Agency, and now she is in mandate Member of the Evaluation Panel of Croatian Science Foundation for scientific field of Biomedicine and Health, Public Health and Health Protection, and Pharmacy. She was Principal Investigator of a scientific grant and researcher on many scientific projects and gained two scientific awards. She was Supervisor of more than 50 student’s diploma thesis, and received 4 Rector Awards and two Dean Awards.

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Investigation of lidocaine-containing NLC systems for dermal application

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Topically applied anaesthetics are employed in order to eliminate pain caused by needle insertion and injection, thus ameliorating patient compliance. Furthermore, they are devoid of symptoms of superficial trauma and local reaction. Therefore, the aim of this work was to develop a new formulation of lidocaine, proposed to improve its clinical effectiveness in topical anaesthesia in terms of both enhanced anaesthesia and a prolonged duration of action. For this purpose, we incorporated lidocaine in nanostructured lipid carriers (NLC). Particle size and zeta potential measurements, Fourier transform infrared spectroscopy and Raman spectroscopy were performed to characterize the NLC system. Furthermore, DSC and XRD measurements were conducted to investigate lipid crystallization which plays a very important role in the performance of NLC carriers. Additionally, membrane diffusion and penetration studies were completed \textit{in vitro} and \textit{ex vivo}, followed by measurements on skin hydration and transepidermal water loss \textit{in vivo}. Our results lead us to the conclusion that the developed nanostructured lipid carrier is a promising vehicle for the topical delivery of lidocaine. The penetration of the NLC formulation was remarkable through heat separated epidermis after 24 hours, and the observed skin hydrating and occlusive effect also makes this formulation a favourable dermal carrier system.

Recent Publications


Biography

Mónika Bakonyi completed her Master's degree in Pharmaceutical Sciences in 2015 at University of Szeged. Since 2015, she is a PhD student at the Institute of Pharmaceutical Technology and Regulatory Affairs of the University of Szeged. Her research focuses on transdermal delivery of active agents, active and passive penetration enhancement techniques and electroporation. Her studies include experiments with Franz cell diffusion method, tape stripping method, Corneometer and Tewameter, ATR–FTIR and Raman spectroscopy. She has done a three month internship at the University of Freiburg, learning liposomes preparing and evaluating methods.

Notes:
Transfer behavior of the weakly acidic BCS class II drug valsartan from the stomach to the small intestine during fasted and fed states

Rania Hamed and Sabrine Hassan
Al-Zaytoonah University of Jordan, Jordan

Weakly acidic biopharmaceutics classification system (BCS) class II drugs may exhibit gastric supersaturation and precipitation. The objective of this study was to investigate the transfer behavior of the weakly acidic BCS class II model drug valsartan from the stomach to the small intestine during fasted and fed states. An in vitro transfer method, previously introduced by Kostewicz et al., based on a syringe pump and a USP paddle apparatus was used to obtain the concentration profiles of valsartan in the small intestine. Donor phases of fasted and fed states simulated gastric fluids (FaSSGF of pH 1.2 and FeSSGF of pH 5.0, respectively) were used to pre-dissolve Diovan®, immediate release tablets containing 160 mg valsartan. The initial concentrations of valsartan in FaSSGF and FeSSGF were determined before the transfer experiments. The pre-dissolved valsartan dispersions were transferred to acceptor media that simulate intestinal fluid at a flow rate of 2 mL/min. pH measurements were reported at time intervals corresponding to those of the transfer experiments to investigate the effect of % dissolved valsartan in the donor phase on lowering the pH of the acceptor media. The similarity f2 test was used to compare the concentration profiles in the acceptor media. Results showed that the initial concentration of valsartan in FaSSGF was very low of 6.2±0.6%, whereas in FeSSGF, the initial concentration was high of 91.8±4.2% after 30 mins. The concentration profiles for valsartan pre-dissolved in FaSSGF ranged between 13.1–86.5% after 60 mins, based on the physicochemical properties (buffer capacity and ionic strength) of the acceptor media. Whereas, valsartan pre-dissolved in FeSSGF was fully dissolved in the acceptor media after 60 mins. Therefore, the transfer model provides a useful screen for the concentrations of valsartan in the small intestine after oral administration during fasted and fed conditions.

Biography
Rania Hamed received her PhD in Pharmaceutical Sciences and Experimental Therapeutics at The University of Iowa in 2011, where she worked under the supervision of Professor Jennifer Fiegel. Her research was focused on developing a more physiologically relevant in vitro model mimetic of native, non-diseased tracheal mucus to understand the surface rheology of the airway-lining fluid and to elucidate bioaerosol formation from the trachea. She is currently an Associate Professor in the Faculty of Pharmacy at Al-Zaytoonah University of Jordan. Her current research focuses on developing controlled-release drug delivery systems based on hydrophilic/hydrophobic polymeric matrices and nanoemulsion-based gel and oleogel formulations for transdermal delivery. In addition, she is interested in determining the key parameters of the physiologically-relevant dissolution media that control the rate of dissolution of BCS class II drugs along the gastrointestinal tract to better predict its in vivo performance.

Notes:
Analysis of adverse drug reactions based on an electronic reporting system in a single hospital

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Monitoring the ADR (adverse drug reaction) is very important because of the characteristics of VHSMC where the proportion of elderly patients who are most likely to have ADR is large. Since 2015, we have developed a monitoring system for ADR in the hospital and have been monitoring the ADRs. This study attempts to analyze the report case. A retrospective study was conducted; the ADR was reported and evaluated through the hospital monitoring system in the EMR for 32 months from January 1, 2015 to August 31, 2017. This study analyzed the following: (1) by numbers of reporting case; (2) by reporter; (3) by drug classes (coding into the drug classification number of KFDA [Ministry of Food and Drug Safety of Korea]/possible multiple suspicious drugs in one report); (4) by symptoms (WHO-ART preferred term is used for coding/possible multiple symptoms in one report). A total of 757 evaluations were completed and the average number of reports per month was 22 in 2015, 23 in 2016, and 27 in 2017. According to reporter analysis, pharmacists were 78.7% (596 cases), followed by 11.4% (86) of nurses, 9.6% (73) of physicians and 0.3% (2) of radiation engineers. By drug classes, No. 114 antipyretic/analgesic/anti-inflammatory drug was 15.5% (136 cases), followed by 6.6% (58) of No.618 antibiotics for Gram positive and negative and 5.9% (52) of No.119 other central nervous system drugs, 5.7% (50) of No.117 psychotropic drug and 4.6% (40) of No. 219 other circulatory drugs. By symptoms, dizziness was 10.2% (120 cases), followed by 7.5% (88) of nausea, 7.4% (87) of vomiting, 5.3% (62) of pruritus, 4.2% (50) of dyspepsia. In this study, it is significant that the adverse drug reaction terminology is unified with the WHO-ART preferred term. We aim to improve the adverse drug reaction monitoring system using the WHO-ART preferred term, which can give ease of referral and accuracy of the evaluation. This is expected to contribute to manage the patient's safe use of medicines and adverse drug reactions.

Biography

H J Cho obtained her Bachelor of Pharmacy Degree from Chung-Ang University and a Pharmacist License in 2004. She currently serves as a Pharmacist of Seoul Veterans Health Service Medical Center. She was a Member of Adverse Drug Reaction Evaluation Team of Seoul Veterans Health Service Medical Center from 2016 to 2017. She serves as the Preceptor for the Hospital Pharmacy Practice Learning Experience since 2016 and she is an active Member of the Nutrition Support Team of Seoul Veterans Health Service Medical Center since 2017.

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Electrically responsive hydrogel films mediated iontophoretic transdermal drug delivery

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Hydrogels that are used for biomedical purposes such as controlled drug delivery systems should be biocompatible and often biodegradable. Depending upon the hydrogel type, their swelling ratios are dramatically changed, due to changes in external pH, temperature, ionic strength and electromagnetic radiation. This study describes the effect of hydrogel crosslink density upon the swelling kinetics and electro-responsive nature of the hydrogel, such that a formulation with the highest degree of swelling and greatest enhancement in solute permeation following the application of an electric current could be identified for subsequent microneedle (MN) production. The intention is to obtain electrically responsive hydrogel systems suitable for the production of a novel hydrogel forming, MN mediated iontophoretic transdermal drug delivery. In order to achieve hydrogels with good mechanical properties to be used as MN, network parameters, ionic conductivity, solute permeation, the mechanical and electrical properties of hydrogel films were investigated. Based upon the equilibrium swelling and ionic conductivity studies, a formulation producing a hydrogel of high swelling and conductivity at F7 6 hrs, F16 6 hrs, and F18 were identified to investigate the effect of electric current upon the electro-responsive nature of these hydrogel systems. In conclusion, the more open network structure of low crosslink density hydrogels enables solute permeation to occur more readily and the greater ionic conductivity of these formulations allows a greater solute permeation enhancement to occur when subjected to an external electric field.

Recent Publications


Biography

A Zaid Alkilani is an Assistant Professor, Dean of the Faculty of Pharmacy, Zarqa University, Jordan. She graduated from Jordan University, College of Pharmacy in 2006. Then she completed her MSc Degree in Pharmaceutical Science from Jordan University in 2010. After that she completed her PhD in Drug Delivery and Pharmaceutical Technology at the Faculty of Pharmacy, Queen’s University of Belfast, United Kingdom in 2013. Her research interests in the field of Transdermal Drug Delivery, Microneedle, Controlled Release, Formulations and Iontophoresis. She has presented her work at many international conferences such as, Proceedings of the 2nd International Conference on Microneedles, Cork, Ireland; Proceedings of the 2013 UKICRS Symposium, Belfast, UK; Proceedings of the UK PharmSci Conference, Nottingham, UK; Stratum Corneum VIII Conference, Cardiff, UK; 8th International Conference and Exhibition on Pharmaceutics and Novel Drug Delivery Systems 2016, Madrid, Spain and 6th FIP Pharmaceutical Sciences World Congress 2017, Stockholm, Sweden.
The relation between antibiotic use and changes of antimicrobial resistance at intensive care unit

Y S Chu, S Y Min, S M Yoo, Y J Jung and H K Jung
Veterans Health Service Medical Center, South Korea

Statement of the Problem: Antimicrobial resistance in major bacterial pathogens has become a serious medical health problem. To provide reference data or guideline for treatment of antimicrobial therapy, we studied a change pattern in the antimicrobial resistance rates of clinically important microorganisms at a veteran's hospital. In general, higher resistance rates are observed among intensive-care-unit (ICU) isolates than non-ICU isolates. Antimicrobial resistance is an emerging problem for ICU. Therefore, we also studied the trend of antibiotic consumption in ICU at the same hospital between 2012 and 2016.

Methodology & Theoretical Orientation: Susceptibility data were collected from Seoul VHS Hospital's EMR (Electronic Medical Record) system and antimicrobial resistance monitoring system annual report between 2012 and 2016. We used days of therapy (DOT) to calculate the annual antibiotic consumption for 17 antibiotic groups, retrospectively.

Findings: Total number of detected bacteria in the medical center was 96,410. Frequently isolated organisms in decreasing order were Staphylococcus aureus (12%), Pseudomonas spp. (10%), Acinetobacter spp. (10%), Klebsiella spp. (9%). Methicillin-resistant S. aureus (MRSA), vancomycin-resistant S. aureus (VRS), vancomycin-resistant Enterococcus spp. (VRE), multidrug-resistant P. aeruginosa (MRPA), multidrug-resistant Acinetobacter baumannii (MRAB) and carbapenem-resistant Enterobacteriaceae (CRE, Klebsiella pneumoniae) were isolated at 75~80%, 0%, 12~37%, 10~15%, 55~68% and 2~15%, respectively; the resistance rate increased gradually. Average annual antibiotic consumption during 2012–2016 was 18002 DOT/year. The prescription rates of injection antibiotics are in the order of glycopeptide, carbapenem, β-Lactam/β-Lactamase inhibitor, 3rd generation cephalosporin, 1st generation cephalosporin and quinolone. However, no statistically significant change in the total amount of antibiotics was observed during the study period. Consumption of 2nd generation cephalosporin, lincosamide, monobactam and aminoglycoside was significantly decreased, while that of β-lactam/β-lactamase inhibitor, 3rd and 4th generation cephalosporin, carbapenem, quinolone, polymyxin, glycycline and oxazolidinone with broad spectrum increased significantly.

Conclusion & Significance: High rates of antibiotic consumption were associated with high resistance rates of microorganisms. The increase of multidrug-resistant microorganisms requires an update of guidelines and a more strict control of antibiotics.

Recent Publications

Biography
Y S Chu is a Pharmacist working on improving patients' health through patient safety management and system improvement since four years at the Seoul VHS Hospital, the largest veteran's hospital in Korea. She has 15 years of experience both in hospitals and pharmacies, contributing to social healthcare and education.
In silico analyses of several signal peptides for the excretory production of phenylalanine ammonia-lyase in Escherichia coli

Hajar Owji and Shiva Hemmati
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Statement of the Problem: Day by day, the demand for biotherapeutics and recombinant proteins is increasing. Herein, cytoplasmic expression in prokaryotic and eukaryotic hosts has been widely accepted. However, there are several obstacles in the large-scale production of recombinant proteins. Recombinant proteins might form inclusion bodies or be degraded by proteases. Endogenous proteins might also interfere with the folding of a recombinant secretory protein. These factors, as well as the complicated downstream purification process, will result in loss of protein yield. Moreover, the yield of recombinant protein is not only related to expression levels, but also to translocation efficiency. Thus, the translocation efficiency could be increased by using signal peptides. Phenylalanine ammonia-lyase (PAL), involved in the first step of the phenylpropanoid pathway, catalyzes the deamination of phenylalanine to cinnamate and ammonia. PALs are ubiquitous in plants and also commonly found in fungi; however, animal lacks it. They are of special interest in several medical and industrial applications, including preparation of low phenylalanine diet, treatment of phenylketonuria and certain neoplastic tumors. Although several methods have been applied in the production of PAL, the final titers of PAL are still low, thereby impeding considerable industrialization of this enzyme.

Objective: This study aims to evaluate a vast number of signal peptides, previously deposited in databases (1168 signal peptides), in order to select the most appropriate ones for secretory production of PAL.

Methodology & Theoretical Orientation: Herein, the SignalP tool was applied to determine the secretion efficiency as well as cleavage sites. Moreover, various physiochemical properties of signal peptides linked to the protein as well as secretory pathways were identified. Effects of signal peptide addition on antigenicity, allergenicity, and mRNA secondary structure of PAL were evaluated.

Findings: The appropriate candidates for high yield and efficient production of phenylalanine ammonia-lyse in E. coli were identified.

Recent Publications

Biography
Hajar Owji completed her PharmD from Shiraz University of Medical Sciences. She is now working as a Research Pharmacist affiliated to the Department of Pharmaceutical Biotechnology. Her research interests are focused on Bioinformatics, Molecular Biology, and Biomolecular Pharmaceutical Sciences.
Temperature-responsive PVCL-based hydrogel as a promising novel nanocarrier for drug delivery

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Shiraz University of Medical Sciences, Iran

Among various dedicated nanoparticles for drug delivery applications, hydrogels have been mostly studied. Hydrogels are 3D structures with high water-content capacity that is made up of hydrophilic polymers. In addition, hydrogels have significant physicochemical properties, such as permeability, porosity, physical interactions and some smart ones are capable of responding to environmental stimuli like temperature, pH and ionic strength. Poly vinyl caprolactam (PVCL) as one of the most extensively studied thermo-responsive polymers, has a continuous coil-to-globule phase transition behavior with the lower critical solution temperature (LCST) ranging from 32 to 50°C, which depends on PVCL molecular weight and concentration. In this study, novel temperature responsive hydrogel based on poly(vinylcaprolactam) (PVCL) were prepared via reversible addition-fragmentation chain-transfer (RAFT) polymerization, where PEG-diacrylate served as cross-linker, and lysine was used as linking agent and applied for drug delivery. First, PVCL-PEG nano-hydrogel was prepared by RAFT polymerization in dioxane solvent, and then lysine was added to PVCL-PEG. After that, doxorubicin as an anti-cancer drug, was conjugated to lysine moiety of a prepared structure via Schiff-base reaction. Obtained nano-gels were characterized by FT-IR, 1H-NMR and their effective sizes were checked by dynamic light scattering analysis. LCST were determined and the drug release profile was tested in vitro. The 1H-NMR analysis of PVCL-PEG and PVCL-PEG-lysine confirmed the synthetic steps. DLS analysis represents the particles hydrodynamic size with average diameter of 20 nm. The LCST behavior was measured to lie at 37°C. Synthesized PVCL-PEG-lysine were observed to disperse well in aqueous solution without precipitation which show their high potential as a nanocarrier for drug delivery.

Biography
Elaheh Entezar-Almahdi completed her PharmD at Shiraz University of Medical Sciences in 2016. Currently, she is a PhD student of Pharmaceutics. Her research interests include, designing novel smart DDS, targeted drug/gene delivery system for cancers, and nanoparticulate DDS.

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Notes:
Preliminary studies regarding biocompatibility of encapsulated dopamine in a nanoporous matrix of TiO$_2$ as a material for store and release of dopamine


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The development of formulations based on titanium dioxide to store dopamine (TiO$_2$/DA) minimizes the oxidation of it by protecting it from direct exposure to natural light and air. It also fulfills a second function that is the release of dopamine (DA) for long periods in a rat model of hemiparkinsonism. A critical point is the toxicity of these materials that has led us to perform biocompatibility tests on these TiO$_2$/DA implants. The first biocompatibility studies on TiO$_2$/DA implant are presented here. Presterilized samples of the matrix were implanted subcutaneously and intraperitoneally in male Wistar rats. Scanning electron microscopy and histological examination of implanted samples and surrounding tissues were performed; subcutaneous implant was 0.095 g/DA per 20 ml of TiO$_2$. Histological examination of implanted samples and surrounding tissues revealed no evidence of acute or chronic foreign body inflammatory response. The fibrous capsules surrounding the implant remained thin (<100 μm) after more than three months in situ, while the surrounding tissue remained well vascularized; intraperitoneal implant was 0.02 ml/DA per 20 ml of TiO$_2$. The histological analysis for the liver, heart, lung, kidney, spleen, muscles and brain did not show structural macroscopic changes. It did not show an inflammatory response either (TNF-α, IL-6 and cellular infiltration), between the control group and the experimental groups. Also, the implants lingered encapsulated on tissue after three months; intraperitoneal implant was 0.13 g/DA per 20 ml of TiO$_2$. It was observed that a mild inflammatory effect and the presence of mononucleocytes within the group which received the highest dose of TiO$_2$/DA. The results of this analysis suggest that there is no contamination across the organs due to the implants. It is possible to suggest the compatibility of the TiO$_2$/DA implant with the rat tissue, and thus, justify a further investigation about its potential use as biomaterial for storing and releasing drugs.

**Recent Publications**


**Biography**

P Vergara-Aragón is an MD and PhD in Psychological Research and has worked in the Faculty of Medicine, UNAM in Mexico for more than 30 years. She collaborates with the Physics Institute of the National Polytechnic Institute. Her research is focused in the field of Parkinson’s disease (PD), study of the nigrostriatal pathway degeneration, and involved mechanism caused by rotenone and 6-OHDA; stabilization of dopamine and its use as treatment for PD; the study of the effects produced in vivo of a TiO$_2$ amorphous matrix as a reservoir for dopamine in a PD model in rats; description of the cognitive implications of PD in patients; toxicity and biological implications of rotenone exposure in animal models.

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Dopamine urinary content and dopamine striatal levels could be relations with the disturbed dopaminergic system of the hemiparkinsonism rat model?

B Hernández-Téllez1, P Vergara-Aragón1, Valverde-Aguilar2, M Vázquez-García1, A Sánchez-García1, S M Castillo Alejo1, E A Rodríguez-Pérez1, L G Luna León1, E García-Ramírez1 and R Bustamante García1

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The aim of the present study was to establish the relation that exists between the striatal dopamine levels and urine dopamine content in hemiparkinsonism rat model. 20 Wistar rats were used and were randomized into two groups as follows: a) control group and b) lessoned injured group induced by (6-OHDA). All animals were re-tested on the same battery of motor tests that before lesion. The rotation test behavior test was assessed and striatal DA levels and urine DA were determined by HPLC, motor behavior fine tests were done and finally immunohistochemical (Hir+) striatum was done. We found a positive correlation between the dopamine levels in the striatum and the content dopamine in urine of rats (control vs. 6-OHDA group). Respect motor performance, the 6-OHDA group showed a significant fine motor impairment (grasp and advance) vs. control group (p<0.01). Immunostaining for tyrosine hydroxylase (TH) expression revealed no TH-immunoreactive (THir) neurons in any 6-OHDA animals vs. control group (p<0.01). Positive correlation between the dopamine levels in the striatum and the content dopamine in urine could be talking also, about a major proportion of urinary dopamine could be derived from the renal decarboxylation of circulating dopa and not dopaminergic system disturbance. The other hand, alterations of a forelimb motor function in rats could be only due to more vulnerability of striatal dopaminergic depletion and not to low periphery dopamine levels.

Recent Publications


Biography

B Hernández-Téllez is a Biology graduate and has worked in the Faculty of Medicine UNAM in Mexico for more than 20 years. Her research is focused in the field of Tissue Engineering and collaborates in toxicity and biological implications of rotenone exposure in animal models. She is a Professor of Histology in the Biology Cellular and Tisular Department, Faculty of Medicine, National Autonomous University of Mexico, Mexico.

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E-Poster

Pharma Europe 2018
Assessment for the use of nutritional support in Turkey

Beril Koparal, Aysenur Koç, Kübra Erdoğan, Nazan Arslan, Sıdia Büyükhelvacil Öztürk and Ali Aysakar
Zade Vital® Natural Supplements, Turkey

Dietary supplement market is growing in Turkey. Local and multinational companies develop and introduce many new products for Turkish dietary supplements market. However, in marketing literature, little academic research could be found regarding Turkish consumers’ behavior about dietary supplements. However, it is found that there is extremely low consumption of these products in the field of marketing research studies in Turkey. Understanding the awareness and utilization rates of nutritional support products is important at the point of designing strategies for producers, the state and related organizations. This general exploratory research in 60 different pharmacies located in different regions of Turkey (Mediterranean, Black Sea, Eastern Anatolia, Southeastern Anatolia, Central Anatolia Region) was carried out. Face-to-face interviews were conducted with 253 people aged 18 years and over from September 2017 to February 2018 (5 months). The data collected by the questionnaire includes the factors that affect the use of nutritional support products by respondents in the study, the recognition and consumption rates, the product content and how regularly they use it. Respondents were found to be immunocompromised (21.03%) at the beginning of their use of nutritional support products. Omega 3 fish oil (26.98%), multivitamins (17.86%) and CoQ10 (7.94%) were the most common sources of preference for the product (71.43%) and many factors have been found to be effective. It is thought that this research will lead the causal researches to be made in the market of healthy lifestyle products in the future.

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Construction of serum-resistance cationic polymer α-CD-PAMAM and evaluation of its performances as gene delivery vector

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Polyamidoamine (PAMAM) dendrimers as synthetic gene vectors have been proved to be efficient gene delivery systems. In this study, a kind of α-cyclodextrin-PAMAM conjugate polymer was synthesized as gene delivery vector. Based on 1H-NMR detection, about 6.4 PAMAM-G1 molecules were grafted onto an α-CD core. Agarose gel electrophoresis results revealed that CyD-G1 could efficiently bind with DNA and condense them into nano-scale particles which showed similar binding capacity of PEI-25K. Besides, it could protect DNA from DNase I degradation in a low N/P ratio. When N/P ratio in the CyD-G1/DNA polyplex was 40, the average particle size of CyD-G1/DNA polyplex was about 120nm, and zeta potential was +21mv. Also, this polyplex could maintain its particle size in a serum-containing solution within 360 mins. In comparison with PEI-25K carrier, CyD-G1 showed low cytotoxicity in various cell lines. Cell transfection results showed that CyD-G1 could efficiently deliver DNA into cells at N/P=80 compared with lipofectamine2000 and PEI-25K. Unlike lipofectamine2000 and PEI-25K, in serum-containing test condition, CyD-G1/DNA polyplex could maintain the transgene activities. The results of confocal laser scanning microscopy indicated that most DNA entered into cell nuclei within 4h, and this phenomenon was consistent with the results calculated by flow cytometry. Above all, CyD-G1 showed good transgene activities and this gene delivery vector could be used not only for in vitro but also for in vivo testing.

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Solubility strategies in pharmaceutical research and development

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The ideal drug attributes allow easy formulation into common and already registered dosage forms. Solubility into conventional oral (per os) and intravenous formulations as well as good absorption in the gastrointestinal tract always facilitate achieving desired therapeutic goals as well as demonstrating acceptable pharmacokinetic profiles. However, during drug discovery optimization phase, the low solubility of drug candidates has become one of the most frequent issues that prevent these attributes from being fulfilled. Low solubility impacts the intravenous formulation feasibility and the oral bioavailability. In parallel, safety and toxicity concerns have to be anticipated, thus challenging clinical development. This lecture describes comprehensive strategies towards these ends, at the interface between research and development, to alleviate solubility deficit in order to realize essential animal studies. The main enabling formulations to tackle solubility will be described through several unpublished case studies. Some undisclosed formulations for low water soluble molecules will be presented. A focus on nanotechnology, enabling formulation to deliver drug substance via an intravenous administration will be discussed, including feedback from the FDA for incrementally modified drug (IMD) submission. However, to avoid labor intense and resource-consuming pharmaceutical development, approaches to design solubilizing prodrugs or salts compatible with standard drug formulation technologies will be considered. Finally, these approaches either based on enabling formulation or molecule design will be compared to allow making strategic choices as early as possible in the discovery phase to ensure fast and smooth pharmaceutical development.

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Structure-based design for binding peptides in anti-cancer therapy

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The conventional anticancer therapeutics usually lack cancer specificity, leading to damage of normal tissues that patients find hard to tolerate. Ideally, anticancer therapeutics carrying payloads of drugs equipped with cancer targeting peptides can act like “guides missiles” with the capacity of targeted delivery towards many types of cancers. Peptides are amenable for conjugation to nano drugs for functionalization, thereby improving drug delivery and cellular uptake in cancer-targeting therapies. Peptide drugs are often more difficult to design through molecular docking and in silico analysis than small molecules, because peptide structures are more flexible, possess intricate molecular conformations, and undergo complex interactions. In this report, the development and application of strategies for structure-based design of cancer-targeting peptides against GRP78 are discussed. This presentation will also cover topics related to peptide pharmacokinetics and targeting delivery, including molecular docking studies, features that provide advantages for in vivo use, and properties that influence the cancer-targeting ability. Some advanced technologies and special peptides that can overcome the pharmacokinetic challenges have also been included.

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Building a culture of employee engagement

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With the complexity in the pharmacy profession and with advancement of technologies in hospital pharmacy setting, the human factor tends to be forgotten or ignored which might lead to major employee disengagement. Studies show that when the employees are involved in and are enthusiastic and committed to his or her work, an increased retention, reduced sick call, increased profitability, accountability and improved customer retention are observed. One of the many tools to measure employee engagement is through Gallup Q12 survey which is currently used in many health care institutions in the United State of America including Cleveland Clinic Abu Dhabi. This presentation shares the Cleveland Clinic Abu Dhabi Hospital pharmacy experience focusing on initiatives and strategies in building the culture of engagement in the Pharmacy Department in Cleveland Clinic Abu Dhabi.

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Influence of hot melt extrusion processing parameters on the properties of a pharmaceutical formulation

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Prince Sattam Bin Abdulaziz University, Saudi Arabia

Hot melt extrusion (HME) is an old technology that has been recently adapted to be used in the pharmaceutical industry. HME is a continuous process that is widely used to produce a solid dispersion matrix. The aim of this dissertation is to evaluate different factors that will affect the pharmaceutical formulation properties that are produced using HME. For HME, there are different variables that will affect the product quality such as processing parameters, material selection, material ratio and the presence of gas or moisture. One aim of this study is to find the most significant factor that affects the product properties using the simplest design of experiment. Material selection and the ratio between the materials will be extensively evaluated using carbamazepine as a model drug. Moisture content and gas introduced during the process will be assessed to illustrate the best method to remove them. Process parameters show a significant effect on the product quality. Polymer selection and the ratio between the polymers show a great impact on drug dissolution and stability studies. Effective degassing has successfully enhanced the overall product quality features such as dissolution, shape, drug content and stability.

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Advancing pharmacotherapy services: A futuristic model of Cleveland Clinic Abu Dhabi

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Cleveland Clinic Abu Dhabi (CCAD) opened its doors in March 2015, providing inpatient and outpatient services through five major institutes of practice through a state of art facility with the highest level of automation. Establishing a unique and advanced practice pharmacotherapy services at CCAD was a requirement, a vision and a challenge. We had to consider the scope of services and identify the necessary infrastructure to operate including the necessary manpower and needed expertise; add to that identify challenges and pertinent solutions. Establishing a therapeutic drug formulary and putting it into effective use was one of our early tasks as the cornerstone for the pharmacotherapy practice of any medical center. As such, the pharmacotherapy services had the privilege to establish the formulary at CCAD that subsequently got endorsed and approved by the executive medical board. Putting the formulary into effective use through build of drug records, order sets and protocols was our next lightening success where we worked to optimize the use of the provided technology with pertaining complexity to implement best practices and ensure safe and effective drug therapy. We managed to apply pharmacotherapy through technology; a comprehensive system based approach. This was not without major challenges that had to be addressed including difficulties in medication procurement, variations in clinical practices in a facility that is employing over 70 nationalities coming from different practice models. In addition to the contributions at the system level, we laid the infrastructure for direct patient care. We established our own managed inpatient pharmacotherapy consult services and anticoagulation and heart failure clinics with policies and procedures, workflows and electronic medical records functionalities required to facilitate our services and allow us to measure key performance indicators. In parallel, equally important and essential was to recruit qualified highly trained pharmacotherapy specialists needed to support these services. We are privileged with a team that is very cohesive, positive and highly qualified working passionately to establish additional services in a futuristic model of practice supporting the “patient first” philosophy, the Cleveland Clinic philosophy.

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Caffeic acid-derived polyether from medicinal plants: Structure and biological activity

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A new series of linear and regular 3-arylglyceric acid-derived polyether, namely, poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA) was isolated and identified in the water-soluble, high-molecular weight fractions obtained from extracts of different species of Comfrey. Symphytum asperum, S. caucasicum, S. officinale, S. grandiflorum and Bugloss Anchusa italica. According to data of 13C, 1H NMR, APT, 2D 1H/13C HSQC, ID NOE and 2D DOSY experiments, the polyoxyethylene chain is the backbone of the polymer molecule. 3, 4-dihydroxyphenyl and carboxyl groups are regular substituents at two carbon atoms in the chain. The repeating unit of this regular polymer is 3-(3, 4-dihydroxyphenyl)glyceric acid residue. This compound is a first representative of a new class of natural polyethers. Then the racemic monomer 2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid (DDPPA) and its virtually pure enantiomers (+)-(2R,3S)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid and (-)-(2S,3R)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid were synthesized for the first time via Sharpless asymmetric dihydroxylation of trans-caffeic acid derivatives using a potassium osmate catalyst, a stoichiometric oxidant N-methylmorpholine-N-oxide and enantiocomplementary catalysts cinchona alkaloid derivatives (DHQ)2-PHAL and (DHQD)2-PHA as chiral auxiliaries. It is well known that epoxides are valuable synthons in organic synthesis and have been introduced into pharmaceutical applications, such as in the synthesis of antitumor drugs. Subsequently, the building block for the production of derivatives of PDPGA, methyl 3-(3,4-dimethoxyphenyl)glycidate was synthesized based on the Darzen reaction or by oxidation with oxone in order to produce future derivatives of synthetic analogue of natural polymers through ring-opening polymerization of 2,3-disubstituted oxirane. PDPGA is endowed with intriguing pharmacological properties as anticomplementary, antioxidant, anti-inflammatory, burn and wound healing and anticancer properties. PDPGA and DPGA exerted anticancer activity in vitro and in vivo against human prostate cancer (PCA) cells. However, anticancer efficacy of PDPGA is more effective compared to its synthetic monomer. Overall, this study identifies PDPGA as a potent agent against PCA without any toxicity, and supports its clinical applications.

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Iran’s pharmaceutical industry: Structure, players and institutions and regulatory system

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The present research seeks to understand the behavioral logic of the players of Iran’s pharmaceutical industry so as to infer the innovative treatment of the firms. The structure of such an approach is composed of some components through which performance analysis of certain technological industry could be made possible. In this research, we use two steps of expert panel review: first step is 17 experts and second step is 11 experts from universities, companies and governmental institutes. The current study wishes to explain structural model of institutional elements in this technological sector. Subsequently, in light of such an explanation, structural elements of this sector would be analyzed through identification of legal and regulatory framework, innovative culture, innovative infrastructure, financial resources, information resources, technology transfer mechanisms, commercialization support and marketing.

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Synthesis, anti-bacterial activity and molecular docking of novel pyrazole-thiazolidinone conjugates

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A novel series of pyrazole conjugates were synthesized through Vilsmeier Haack and nucleophilic substitution reaction. The chemical structures of these compounds were established using 1HNMR, 13CNMR, IR and elemental analyses. The synthesized compounds were assayed for antimicrobial activity against two Gram positive bacteria (methicillin-resistant Staphylococcus aureus, Staphylococcus aureus) and four Gram negative bacteria (Escherichia coli, Salmonella typhimurium, Klebsiella pneumonia and Pseudomonas aeruginosa). Interestingly, among the compounds tested, 3-(2,4-dichlorophenyl)-1-(2,4-dinitrophenyl)-1H-pyrazol-4-yl)methylene)hydrazinecarbothioamide (3a) and 2-((3-(2-chlorophenyl)-1-(2,4-dinitrophenyl)-1H-pyrazol-4-yl)methyleneamino)thiazolidin-4-one (4b) were the most cogent antimicrobial compounds with minimum bacterial concentration (MBC) of 0.08, 0.08, 0.16 and 0.16 μg/mL against MRSA and S. aureus respectively. To explore the antimicrobial result on a structural basis, molecular docking studies of the synthesized compounds into the crystal structure of topoisomerase II and topoisomerase IV using AutoDock Vina suggested that compounds 3a and 4b would form hydrogen bonds with the active site of the target.

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Nivolumab radiolabelling with Ga-68: Two different approaches for the formulation of an immunoPET tracer to detect PD-1 expressing tumors

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In recent years, immunotherapy with drugs that inhibit immune checkpoints has shown clinical efficacy in several different types of cancer by blocking PD-L1/PD-1 and CTLA-4 checkpoint pathways. Direct imaging of cell surface targets for immunotherapy using monoclonal antibodies (Mo)Abs labeled with PET and SPECT radioisotopes can visualize drug distribution and tumor characteristics. The aim of this study was to develop an immunoPET probe labeled with the PET radioisotope gallium-68 for imaging PD-1 expressing tumors. For noninvasive detection of PD-1, we chose Nivolumab (Opdivo®; Bristol-Myers Squibb, Princeton, NJ, USA), the first-in-human immunoglobulin G4 (IgG4) PD-1 immune checkpoint inhibitor antibody. We developed direct (free nivolumab) and indirect (functionalized nivolumab with bifunctional cyclic chelators, DOTA/NOTA) labeling approach procedure using the PET isotope Ga-68 obtained from a pharmaceutical grade 68Ge/68Ga generator (Eckert & Ziegler, Berlin, Germany). The 68Ge/68Ga generator was eluted with 0.1 M HCl following the manufacture’s protocol. A solution of ultrapure NaOAc 1.25M (Fluka Traceselect, ≥99.99%, metal basis) was added to nivolumab or DOTA/NOTA-nivolumab protein solution and then the eluate 68GaCl3 (ca. 50-100 MBq) bringing the pH to 5–6. The reaction mix was incubated in a heat block at 37°C for 40 minutes and after that the resulting radiopharmaceutical was isolated from free Ga-68 by centrifugation. The radiochemical purity percentage of [68Ga]Ga-nivolumab and [68Ga]Ga-DOTA/NOTA-nivolumab was determined using instant thin layer chromatography (TLC); TLC-SG strips are used as stationary phase and sodium chloride (0.9%) as mobile phase to separate the radiolabelled (Mo)Abs, which remains at the bottom, while the free gallium-68 moved to the top. Our results showed that the indirect approach is a site-specific labeling procedure and these radioimmunoconjugates are more stable than the direct approach. The promising labeling results showed an efficient procedure to label the antibody with Ga-68 providing the model for the future production of immunoPET imaging probe.

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Exploring 3D structure of human gonadotropin hormone receptor at antagonist state using homology modeling, molecular dynamic simulation, and cross-docking studies

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Human gonadotropin hormone receptor, a G-protein coupled receptor, is the target of many medications used in fertility disorders. Obtaining more structural information about the receptor could be useful in many studies related to drug design. In this study, the structure of human gonadotropin receptor was subjected to homology modeling studies and molecular dynamic simulation within a DPPC lipid bilayer for 100 ns. Several frames were thereafter extracted from simulation trajectories representing the receptor at different states. In order to find a proper model of the receptor at the antagonist state, all frames were subjected to cross-docking studies of some antagonists with known experimental values (Ki). Frame 194 revealed a reasonable correlation between docking calculated energy scores and experimental activity values (\(|r|=0.91\)). The obtained correlation was validated by means of stratum-specific likelihood ratios (SSLR) and showed the presence of no chance correlation for the obtained model. Different structural features reported for the receptor, such as two disulfide bridges and ionic lock between GLU90 and LYS 121 were also investigated in the final model.

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Trichiliasinenoids A–C, three novel 6, 7-secomexicanolide limonoids with a 7, 29-linkage from *Trichilia sinensis*

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Meliaceous limonoids, characteristic chemical markers of the Meliaceae family are natural products with both fascinating structures and potential bioactivities that have attracted interest from natural products chemists and synthetic chemists in the past half century. As part of a continuing search for structurally interesting and biologically important limonoids from the Meliaceae family, the leaves and twigs of *Trichilia sinensis* collected from Xishuangbanna, Yunnan province of China were investigated. *Trichilia sinensis* Bentv, a shrub, is native to the south of China and Vietnam, having traditional applications in the treatment of several diseases such as abdominal pain caused by *Ascaris lumbricoides*, chronic osteomyelitis, scabies, and eczema in folk medicine. The three novel rearranged mexicanolide-type limonoids (trichiliasinenoids A–C) with an unprecedented C-29-C-7 connecting carbon skeleton formed by migration of C-7 from C-6 to C-29 of a mexicanolide-type limonoid precursor were isolated from the leaves and twigs of *Trichilia sinensis*. Their structures were assigned by spectroscopic analysis, and the absolute configurations were determined by X-ray crystallography and CD calculation. A possible biosynthetic pathway of trichiliasinenoids A was also proposed. The three new limonoids were evaluated for their cytotoxic activity against human myeloid leukaemia (HL-60), hepatocellular carcinoma (SMMC-7721), lung cancer (A-549), breast cancer (MCF-7), and colon cancer (SW480) cell lines by MTS assay. Trichiliasinenoid B showed cytotoxicity against HL-60 cells, SMMC-7721 with an IC₅₀ value of 5.2 μM and 30.6 μM, respectively, whereas other limonoids were inactive and comparable to the cisplatin positive control (IC₅₀: 1.1–17.3 μM).
Preparation, characterization and in vivo antiplasmodial activity of magnesium oxide nanoparticles on *Plasmodium berghei* infected mice

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The search for new antimalarial agents remain an illusion to some extent in the global fight against antimalarial drug resistance. Malarial treatments now have taken a toll from single dose regimen to combinations of drugs over a period of three days to intravenous or intra muscular injections for three days followed by oral treatment for another three days. This change is surely a problem and fuels the search for newer and more rapid antimalarial agents. In this research, the potentials of magnesium oxide (MgO) nanoparticles were discovered to the fullest. MgO nanoparticles were synthesized using sol-gel process and characterized using SEM, FTIR and UV-VIS spectral study to confirm the formation and size of the nanoparticles. LD50 was carried out using 13 of the mice and was found to be 1131.4 mg/kg. 20% of this value was used to formulate a graded dose of 20, 10 and 5 mg/ml/kg. Then 30 mice divided into a group of five, containing six mice each and were inoculated with 0.2ml of ANKA strain of *Plasmodium berghei*, intraperitoneally; they were left for the next seven days before treatment with the graded doses based on their body weight. 20/120mg/kg standard dose of artemether/lumenfantrine was used as a positive control while negative control were given no treatment at all. Data were analyzed using mean percentage parasite clearance rate and with that, MgO nanoparticles showed a remarkable clearance rate of 98.8% just after 24 hours of administration and at the end of the four day curative model all the parasites were cleared from the blood; however, one shizoint was seen in two cases. Coartem on the other hand had 81% clearance rate after 24 hours and at the end of the curative model, 98% clearance rate was achieved. This clearly showed that MgO nanoparticles are superior in the clearance of the ANKA strain of *Plasmodium berghei* in infected mice than Coartem.

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Hot-melt extrusion (HME) and its application for bioavailability improvement of poorly water soluble drugs

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**Statement of the Problem:** For orally administered drugs, water solubility and permeability are the rate-limiting factors to achieve their desired concentration in systemic circulation for the pharmacological response. Poor water solubility of new chemical entities belonging to biopharmaceutical classification system (BCS) class II and IV accounts for 40 to 70% incidence of delay or failure during the drug product development process. Therefore, turning poorly water soluble drugs into viable therapeutics is the recurring and most challenging aspect facing by formulation scientist for drug product development. Hence, the poor bioavailability of the drugs has intensified demand for technologies and methods in the pharmaceutical industries to overcome their traits and meet the aforesaid challenges.

**Solution for the Problem:** Development of the formulations of BCS class II and IV drugs by converting the poorly water-soluble crystalline form into a more soluble amorphous form within the polymeric blends that will enhance the solubility which in turn leads to the improved bioavailability. These formulations can be developed by adopting various solid dispersion technological approaches like hot-melt extrusion (HME), kneading technique, co-precipitation, co-grinding, spray-drying, lyophilization, melt agglomeration process and supercritical fluid process. Among all these approaches, solid dispersion prepared by HME has gained popularity in the pharmaceutical industry as a means of improving the bioavailability of drugs due to its wide applications, simple process and low cost.

**Conclusion & Significance:** HME is an efficient technology for producing solid molecular dispersions with considerable advantages including the absence of solvents, few processing steps, and continuous operation over solvent-based processes such as spray drying and co-precipitation. Also, HME is one of the recommended processes by FDA to encourage move from batch-to-continuous manufacturing. Moreover, it is a value addition to intangible property of organization and can be used as noninfringing strategies for product development.

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Hypoglycemic, hypolipidemic and histological effects of ethylacetate extract of *Combretum platypterum* leaves in alloxan induced rats

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**Statement of the Problem:** Plants with medicinal properties are rich in phytochemical compounds. Some botanical polysaccharides have important bioactive components responsible for hypoglycemic effect, while some plants are known to have hypolipidemic activity. The purpose of this study is to determine the hypoglycemic, hypolipidemic and histological effects of ethylacetate extract of *Combretum platypterum* leaves in alloxan induced rats.

**Methodology & Theoretical Orientation:** Sequential extraction was carried out on the plant leaves using n-Hexane, ethylacetate and methanol. These were concentrated to constant weights. Phytochemical screening was carried out on the crude sample of *Combretum platypterum* leaves. Diabetes was induced in the albino rats by the administration of alloxan monohydrate (150 mg/kg i.p.). The ethylacetate extract of *Combretum platypterum* at different doses of body weight were administered orally at a single dose per day to the diabetic induced rats for a period of 13 days. The effects of the ethylacetate extract of *Combretum platypterum* leaves and glibenclamide on blood glucose, plasma lipid and blood chemical parameters were measured in the diabetic rats. Histological effect of the ethylacetate extract of *Combretum platypterum* leaves was also carried on the liver, spleen, kidney and heart of the diabetic rats.

**Findings:** Phytochemical screening showed the presence of flavonoids, saponins, cardiac glycosides, cyanogenetic glycosides, tannins and alkaloids, while anthraquinones were absent. Hypoglycemic effect of the ethylacetate extract of *C. platypterum* showed a significant positive effect. Administration of glibenclamide and the ethylacetate extract of *C. platypterum* showed significant hypolipidemic effect when compared with the reference range. This also caused reduction in total triglyceride and total cholesterol levels. Histological result showed that *C. platypterum* has no toxic effect on the organs.

**Conclusion & Significance:** The ethylacetate extract of *C. platypterum* showed both hypoglycemic and hypolipidemic activities. *Combretum platypterum* has a great potential with activities to lead to desired drug design.

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Electromembrane extraction combined with capillary electrophoresis for the determination of metoclopramide and ondansetron in urine samples

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Electromembrane extraction (EME) is a sample preparation technique in pharmaceutical, chemical, clinical and environmental analysis. This technique uses electromigration across artificial liquid membranes for selective extraction of analytes and sample enrichment from complex matrices. This method has many advantages such as simplicity, rapid, low-cost, low LOD, high preconcentration factor and high recovery. In the present work, simultaneous preconcentration and determination of two basic drugs namely metoclopramide (MCP) and ondansetron (OSN) were studied using EME as a suitable extraction method, followed with capillary electrophoresis (CE) using ultraviolet (UV) detection as separation technique. The drugs were extracted from 4 ml sample solutions, through a supported liquid membrane (SLM) consisting 2-nitrophenyloctylether (NPOE) impregnated in the walls of a polypropylene hollow fiber, and into a 20μL acidic aqueous acceptor solution resent inside the lumen of the hollow fiber with a potential difference applied over the SLM. The variables of interest, such as chemical composition of the organic liquid membrane, stirring speed, extraction time and voltage, pH of donor and acceptor phases and salt effect in the EME process were investigated and optimized. Under optimal conditions NPOE as SLM, stirring rate of 1000 rpm, 200 V potential differences, 20 min as the extraction time, acceptor phase HCl (pH 1.0) and donor phase HCl (pH 1.5). After the microextraction process, the extracts were analyzed by CE with optimum conditions phosphate running buffer (pH 2.0), applied voltage of 20kV and 25°C. Under the optimum conditions, limits of detection (LOD) and quantification (LOQ) for MCP and OSN were 2.31-2.68 and 7.72-8.91 ng mL⁻¹ respectively. Preconcentration factor and RSD for five replicates of each drugs were calculated to be 200 and 4.06-3.93 respectively. Finally, the applicability of this method was studied by the extraction and determination of these drugs in urine samples with recovery percentages of 87–92%.

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