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Chemotaxonomic investigation of South African *Portieria* species

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Purpose: The red marine algal genus, *Portieria*, is known to produce a number of potent cytotoxic compounds with anticancer potential. The most important anticancer lead produced by this genus is the compound halomon. Unfortunately, the lack of sufficient quantities of this compound hampered its further development. Two *Portieria* species, *Portieria hornemannii* and *Portieria tripinnata*, are found along the South African coastline. Recent studies, based on DNA analysis, suggest that *Portieria hornemannii* may in fact be divided into several cryptic species. The current project is part of a larger study designed to investigate the use of secondary metabolites to identify new marine algal species. In this study ^{1}H NMR profiles of the organic extracts of selected *Portieria* spp were compared in order to identify new species. Selected compounds were then isolated and characterised as potential chemotaxonomic markers.

Method: Seventeen seaweed samples were collected along the South African coastline of which twelve were identified as *Portieria hornemannii* on the basis of their morphology. One gram of each sample was extracted with DCM-MeOH (2:1), the organic layer was separated and dried under reduced pressure. The crude extracts were reconstituted in $CDCl_3$ (~ 600 mL) and 1H NMR spectra were obtained on a 600 MHz spectrometer. In order to identify specific chemotaxonomic markers a "large scale" extraction was undertaken. The algae was sequentially extracted with MeOH and DCM-MeOH (2:1). This crude extract was further separated via a step gradient silica gel column chromatography using hexane and EtOAc as solvents. The fraction containing the major metabolite (Fraction **A**) was further fractionated by silica gel column chromatography to give pure compound **1**. The structure of compound **1** was determined from one- and two-dimension NMR spectroscopic data. A second fraction (Fraction **B**) containing another metabolite was further separated using High Performance Liquid Chromatography (HPLC) to give rise to pure compound **2**, and the structure of this compound was also determined from one and two-dimensional spectroscopic data.

Results and Conclusion: Of the seventeen specimens analysed, eight showed almost identical ^{1}H NMR chemical profiles, containing one major metabolite, while the remainder showed completely different metabolite profiles. Further morphological, microscopic and DNA analyses are required in order to confirm the utility of the ^{1}H NMR metabolite profiles in the identification of cryptic species of *Portieria hornemannii*.

Synthesis and biological evaluation of marine bromopyrrole alkaloid-based conjugates for their anti-inflammatory activity

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We are reporting with this poster few hybrids of bromopyrrole alkaloids with aroyl hydrazone feature, synthesized and evaluated for their anti-inflammatory activity using the carrageenan induced rat paw edema method. All these tested hybrids showed good anti-inflammatory activity with 64.78–86.03 % inhibition of rat paw edema. In order to understand mechanism of action, most active hybrids of this series, 4b and 4f were further investigated for antihistaminic H1 [4b - 8.09 μg/mL (18.5 μM); 4f - 9.26 μg/mL (24.05 μM)] and anti-serotonergic 5-HT3 [4b - 7.01 μg/mL (16.04 μM); 4f - 9.64 μg/mL (25.04 μM)] activities. Molecule 4f with anti-inflammatory, anti-histaminic and anti-serotonergic activities emerges as a potential anti-inflammatory lead from this study.

Should academic pharmacy be recognised as a pharmacy speciality?

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Purpose: Integral to the success of pharmacy education is the availability of sufficient numbers of appropriate and well-qualified pharmacy educators. However, in South Africa there is a shortage of pharmacy educators which is disproportionate to the general shortage of pharmacists. One of the ways in which academic pharmacy might be a more attractive career opportunity is if it was recognised as a speciality by the South African Pharmacy Council (SAPC). The aim of this study was to determine if academic pharmacists in South Africa thought that academic pharmacy should be recognised as a speciality and to determine the underlying motivations for their responses.

Methods: As part of a larger study to explore the professional identity of pharmacy educators, this study involved a qualitative online survey conducted with 32 academic pharmacists in South Africa. Respondents were asked whether they thought academic pharmacy should be recognised as a speciality by the South African Pharmacy Council and to motivate their responses. Thematic analysis and interpretation of questionnaire responses was conducted using qualitative data analysis software – Atlas.ti®.

Results: The majority of respondents, 75% (24), believed that academic pharmacy should be recognised as a speciality, 6% (2) were uncertain, and 19% (6) of respondents believed that it was not necessary. The motivations provided for its recognition as a speciality included: the requirement for specialist knowledge and a postgraduate qualification and the potential to create an attractive career path. In addition some felt that since there is a constant need to graduate increasing numbers of pharmacists to meet society's needs for pharmaceutical services at all levels, academic pharmacy is needs driven. However, some respondents felt that in addition to a pharmacy related post-graduate degree and experience in pharmacy education, a formal qualification in education should be a requirement for registration as a specialist pharmacist. The reasons against having academic pharmacy registered as a speciality included the beliefs that: academic pharmacy was already well recognised and accommodated by the SAPC, academic pharmacists had a well-formed sense of identity and did not require further recognition from others and the fear that it had the potential to limit the scope of practice of pharmacy educators.

Conclusion: The results of this study suggest that since academic pharmacy is based on advanced knowledge and practical experience in the specialist field of pharmacy education, the SAPC should be lobbied to recognise academic pharmacy as a speciality.

An exploration of barriers to contraception use by visually impaired persons

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Purpose: The use of contraception specifically by the visually impaired community has not been widely explored in South Africa. The aims of the study were to investigate the experiences visually impaired men and women have encountered with various contraception methods available in the public sector.

Methods: Available contraceptive methods and packaging were assessed for potential barriers to method use by visually impaired persons. A non-experimental, qualitative and explorative study was subsequently conducted with male and female, temporary and permanent residents of the League of Friends of the Blind (LOFOB) facility in Grassy Park, Cape Town, who were current, past or future contraceptive users. Consent forms and information sheets in 3 languages were available as audio recordings (CD-Rom) and printed in Braille. Interviews were conducted on a one-on-one basis, according to the language preference of the individual participant in English, Afrikaans or Xhosa. Interview questions were based on knowledge, barriers and method use by the individual.

Results: The contraceptive methods which were found to present significant potential barriers to use by visually impaired persons were the oral contraceptive, the contraceptive patch and both male and female condoms. Thematic analysis of the interviews revealed that the majority of the participants interviewed were knowledgeable about the importance and the use of contraception. They identified the attitudes of health care personnel and the public as having a negative impact on their confidence to physically use contraceptive methods. The impact of the environment with regards to the placement of condoms within the clinic also hindered accessibility to the use of this method as other persons had to be involved. Participants also revealed a further barrier, being the associated costs incurred of having a person to accompany them to the clinic, which also infringed on their independence and confidentiality.

Conclusions: This exploratory study clearly identified the existence of barriers to the use of contraception by visually impaired persons and supports further investigation in this regard in order to clearly define the role of the pharmaceutical industry and health care providers, including pharmacists.

Teenage pregnancy: Experiences of community care workers in two rural communities

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Purpose: The aim of this study was to interview the community care workers (CHWs) with regards to teenage pregnancy in Glenmore and Ndwayana, two rural villages in the Eastern Cape Province. The CHWs are based at the primary health care centres in the two communities.

Method: Semi-structured interviews were carried out with community care workers to generate their response to the issues arising from teenage pregnancies from their point of view. A question guide was used to interview 13 participants in total. Note-taking and tape recording were used to record the interview responses.

Results: According to the experiences of community care workers, there are a number of teenagers that fall pregnant each year. Teenage pregnancy has always been a cause for concern in the two communities. They identified that lack of parental support in informing and educating teenagers about sexual health was a contributing factor to teenage pregnancy. Teenagers themselves lack the maturity to recognise the risks and consequences of teenage pregnancy. Peer pressure is one of the main factors contributing to teenage pregnancy. Despite sex education being taught in schools and clinics, use of contraceptives is still low as shown by the low turn up at clinics for contraceptives. Other factors included lack of health promotion materials and activities with information about preventing of teenage pregnancy, and if available, the material is in English, that the teenagers may not comprehend.

Conclusion: Community care workers identified various factors contributing to the issues of teenage pregnancy relevant in the two villages. These factors will be incorporated in the training manual being developed as a participatory collaborative initiative with the CHWs during the next phase of this research project.

Novel tricycloundecane derivatives as potential *N*-methyl-D-aspartate receptor and calcium channel inhibitors for neuroprotection

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Purpose: Neurodegenerative disorders are debilitating conditions characterised by progressive dysfunction and death of neuronal cells by means of apoptosis, necrosis or autophagic degeneration. Amidst the proposed mechanisms of neurodegeneration, the effects of excitotoxicity *via* glutamate receptor stimulation on neuronal cells are prominent. Phencyclidine (PCP) and dizolcipine (MK-801) have proven to noncompetitively block NMDA receptors but are marked by undesirable side effects. Uncompetitive blockers such as memantine and amantadine proved to be neuroprotective with fewer side effects and are approved for clinical use. This has led to the development of structurally related polycyclic molecules such as NPG1-01, which exhibit neuroprotective properties through NMDA receptor and VGCC inhibitions with lower side effect profile. This study focused on the synthesis of a series of novel tricycloundecane derivatives and evaluation of these compounds for neuroprotection.

Method: The cycloaddition reaction between *p*-benzoquinone and monomerised dicyclopentadiene yielded tricycloundeca-4,9-diene-3,6-dione which was used as the base structure and further derivatised. These derivatives were conjugated with benzylamine to form a series of imines and amines. A total of 10 compounds were synthesised for evaluation of inhibition of calcium influx through NMDA receptor channels and voltage-gated calcium channels.

Results: The structures were confirmed using NMR, IR and MS. In the NMDA receptor inhibition assay, MK-801, memantine and NGP1-01 were used as reference compounds and all showed statistically significant ($p < 0.05$) NMDA receptor inhibitory activity of 97.47%, 57.90% and 57.20% respectively at a 100 µM concentration. Significant inhibition were observed for compound **2** (78.00%) and **3** (96.07%). The highest inhibitory activity ($p < 0.05$) was observed with compound **7**, which exceeded the inhibitory activity of MK-801 in this assay. In the VGCC inhibition assay, nimodipine, amantadine and NGP1-01 were used as the reference compounds. Nimodipine and NGP1-01 showed statistical significant VGCC inhibition of 90.19% and 25.63% respectively at a 100 µM concentration. Compound **6** (34.03%), **7** (38.07%) and **10** (40.33%) showed statistically significant ($p < 0.05$) VGCC inhibitory activity compared to NGP1-01 (25.63%). These compounds (**2**, **3**, **6**, **7** and **10**) demonstrated potential ability to attenuate calcium influx through NMDA receptor and/or VGCC.

Conclusion: The potential NMDA receptor and/or VGCC inhibitory activities of the tricycloundecane derivatives (**2**, **3**, **6**, **7**, and **10**) were demonstrated in this study. However, the true potential benefit as neuroprotective agents and safety in patients is yet to be established. The compounds could serve as lead structures for the development of novel neuroprotective drugs.

Integrated practical training for large groups of pharmacy students: From product to patient

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Purpose: Students enrolled in the B.Pharm curriculum are required to register as pharmacy students with the South African Pharmacy Council. This allows students to perform duties within the scope of practice as post basic pharmacy assistants, after completion of their second academic year. The aim of this study was to determine whether students have valuable learning experiences when they perform unstructured compulsory work in a pharmacy which accounts for integrated practical training in the B.Pharm curriculum.

Method: After obtaining permission from the NWU ethical committee, a self-administered structured questionnaire was distributed to 172 undergraduate fourth year pharmacy students in the NWU School of Pharmacy. There was a 100% response rate. Data was analyzed by Statistical consultation services of the NWU.

Results: The results showed that only 93 students have worked in pharmacies more than 201 hours, 49 students worked between 151 – 200 hours, 10 students worked between 101 – 150 hours, 12 students between 51 – 100 hours and 8 students completed less than 50 hours. The students indicated that they have never been given the opportunity to perform the following housekeeping tasks in practice: never worked at the OTC counter (10 students (5.8%),) have registered items sold on the cash register (52 students, 30.2%), worked as a front shop assistant (70 students, 40.7%), received stock from delivery companies (27 students, 15.7%), unpacked stock (13 students, 7.6%), captured invoices (88 students, 51.2%), packed stock on the shelves (4 students, 2.3%), ordered stock from pharmaceutical companies (86 students, 50%), washed and organised shelves (33 students, 19.3%), checked expiry dates (16 students, 9.3%), took stock (44 students, 25.6%) and done pre-packing (12 students, 7.0%). Evaluating the statistical results of the dispensing of prescriptions, the researchers divided the dispensing process into three phases according to the Good Pharmacy Practice (2010:33 - 35). Eight students (4.7%) never interpreted and evaluated prescriptions, 9 students (5.2%) never performed phase 2, the preparation and labelling of the prescribed medicine and 14 students (8.1%) never provided information and instructions to patients to ensure the safe and effective use of medicine under direct supervision of a pharmacist. More than 55 students never performed diagnostic tests and procedures: blood pressure (55 students, 32.0%), glucose testing (83 students, 48.3%), cholesterol testing (93 students, 54.1%) and administration of injections (132 students, 76.7%).

Conclusion: Students' inadequate exposure to the pharmacy practice environment could be attributed to large student numbers, shortage of pharmacists, the lack of knowledge of pharmacists regarding the scope of practice of the students, in which areas of the pharmacy they can be utilised and the amount of hours allocated to the specific tasks. Formal agreements and structured training of the community pharmacists may contribute towards a global focus change in the community pharmacy sector.

Optimisation of formulation variables of drug free lipid polymer hybrid nanoparticles

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Purpose: Lipid-polymer hybrid nanoparticles (LPHNs) are an attractive alternative dosage form which simultaneously displays the high structural integrity of polymeric nanoparticles as well as the superior biomimetic characteristics of liposomes. Since LPHNs are a recent and emerging drug delivery system in the literature, there is a need to identify optimal lipid-polymer formulations that can be used for various classes of drugs. Therefore, the aim of this study was to identify an optimal drug free formulation containing Eudragit RS100 for future drug incorporation studies.

Methods: Drug free LPHN's were prepared by hot high pressure homogenisation followed by ultra-sonication. The formulation variables that were investigated included polymer, lipid and surfactant concentration, lipid to polymer ratio and process variables. The drug free particles were characterised in terms of particle size (PS), polydispersity index (PDI) and zeta potential (ZP). Morphology of the particles was determined by Transmission Electron Microscopy (TEM).

Results: The initial formulation comprising of stearic acid (2% w/v), Eudragit RS100 ((1% w/v) and Poloxamer 188 (1% w/v) resulted in LPHNs with PS of 537.7 ± 4.60 nm, low PDI (0.391 ± 0.17) and high ZP (+36.0 ± 1.77 mV). Subsequently, various surfactants (Solutol HS15, Lutrol F68, Tween 80), at 1% (w/v) concentration showed Solutol HS15 as the most suitable surfactant based on the smallest PS (438.9 ± 39.26 nm), acceptable PDI (0.361 ± 0.04) and ZP (+9.26 ± 0.63). Further investigations with various lipids (glyceryl tripalmitate, comprtitol, glycerol monostearate) found glyceryl tripalmitate to be the best lipid (PS= 246.2 ± 11.78 nm, PDI= 0.340 ± 0.04, ZP= +16.52 ± 1.41 mV). This formulation comprising of Eudragit RS100 1% (w/v), glyceryl tripalmitate 2% (w/v), and 1% (w/v) surfactant Solutol HS15 was further optimised by changing homogenisation speed and time, and sonication amplitude and time. The particle size, PDI and ZP at these conditions was 217.3 ± 3.81 nm, 0.259 ± 0.004 and +18.23 ± 0.21 mV respectively. Morphology showed particles that were spherical, discreet and homogenous.

Conclusion: Optimising the formulation for synthesis of LPHN's is crucial in obtaining suitable and acceptable results in terms of size, PDI and ZP. We have successfully optimised the LPHN formulation containing Eudragit RS100 as a polymer for the first time. Further drug loading studies are in progress in our laboratory.

Exclusive breastfeeding; a community care worker perspective

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Purpose: Exclusive breastfeeding is the single most effective feeding practice which promotes good infant health and growth. In 2003, the South Africa Health and Demographics Survey reported that the exclusive breastfeeding rates within the country are low; therefore it is necessary to identify and address the barriers to exclusive breastfeeding. The aim of this research was to explore the beliefs that affect exclusive breastfeeding practices as perceived by community care workers (CCWs) in two rural Eastern Cape communities.

Method: Semi-structured interviews were conducted with 13 CCWs in the two clinics situated in Ndwayana and Glenmore rural communities. A question guide was used during the interviews and probes were used whenever necessary. Note taking and a recording device were used during the interviews, which were conducted in English and a translator assisted.

Results: The CCWs perceived that the community actually appreciates breastfeeding because it is a cheaper option when compared to formula feeding. However, beliefs such as that of women not being able to be sexually involved when breastfeeding, and that breast milk is insufficient for the baby , pose barriers to breastfeeding, specifically exclusive breastfeeding. Other beliefs such as the size of breasts having an impact on the amount of milk that is produced, and the breast feeding practice actually affecting the shape and size of breasts, were also reasons why the mothers preferred to practice mixed feeding. Although the CCWs provided information about breastfeeding, the community still had beliefs which affected negatively exclusive breastfeeding.

Conclusion: Although breastfeeding is common and accepted practice within the two communities, some beliefs actually hinder exclusive breastfeeding practices and the CCWs suggested that it could be a lack of clarity and/acceptance of the information from them. The CCWs acknowledged that exclusive breastfeeding is a practice that ought to be encouraged since it has many benefits for the baby, the mother and the community at large. The development of material to promote breastfeeding (which is the next phase of this research), is therefore an essential strategy that can be useful to reaffirm the positive beliefs which promote exclusive breastfeeding and negate the beliefs which discourage exclusive breastfeeding.

Ascorbic acid content and prebiotic activity of wild edible plants from the Limpopo Province of South Africa, Lesotho, and Swaziland

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Purpose: Wild edible plants (WEP) may be affordable potential sources of prebiotics and ascorbic acid especially for people in urban areas of the Limpopo Province of South Africa, Lesotho and Swaziland. This study investigated the ascorbic acid content and prebiotic activity of wild edible plants from the above-mentioned regions.

Methods: Samples of 30 air-dried, ground plant species were extracted using water for ascorbic acid content and using 50 %v/v ethanol for prebiotic activity. The ascorbic acid content was determined according to a modified Reiss (1999) method. The amount of ascorbic acid in the plant extracts, which changed a predetermined volume (known concentration) of corn starch-iodine dye from blue to colourless, was determined through titration. Changes in microbial counts of a pure commercial culture of *Lactobacillus acidophilus, ATCC 314* (Sigma, RSA), grown in broth media containing the test fibres were observed over 72 hours. Inulin and Lactulose (Sigma, RSA) were used as positive controls. The cultures were plated on MRS agar for colony counting.

Results: Extracts of 27 plant species had ascorbic acid content ranging from 20 mg/100 g to 640 mg/100 g of dried plant material. *Cyprus ututatus* species had the highest ascorbic acid content (640 mg/100 g) while *Discorea minutiflora* species had the least ascorbic acid content (20 mg/100 g). *Tragopogon porrifolius* species showed better prebiotic activity while *Chenopodium album* had the least prebiotic activity as compared to Inulin and Lactulose. *Urtica dioica* species inhibited the growth of *L. acidophilus*.

Conclusions: Wild edible plants are possible affordable and renewable sources of ascorbic acid and prebiotics especially for people living in urban areas.

Effects of 20 wild edible plant extracts on Cytochrome P450 3A4 metabolic activity in pig intestinal and liver microsomes

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Purpose: Wild edible plants (WEP) are commonly used concomitantly with allopathic medicines with potential to cause herb-drug interactions. The effects of WEPs on drug metabolizing systems such as the Cytochrome (CYP) 450 3A4 isozyme, which play a major role in these interactions, were investigated.

Methods: The effect of 20 ethanol-based wild edible plant extracts (0.5 and 1.0 mg/ml) from the Limpopo Province of South Africa, Lesotho and Swaziland on CYP450 3A4 metabolic activity in pig intestinal and liver microsomes was assessed by a chemiluminescence assay. Cimetidine, a general CYP inhibitor, was used as a positive control. The effects of plant test extracts were expressed as % inhibition of CYP activity.

Results: *Rorippa nudiuscula, Urtica dioica*, *Wahlengergia androsacea* and *Lepidium capense* showed varied inhibitory effects on the metabolic activity of CYP450 3A4 on Luciferin-BE (substrate) compared to cimetidine (positive control) in both pig intestinal and liver microsomes. The inhibitory effect of *Rubus Cuneifolius, Opuntia megacantha, Sonchus dregeanus, Rosa rubiginosa, Amaranthus retroflexus* and *Chenopodium album* on CYP450 3A4 activity showed concentration dependence with enhancement at low concentration (0.5 mg/ml) and inhibition at the higher concentration (1.0 mg/ml) in pig intestinal microsomes. *Rhynchosia totta, Sochas integrifolius, Solanum retroflexum Dunal, Momordica foetida Schumach, Corchorus tridens L, Amaranthus hybridus L, Amaranthus spinosus, Bidens pilosa, Momordica involucrate* and *Discorea minutiflora* enhanced CYP450 3A4 activity.

Conclusion: The CYP450 3A4 modulatory activities of the wild edible plants should be investigated further using *in vivo* models.

Clozapine usage in a public sector psychiatric hospital in the Nelson Mandela Metropole

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Purpose: Patients receiving clozapine therapy may develop serious adverse effects such as agranulocytosis, neutropenia and metabolic syndrome. Therefore guidelines are required which recommend that regular haematological and metabolic monitoring be performed. South Africa lacks uniform provincial or national guidelines regulating practices in the treatment of mental disorders. International guidelines may be considered, which are not specifically adapted for the South African setting. The general aim of the study was to determine the prescribing and monitoring patterns of clozapine at Elizabeth Donkin Hospital in the Nelson Mandela Metropole. Due to the absence of specific South African guidelines and the severe side effect profile of clozapine, some of the research objectives were to determine whether the initiation of clozapine, as well as the haematological and metabolic monitoring performed, was compliant with international clinical guidelines.

Methods: In this pharmacoepidemiological study a retrospective drug utilisation review was performed. The study was observational in design and included quantitative data. Data were collected from the files of 65 patients (N=65) discharged on clozapine between 1 December 2010 and 29 February 2012. Follow-up investigations were performed at the clinics and long-term care centres both three months and six months after discharge.

Results: Compliance with the National Institute for Health and Clinical Excellence (NICE) guidelines for the appropriate initiation of clozapine was 63.10% (n=41). Compliance with the Standard Treatment guidelines for the initiation of clozapine by a psychiatrist was 63.10% (n=41). Non-compliance with the recommended guidelines for haematological monitoring occurred in 77.40% of patients in the hospital setting (n=48) as well as in 95.70% of patients during the three-month follow-up at the clinics (n=44). Non-compliance with the guidelines for metabolic monitoring occurred in all the observed patients in the hospital setting (n=62) as well as in 45.70% of patients in the clinic setting (n=21). It was found that 71.00% (n=46) of patients were still on clozapine three months after discharge and 65.00% (n=42) were still on clozapine six months after discharge from hospital, resulting in discontinuation rates of 29.00% and 35.00% respectively.

Conclusions: It was found that clozapine was inadequately monitored although in most cases the initiation of clozapine was compliant with the recommended guidelines. However, practitioners should be trained on the existing prescribing and monitoring guidelines to promote the rational use of clozapine in the public health sector of South Africa.

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Monogalactosyldiacylglycerols (MGDGs) from the brown algae *Brassicophycus brassicaeformis*

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Purpose: Monogalactosyldiacylglycerols (MGDGs) are components of photosynthetic organelles found in plants, marine algae and bacteria. Some researchers have postulated that these have been produced as herbivore deterrents in chemical defence of the plants and algae. MGDGs are galactolipid molecules comprising of a galactose moiety, a glycerol unit and two fatty acid chains. They have been found to possess biological activities that include anti-tumour, anti-viral and anti-inflammatory activities, with the degree of unsaturation of the fatty acid chain being linked to the extent of biological activity. As medicinal chemists constantly in search of new and novel drug molecules, these MGDGs are suitable candidates for novel drug discovery to combat disease states such as cancer.

Method: Frozen *B. brassicaeformis* was extracted with CH_2Cl_2/MeOH (2:1) solvent system, and the crude extract fractionated using silica gel column chromatography (hexane-EtOAc gradient). The fraction of interest was eluted by 100% EtOAc which was further purified using Reverse phase HPLC (100% MeOH) to give two MGDGs (**G** and **P**). The structures of the pure compounds were determined using one- and two-dimensional NMR spectroscopic techniques, mass spectrometry and Fatty acid methyl ester (FAME) analysis.

Results: Fractions **G** and **P** displayed ^{1}H NMR signals characteristic of a sugar moiety (δ 3 – 4) and unsaturated fatty acids (δ 5.4). Complex overlapping signals (δ 0.5-2.5) are characteristic of a fatty acid chain, and differences in this spectral region between **G** and **P** highlighted that these compounds differed in the fatty acid chain composition. Analysis of its NMR spectroscopic data allowed the assignment of two galactosylglycerol lipids (**G** and **P)**.

Conclusion: Isolation of the two MGDGs **G** and **P** is part of the first phytochemical study of the brown algae *Brassicophycus brassicaeformis*. FAME analysis and Mass spectrometry of these two compounds are currently underway. Biomimetic catalysis of these two galactolipids shall be conducted as an extension of this project in order to determine the possible metabolites of these potential drug molecules and also to test the potential physiological effects of these metabolites in the human body.

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Solubilisation of triclosan with sodium deoxycholate and assessing dissolution characteristics

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Purpose: Triclosan scientifically known as 5-Chloro-2-(2,4-dichlorophenoxy)phenol is an active ingredient used in a variety of health care and consumer products. Triclosan inhibits the enoyl reductase thus blocking the fatty acid synthesis of bacteria. Aim of the current project is to investigate the fate of antibacterial residues in sewage treatment systems in Tiaret, Algeria and Grahamstown, South Africa. Chemical analyses of sludge must quantify the concentrations of heavy metals, namely nickel, zinc, copper, mercury, lead, chromium and cadmium. Organic micropollutants in question include Triclosan and the total hydrocarbons. The microbial characterisation of the sludge biofilm will be done by enumeration of the aerobic and anaerobic bacteria, actinomycetes and fungi; and faecal coliforms as indicators for the possible presence of pathogens. Mutual inter-relations between the above-listed variables are also critical.

Method: Our study has been based on optimizing methods for Triclosan analysis. Various compounds have been used in combination with TCS, so as to mimic the sludge residues. The compounds used included Chromosorb G (adsorbent), deoxycholic acid (bile acid), sodium hydroxide and milliQ water.

Chromosorb G was coated with 0.5g/L solution of TCS in acetone. The adsorbent coated with TCS was mixed with 1g/l of sodium deoxycholate, and shaken for 72hours. Samples were collected at various time intervals to assess the release rate of TCS in a solubilized system in the presence of an adsorbent. The experimental progress was analyzed using High performance liquid-chromatography and HPLC/UV and UV-VIS Spectrophotometer at a wavelength of 281nm, and absorbance was recorded.

Results and conclusion: From the experiments that have been conducted, the release of TCS from Chromosorb G and sodium deoxycholate has been assessed at different concentrations and 0.5g/L was the maximum point of detection that was established. The release of TCS has been analyzed using HPLC/UV and UV-VIS Spectrophotometer. Further studies are being done with different salts of deoxycholate, and the cations will be Calcium (Ca), Magnesium (Mg) and Potassium (K). After these experiments have been done, we are looking forward in introducing other bile acids such as Lithocholic acid, with various cations and further assess the impact of surfactant Solubilisation on release of Triclosan in sludge residues. Further quantitative analytical methods will include solvent extraction of metals and organic micropollutants; gas chromatography with flame-ionisation and mass-spectrometric detection; and the inductively coupled plasma spectroscopy.

Polymorphism of Bis [adamantane-1-aminium] carbonate

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Salt formation is one of most traditional techniques used to optimize the solid parameters of an active pharmaceutical ingredient (API) due to the presence of its ions. The limitations of salt formation from strong acids or bases are known to be very high solubilities and the presence of hygroscopic properties. Four polymorphic forms of bis [adamantan-1-aminium] carbonate (Figure 1) were prepared and analysed. Bis [adamantan-1-aminium] carbonate salt ($ADTCO_3$) is a derivative of 1-adamantanamine, the antiviral and antiparkinson drug usually used in its hydrochloride salt form.

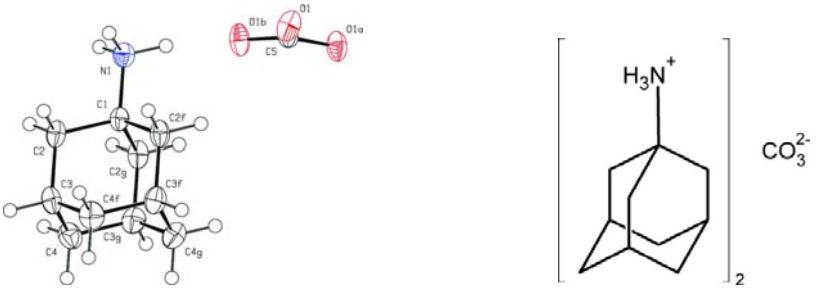

Figure 1: Bis (adamantan-1-aminium) carbonate.

Studies show that a change in the polymorphic properties may occur during the manufacturing and storage process of an API which could directly impact on the bioavailability of a drug and hence have serious consequences on the patient.[1, 2, 3] This could either be advantages or detrimental to both the manufacturing process and/or patient.

Dry grinding, solvent-drop grinding, co-precipitation, sublimation and vapour diffusion were used to prepare the different polymorphs of $ADTCO_3$ salt. Each form was fully characterised using a combination of techniques such as hot stage microscopy (HSM), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), fourier-transform infrared spectroscopy and X-ray diffraction.

Selection of the desired form is an important step for the formulation process. Compared to the other 3 polymorphic forms, form IV is the most stable thermodynamically, however from a manufacturing perspective all four polymorphic forms require further testing.

1. Bernstein J., Polymorphism in Molecular Crystals – IUCr Monographs on Crystallography, Oxford: Clerendon Press, 2002, 14.
2. Guillory J.K., In: Polymorphism in Pharmaceutical Solids, Brittain H.G. (Ed.), New York: Marcel Dekker, Inc., 1999, 5, 183-226.
3. Hancock B. C. and Zografi G. J. Pharm. Sci., 86 (1997) 1.

Phytochemical variation and development of a quality control protocol of *Leonotis leonurus*

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Purpose: *Leonotis leonurus* has been widely used by traditional healers in Southern Africa for treatment of various ailments and is known for its psychoactive properties. The present study focused on the determination of the phytochemical variation within and between geographically distinct populations of *Leonotis leonurus* in South Africa. These data will be potentially useful in developing a comprehensive quality control protocol for *Leonotis leonurus* as the general regulations of the Medicines and Related Substances Act (Act 101 of 1965 as amended) require that all herbal products are regulated for safety, quality and efficacy.

Methods: Plant samples (50) were collected in the late summer season from the following population sites: KwaZulu-Natal (14), Mpumalanga (15), Eastern (10) and Western Cape (11). The volatile essential oils were isolated from the freshly collected leaves and stems using hydrodistillation and the chemical composition determined by one and two dimensional GC-MS. The chemotypic variation was explored using targeted and untargeted chemometric approaches.

Results: The data collected from both one and two dimensional GC-MS present two distinct clusters in which samples collected from Mpumalanga and Kwa-Zulu Natal (in land) were separated from samples from Western and Eastern Cape (coastal). Distinction between the two clusters was mainly quantitative.

Conclusion: The chemical composition of different oil samples of *Leonotis leonurus* showed almost the same pattern in both one and two dimensional GC-MS. This implied that there are similarities in chemistry between different plant materials collected at various locations in South Africa. However, due to the difference in concentration, variations tend to be more quantitative then qualitative.

Synthesis of novel mono-substituted 2-chloro-3-(thiazol-2-ylamino) naphthalene-1,4-diones

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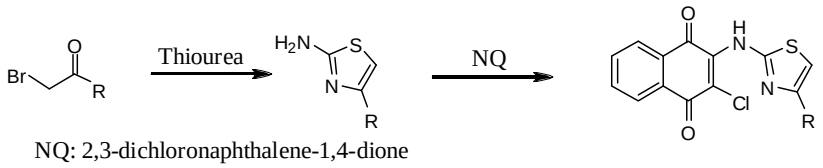
Purpose: Naphthalene-1,4-dione and 2-aminothiazole moieties have been reported in literatures for different biological activities, such as antibacterial, anti-parasitic and anticancer. The synthesis of aminonaphthalene-1,4-diones have been achieved mainly in ethanol, methanol or toluene at refluxing condition. Thus, this study was designed to synthesise 2-chloro-3-(thiazol-2-ylamino) naphthalene-1,4-diones using a different optimised milder reaction conditions.

Methods: This study involved the synthesis of new mono-substituted 2-chloro-3-(thiazol-2-ylamino) naphthalene-1,4-diones via nucleophilic substitution of various 2-aminothiazoles on 2,3-dichloronaphthalene-1,4-dione after an initial optimization processes under different reaction conditions. The 2-aminothiazoles were synthesized using the classical Hantzsch thiazole synthesis. This was followed by the nucleophilic coupling of the to 2,3-dichloronaphthalene-1,4-dione using dimethylformamide as solvent at room temperature for 6-8 hours. The reaction progress was monitored by thin-layer chromatography and the crude mixture was poured into ice water, filtered and further purified by column chromatography using hexane-ethylacetate (4:1) as the eluent.

Results: The coupling reaction was not successful when the reaction was done in ethanol, pyridine, tetrahydrofuran and toluene at varied temperatures ranging from room temperature to refluxing condition. Similarly, no product (2-chloro-3-(thiazol-2-ylamino)naphthalene-1,4-diones) was formed under a microwave assisted reaction even at 150 ^{0}C. However, 2-chloro-3-(thiazol-2-ylamino)naphthalene-1,4-diones were isolated in good yields ($\leq$ 50%) when 2-aminothiazoles and 2,3-dichloronaphthalene-1,4-dione were stirred together overnight in dimethyformamide at room temperature in presence of potassium carbonate. In addition, the use of naphthalene-1,4-dione to aminothiazole in 1: 2 ratio did not give any di-coupled product.



NQ: 2,3-dichloronaphthalene-1,4-dione

Conclusion: Mono-substituted ethyl 2-(3-chloro-1,4-dioxo-1,4-dihydronaphthalen-2-ylamino) thiazole-4-carboxylate and other five 2-chloro-3-(4-phenylthiazol-2-ylamino)naphthalene-1,4-diones were successfully synthesized under a mild condition and in good yields.

Preliminary investigation on reflective practice as a tool for reviewing and developing pharmacy curriculum

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Purpose: Planning, implementing, reviewing and developing a curriculum involves a reflective practise. Reflective practise is used as a tool by educators consisting of continuous feedback that targets specific problems in a curriculum. The information obtained through feedback helps in making better interventions into future teaching and learning to meet the needs of the students. In 2012, the Department of Pharmacy at University of Limpopo (Turfloop) has initiated an integrated Pharmacy curriculum for undergraduates over the existing traditional curriculum with the aim of preparing students for work place by improving application knowledge. The aim of the study was to investigate how the reflective practice can help in evaluating the quality and effectiveness of an integrated Pharmacy curriculum.

Methods: Student evaluation questionnaires have been developed for each module, where the evaluation criteria was based on content of the module, methods of teaching, assessment methods and overall administration and co-ordination of the module. The questionnaires contained both open and close ended questions, allowing the students to suggest changes. The target students for this study were first, second and third year undergraduates of the academic session 2014. At the end of every module students were asked to rate using the evaluation questionnaire. The student evaluation questionnaires were analysed to group their responses for each criteria: helped a lot, helped a bit or didn't help at all. These were evaluated quantitatively. Associated with each category, there were remarks which were evaluated qualitatively.

Results: A 100% response rate, suggests that students were enthusiastic to highlight the constraints of the modules. More than two-thirds of the respondents from all the modules found that the overall administration of the modules were poor, and half of the respondents attributed difficulties to methods of teaching and these were mostly related to lack of infrastructure. Only 50% of respondents found assessment methods used to be satisfactory but the satisfactory levels increased in modules where a constant feedback was provided on the status of assessments. However, considering the content of the module, the satisfactory levels were as high as 80%.

Conclusions: Working in education sector involves managing regular, rapid, and often confusing change. Using the technique of reflective practice, it has helped in organised thinking and action. The reflective practice used for reviewing and developing the Pharmacy curriculum, has so far resulted in positive improvements, solutions and also found to be helpful in managing the change effectively.

Development and validation of an *in vitro* release test for ketoconazole (KZ) on semi-solid dosage forms

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Purpose: Vaginal formulations are novel products on the pharmaceutical market. Extensive research is currently being undertaken exploit this route of administration. This present work aims to develop and validate an *in vitro* test method for semi-solid and vaginal gel formulations containing KZ.

Method: Franz diffusion cells (n= 3) were used for each test. The temperature of the water jacket was maintained at 37 ±0.5°C to mimic the temperature in the vagina since the target tissue is the vaginal mucosa. A 0.2µm Sartorius® cellulose acetate membrane was used as the artificial membrane. Samples were withdrawn at 0.5, 1, 2, 4, 8, 12, 20, 24, 48, 72 hours and 800 µL aliquots were withdrawn for HPLC analysis. The Franz cells were completely emptied at each time and the receptor fluid was replenished with fresh medium after withdrawal. The donor compartments were filled with 500 mg of test formulation and 1mL simulated vaginal fluid to mimic conditions of the intra-vaginal environment. The commercial products tested were Ketazol® cream, Kez® shampoo and Xolegel®. Analysis of Variance (ANOVA) was used to compare the *in vitro* release profiles of the formulations.

Results: The *in vitro* release profiles obtained reveal that the receptor medium of choice for aqueous based formulations included 50 % v/v 50 mMol phosphate buffer, ethanol made to a pH of 4.5 using orthophosphoric acid. The % RSD values for the tested formulations at most time points for inter-day and intra-day release testing were ≤ 10. Therefore, the developed *in vitro* method was considered accurate and precise for the purposes of release testing. One-way ANOVA demonstrated that the mean % KZ released of the tested formulations were significantly different. However, two-way ANOVA showed that as from two hours, there was no significant difference between the mean % KZ released from the shampoo and gel. No significant difference was observed for Ketazol® cream and Xolegel® at half and one hours using two-way ANOVA analysis. However a significant difference was observed at all other time points. The cream and shampoo were significantly different at all time points analyzed using two-way ANOVA. The % released after 72 hours from Ketazol® cream, Kez® shampoo and Xolegel® were 61 %, 103 % and 104 % respectively.

Conclusion: The *in vitro* release test method of commercially available KZ formulations for application in vaginal gel delivery was successfully developed and validated for accuracy and precision. This method can be used to assess drug product quality for vaginal gel formulations.

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In vitro high-throughput chemiluminescence screening for medicinal herb-drug metabolic interactions

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Purpose: Lesotho has a remarkable population that relies on herbal medicines for treatment and prevention of diseases. These herbal medicines are commonly used concomitantly with allopathic medicines with potential to cause herb-drug interactions in which drug metabolizing systems such as Cytochrome (CYP) 450 3A4 isozyme play a major role. These interactions, which may result in major and even fatal adverse reactions, are reported.

Methods: Methanol-based (11 %v/v) crude extracts of various plant parts (0.5 and 1.0 mg/ml) of *Helichrysum caespititium, Ledebouria marginata, Xysmalobium undulantum, Hermannia depressa, Rhus erosa, Agapanthus campanulatus, Malva paviflora, Gunnera perpensa, Ajuda ophryds* medicinal herbs from Lesotho and a Moringa commercial product (South Africa) were assessed using a chemiluminescent assay on CYP450 3A4 modulatory activity with a P450-Glo Assay kit™ (Promega), pig intestinal and liver microsomes. Cimetidine, a general CYP inhibitor, was used as a positive control.

Results: The nine medicinal plants and Moringa showed inhibitory effects on the metabolic activity of CYP450 3A4 on Luciferin-BE (substrate) that were lower than that of cimetidine (positive control) at both concentrations while *Helichrysum caespititium* had a higher inhibitory effect at the higher concentration (1.0 mg/ml) than cimetidine.

Conclusion: The inhibitory activity of the herbal medicines and Moringa on the metabolism of CYP450 substrate drugs requires further *in vivo* investigation.

Preparation and characterization of ultra-small curcumin nanoparticles

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Purpose: Most nanomaterials currently used for biomedical purposes are about 100 nm in size and to improve targeting, it is necessary to make them smaller (approximately 10-30 nm). Smallest average size reported for curcumin nanoparticles (CNPs) is 30 nm. Thus, the main aim of this study was to develop a method for preparation of ultra-small CNPs and also to address the solubility issue of curcumin.

Methods: CNPs were prepared by an ultrasonication method. Curcumin (100 mg) was dissolved in dichloromethane (20 ml) and this solution (1 ml) was added over a period of 5 min to the boiling aqueous solution (50 ml) of a surfactant under sonication. The yellow solution formed was sonicated further for 10 min and stirred at room temperature for 20 min. The resultant CNPs were lyophilized, diluted with milli-Q water and analyzed for size and polydispersity index (PI) at 25 °C using a Zetasizer Nano ZS90. Surface morphology of CNPs was examined using a transmission electron microscope (TEM). The stability of CNPs was evaluated at 4 °C over a period of 3 months.

Results: The particle size and PI of CNPs prepared without the use of any stabilizing agent were 103.5 ± 1.5 nm and 0.213 ± 0.02 respectively at 30 % sonication amplitude. Increasing the sonication amplitude to 50 % generated CNPs with a size of 90.6 ± 0.8 nm and PI of 0.210 ± 0.01. Further increases in the sonication amplitude to 70 % resulted in an increased size (97.15 ± 0.4 nm) and a slight decrease in PI (0.171 ± 0.02). Therefore, sonication amplitude of 50 % was considered to be optimum amplitude for the preparation of CNPs. The size and PI were found to be 103.6 ± 13.46 nm and PI: 0.221 ± 0.03 after using 1 % sodium dodecyl sulfate as a stabilizing agent whereas there was marked decrease in particle size (13.13 ± 0.24 nm) and PI (0.191 ± 0.05) after using solutol HS15 as a stabilizer. Further decrease in solutol HS15 concentration from 1 to 0.5 % resulted in increased particle size and PI. TEM images revealed that the formed CNPs were almost spherical with particle sizes in the range of 8.45 to 10.11 nm.

Conclusion: A new method for the preparation of ultra-small CNPs has been developed. Curcumin, a polyphenol derived from *Curcuma longa* plant exhibits several pharmacological actions such as anti-oxidant, analgesic, anti-inflammatory, antiseptic and anticancer but its use is limited due to poor aqueous solubility. CNPs prepared in this paper will certainly improve these actions of curcumin by two ways: i)increasing its solubility and ii) its nano size will allow its penetration well into the targeted cells. Further studies on pharmacological evaluation of CNPs are in progress in our laboratory.

Knowledge, attitudes and perceptions (KAPs) of pharmacists' assistants towards mid-level pharmacy personnel training in South Africa

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Purpose: The South African Pharmacy Council has introduced two new qualifications in pharmacy aimed at increasing the human resource capacity in pharmacies in the country. The qualifications are a higher certificate for a pharmacy technical assistant (PTA) and an advanced certificate for a pharmacy technician (PT). These new qualifications will have impact on the current pharmacists' assistants. Therefore the knowledge, attitudes, and perceptions of current pharmacists' assistants towards the proposed mid-level pharmacy personnel training were assessed.

Methods: A cross-sectional survey with ethics clearance was conducted in June 2014 using a self-administered validated questionnaire with 34 pharmacists' assistants in private hospitals and the community sector in Pretoria. Data was captured in Microsoft Excel using a double entry method and was analyzed using Epi Info and Microsoft Excel (ANOVA, $P<.05$).

Results: A 100% (n=34) response rate was realized with 29% (n=10) being males. Most of the participants (88%, n=30) indicated that they would like to upgrade for career growth, to increase their knowledge and monthly salary while participants with more than 11 years of experience were the most reluctant to upgrade (OR = 40.95 ± 1.54, $P=.03$). Only 43% (n=13) of (n=30) participants who were willing to upgrade met the PT entrance criteria. Among these (n=30) participants, 87% (n=26) preferred to study part time, 70 % (n=21) have dependents and 57 % (n=17) prefer to hold a paid job while studying to pay their study fees.

Conclusion: Less experienced, younger participants with dependents would undertake PT studies on a part-time basis. We thus recommend that a part-time study program is developed for these assistants. Entry requirements would determine the uptake into the PT program.

Solubility enhancement of curcumin by formulating it as a SMEDDS using a novel oleic acid derived heterolipid

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Purpose: Though curcumin (Curc) has anti-oxidant, anti-inflammatory, antibacterial and anticancer activities, its poor aqueous solubility limits its applications. Therefore, the purpose of the present study was to enhance the aqueous solubility of Curc by developing self-microemulsifying drug delivery system (SMEDDS) using a novel oleic acid (OA) based heterolipid which has the potential to improve solubility of poorly soluble drugs.

Methods: Heterolipid, OA1E was synthesized following a previously reported proceudre[1] and was characterized by FT-IR, NMR and ESI-MS. A shake flask method was used to determine the solubility of Curc in oils (OA1E and OA), surfactant solutions and co-surfactants. The pseudo-ternary phase diagrams were constructed by titration of homogenous liquid mixtures of oil, surfactant and co-surfactant with water at room temperature. Mean globule size and polydispersity index (PI) were measured at 25 °C using a Zetasizer Nano ZS90 (Malvern Instruments Ltd., UK). Surface morphology was examined using a transmission electron microscope (TEM) (Jeol, JEM-1010, Japan). Curc content was measured spectrophotometrically at 425.7 nm (Schimadzu UV 1601, Japan). Stability studies on developed Curc-SMEDDS were carried out at 4 °C (RH: 70 ± 5 %) and 40 °C (RH: 75 ± 5 %) for 3 months in a sealed glass vial and protected from light.

Results: The structure of synthesized OA1E was confirmed by FT-IR, NMR (^{1}H and ^{13}C) and ESI-MS. Solubility of Curc in OA1E was 0.83 % w/w which was almost 28 times higher than OA (0.03 % w/w). With surfactants, Curc showed greater solubility in 10 % w/w solutol HS 15 (0.62 % w/w). Gelucire 44/14 was selected as a co-surfactant because it is a known bioavailability enhancer and also plays a role in the reduction of mean globule size.[2] The phase diagrams revealed that the existence of microemulsion area was greater at K_m of 2. Mean globule size and PI for the developed SMEDDS were 57.06 ± 1.96 nm and 0.272 ± 0.04 respectively. TEM images showed existence of spherical globules in the size range of 27.9 to 57.9 nm. Curc content was found to be 99.69 ± 4.19 %. There were no significant changes in color, appearance, globule size and PI of developed Cur-SMEDDS on storage at 4 °C (RH: 70 ± 5 %) and 40 °C (RH: 75 ± 5 %) for 3 months indicating stability of the formulation.

Conclusion: Novel biocompatible oleic acid based heterolipid, OA1E, significantly enhanced the solubility of Curc than the parent oil, OA. This confirms its utility as a novel oily excipient for solubility enhancement of BCS class II and IV drugs. Further, its application in a nano drug delivery system was proved by using it as an oily phase in the formulation development of stable Curc-SMEDDS. Further investigations on the evaluation of antibacterial and anticancer activity of Curc-SMEDDS are in progress.

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Determining the solubility of poorly aqueous soluble drugs and drug complexes utilising a nephelometer

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Purpose: A lot of pharmaceutical substances are poorly soluble in aqueous media and this affects their bioavailability. Developing poorly soluble drugs is time consuming and costly. An effective, simple method for the determination of the solubility of poorly soluble aqueous drugs based on laser nephelometry can overcome most of the current problems. Laser nephelometry measures light scattering due to particles in suspension. It is a simple and cost-effective *in-vitro* screening assay that can be used to determine the solubility of drugs early in the process of formulation and development in a short period of time. The purpose of this study was to investigate solubility of poorly aqueous soluble drugs in solution and as cyclodextrin complexes using laser nephelometry.

Methods: Experiments were conducted by using a BMG LABTECH NEPHELOstar Galaxy Laser-nephelometer for all determinations. Test drugs, as 30 mg/ml and 10 mg/ml stock solutions or suspensions were dissolved in 100% DMSO/PBS and 1% v/v DMSO/PBS (pH 7.4) for each method respectively. Initial solubility of pure drugs were determined. The same drugs were then complexed with cyclodextrins (2-hydroxypropyl-β-cyclodextrin) in a 1:1 molar ratio after which the solubility was determined again. Solubility measurements were performed in 96-well plates at different time intervals up to 24 hours. A number of drugs including prednisone, ibuprofen and imipramine as well as natural drugs stevioside, caffeic acid, rosmarinic acid and glycyrrhizic acid were used for the study. Complex formation was confirmed by differential scanning calorimetry (DSC) (Shimadzu 60-A model) and Fourier transform infrared spectroscopy (FT-IR).

Results: The solubility of drugs before complexation were determined using nephelometry. A close to 30 fold increase in solubility could be determined as a result of inclusion complexes formed with cyclodextrins. Initially, the solubility of prednisone, ibuprofen and glycyrrhizic acid was found to be 0.200 mg/ml using nephelometry. After complexation however, the solubility was found to be 5.294, 5.191 and 5.610 mg/ml respectively. The DSC thermograms indicated formation of complexes between the cyclodextrin and drug compounds based on shifts, disappearance or the presence of peaks obtained.

Conclusion: The solubility of poorly soluble drugs were determined using a nephelometer. Nephelometry proved a simple and cost effective method for predicting the aqueous solubility of drug compounds in drug-complex systems in a relatively short period of time.

Synthesis of novel silver salts of generation 1 poly (propyl ether imine) (PETIM) dendron and dendrimers enhance antimicrobial activity against *S.aureus* and MRSA.

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Purpose: Novel therapeutic strategies are essential to address the current global antimicrobial resistance crisis. Silver displays activity against several micro-organisms only in its positively charged form. Branched molecules with multiple peripheral functionalities, known as dendrimers, have gained interest as antimicrobials with low toxicity. In this study, silver salts of generation 1(G1) poly (propyl ether imine) (PETIM) dendron and dendrimers were synthesized and evaluated for their antimicrobial potential against sensitive and resistant bacteria. The purpose was to exploit the multiple peripheral functionalities of G1 PETIM dendron and dendrimers for the formation of silver salts containing multiple silver ions in a single molecule for enhanced antimicrobial activity at the lowest possible concentration.

Methods: G1 PETIM dendron, dendrimers and their silver complexes were synthesized and characterized by FT-IR, ^{1}H NMR and ^{13}C NMR. PETIM silver salts were evaluated for their cytotoxicity using MTT assays. The G1 PETIM dendron/dendrimers, silver nitrate and silver salts of the G1 dendron (compound **A**), dendrimer with an aromatic core (compound **B**) and an oxygen core (compound **C**) were evaluated for activity against *S. aureus* and methicillin-resistant *S. aureus* (MRSA) by the broth dilution method.

Results: The structures of the dendron/dendrimers were confirmed by FT-IR, ^{1}H NMR and ^{13}C NMR; and the formation of compounds **A**, **B** and **C** were confirmed by FT-IR analysis. PETIM silver salts were found to be non-cytotoxic even up to 100 µg/ml. Minimum inhibitory concentration values of compounds **A**, **B** and **C** against *S. aureus* were 52.1, 41.7, and 20.8 µg/ml while against MRSA they were 125.0, 26.0 and 62.5 µg/ml respectively. The calculated fractional inhibitory concentration index further indicated that compound **B** specifically displayed additive effects against *S. aureus* and synergism against MRSA.

Conclusion: The enhanced antimicrobial activities of the novel PETIM dendron/dendrimer-silver salts against both sensitive and resistant bacterial strains widen the pool of available pharmaceutical materials for optimizing treatment of bacterial infections.

Synthesis of novel α-aryl substituted 3-indolylethanones as potential antimalarial agents

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Purpose: According to the World Health Organisation (WHO), deaths attributed to *Plasmodium falciparum* exceeded 600 000 in 2012, with 207 million cases of malaria being reported. One contributing factor to this statistic is the emergence of drug resistance against the available antimalarial agents. Therefore there is a critical need to develop new therapeutic antimalarial drugs with novel mechanisms of action in order to curb the increasing spread of malaria. The indole scaffold is often associated with biologically active compounds, recently exemplified by the new antimalarial agent NITD609, which is currently in Phase 1 clinical trials. Based on a current SAR study of 3-acylindole derivatives which show promising antimalarial activity, we are looking into the synthesis and in vitro evaluation of a series of α-arylated 3-indolylethanones as potential inhibitors of *P. falciparum*.

Methods: Our study explored the synthesis pathway of a two-step reaction toward our target compounds, with the initial α-bromination of 3-acetylindole, followed by substitution of the halogen with an appropriate nucleophile. Various reagents were explored to optimise the nucleophilic displacement step, including potassium carbonate and various silver containing compounds.

Reaction progress was analysed using thin-layer chromatography (TLC); purification of the products was done using a step gradient column chromatography. Nuclear magnetic resonance (NMR) was used to resolve the structures of the products.

Results and Conclusion: While many of the silver compounds were found to assist in nucleophilic substitution, none were superior in to the addition to the addition to potassium carbonate. We have synthesised a small series of new indolyl-3-ehtanone analogues, and are looking to expand our collection with a view to biological evaluation.

The use of hydrogen-sulphide test kit to monitor fecal contamination of various water sources using a community based approach in underprivileged South Africa

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Purpose: South Africa is a water scarce country and the potable water supply suffers from problems such as pipe breaks and interruption of supply. Problem with water supply forces a large part of the population to use rainwater for domestic consumption. This paper is aimed at designing information tools using a community based approach.

Methods: A modified hydrogen-sulphide (H2S) test kit was used to detect faecal contamination of different water bodies. A workshop was conducted with youth comprising of (7 males and 7 females) to educate them about the study at hand. These youth worked with the municipality as community environmental facilitators. Tasks included providing the trainees with overview with laboratory healthy and safety of the laboratory, practical manufacturing of the H2S kits, lectures in the form of videos and handouts containing, home tasks including water sampling and assignments, reflections in terms of focus group discussions and questionnaires. The participants followed the theory and the practical however the assignment posed a challenge since only 33% of the participants managed to get above 50%. Samples were collected from house taps, tanks, communal taps, community halls and schools.

Results: Ninety two percent of the results were negative and 8% were positive for faecal contamination. From the questionnaire the participants indicated that the H2S kit might be beneficial to the community. Lack of the information and inadequate sanitation may result in an increased outbreak of waterborne diseases.

Conclusion: The community based approach is a platform that will be of benefit to elucidate water issues in communities.

Benzodiazepine prescribing in South Africa with the focus on half-life and the associated potential for misuse

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Purpose: Benzodiazepines are a frequently misused class of medicine. Benzodiazepines are Schedule 5 medicines in South Africa. Alprazolam is indicated for anxiety and panic disorder, and was recently rescheduled in Australia to be more strictly controlled due to its potential for illicit drug use. The aim of this study was to investigate benzodiazepine prescribing patterns in South Africa in general with a specific focus on half-lives and the associated potential for misuse of this class of medicines.

Methods: A retrospective, cross-sectional drug utilisation study was conducted on prescription data of a medical insurance scheme administrator in South Africa for 2010 and 2011. The databases contained approximately 5 million records for medicine, medical devices and procedures.

Results: In 2010 and 2011, a total of 71 390 prescriptions for benzodiazepines and benzodiazepine-related drugs were dispensed to 16 601 patients. The average age of patients was 43.92 (SD=16.36) years, with 53.73% female patients. Approximately 60% of prescriptions were dispensed to females. Benzodiazepines constituted 64.9% of prescriptions, sedative hypnotics (other) for 29.17% and anxiolytics (other) for 6.04%. Twenty-six different active ingredients were dispensed, with 45.27% of prescriptions classified as ultra short-acting or short-acting. In both years, alprazolam constituted the third most often prescribed benzodiazepine accounting for 17.27% of all benzodiazepine prescriptions in 2010 and 15.64% in 2011. Zolpidem, diazepam and bromazepam were other frequently prescribed benzodiazepines. In a second South African study conducted on a claims database, alprazolam was the most often claimed benzodiazepine, with 31.41% of benzodiazepine claims in 2006 and 32.03% in 2008. A study conducted in South African treatment centres found that benzodiazepines are the most widely misused medicines in Cape Town (consistent with USA and European studies) and that more (middle-aged, higher income) women reported them as their primary substance of abuse. Alprazolam is often used in higher dosages and mixed with alcohol to enhance the “high” feeling that the drug generates.

Conclusions: Further studies on benzodiazepines and their use should be conducted in South Africa, and comparative studies with Australia may yield important results. The length of therapy, dosages and indication for use are aspects that could be investigated.

Proton pump inhibitors in South Africa: Role of branded generics

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Purpose: Originator products dominate the market, and as soon as patents expire prescribing patterns change as branded generics become the most often prescribed due to mandatory generic substitution in South Africa. This study investigated the prescribing patterns of proton pump inhibitors (PPIs).

Methods: A retrospective, cross-sectional drug utilisation study was conducted on prescription data of a medical insurance scheme administrator in South Africa for 2011. The database contained 2 298 312 records for medicine, medical devices and procedures.

Results: A total of 22 198 PPIs were prescribed to 7 504 patients (average age: 45.09 (SD=15.82) years) at a cost of R3 931 241.43. The average cost per PPI prescription was R177.10 (SD=R140.62). The average cost for a generic PPI prescription was R147.01 compared to R276.17 for a prescription for an originator product. Five different PPIs were prescribed. Omeprazole, lansoprazole and pantoprazole had branded generics available on the market, whereas esomeprazole and rabeprazole only had originator products on the market. Omeprazole was the most frequently prescribed (47.05% of all PPI prescriptions). Nearly all omeprazole prescriptions (98.90%) were for one of its eight branded generics. Esomeprazole had the highest average cost per prescription of R289.23. The 40mg tablet formulation of esomeprazole was the most commonly prescribed. Less than 2% of PPI prescriptions were for rabeprazole. Most prescriptions were for Schedule 4 products (prescription-only), with only 3.91% Schedule 2 prescriptions (over-the-counter, prescribed in lower dosages for acute symptoms over a short period of time). Overall in this study, 76.70% of PPI prescriptions were for branded generics.

Conclusions: Omeprazole dominated PPI prescribing, whilst esomeprazole was the most expensive PPI. It will be important to further investigate the impact of patent expiry and the introduction of new branded generics on PPI prescribing patterns. The study confirmed the significant price differences for PPIs between branded generics and originator products.

Supporting integration of research and practice into pharmaceutical education - collaboration between a university and health system strengthening organisation

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Building healthcare professional's capacity in operational research is key to improving work place practice. In 2014, Systems for Improved Access to Pharmaceuticals and Services (SIAPS) a United States Agency for International Development (US-AID) funded Management Sciences for Health (MSH) project is working with Nelson Mandela Metropolitan University (NMMU) to support the Final Year Bachelor of Pharmacy Research Elective Module. Three SIAPS consultants in collaboration with NMMU faculty are coordinating (a) one full research project (1 student), and two elective courses on (b) Managing Medicine Supply at Health Institutions (8 students), and (c) Pharmacovigilance (5 students).

a) The ***Research Project*** involves the analysis of trends and cost of dispensing chronic medication using a public sector electronic database. The results from the project will be shared with the National Department of Health and will be used to develop recommendations for improved use of the electronic medical database. SIAPS has designed the mentorship to teach the student overall qualitative, quantitative and project management skills that can be carried into a consulting environment or academia.
b) The main objective of the ***Managing Medicine Supply at Health Institutions*** elective is to help students understand the importance of managing medicine supply in order to ensure optimal delivery of health care services. Cold chain management of vaccines used in South Africa's Expanded Programme on Immunisation (EPI-SA) took the centre stage where students investigated the level of compliance with cold chain management practices. Such information will assist the profession in developing suitable interventions to ensure improved health outcomes by ensuring patient safety, improving knowledge and/or behaviour and minimising wasteful expenditure.
c) The ***Pharmacovigilance*** component is designed to help students understand the basic concepts of Pharmacovigilance, define key terms used in Pharmacovigilance ; including the history of Pharmacovigilance and drug safety, the World Health Organization Medicines Safety Program; identify Pharmacovigilance methods applicable for data collection for safety monitoring and national regulatory decision-making, understand the importance of spontaneous reporting and the role it plays in reporting of adverse drug reactions; know the source of adverse drug reaction reports, and levels and forms of reporting adverse drug reaction. The course exposes participants to key features of the various Pharmacovigilance methods and their advantages and disadvantages.

The collaboration between NMMU and SIAPS brings research and practice into pharmacy student's education, ultimately strengthening the students' understanding of some components of the South African health system.

Development and validation of a RP-HPLC method for the quantitation of captopril in tablets

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Purpose: The purpose of the research was to develop a reversed-phase HPLC method for the determination of captopril in tablets. From a literature review it is apparent that HPLC methods that have been reported for captopril use UV and electro-chemical detection. A capillary-zone electrophoresis method using UV detection has also been reported. The objective of this study was to develop a sensitive, simple, selective and stability indicating analytical method, specifically in terms of efficient elution characteristics and economical in terms of mobile phase costs. The method will be validated in terms of linearity, precision and accuracy for the quantitative analysis of captopril in formulations.

Methods: A standard HPLC system consisting of a Waters Alliance® solvent delivery module equipped with a Waters 2996 PDA detector was used. Separation was achieved using a 5µm Phenemenox Luna® C_{18} 150mm x 4.6mm i.d. as the stationary phase and a mobile phase consisting of 29.7:70.3 % v/v acetonitrile:water adjusted to a pH of 2.98 using ortho-phosphoric acid. The column temperature was maintained at 24.0°C and a flow rate of 1.0 ml/min with phenobarbital as internal standard was used. Detection was achieved at 210nm using a photo diode array (PDA) detector. The Design of Experiments using a Central Composite Design (CCD) approach was used for method development and optimization. Mobile phase composition, pH of mobile phase and column temperature were selected as critical factors to establish retention time and better resolution of captopril and phenobarbitol. Twenty experimental runs were performed in the range of acetonitrile concentration between 28% and 36%, pH range between 2.8 and 3.6 and temperature range between 22°C and 32°C. The experimental data obtained was used to derive a quadratic model for retention time for captopril.

Results: The optimized method was found to produce sharp peaks with good resolution for captopril and phenobarbital at 3.1 min and 6.2 min., respectively. The calibration curve showed a good linear relationship with a correlation coefficient of 0.9999 over the concentration range 2-60 µg/ml and the regression equation was y=0.0367x-0.0117. The experimental data revealed that acetonitrile concentration in mobile phase and pH are the significant factors that affect the retention time and resolution of captopril and the internal standard.

Conclusions: A sensitive, simple, selective analytical method was developed successfully and will be further validated in terms of precision, accuracy, linearity, limits of detection (LOD) and quantitation (LOQ) according ICH guidelines for the determination of captopril.

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