DIRECT COST ASSOCIATED WITH ADVERSE DRUG REACTIONS AMONG HOSPITALISED CHRONIC KIDNEY PATIENTS IN A PUBLIC HEALTHCARE FACILITY IN MALAYSIA: A RETROSPECTIVE 3-YEAR STUDY

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ABSTRACT

Adverse reactions which are clinically diverse increases the overall cost of care, as it often results in additional days of hospitalisation, clinical investigations and treatment drugs. Thus, the main objective of this study is to evaluate direct medical costs among chronic kidney disease (CKD) patients who experienced adverse drug reactions (ADRs) during hospitalisation and identification of associated drug classes and clinical symptoms. Individual direct medical costs from the perspective of Ministry of Health (MOH), Malaysia among stages 3 to 5 CKD patients who experienced ADRs during hospitalisation were evaluated from 2014 till 2016. A higher number of days of hospitalisation (11.5 [4.25–39.25] days), ward and laboratory costs (RM48.50 [0–195.75]) plus drug costs (RM2.05 [0–91.30]) were observed among patients who did not survive ADRs. The highest number of hospitalisations, monitoring and laboratory costs were attributed to anti-arrhythmic drug class (11.0 [4.00-] days; RM326.00 [0-]) and haematological reactions (11.0 [1.00–19.00] days; RM116.80 [±112.38]). Furthermore, the highest treatment drug cost was attributed to anti-platelet (RM104.60 [0-]) and psychiatric reactions (RM17.50 [±24.13]). Top five major treatment drug classes contributed to ADRs were anti-infectives (*n* = 63 [39.4%]), anti-hypertensive (*n* = 23 [14.4%]), analgesic (*n* = 12 [7.5%]), statin (*n* = 10 [6.3%]) and anti-diabetic (*n* = 8 [5.0%]). Antibacterial constitutes the majority of the anti-infectives reactions. Vancomycin (*n* = 7 [13.7%]) tops the most ADRs contributing antibacterial. ADRs experienced during hospitalisation caused prolongation of hospitalisation and its associated investigational and treatment charges. The true value of the cost estimate could be much higher than the calculated value as the indirect costs were not included in the final estimates of this study and as a result of the Malaysian government's waiver policy.

Keywords: Direct cost, Adverse drug reactions, Chronic kidney disease

DEVELOPMENT OF GAS CHROMATOGRAPHY-MASS SPECTROMETRY FINGERPRINTS FOR *WARBURGIA UGANDENSIS* HERBAL MATERIALS

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ABSTRACT

Warbugia ugandensis is among the 10 most utilised medicinal plants in East Africa. Stem-bark and leaves are used as remedies for malaria, stomach ache, coughs and skin diseases. Consequently, the plant is endangered because of uncontrolled harvest and lack of domestication. There is therefore fear of poor quality commercialised products due to lack of evaluation mechanisms. This study explored the chemical profiles that could be used to confirm its authenticity and purity. *Warburgia ugandensis* used as reference during method development was harvested from Kenyatta University Medicinal Plant Research Garden. Six other samples were obtained from different geographical locations in Kenya. The samples were identified by a botanist and a voucher specimen (MO/002-008/2013) deposited in the East African Herbarium, National Museums of Kenya, Nairobi. Samples were harvested and processed by WHO recommended methods. Chromatographic profiles of the leaf and stem-bark were established based on parameters arrived at iteratively. The study characterised over 100 compounds in leaf and stem-bark. Based on area percent and known medicinal value, 22 compounds from the leaf and 38 from the stem-bark were selected as major chemical profiles. The compounds in the stem-bark included gamma sitosterol (1.0%–2.5%), squalene (0.2%–4.6%), isolongifolene (1.2%–2.8%), phenol 2 methoxy (0.8%–1.8%) and nerolidol (0.3%–1.5%). Those in the leaf included nerolidol 2 (0.3%–1.1%), phytol (0.6%–1.7%), 2-methoxy phenol (0.2%–2.2%), gamma tocopherol (0.2%–0.9%), vitamin E (0.4%–1.5%) and gamma sitosterol (1.8%–4.9%). Most of these compounds were characterised in *Warbugia ugandensis* for the first time. The profiles therefore can form fingerprints for use to evaluate its quality, purity and authenticity.

Keywords: Chromatographic, Fingerprints, Warburgua, Ugandensis, Quality

A MULTICENTRE STUDY ON AVERAGE WARFARIN DOSE TO MAINTAIN THERAPEUTIC INTERNATIONAL NORMALISED RATIO WITH TIME IN THERAPEUTIC RANGE OF MORE THAN 75% IN ATRIAL FIBRILLATION PATIENTS

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ABSTRACT

Large interindividual variability and over-anticoagulation resulting bleeding complications due to narrow therapeutic index of warfarin has causes its pharmacodynamic activity to be highly variable. Studies shown that ethnicity, age and gender contribute to warfarin response variability. Good coagulation control of Time in Therapeutic Range (TTR)>75% was chosen to determine the average warfarin dose in atrial fibrillation (AF) among ethnicity, age and gender. Data from Warfarin Medication Therapy Adherence Clinic of selected Penang hospitals were used for the analysis of average warfarin dose in AF among ethnicity, age and gender. Patients who fulfilled the inclusion criteria from 2015-2016 were followed up for a year. Of 576 patients, 210 patients had good coagulation control of TTR >75% with mean warfarin dose of 3.05 mg ± 1.25 mg. Only Chinese and Indian have significant difference in average warfarin dose with 2.86 ± 1.10 mg and 4.11 ± 1.40 mg, respectively (p = 0.008). Average warfarin dose was found not significantly different among gender and age. As for TTR achievement, 210 (36.4%) were able to achieve TTR >75%, 134 patients achieved TTR 60%–75% and 232 patients has TTR <60%. The median day to achieve three consecutive targeted INR is 186.5 days for atrial fibrillation patient newly started on warfarin therapy in 2015 until 2016. Indian patients required a higher warfarin dose than Chinese patients. This study found that mean warfarin doses were not affected by age and sex.

***Keywords*:** Warfarin, Atrial fibrillation, Time in therapeutic range, International normalised ratio

EFFECT OF GENETIC MODIFICATION OF MAIZE PLANT ON PHARMACEUTICALLY IMPORTANT PROPERTIES OF ITS STARCH

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ABSTRACT

Genetic engineering of maize plants for improved yield, drought and pest resistance has received considerable attention in agricultural research. The aim of this work is to determine the effect of genetic modification of maize plant on some pharmaceutically relevant fundamental properties of its isolated starches. Properties of starches isolated from PVA 39 and IWD 15 maize genotypes were compared with starch from unmodified maize grains. Morphology was studied by scanning electron microscopy (SEM); Fourier infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC) were evaluated. Swelling capacity, amylose content, pasting behaviour of the starches were also determined. SEM revealed that all the starches are largely irregular and polygonal with few round shaped granules. FTIR showed identical peaks in all the starch samples and DSC revealed higher enthalpies of starch gelatinization from the modified grains. Modification also increased amylose content, swelling capacity and viscosity of the starches. Genetic modification increased amylose content which positively affected pharmaceutically important properties like moisture sorption and viscosity thus, increasing their value in formulations especially as binders.

Keywords: Genetic modification, Amylose content, Maize starch, Pharmaceutical properties, Swelling capacity

IN-VITRO BIOPHARMACEUTICAL AND PHYSICOCHEMICAL EVALUATION OF DIFFERENT BRANDS OF CIPROFLOXACIN MARKETED IN ADEN-YEMEN

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ABSTRACT

The current study conducted to evaluate the biopharmaceutical and physicochemical equivalence of the three available pharmaceutical dosage forms of CIP in the local markets (tablets, infusion and eyedrops). Three brands for each dosage form were selected and coded as [tablets I, II and III), CIP infusion (Infusion I, II and III) and CIP eye drop (Eyedrop I, II and III)]. Different *in vitro* quality control tests, physiochemical and determination of active ingredients contents were performed. All brands of tablets have a satisfactory result that complies with the pharmacopeia specification except the hardness of the tablets was more than the recommended value, and the salinity of Infusion II and III was lower than 0.9, the viscosity of the eye drops was lower than the specified value. Post-marketing surveillance is an essential issue to distinguish poor-quality medicines and must be routinely performed to weed out substandard and counterfeit medicine.

Keywords: Ciprofloxacin, Biopharmaceutical, Quality control tests, Physicochemical, Pharmacopeia

A META-ANALYSIS OF THE GENETIC FACTORS THAT PREDISPOSED ASIAN WOMEN TO GESTATIONAL DIABETES MELLITUS

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ABSTRACT

A meta-analysis was conducted to determine the significant risk alleles which increase the risks of gestational diabetes mellitus (GDM) in Asian to help in decision-making for genotyping of women at risk. PubMed, Science Direct and HuGE navigator were used to identify relevant studies from January 2000 to November 2018. Data extraction was done by five reviewers. Using Review Manager 5.3, association between 11 SNPs and risks of GDM was determined. Odds ratios (ORs) with 95% confidence intervals (95% CI), test of heterogeneity and publication bias were calculated. The result was considered significant if *p*-value ≤ 0.05. Twenty-one studies were identified based on the inclusion and exclusion criteria. From 11 genetic variants studied, nine were found to have significant association with GDM susceptibility with different heterogeneity. Allelic, dominant and recessive genetic models show MTNR1B (rs138753, rs10830963) and CDKAL1 (rs7754840) are significantly associated with GDM. IGF2BP2 (rs4402960) was found to have significant association with GDM using allelic and recessive models. For TCF7L2 (rs7903146), significant association was found using allelic, dominant and over dominant models. KCNQ1 (rs2237892) showed association with GDM in dominant model only. Strong associations with increased susceptibility for GDM were also found for GSTM1 (deletion), GSTT1 (deletion) and GSTP1 (rs1695). However, MTNR1B (rs10830962), and PPARγ2 are lack of association with GDM risk in Asian population. Nine genetic variants were associated with increased GDM risk in Asian population. Screening of these polymorphisms to identify pregnant women at risk is recommended for prevention and personalised intervention.

Keywords: Gestational diabetes mellitus, Meta-analysis, Genetic model, Odds ratio, Single nucleotide polymorphism

TREND OF HBsAG SEROPREVALENCE AMONG BLOOD DONORS IN A NIGERIAN TEACHING HOSPITAL: A FIVE-YEAR RETROSPECTIVE STUDY

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ABSTRACT

World Health Organization (WHO) classified Nigeria as a hyper-endemic hepatitis-B surface antigen (HBsAG) positive nation with prevalence ≥ 8%. This study intends to add information that could strengthen established database to improve awareness and prevention of hepatitis-B virus (HBV) infection. We aimed to evaluate seroprevalence and trend of HBsAG among blood donors in Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Ogun State, Nigeria over a five-year period. Data from records of the 7,102 individuals aged ≥ 20 years who donated blood to blood bank in this hospital from January, 2012 to December, 2016 were analysed for gender, age, number of donors per year and HBsAG status. Data analysis was done with Statistical Package for Social Sciences software. $P \leq 0.05$ was considered statistically significant. Males were in the majority, 6,547 (92.2%). Age 30–39 years old was the major group, 3,052 (43.0%). Pooled HBsAG seroprevalence was 486 (6.8%). Females had the highest HBsAG seroprevalence across board with highest rate of 10 (19.6%) in year 2012 and pooled prevalence of 73 (13.2%). Age group ≥ 50 years had highest HBsAG seroprevalence 39 (8.5%) while age group 20–29 years old had least 128 (5.8%). Stratified HBsAG positivity decreased steadily from year 2012 to year 2016. This location was HBV intermediate-endemic. There were age, gender and yearly seroprevalence of HBsAG related trends which could be leveraged upon in finding effective preventive measures against the disease. We recommend mass vaccination by government against hepatitis B virus infection in addition to provision of sensitive blood investigational equipment.

Keywords: Trend, Seroprevalence, HBsAG, Blood donors, Teaching hospital

DRUG-RELATED PROBLEMS IN EMERGENCY DEPARTMENTS VISITS AND INTENSIVE CARE UNITS AT HEALTHCARE FACILITIES IN SAUDI ARABIA: A REVIEW OF THE LITERATURE

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ABSTRACT

The burden of drug-related problems (DRPs) is becoming an issue of healthcare concern. It has been responsible for many intensive care unit (ICU) admissions and emergency department (ED) visits in Saudi Arabia. We aim to summarise available data on ED visits and ICU admissions linked to DRPs in Saudi Arabia and provide recommendations for preventive measures. A systematic search of the literature was conducted using PubMed and Google Scholar databases to identify eligible studies. The review included research on ED visits and ICU admissions linked to DRPs performed in Saudi Arabia from the database's inception to January 2020. Study selection, data extraction, and assessment were performed based on PRISMA guidelines. The initial search of literature generated 267 articles. After the study selection, 15 articles met our eligibility criteria and were included in the review. The commonly implicated DRPs were adverse drug reactions, medication non-adherence, drug overdose, drug interactions. Central nervous system drugs and cardiovascular drugs were the most frequently involved drugs. Most of these visits resulted in moderate harm. The prevalence of DRPs associated with ED visits and ICU admissions is high in Saudi Arabia. Sixteen out of a hundred ED visits and ICU admissions are related to DRPs. Therefore, the Saudi government should implement interventions to improve the awareness of rational drug use in the general public.

Keywords: Emergency department, Drug-related problems, Drugs, Saudi Arabia, Intensive care unit

THE EFFECTIVENESS OF PHARMACIST-LED MEDICATION REVIEW IN PEJABAT KESIHATAN DAERAH PETALING, SELANGOR, MALAYSIA

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ABSTRACT

Medication review is an important service in optimising medicine use and improves clinical outcomes. This study aims to assess the effectiveness of pharmacist-led medication review on patients' knowledge and adherence. For this prospective study, 480 patients were randomly recruited in six primary healthcare clinics at the Petaling District Health Office, Selangor, Malaysia. Patients were interviewed with a questionnaire and validated medication adherence scale during recruitment and at follow-up visits to assess their medication knowledge and adherence. The data was analysed using Chi-square tests and paired *t*-tests to determine the correlation between medication knowledge and adherence with patient demographics. Among 408 patients that had completed the follow-up, 16.9% of patients showed medication knowledge deficits on recruitment. However, there is a significant improvement in the medication knowledge indices during the follow-up session ($p < 0.001$). Elderly patients were found to benefit from medication review with better medication knowledge and adherence post-medication review. The study found that the number of good adherers increased by 29.3% after the medication review. A further study demonstrating the effectiveness of medication review in cultivating knowledge retention and sustained adherence in the longer-term is warranted. Future work shall also focus on measuring the cost-effectiveness of pharmacist-led medication review implementation in primary healthcare settings. Pharmacist-led medication review is an essential and effective service in primary health care facilities for patients to enhance their knowledge on their medications, and adherence especially in elderly patients on chronic medications.

Keywords: Pharmacist, Medication review, Patient medication knowledge, Medication adherence, Primary care

EFFECT OF VITAMIN E ON POLYCYSTIC OVARY INDUCED BY DHEA IN FEMALE ALBINO MICE: A HISTOLOGICAL STUDY

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ABSTRACT

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder of reproductive-aged women. Vitamin E is used in combination with clomid, metformin, melatonin, or other drugs to ameliorate and improve the symptoms of PCOS. The aim is to investigate the histological effect of vitamin E on PCOS. PCOS model Using DHEA was adopted. Female mice were divided into eight group (n = 6). Group I, administered 1%T80; Group II, administered DHEA; Group III, administered clomid; Group IV, administered vitamin E; Group v, administered DHEA and vitamin E; drugs were administered for 20 days. Group VI, administered DHEA per day for 20 days followed by clomid, a dose per day, for the next 10 days; Group VII, administered DHEA per day for 20 days followed by vitamin E, a dose per day, for the next 10 days; group VIII, administered DHEA every day for 20 days followed by no treatment for the next 10 days. Mice were sacrificed, at the end of experiment, by neck dislocation. Ovary was surgically separated and kept in 10% formalin for histological analysis. DHEA administration produces PCOS changes in ovary. Clomid did not improve PCOS induced by DHEA, while vitamin E ameliorates PCOS to nearly normal. Vitamin E showed marked recovery of the ovarian tissue with the presence of many follicles in the various stages of development, indicating normal oogenesis. Follicles showed normal granulosa layer with defined thecal layers. The presence of corpora lutea was also seen, indicating that vitamin E treatment restore normal estrous cycle.

Keywords: PCOS, DHEA, Vitamin E, Clomid, Mice

IN VITRO INTERACTIONS OF *COSTUS SPECIOSUS* (J. KOENIG) SM., *CYMBOPOGON CITRATUS* (DC. EX NEES) STAPF. AND *TABERNAEMONTANA CORONARIA* (L.) WILLD WITH FIRST-LINE ANTI-TUBERCULOSIS DRUGS AGAINST *MYCOBACTERIUM TUBERCULOSIS* H37Rv

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ABSTRACT

The current study conducted to evaluate the biopharmaceutical and physicochemical equivalence of the three available pharmaceutical dosage forms of CIP in the local markets (tablets, infusion, and eyedrops). Three brands for each dosage form were selected and coded as (Tablets I, II, III), CIP infusion (Infusion I, II, III) and CIP eye drop (Eyedrop I, II, III)]. Different *in vitro* quality control tests, physiochemical and determination of active ingredients contents were performed. All brands of tablets have a satisfactory result that complies with the pharmacopeia specification except the hardness of the tablets was more than the recommended value, and the salinity of Infusion II and III was lower than 0.9, the viscosity of the eye drops was lower than the specified value. Post-marketing surveillance is an essential issue to distinguish poor-quality medicines and must be routinely performed to weed out substandard and counterfeit medicine.

Keywords: Plant fractions, Checkerboard, Fractional Inhibitory Concentration Index, Synergism