



YOUNG SCIENTISTS

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Documentation and verification of self-reported drug allergies in hospitalized patients

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Purpose: Pharmacists often have only the documented patient history to guide assessment of therapy. There is a lack of information on the incidence of claimed drug allergies or the validity of these self-reported drug allergies in the South African population¹. Mislabelling of patients as allergic to medication often excludes important therapeutic drugs and alternative agents may be more dangerous, less effective and more costly². The aim of the research was to determine the incidence of drug allergies in patients admitted to a private hospital and to assess the validity of these self-reported drug allergies.

Methods: A descriptive, non-experimental study design was used. Data was collected using a concurrent, cross-sectional approach data was obtained from patients admitted to hospital using medical chart reviews and researcher-led, questionnaire based interviews. During the seven month sampling period, 693 patients were identified with one or more self-reported drug allergies. A subset of 99 patients (14.2%) consented to a researcher-led interview. The allergies were assigned to one of three groups based on the history.

Results: A total of 953 allergies were identified in the 693 patients, with a ratio of drug allergy to patient of 1.4:1. The majority of claimed allergies were to penicillin (39.2%) and opioid analgesics (17.6%). Descriptions of the “allergic” reactions were only recorded on 8.9% (62, n=693) of the reviewed charts. In total, 1.3% (9, n=693) of the patients with a self-reported allergy received the allergen while in hospital. A total of 118 allergies were identified in the 99 interviewed patients, with a ratio of drug allergy to patient of 1.2:1. Inaccurate allergy history was found in 9.1% (9, n=99) of the interviewed patients. Overall, the majority of self-reported drug allergies (67.8%) had a “high probability” of being a true drug allergy.

Conclusion: In summary, the validity of self-reported drug allergies needs to be determined by a pharmacist before excluding medication from a patient’s treatment options. Detailed descriptions can assist in the evaluation of self-reported allergies which would be advantageous to both prescribers and patients.

References:

1. Potter, P.C. (2010). Discussion on drug allergies prevalence studies in South Africa. [Personal Communication, Head of Allergology, Department of Medicine, Groote Schuur Hospital].
2. Hung, O.R., Bands, C., Laney, G., Drover, D., Stevens, S. & MacSween, M. (1994). Drug allergies in the surgical population. *Canadian Journal of Anaesthesia*, 41(12):1149-1155.

Assessing inventory management practices at antiretroviral community health centres in the Cape Metropole

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Purpose: South Africa has the largest population living with HIV/AIDS, along with guidelines promoting earlier initiation of antiretroviral treatment (ART), task shifting that allows nurse-initiated ART, and awareness of available treatment options in people living with HIV (PLHIV), increases the demand for sustainable supply of antiretroviral drugs (ARVs) to the primary health care level. In recent years stock outs of ARVs and other chronic medicines have been reported at facilities across the country. The extent to which the management of these pharmaceuticals at facility level contributed to these stock outs is unknown. The aim of this study was to characterise the inventory management practices and medicine store maintenance of ARVs in community health centres (CHCs) in the Cape Metropole.

Methods: This was a cross-sectional study, using key indicators and interviews at all community health centres (CHCs) accredited to provide ARVs (N=23) in the Cape Metropole district of the Western Cape. An adapted MSH tool and a semi-structured questionnaire were used to collect data. Data sources included stock cards, electronic software, requisition forms and delivery notes. Respondents were the personnel responsible for ARV management, i.e. either a pharmacist or a post basic pharmacist assistant. Approval was granted for 15 (65 %) sites. Data was analysed using STATISTICA.

Results: 86.7% of CHCs utilised a logistics tool (either manual or electronic) to manage ARVs, while 13.3% did not use any tool. Although records were kept for an average of 82.7% of ARVs in facilities, only 32.9% were up to date (physical stock count matched recorded stock on hand) and 21.9% were found to be accurate (logistics tool existed for each ARV, filled in with all information on the ARV drug identification, with updated quantities). No historical data on stock outs or on monthly usage (monthly consumption) were recorded in any of the facilities, however, on the day of the visit no ARVs were out of stock. Despite the poor record-keeping, staff reported very few problems with stock availability owing to high ordering frequency (weekly on average), short lead times (3days) from the depot and a high order fill rate (91.9%). No expiries were found on the day of the visit. Only 80% of facilities met the criteria for space allocation in accordance with Good Pharmacy Practice (GPP) and 66.7% had appropriate labelling on shelves in the dispensary and storeroom.

Conclusions: This study has demonstrated poor record-keeping practices and challenges with respect to the size and organisation of medicine store rooms. While there was no conclusive evidence of poor stock availability or medicine expiries resulting from these practices, the high ordering frequency and associated costs raises questions about the effective management of budgets. While logistics management systems are generally in place, there is evidence that are not being utilised optimally to ensure the effective use of state resources.

The effect of an educational intervention on frequency and extent of documentation of adverse drug reactions to antipsychotic drugs

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Purpose: Antipsychotic drugs are the mainstay of treatment for psychotic disorders according to the Standard Treatment Guidelines (2012). However, these drugs are associated with multiple severe adverse drug reactions. In order to limit the effect of adverse drug reactions on patient care, documentation is necessary. Documentation of adverse drug reactions entails recording the reaction experienced, as well as supplementary information. Proper documentation can prevent future occurrences of the same or similar adverse drug reactions. The aim of this study was to determine the effects of an educational intervention targeting increasing documentation of the adverse effects of antipsychotic drugs.

Methods: A before-and-after method was employed, with an educational intervention forming the central point. The intervention consisted of the introduction of a purpose-designed adverse drug reaction documentation form, with accompanying education. A clinical audit of patient medical files was performed to determine the effect of the intervention on frequency and extent of documentation.

Results: A total of 102 patient medical records were screened during the pre-intervention phase, as well as another, separate 102 patient medical records in the post-intervention phase. During the pre-intervention phase 185 instances of adverse drug reaction documentation were recorded. Comparatively, 352 instances were recorded during the post-intervention phase. Documentation by doctors specifically increased from 70 instances to 216 instances after the intervention. Two cases of adverse drug reaction documentation using the supplied intervention tool were recorded.

Conclusion: Initial findings indicate that the frequency of documentation increased considerably between the pre-intervention and post-intervention phases, although the extent of documentation remained the same. The introduced adverse drug reaction documentation form proved to be largely unused and unsuccessful.

Pharmacists' perceptions of occupational specific dispensation (OSD): exploratory study of career and human resource perspectives

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Purpose: One of the strategies suggested and implemented by the South African government to alleviate the strain of health staff shortages in the public sector was the introduction of a remuneration structure and reward strategy known as occupational specific dispensation (OSD). The structure was developed specifically for some categories of public employees and was introduced in 2007 to “attract and retain skilled employees” (DPSA, 2007). This dissertation explores the perceptions of pharmacists' with regard to OSD. The areas of exploration were: 1) **pharmacists' perceptions on how OSD has altered their opinions on public sector employment.** Perceptions indicating that public sector is the organization of choice for employment would indicate OSD's potential to attract pharmacists. 2) **Pharmacists' perceptions of career advancement and the promotional structure of OSD** as an indication of possible organization commitment and motivation.

Methods: Key-informants were interviewed one-on-one and focus group interviews were conducted with production and supervisory pharmacists employed in academic hospitals, district hospitals and community health centers in the Western Cape; thus ensuring multiple perspectives. **Thematic analysis** was applied to all interviews with the help of qualitative analysis software, Atlas.ti®. One-on-one interview data analysis produced foundational themes and an *a priori* code framework for focus group interview analysis. Foundational themes were modified to produce final themes. Strategies to ensure validity included data saturation, reflexive interpretation and member checks. Reliability was demonstrated through inter-dataset code application and an audit trail transparency.

Results and conclusion: In the broad theme of **OSD and attraction**, elements of OSD have positively influence the image of public sector employment by: 1) offering a market-related remuneration package; 2) attracting a better caliber of professional and 3) offering management opportunities to junior pharmacists. In the broad theme of **overlapping of production level 3 and supervisory level 1 salary grades**, the major perception was that this part of the structure did not encourage pharmacists to progress and has led to many experienced pharmacists stagnating in their career while many inexperienced pharmacists have been promoted to management. This indicated that career advancement could not be envisaged by pharmacists.

References:

Department of Public Services and Administration (DPSA). (2007). Occupation specific dispensation (OSD) in the public service. [official notice]. Retrieved June 02, 2013, from <http://www.info.gov.za/speeches/2007/07061811451001.htm>.

Impact of selected herbal products on the *in vitro* transport and metabolism of indinavir

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Purpose: Patients infected with the human immunodeficiency virus (HIV) whom receive anti-retroviral (ARV) drug treatment are sometimes also taking herbal remedies. Pharmacokinetic herb-drug interactions are a realistic outcome in these patients. The aim of this study was to investigate the effect of selected herbal products, namely Linctagon C[®], Viral Choice[®] and Canova[®] on the *in vitro* transport and metabolism of indinavir in cell culture models.

Methods: Bi-directional transport of indinavir was conducted across Caco-2 cell monolayers in the absence (control group) and presence of three selected herbal products namely Linctagon C[®], Viral Choice[®] and Canova[®]. The apparent permeability coefficient (P_{app}) and efflux ratio (ER) values were calculated from the transport results. The metabolism of indinavir was determined in LS180 cells in the absence (control group) and presence of the four selected herbal products (experimental groups).

Results: The efflux of indinavir across Caco-2 cells increased in the presence of some of the herbal products in a concentration dependent way. However, one of the herbal products caused a reduction in the efflux of indinavir. All the selected herbal products promoted indinavir metabolism in LS180 cells.

Conclusions: Some of the herbal products investigated promoted indinavir efflux across Caco-2 intestinal epithelial cells and increased metabolism of indinavir in LS180 cells. This may negatively affect indinavir's bioavailability, but this needs to be confirmed with *in vivo* studies before conclusions regarding the clinical significance of this effect can be made. The product that reduced indinavir efflux may enhance its metabolism.

Type 2 Diabetes Mellitus: Disease pathogenesis and treatment

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Purpose: Type 2 diabetes mellitus (T2DM) is expected to be the 7th leading cause of death in 2030. Insulin resistance (IR) is synonymous with T2DM. It is widely accepted that inflammation plays a vital role in disease pathogenesis and can directly result in insulin resistance. Available therapies are few and ineffective at completely reversing and/or preventing disease progression. The following study was conducted to investigate the role of colon inflammation in the onset of insulin resistance and ascertain the role of the medicinal plant, *Sutherlandia Frutescens*, in disease prevention.

Methods: To investigate this, we fed three groups of male Wistar rats a HFD (40% calories from fat), a standard low-fat diet and a HFD + treatment with *Sutherlandia frutescens* respectively. 7 rats from each group were killed on days 7, 14, 28 and 56. Colon and mesenteric adipose tissue samples were taken and analysed for occludin, IL-1 β and COX-2 using RT-qPCR.

Results: Rats fed the HFD developed IR on day 56 as assessed using HOMA-IR. Plasma FFA's were significantly elevated in the HFD group compared to LFD ($p < 0.05$) and HFD + *S. frutescens* ($p < 0.01$) treated rats on day 56. In the colon, IL-1 β mRNA was down-regulated on day 7 (0.43-fold*) and conversely up-regulated on day 14 (2.63-fold*) and further down-regulated on day 56 (0.65-fold) compared to LFD. COX-2 mRNA was increased on day 14 (1.67 fold), but dropped precipitously to day 56 compared to LFD rats. In The mesenteric adipose tissue, the inflammatory markers were down-regulated in HFD compared to LFD although only reaching statistical significance on day 56 for IL-1 β (0.173-fold*). *S. frutescens* showed a statistically significant down-regulation for IL-6 (0.121-fold*), IL-1 β (0.0336-fold*) on day 56 compared to LFD.

Conclusions: Therefore FFA's do not mediate IR through inflammation in HFD fed rats in the current model. An aqueous extract of *S. frutescens* appears to have anti-inflammatory properties. ((*) shows statistical significance using one-way ANOVA)

Combining chemical permeation enhancers for synergistic effects

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Purpose: Therapeutic proteins are currently mainly administered by means of injections because of its low intestinal epithelial permeability. The purpose of this study is to investigate binary combinations of permeation enhancers to create synergistic drug permeation enhancer formulations for effective oral delivery of peptide drugs.

Methods: The effect of combinations of *Aloe vera*, *Aloe ferox* and *Aloe marlothii* leaf gel materials as well as *N*-trimethyl chitosan chloride (TMC) was measured on the transepithelial electrical resistance (TEER) of Caco-2 cell monolayers as well as the transport of FITC-dextran across Caco-2 cell monolayers. Each combination consisted of two materials mixed in five different ratios namely 10:0, 8:2, 5:5, 2:8, 0:10 at concentrations of 0.1% w/v and 0.5% w/v. The data was processed by the isobole method to determine the type of interaction between the absorption enhancers (e.g. synergistic, additive or antagonistic).

Results: The results showed synergism for the following combinations: *A. vera* and *A. marlothii*, *A. marlothii* and *A. ferox* as well as *A. vera* and TMC in terms of TEER reduction. Synergism occurred at some concentrations and at some ratios, while antagonism was detected at other concentrations and ratios. The antagonism interactions can probably be explained by chemical reactions between the chemical permeation enhancers such as complex formation. Antagonistic effects were found between *A. marlothii* and TMC as well as *A. ferox* and TMC at both concentrations.

In terms of FITC-dextran transport, synergism was found for the following combinations: *A. vera* and *A. marlothii*, *A. vera* and *A. ferox* and *A. marlothii* and *A. ferox* at concentration 0.5% w/v, whereas antagonism was observed for these same combinations at 0.1% w/v. From these results it is evident that the presence of FITC-dextran may have influenced the chemical reactions between the chemical permeation enhancers.

Conclusion: This study indicated that combinations of certain drug absorption enhancers resulted in synergetic effects in terms of tight junction modulation, while others caused additive or antagonistic effects. The combinations where synergism was obtained have potential to be used as effective drug absorption enhancers. The antagonistic interactions can possibly be explained by chemical reactions such as complex formation between the chemical permeation enhancers when a threshold concentration is exceeded.

Aloe gel materials as absorption enhancers in multiple-unit solid oral dosage forms for effective peptide drug delivery

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Purpose: The most popular and convenient route of drug administration remains the oral route; however, protein and peptide drugs such as insulin have poor membrane permeability and stability in the gastrointestinal tract. Absorption enhancers can be added to the drug delivery system to overcome the epithelial cell membrane permeability problem. Although previous studies have shown that aloe leaf materials improve the transport of drugs across intestinal epithelia, their performance in solid oral dosage forms has not been investigated yet.

Methods: Beads containing insulin and each of the absorption enhancers were produced by extrusion-spheronisation using a full factorial design to optimise the formulations based on transepithelial electrical resistance reduction of Caco-2 cell monolayers as response. The optimum bead formulations were evaluated in terms of friability, mass variation, particle surface texture, shape, size and dissolution. The transport of insulin across Caco-2 cell monolayers from the optimised bead formulations were determined over a 2 h period and compared to that of the aloe gel materials in solution. The samples obtained from the transport studies were analysed for insulin content by means of high-performance liquid chromatography (HPLC).

Results: The results showed that the TEER reduction, as an indication of tight junction modulation, obtained for the bead formulations containing aloe materials was concentration dependent. Furthermore, inclusion of croscarmellose sodium (Ac-di-sol®) as disintegrant showed an enhanced TEER reduction effect in combination with the aloe gel materials. Dissolution profiles were seen to release the insulin within the first hour from the beads. In accordance with the TEER reduction results, the aloe material containing beads showed similar insulin delivery across Caco-2 cell monolayers compared to the solutions, which were pronouncedly higher than that of the control group (insulin alone).

Conclusion: The optimised aloe gel material containing bead formulations showed high potential to deliver insulin effectively across human intestinal epithelial cells.

A novel semi-interpenetrating polymer network (IPN) matrix system for the delivery of sulpiride in schizophrenia

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Purpose: Schizophrenia is a neurodegenerative disease that affects the primary functional areas of the central nervous system, leading to memory dysfunction and reduction in social functionality. For the purpose of the current study sulpiride has been elected as the model drug to be delivered via a novel semi-IPN xerogel matrix drug delivery system.

Methods: A 3-factor, 3 level Box-Behnken experimental design was generated for statistical optimization which produced 15 formulations. A semi-IPN was formulated via crosslinking Gellan Gum (GG) in the presence of Poly (ethylene) oxide (PEO) the resulting polymeric was precipitated, dried and crushed to form matrix tablets. Characterization studies such as Fourier Transform Infrared spectrometry (FTIR), Differential Scanning Calorimetry (DSC), *in vitro* drug release studies, Textural Analysis and Scanning Electron Microscopy (SEM) were conducted. The properties of the synthesized xerogel as compared to crude polymers were evaluated.

Results: The fabrication of the semi-IPN xerogel was successful as evident from data derived from characterization studies such as SEM. Formulated matrix tablets displayed zero- order sustained release kinetics, extending over a period of 24 hours. The mechanism of drug release was observed to be initiated by swelling followed by surface erosion. A 100% drug release was achieved at 24 hours, thus proving its oral applicability. Crosslinked formulations displayed water uptake majorly between 450-500% which indicated a controlled rate of swelling and erosion further allowing for sustained release. Surface morphology of the crosslinked system depicted a porous structure formed by interpenetrating networks of polymers, thereby allowing for a greater degree of controlled penetration into the system affording it the ability to sustain drug release. Brinells hardness number ranged from 200-238, these results illustrate that despite its porous structure the matrix tablet maintains its structural integrity under compression. A peak at 215°C due to crosslinking was observed in the DSC profile. FTIR showed an additional NaOH group at 3276 cm⁻¹ due to crosslinking with EPI. An erosion of 80-86 % was observed in all formulations at the 24 hour mark.

Conclusion: The study validated that the crosslinking of PEO and GG enhanced the physiochemical and physicomechanical properties of the individual polymers, as well as the formation of a semi-IPN xerogel matrix that allows for sustained drug release. The porous structure of the matrix system further enhanced the ability to achieve sustained drug release.

Formulation and process optimisation of an immediate release tablet using quality by design

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Purpose: Designing a pharmaceutical product and its manufacturing process that is efficient, safe and fit for its intended use for patients is the primary focus of pharmaceutical development. Quality by Design (QbD) emphasises that the product quality should be built into the product and not merely tested post production. This systematic concept of QbD is the successor of the empirical Quality by Testing (QbT) and forms part of the modern approach to pharmaceutical quality. The aim of the study is to optimise the formulation and manufacturing process of an immediate release tablet using QbD.

Methodology: The methodology employed in this investigation was done in accordance with the International Conference on Harmonisation Q8 and Q9 guidelines. Established the quality target product profile (QTPP). Identified the critical quality attributes (cQAs) of the product. Performed a risk assessment to identify the critical material attributes and process parameters that may impact the cQAs. Design of experiments (DoE) was applied to the risk factors. The screening trial batches using a 2-level fractional factorial design screened the factors to determine which of the critical factors identified during the risk assessment are significant. Following the screening trial, the pivotal study using a central composite design (CCD) determined the effects of the significant factors on the cQAs.

Results: The risk assessment identified the active pharmaceutical ingredient (API) particle size; binder content (povidone); impeller speed during dosing; massing time; impeller speed during wet mix; and moisture content (after drying wet granule) as factors that may impact the extent of dissolution (%) at 15 minutes (cQA). ANOVA analysis of the experimental designs showed that the model (quadratic) chosen for the analysis had significant fit ($p=0.030$). The response optimiser, indicated that to reach optimum desirability for the extent of dissolution (%) at 15 minutes, i.e. 100.6%, impeller blade speed during dosing should be 115 rpm and moisture content at 2.5% m/m.

Conclusion: QbD provided an effective means to optimise the formulation and manufacturing process of the immediate release tablet by determining the influence of the selected input variables on the product cQA.

Comparison of drug permeability in rat, pig and human *in vitro* models

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Purpose: High throughput, but less predictive *in vitro* models are preferred for primary screening purposes. The aim of this study is to compare three different *in vitro* models, namely the excised rat intestinal tissue, the excised pig intestinal tissue and the Caco-2 human cell culture in terms of drug permeability. Furthermore, the Sweetana-Grass Ussing type diffusion and everted sac techniques were used for both of the excised animal tissue models.

Methods: The transport of abacavir was determined in two directions (i.e. apical-to-basolateral and basolateral-to-apical directions) in all three *in vitro* models and in both techniques. The test solution was applied to the donor side and samples (200 µl) were drawn from the acceptor side at 20 min intervals for a period of 2 h. The concentration of abacavir in the samples was measured by means of a validated high performance liquid chromatography (HPLC) method. The transepithelial electrical resistance (TEER) was measured before and after the transport experiments in all models to determine if membrane integrity was maintained. The models were compared in terms of apparent permeability coefficient (P_{app}) values and efflux ratio (ER) values.

Results: All three the *in vitro* models, in both the techniques employed, showed higher transport of abacavir in the BL-AP direction than in the AP-BL direction. This indicates that all three *in vitro* models contained intact active efflux transporters over the entire study period. The excised rat intestinal model showed similar drug permeability characteristics in both techniques compared to that of Caco-2 cell monolayers. On the other hand, the excised pig intestinal model only showed similar drug permeability characteristics in the Sweetana-Grass diffusion apparatus compared to that of the Caco-2 cell monolayers, but not in the everted sac technique. This phenomenon can possibly be explained by the relatively large size of the pig tissue used in the everted sac technique where the role of physiological and other factors take effect. These factors may include the thickness of the membrane and mucus layer as well as variables such as diet, age, gender and size of the pigs obtained from the abattoir that cannot be controlled.

Conclusions: The Sweetana-grass Ussing type diffusion chamber technique rendered drug permeability results comparable to that of the Caco-2 cell line for both the excised rat and pig intestinal tissue models. The everted sac technique, on the other hand, proved to be relatively predictive with rat intestinal tissue and less predictive with pig intestinal tissue in terms of drug transport across human intestinal epithelial cells.

Synthesis of a semi-Interpenetrating polymer network as a bioactive curcumin film for wound healing

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Purpose: Wound healing and management has been proven to be challenging due to the fact that various extrinsic and intrinsic factors govern significant roles during the healing process. Wound healing is a dynamic and complex process that involves a complex sequential cascade of events. Wounds occur on a daily basis and can result in a declined quality of life depending on the severity. The purpose of this study was to focus on the synthesis and characterisation of a natural polymeric system employing techniques such as the interpenetrating polymer network, cast and electrospinning.

Methods: Using a statistically derived Box-Behnken Design Template, the paramount concentration of biopolymers was generated to produce 14 various formulations to fabricate wound healing films and nanofibrous mats. These were then investigated in terms of their physicochemical, physicomechanical and biological properties by quantification by FTIR, DSC, Young's Modulus, *In Vivo* and *In Vitro* characterisation. Upon the retrieval of results an optimised formulation was then synthesised.

Results: Chemical analysis by FTIR revealed greater shifts in wavelengths from 3260.11cm^{-1} to 3278.79cm^{-1} when the concentration of crosslinker was increased by the formation of crosslinking bridges which impacts on the stability and physicomechanical properties of the film. Furthermore thermodynamic evaluation revealed both semi-crystalline and crystalline behaviour amongst the various formulations which was dependent on the degree of crosslinking. Degradation of all systems occur between a temperature spectrum of 230 and 300°C as all known natural polymers tend to be highly degradable. Structural morphological analysis of films illustrate relatively smooth, non porous and homogenous surface texture whereas nanofibrous mats revealed the presence of nanofibres of varying diameters dependent upon the viscosity and concentrations of polymer used. The presence of nanobeads in some instances was also revealed but varies from formulation to formulation. Nano tensile analysis reveals the Young's Modulus of the various formulations. Nanofibres of formulation 1 show a lower Young's Modulus of 4.25MPa thus resembling greater flexibility whereas formulations with a greater Young's Modulus such as nanofibrous mats of Formulation 3 and 4 reveal greater rigidity and stiffness. Further studies undertaken in terms of *in vivo* and *in vitro* reveal successful release of the bioactive compound curcumin, whereby an initial burst release was observed occurring within the first hour at 1.1mg *in vivo* and 2.23mg *in vitro*. Interestingly these results relate that the bioactive release rate from the system is greatly affected by the Lipophilic nature of the skin. Thus when exposed to the skin a superior release rate is seen improving the system performance.

Antibiotic Stewardship: The role of the clinical pharmacist - the intervention phase

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Purpose: Antibiotic stewardship initiatives consist of direct interventions in antibiotic therapy, educating of healthcare professionals involved in patient therapy and developing antibiotic policies and guidelines. The aim of this study is to assess the role of the clinical pharmacist in antibiotic stewardship through pharmacist interventions in a public hospital setting.

Methods: A prospective, experimental and cross-sectional approach was employed for the study. The study consisted of an intervention design, incorporating a pre-intervention audit phase, an intervention phase and a post-intervention phase. The intervention phase was carried over a six-week period whereby the researcher collected data using a purpose designed data collection tool from patient files during weekday mornings from 08:00 to 12:00 (excluding public holidays). The study sample included adult patient files (both males and females, aged 18 years or older) that were prescribed antibiotics, after being admitted to the medical ward. An antimicrobial communication form was used for the interventions together with verbal discussion with the prescribers during the doctor's ward rounds.

Results (Intervention Phase): A total of 101 patient files (62.38% females) were included in the study during the six-week intervention phase. Forty-one interventions (n=41) were made during the intervention phase, out of which 43.90% of the interventions were incorrect duration, 17.07% were inappropriate dosing regimen, 14.63% were incorrect indication, 12.20% required IV to oral switch, 4.88% were inappropriate agent used, 2.43% were risk of adverse drug reaction, 2.43% were re-boarding of medication and 2.43% were ordering of microbial cultures. The pharmacist interventions had a 73.17% (30, n=41) prescriber acceptance rate and were mostly through verbal recommendations when the prescribers were present in the ward. 19.51% (8, n=41) of the recommendations were not accepted and 7.32% (3, n=41) of the interventions made, were unclear with regards to the outcome. Of the total 41 interventions made, 82.93% (34) were supported by verbal discussion in addition to using the antimicrobial communication form, out of which 82.35% (28) were accepted, 17.65% (6) were not accepted.

Conclusions: The results from the intervention phase show that the presence of a clinical pharmacist in the ward is essential for the monitoring and influencing of antibiotic prescribing. In addition to direct pharmacist interventions, the education of healthcare professionals and development of antibiotic guidelines and policies need to be introduced and assessed as further antibiotic stewardship initiatives in the ward.

Polycyclic propargylamine derivatives as multifunctional neuroprotective agents

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Purpose: The aim of this study was to design drug-like molecules with multiple neuroprotective mechanisms which would ultimately inhibit N-methyl-D-aspartate (NMDA) receptors, block L-type voltage gated calcium channels (VGCC) and inhibit apoptotic processes as well as the monoamine oxidase-B (MAO-B) enzyme in the central nervous system. These types of compounds may act as neuroprotective and symptomatic drugs for disorders such as Alzheimer's and Parkinson's disease. In designing the compounds we focused on the structures of rasagiline and selegiline, two well known MAO-B inhibitors and proposed neuroprotective agents. Based on this consideration, the compounds synthesised all contain the propargylamine functional group of rasagiline and selegiline or a derivative thereof, conjugated to various polycyclic cage moieties. Being non-polar, these polycyclic moieties have been shown to aid in the transport of conjugated compounds across the blood-brain barrier, as well as cell membranes and have secondary positive neuroprotective effects. An initial series of eight novel synthesized polycyclic derivatives (compounds **1-8**) proved to have significant anti-apoptotic activity ($p < 0.05$) which was comparable to the positive control, selegiline.

When assayed for calcium modulatory effect, compounds **2, 4, 7** and **8** showed the best VGCC and NMDA activity ranging from 18% to 59% in micromolar concentrations and compared favourably to reference compounds. While only compound **2** showed significant inhibition of 73.32% at 300 nM in the MAO-B assay. This compound also reduced the percentage of apoptotic cells by as much as 40% when compared to the control experiments.

With the aim of improving the MAO inhibitory activity (and retaining or improving the established anti-apoptotic and calcium modulatory effect) of these compounds, a second series of four propargylamine derivatives was designed. Based on the preliminary findings from the molecular modeling using Molecular Operating Environment (MOE), this new series of aza-PCU and oxa-PCU compounds show potential interaction with the FAD co-factor of the MAO-B enzyme, suggesting the series to potentially exhibit improved MAO-B activity.

Compounds that render such multimechanistic activity have great potential to serve as future analogues for the treatment and management of neurodegenerative disorders.