Pharmacy Education (2024) 24(7) 158 - 177
https://doi.org/10.46542/pe.2024.247.158177

CONFERENCE ABSTRACTS

FIP CAPE TOWN 2024

82nd FIP World Congress of Pharmacy and Pharmaceutical Sciences in Cape Town, South Africa, 1 to 4 September 2024

Drug delivery medicine

Design, evaluation and optimisation of a paediatric taste-masked azithromycin dry powder suspension using inclusion complexation and microencapsulation

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Introduction: Paediatric medication palatability remains a significant challenge, impacting treatment adherence and therapeutic outcomes.

Objective: This study focuses on designing, evaluating, and optimising a taste-masked azithromycin dry powder suspension for paediatric use. The approach involves employing inclusion complexation and microencapsulation techniques to enhance taste masking while maintaining therapeutic efficacy.

Methods: Microcapsules containing azithromycin-inclusion complex will be prepared using a solvent-evaporation method with varying quantities of Eudragit®. Size distribution, flow properties, drug loading, encapsulation efficiency, and microcapsule yield will be determined. A palatable suspension will be formulated using sucrose, sodium phosphate, hydroxypropyl cellulose, and xanthan gum. Taste assessment will be conducted using an advanced taste sensor system with lipid/polymer membranes.

Results: The microcapsules will exhibit uniform size distribution with desirable flow properties. Drug loading, encapsulation efficiency, and microcapsule yield will be optimally achieved, ensuring high drug content and formulation efficiency. The palatable suspension formulation will demonstrate effective taste masking, enhancing acceptability among paediatric patients. Statistical analysis will confirm the significance of the results, supporting reproducibility and reliability.

Conclusion: This study will successfully design, evaluate, and optimise a taste-masked azithromycin dry powder suspension using inclusion complexation and microencapsulation techniques. The formulation is to show promising characteristics in terms of manufacturability, drug content, taste masking, and palatability. These findings will contribute to addressing the challenges of paediatric medication acceptability, potentially improving treatment adherence and health outcomes in paediatric healthcare globally. Future research could further optimise formulation parameters and explore other taste-masking strategies for paediatric formulations.

The design and development of novel anticancer peptides targeting solid tumours

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Introduction: Conventional cancer treatment modalities possess limitations for solid tumours, such as a lack of selectivity; thus, nanomedicine is explored as an efficient tool in their drug development. To achieve this, the study aimed to design a novel anticancer peptide (ACP) targeting solid tumours using in silico methods as well as formulation strategies to encapsulate the ACP into a lipid-based nanoparticle for efficient delivery to the target site.

Methods: The ACP's were designed using in silico methods; thereafter, optimal ACP was used in a liposomal formulation using a thin-film hydration method containing phosphatidylcholine and cholesterol. Characterisation included the usage of DLS (size, polydispersity, zeta potential), RPHPLCE (peptide quantification), dialysis (drug release), cryoTEM (surface morphology), MTT assays, and hemolysis (activity and biocompatibility of the formulation). The Annexin V-FITC kit was employed for the determination of the peptide apoptotic effect on MCF-7 cell lines. The size, PDI, and zeta potential of the prepared ACP liposome were 193,46 ± 0,10 nm, 0,342 ± 0,12, and -7,67 ± 0,04 mV, respectively, with a %EE of 91,23 ± 0,01.

Results: The ACP liposomes showed concentration-dependent hemolysis, and the in vitro drug release studies showed that the ACP encapsulated liposome had controlled drug release compared to the bare peptide. MTT assays revealed that the ACP-encapsulated liposome induced higher cytotoxic effects on the cancer cell line MCF-7 than Azacitidine and that the peptide formulation (P1CF1) was not toxic to HEK293 cells. The ACP-encapsulated liposomes had no bacterial activity, and the cell apoptosis showed that the ACP-encapsulated liposome (P1CF1) induced early apoptosis in the MCF-7 cell line. The ACP-encapsulated liposome revealed efficient encapsulation with better biocompatibility at lower concentrations. The bare peptide and liposome showed significant anticancer activity in MCF-7 cancer cells.

Conclusion: This study revealed that this formulation can potentially target solid tumours at their target sites.

The comparative disintegrant properties of starches obtained from *Plectranthus edulis* (Ethiopian potato) and Irish potato in paracetamol tablets: Optimisation of formulation parameters using Response Surface Methodology

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Introduction: Starch is one of tablet formulations' most used pharmaceutical disintegrants. Disintegrants are added to tablets to effect the break-up of tablet matrix into granules and particles, thereby facilitating drug dissolution and absorption. Starch occurs abundantly in most plants. Some plants are overexploited for starch extraction and starch used in various industrial applications. Evaluation of starches from other less-utilised plants will allow us to have alternative sources of biomaterials. *Plectranthus edulis* (P. *edulis*) [fam., Lamiaceae] is an ancient Ethiopian tuber crop and one of the traditional root crops indigenous to Ethiopia. Paracetamol, a poorly compressible and sparingly soluble drug, requires an effective binder and disintegrant to disrupt the effects of binder and pressure of tabletting when the tablet is in the aqueous media of the gastrointestinal tract (GIT).

Objective: The present study aimed to assess the disintegrant property of Ethiopian potato (P. edulis) starch in comparison to Irish potato starch and to optimise the formulation factors with respect to the mechanical properties and performance of paracetamol tablet formulations using the Central Composite Design.

Method: The tablets were prepared using the wet granulation method. paracetamol, a binder solution, and various concentrations of disintegrants were mixed to prepare granules for compression. Tablet properties such as crushing strength, friability, disintegration time (DT), and dissolution rate were studied for comparison and optimisation studies. The effects of compression force (CF) and disintegrant concentration (DC) on the characteristics of the tablets on the mechanical and performance of the tablets were studied and optimised using Central Composite Design. A full 2x2 factorial design was combined with five replicates of the centre and 2x2 axial points. Experiments were carried out, and 13 formulations of paracetamol tablets were obtained using Design Expert 8.0.7.1 software.

Results: The results of the comparative study showed that the properties of paracetamol tablets formulated with both starches as disintegrants were affected by their concentration, and the CF and P. edulis starch exhibited a favourably comparable disintegrant property with Irish potato starch in paracetamol tablet formulations. The study also showed that the CF and DC significantly affected the response variables. Therefore, these factors were further optimised using CCD. The optimal conditions experimentally obtained for CF and DC have closely matched the predicted values of the responses, as exhibited by the validation study.

Conclusion: The study concludes that P. edulis can be used as an alternative source of starch for its application as a disintegrant in tablet formulations.

Natural deep eutectic solvents as a potential patient-centred drug delivery strategy

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Background: There is a significant number of inpatients and outpatients who experience difficulty swallowing. This

condition is not only limiting in terms of delivering nutrition but also medication - which can be detrimental to life. This becomes a challenge, especially about the delivery of solid oral dosage forms. To work around this, patients and caregivers resort to crushing tablets or opening and mixing the contents of a capsule with food or drink. This introduces problems that were more likely addressed through formulation design, like taste masking and sustained drug release. Liquid oral dosage forms thus become a more favourable drug delivery method. Natural deep eutectic solvents (NADES) – a novel solvent class synthesised from natural compounds are suggested as a suitable base for a liquid oral formulation. Furthermore, their non-toxic and sweetening properties magnify the opportunity to formulate acceptable formulations suitable to address the aforementioned problem.

Purpose: The aim was to investigate NADES as an alternative liquid base for the extemporaneous compounding of four ARVs.

Method: Several natural compounds and water combinations were heated (60 ± 2 °C) and stirred until the formation of a clear, viscous solution that remained stable at ambient conditions. The solubilisation power of each NADES for abacavir, lopinavir/ritonavir and efavirenz was investigated through equilibrium solubility testing. Solubilised drug concentration was quantified with reverse-phase high-performance liquid chromatography utilising analytical methods as per British Pharmacopoeia. Extemporaneously compounded solutions were evaluated in terms of visual appearance, viscosity, and pH.

Results: The selection of natural compounds yielded NADES with an extremely acidic pH (0.59 - 0.96). The pure NADES's viscosity was over 100 Pa.s, which increased with drug additions to the liquid base. The high viscosity prevented homogeneous drug mixing in the NADES and accurate sampling for quantification analyses. The introduction of the liquid base containing the drug to intestinal pH (6.7) resulted in immediate drug precipitation.

Conclusion: The acidic pH would produce a horrid burning sensation in the mouth and throat during attempts to swallow. The high viscosity of the base suggests extra and potentially difficult steps during extemporaneous compounding to accurately measure the dose (even more so for out-patients). While this enhances difficulty in swallowing, special measuring tools are necessitated to achieve accurate delivery of a dose. Drug precipitation could potentially occur while the dose is in the oral cavity, which would expose the bitter-tasting drugs. This poor palatability further enhances the difficulty of swallowing. Investigations into optimising the said NADES are needed to enable their use in extemporaneous compounding. This is needed to allow pharmacists to provide improved drug dosing strategies customised to patients who struggle to swallow as part of patient-centred care.

Design of anti-VEGF peptide-functionalised superparamagnetic iron oxide nanoparticles for antiangiogenic and targeted delivery of paclitaxel in non-small-cell lung carcinoma

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Introduction: Non-small-cell lung carcinoma (NSCLC) continues to drive the global prevalence of lung cancer, as it constitutes ~85% of all reported lung cancer cases. Angiogenesis is one of the crucial pathways in lung tumour growth and is responsible for tumour vascularisation and metastasis. Therefore, the inhibition of angiogenesis through targeting of the vascular endothelial growth factor (VEGF), as its prominent biomarker, can potentially halt tumour proliferation and metastasis in NSCLC.

Objective: This study set to fabricate superparamagnetic iron oxide nanoparticles (SPIONs) decorated with anti-VEGF peptide, HRH, and loaded with an anticancer drug, paclitaxel (PTX), for targeted antiangiogenic and antitumor activity against NSCLC.

Method: SPIONs were synthesised via the co-precipitation method and coated with conjugated linoleic acid (CLA) for self-assembled loading of PTX to give CLA-coated PTX-SPIONs. HRH peptide was then conjugated via coupling chemistry, yielding the final formulation of CLA-coated PTX-SPIONs@HRH. The size and surface charge of CLA-coated PTX-SPIONs@HRH were determined using a Malvern ZetaSizer, and the overall morphology was ascertained via TEM analysis. The drug loading capacity of the nanosystem, the release behaviour of PTX, and the VEGF receptor targeting ability were determined in vitro. The anti-proliferative activity of CLA-coated PTX-SPIONs@HRH was evaluated on lung adenocarcinoma cells (A549) in vitro, and the in vivo antitumor activity was evaluated on a lung xenograft mouse model.

Results: Formulated CLA-coated PTXSPIONs@HRH exhibited a size and surface charge of 108.5 ± 3.5 nm and −30.4 ± 2.3 mV, respectively, and a quasi-spherical shape. A high PTX loading efficiency of 98.5% and sustained PTX release at acidic pH 6.8 were observed, with a marked dose-dependent anti-proliferative activity on A549 cells, complimented by an enhanced cellular uptake. CLA-coated PTX-SPIONs@HRH significantly reduced secretion levels of VEGF-A, and 76.6% tumour regression was recorded from treated mice, with a

prolonged PTX plasma circulation time and no apparent side effects.

Conclusion: This work provides new insights into the design of targeted nanomedicines for NSCLC and suggests that CLA-coated PTX-SPIONs@HRH could provide a potentially effective treatment modality for NSCLC for enhanced therapeutic outcomes and minimal side effects.

Artificial intelligence in precision drug delivery for the treatment of neurological disorders

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Introduction: Neurological disorders are defined as diseases affecting the brain, spinal cord, and other nerves in the human body (neurons). Brain disease difficulties involving the central nervous system (CNS) and peripheral nervous system (PNS), along with brain cancer, represent some of the most prevalent, lethal, and inadequately treated conditions. Over 1 million of the 6.8 million deaths attributed to CNS-related issues each year are caused by neurodegenerative disorders, including glioblastoma (GBM), Parkinson's disease (PD), and Alzheimer's disease (AD). Several drugs have been developed to address issues related to toxicity, specificity, and delivery while treating diseases of the CNS. However, it is challenging for therapeutic drugs to get across barriers like the blood-brain barrier (BBB), which reduces the efficacy of the therapy. Also, the poor aqueous solubility of some therapeutic agents, their short half-lives, low bioavailability, which requires frequent high dose administrations, and their poor aqueous solubility, which can lead to several severe side effects like dyskinesia, stomatitis, sleep disturbance, anxiety, and depression, limit their use in the treatment of CNS diseases. These problems highlight the need for precision drug delivery, like the use of polydopamine nanoparticles (PN) as a model to alter or manipulate various processes at the cellular level due to the presence of the polydopamine receptors in the CNS to achieve the desired attributes. These nanoparticles are an efficient substitute for delivering drugs and other approaches since they may cross the blood-brain barrier due to their nano size. Given their biocompatibility, high stability, surface modification, and adjustable targeting efficacy, they are useful for transporting bioactive compounds, particularly across the BBB. They have the potential to be an appealing approach for the delivery of drugs to the CNS. Artificial intelligence (AI) has become a crucial technology in the advancement of precision medicine. This is because AI can analyse and interpret biological data and automate intelligent activity. Although AI has been used in drug delivery, there is little to no evidence that computational techniques have been leveraged to study and predict the delivery of polydopamine particles to the CNS.

Objective: The focus of this work and the presentation is on the preparation, physicochemical characterisation of PN and application of AI in the prediction of the delivery and efficacy of polydopamine particles to CNS for the treatment of AD, PD, and GBM diseases.

Method: The synthesis of PN is examined using the self-polymerisation approach. Using the Zetasizer dynamic light scattering technique, the particle size and surface charge will be assessed. Differential scanning calorimetry, thermogravimetric analysis, scanning electron microscopy, transmission electron microscopy, and Fourier infrared spectroscopy techniques will be used to investigate the physicochemical characterisation of the synthesised PN analysis. For the study and prediction analysis of PN particles to CNS, an artificial intelligence neural network (Neurosolution 4.2) software will be employed.

Results: The AI neural network, the Neuro-solution software model, is being developed for the prediction analysis of PN delivery to the CNS disease treatment. The size and morphology analyses confirmed the formation of PN with the intrinsic size and morphological features attributed to PN.

Nanotechnology for cardiovascular diseases

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Introduction: Nanotechnology is being applied to the advancement of drug delivery systems and theragnostic devices in various conditions, including cardiovascular speciality.

Objective: To appraise evidence on the application of nanotechnology cardiovascular disease (CVD) management.

Method: Literature was retrieved from PubMed using the search terms “nanotechnology” AND “cardiovascular”. Inclusion criteria were peer-reviewed articles, available as free full-text, in English and published between 2013 and 2023. Opportunities, types of nanoparticles used, benefits and challenges of nanotechnology in CVD were analysed.

Results: A total of 3,124 records were identified. All records were screened, and after the inclusion criteria had been applied, 46 articles were included in the appraisal. Most articles (n = 39) were reviews, and most originated from Asia

(n = 16), followed by North America (n = 13) and Europe (n = 11). The articles reported on the application of nanotechnology in the treatment (n = 42) and diagnosis (n = 13) of CVD, mostly for atherosclerosis (n=36). Most articles reported on the use of nanotechnology for targeted drug delivery (n = 26). Fourteen articles discussed how nanotechnology can be applied to medical devices, mostly in magnetic resonance imaging (n = 10). The classes of nanoparticles mostly studied are inorganic nanoparticles, such as gold and iron oxide nanoparticles (n = 16), followed by lipid-based nanoparticles (n = 10). Benefits of using nanoparticles include a good safety profile (n = 12), adequate biocompatibility (n = 11), enhanced drug delivery (n = 10), biodegradability (n = 7), and improved bioavailability (n=4). Challenges mostly reported include lack of clinical translation (n = 12), cost issues (n = 8), need for scale-up production (n = 7) and regulatory issues (n = 3).

Conclusion: CVDs persist as the leading cause of morbidity and mortality globally, and nanotechnology represents novel viable approaches for diagnosis and treatment, particularly in atherosclerosis. Nanotechnology still has a long way to go from translational medicine to clinical application, and further evaluation of biocompatibility, pharmacokinetics, and safety of nanomaterials in vivo is required.

Design, evaluation, and optimisation of taste-masked azithromycin by ion-exchange resins

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Introduction: Azithromycin (AZI) is an intensely bitter macrolide antibiotic used to treat both paediatric and adult infections. The bitter taste affects patient adherence to therapy, which may further worsen the condition. Bitter taste is a serious issue in the formulation of most active pharmaceutical ingredients (API); hence, masking the taste of APIs is a useful method for improving patient adherence to therapy. Several taste-masking formulation techniques have been used to develop palatable dosage forms. A taste-masking technique using ion-exchange resins has been used to mask the taste of AZI. Ion exchange resins are pharmacologically inert polymers that bind to substances and exchange mobile ions to produce a tasteless drug-resin complex or resinate.

Objective: This study aimed to develop a taste masked AZI resinate utilising Indion® 234, a weak acidic cation exchange resin.

Method: The parameters influencing the formation of the AZI-resin complex were evaluated. A central composite design was used to generate experiments to optimise response through the evaluation of input variables such as stirring time, temperature, and drug-resin ratio. AZI loading efficiency was assessed using a previously validated HPLC-UV method. Differential scanning calorimetry (DSC), scanning electron microscopy (SEM), and Fourier transform infrared (FT-IR) spectroscopy were used to confirm complex formation. In-vitro taste evaluation of the resinate was performed using simulated salivary fluid.

Results: The optimal AZI-resin ratio, temperature, and stirring time were 1:0.10, 70°C, and 4 hours, respectively, at pH 8. The drug loading efficiency of AZI resinate was 81%. In-vitro taste evaluation revealed 1.72% drug release from the resinate in 5 minutes, implying adequate taste masking.

Conclusion: Using ion exchange resin to mask the bitter taste of drugs in oral dosage forms is a cost-effective and reliable method for improving the taste of medicine. To achieve optimal drug loading, it is important to consider the drug-to-resin ratio, solvent temperature, and contact time between the resin and drug. These studies show Indion® 234 can effectively reduce the bitter taste of AZI.

Protein-coated satin nano delivery system

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Introduction: Atorvastatin is used to treat hypercholesterolemia. However, its low bioavailability (12%) and extensive hepatic first-pass metabolism affect its pharmacokinetics and pharmacodynamics. Bovine serum albumin (BSA) is an endogenous protein characterised by its biocompatibility, water solubility, and potential for active targeting. This research aims to utilise a novel, non-toxicity, and nanoprecipitation-based method to develop an atorvastatin nano-delivery system with protein corona.

Method: The nanoprecipitation approach was used to produce the nano-delivery system. The organic phase, containing a specific proportion of 3-mercaptopropyl and 3-aminopropyltrimethoxysilane, was allowed to stand for 24 hours before the addition of atorvastatin. The mixture was then injected into the aqueous phase and incubated in a 60°C circulating water bath for two hours. Subsequently, nanoparticles were extracted and mixed with BSA. Leveraging the positively charged characteristics of the nanoparticle surface, self-assembly occurred with BSA, resulting in the formation of an atorvastatin nano-delivery system with a protein corona.

Results: The prepared nanoparticles exhibit a spherical structure. The physical properties of an atorvastatin nano-delivery system with a protein corona yield the following observations: the average particle size measures 212.1 ± 44.2 nm, with a zeta potential of –17.5 ± 1.8 mV. It was observed that the drug encapsulation efficiency reached around 50%. The nanoparticles were physiochemically stable for three months.

Conclusion: By encapsulating BSA on nanoparticle surfaces, the anti-aggregation properties is beneficial to the scale-up in the future. Drug conjugation and cross-linking applications of this carrier system improved poorly soluble atorvastatin attribute including loading efficiency and stability. Further examination and bio application will be performed in the following experiments.

Hybrid biopolymer/bioceramic 3D-printed scaffolds embedded with doxorubicin nanoparticulate Systems for local treatment of osteosarcoma

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Introduction: Osteosarcoma continues to present a significant challenge in oncology, owing to its prevalence and the deleterious side effects associated with current treatment modalities. Consequently, there is a critical demand for novel methods. This research contributes to the advancement of the field by investigating the combination of Doxorubicin-loaded nanoparticles with cutting-edge 3D printing technology to fabricate scaffolds tailored for localised tumour treatment and bone regeneration.

Method: The study rigorously assessed four nanoparticulate systems' effectiveness in the treatment of osteosarcoma: liposomes, albumin nanoparticles, spanlastics, and chitosan-coated spanlastics, each imbued with Doxorubicin. In recognition of the necessity to attenuate the toxicity profile of Doxorubicin, these nanoparticulate systems were developed and integrated into hybrid 3D-printed scaffolds comprising a 3% alginate and 9% methylcellulose hydrogel, impregnated with nanocarriers and calcium phosphate cement. An exhaustive array of tests was executed, encompassing the characterisation of particle size, zeta potential, and drug release kinetics. The in vitro analyses included fluorescence imaging for cellular uptake, cytotoxicity against the human osteosarcoma cell lines MG-63, and cell proliferation with human mesenchymal stem cells. Additionally, RT-PCR was utilised to analyse four genes implicated in osteosarcoma within the cells.

Results: A key finding of the study was the exceptional efficacy of the spanlastics and chitosan-coated spanlastics, which demonstrated marked advancements in drug delivery and therapeutic outcomes. Spanlastics, with their innovative elastic vesicular construction, facilitated sustained Doxorubicin release, significantly enhancing bioavailability. The chitosan-coated spanlastics were particularly distinguished by an 85% Doxorubicin encapsulation efficiency and a prolonged release profile, which contributed to a 60% reduction in MG-63 cell viability when contrasted with the control group. The chitosan coating also augmented cellular uptake and the localised delivery of the therapeutic agent. The structural soundness and optimised porosity of the 3D scaffolds were vital in providing the necessary infrastructure for bone regeneration, as evidenced by the proliferation of osteoblastic cells on the scaffold's surface and the support for the attachment of human mesenchymal stem cells to its calcium phosphate elements.

Conclusion: The research establishes the significant effectiveness of Doxorubicin-laden chitosan-coated spanlastics within bespoke 3D-printed scaffolds as a transformative method for the localised treatment of osteosarcoma. The dual-function scaffold not only delivers potent cytotoxicity against osteosarcoma cells but also fosters an environment conducive to the regrowth of bone tissue. The confluence of sophisticated nanoparticle engineering with precision 3D printing technology presents a formidable platform for the development of patient-specific, targeted treatments. This cross-disciplinary breakthrough heralds new pathways in personalised medicine and represents a significant advance in the clinical handling of osteosarcoma, with the potential to markedly enhance patient prognoses and quality of life following therapy.

Solvent deposit onto ion exchange resins combined with microencapsulation for controlled release of water-soluble drugs

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Introduction: Water-soluble drugs are released rapidly in the gastrointestinal tract and have short half-lives. It results in frequent drug administration to maintain a steady plasma concentration. This study used depositing onto ion exchange resins and microencapsulation with ethylcellulose (EC) to control the release of four water-soluble drugs. The hypothesis is that these microparticles will reduce the

frequency of administration and will be better at maintaining therapeutic blood levels.

Method: This study used a combination of depositing for a solvent four water-soluble drugs (propranolol HCl, pseudoephedrine HCl, diclofenac sodium, and dexamethasone sodium phosphate) onto ion exchange resins and then microencapsulating these particles with EC. The change in the zeta potential of the particles was used to monitor the encapsulation of drugs onto the resins. After encapsulation, drug loading was determined using UV or HPLC analysis. Drug release was determined using USP Apparatus II using 900 ml of phosphate buffer (pH = 6.8) as the dissolution medium. The stability of the drug in the microcapsules and crystal form changes during encapsulation were also measured.

Results: Drug loading analysis showed that 14 – 27 mg of either basic or acidic drugs were loaded onto 100 mg of cationic or anionic resin microspheres (14–27%, w/w). Dissolution results showed that drug release from the ion exchange resin microspheres was diffusion-controlled. In the first stage, EC inhibits entry of the dissolution medium into the microspheres. Once the medium enters, the drug dissolves. A drug concentration gradient between the inside and outside of the resin system is produced. This high osmotic pressure drives the drug through the EC wall and releases it into the dissolution medium. This process prolonged the release of the four drugs from less than 20 minutes to 12 hours and longer.

Conclusion: Drugs loaded onto ion exchange resins and subsequently encapsulated within ethylcellulose (EC) provided high drug loading of both cationic (acidic) and anionic (basic) water-soluble drugs. Microencapsulation slowed down drug release while maintaining drug concentration for 12 hours or longer.

Application of the SeDeM Expert Diagram System to multi-component powder mixtures

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Introduction: The SeDeM Expert Diagram System (EDS) is a formulation tool that was initially developed to determine the batch-to-batch reproducibility of active pharmaceutical ingredients (APIs). The application was expanded to determine the suitability of powders for direct compression and to determine the optimal quantity of excipient needed to yield directly compressible tablets. Subsequently, the SeDeM EDS was utilised to evaluate the physical characteristics of numerous powders, granules, and pellets. It has been used in the formulation of orally disintegrating tablets and multiple-unit pellet systems.

Objective: This study investigated the application of the SeDeM EDS to multi-component powder mixtures consisting of more than one active pharmaceutical ingredient (API). These mixtures were evaluated in terms of powder flow and compressibility to predict the mixture's suitability for direct compression.

Method: The SeDeM EDS was applied to three selected API's (i.e. Vitamin B1, B6 and B12), excipients (hydroxypropyl methyl cellulose (HPMC), microcrystalline cellulose (MCC), tricalcium citrate (TCC) and a lubricant mixture consisting of colloidal silicon dioxide, sodium stearyl fumarate and talc) as well as mixtures of these API's and excipients. The mixtures were compressed into tablets that were pharmacotechnically evaluated. These results were compared with SeDeM EDS's predictions to determine whether the SeDeM EDS can be applied to multiple-component powder mixtures.

Results: The study showed that the SeDeM EDS was successfully applied to multi-component powder mixtures to predict the mixture's suitability for direct compression. In addition, a new SeDeM EDS calculation was developed to determine the percentage of corrective excipients required in the event of multiple unsatisfactory incidence factor values.

Conclusion: From the results, it was concluded that the SeDeM EDS is suitable to predict whether multi-component powder mixtures consisting of more than one API have sufficient flow properties and compressibility to yield directly compressible tablets. Tablets containing B vitamins were successfully produced by means of direct compression. A new SeDeM EDS calculation for the determination of the percentage of corrective excipients required in situations where more than one incidence factor requires improvement was also developed. The new calculation for multiple low-scoring incidence factors should be further investigated. The use of tensile strength as a substitute for the cohesion index parameter should also be investigated as it provides more comparable tablet hardness results.

In-silico and in-vitro investigation of antiviral compounds molecular mechanisms for potentially inhibiting dengue virus NS2B-NS3 protease

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Introduction: The recent outlook of Dengue viral infection as a global public health concern, coupled with the reportage of

resistance and lack of efficacy of most anti-dengue drugs, calls for a concerted effort to find new leads.

Method: The study combined in-silico and in vitro approaches to identify novel potential synthetic small-molecule inhibitors targeting the DENV-2 NS2B-NS3 protease. The NS2B-NS3 protease enzyme in the dengue virus transmission pathway is required for the replication of the virus within the host cell. The lack of NS2B-NS3 protease homologue in the human host and its conserved nature among all dengue viruses makes it a viable target for future anti-dengue drugs. Initially, six known inhibitors of dengue NS2B-NS3 protease with IC50 < 10 µM were used to generate a pharmacophore model with a score of 0.9144 using Ligand Scout. The validated model was used to screen a synthetic library of 65,345 compounds obtained from ChemDiv (compound library). Thirty compounds with pharmacophore fit scores above 55 were docked against the modelled three-dimensional structure of NS2B-NS3 protease using AutoDock Vina.

Results: Nine compounds with binding energies ranging from 7.5 to −8.7 kcal/mol were identified as potential hit molecules. Three compounds comprising STOCK6S-06707, STOCK6S-84928, and STOCK6S-65920 with respective binding energies of −8.7, −8.2, and −8.0 kcal/mol, lower than 22,26-azasterol (−7.6 kcal/mol), a known dengue inhibitor, were selected as plausible lead molecules. The compounds were also predicted to have anti-dengue activity with reasonable pharmacological and toxicity profiles.

Conclusion: The identified compounds could be optimised to develop potent anti-dengue therapeutic agents.

Improving access to child-friendly formulations of drug-resistant tuberculosis medicine in South Africa

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Introduction: The treatment journey for drug-resistant tuberculosis (DR-TB) has seen major advances in the past few years with novel new treatment regimens that include new and repurposed medicines. These new agents are safer and less toxic than previous medicine and hold the promise of improved treatment outcomes in this long and difficult journey. Whilst most of the evidence supporting the inclusion of the new medicine into treatment guidelines comes from adults included in clinical trials, the principles of drug selection to obtain the most effective regimen are the same in both populations. Children, however, face barriers to access due to the lack of child-friendly formulations of the new and repurposed medicine that threatens to erode the perceived benefits in this vulnerable population. Adult formulations must be cut, crushed and mixed, making bioavailability questionable and serving as a barrier to decentralisation. Lack of data on the acceptability and tolerability of child-friendly formulations, as well as low demand, are barriers to registration and access.

Method: In 2017, an opportunity presented itself with dispersible formulations becoming available on the global market. The Global Drug Facility coordinated a global pooled procurement to enable the manufacture of dispersible formulations of new medicine. These products were then offered as a donation to encourage countries to gain programmatic experience with the medication and to facilitate global roll out of these products.

Based on the regimen adopted in South Africa, the need was identified, and quantification was done based on the past three-year case registrations of children less than six years old. Approvals were sought from the Pharmacy and Therapeutics Committee, the Affordable Medicines Directorate and the Regulatory Authorities to import and use unregistered products in South Africa. The donation was accepted by the Head of Health, and medicine was procured. Standard operating procedures were drafted based on actual experiences and guided implementation. Informed consent was given prior to use, and progress reports every six months were completed.

Results: Access to child-friendly formulations of pyrazinamide, ethambutol, clofazimine and levofloxacin was facilitated in the first donation for use in one high tuberculosis burden province in South Africa. Based on this experience, a further donation was offered for expanded use in South Africa, with a need identified for delamanid, levofloxacin, clofazimine and linezolid dispersible tablets. Access was extended to three provinces, and based on the successful access project, one province was able to decentralise care for children. A further donation, including child-friendly bedaquiline, is currently being processed.

Conclusion: Prescribers, pharmacists, nurses, caregivers and children in South Africa gained experience in the use of child-friendly formulations of DR-TB medicine. Acceptability and tolerability studies and the impact of child-friendly formulations on treatment outcomes in children are being done and will add to the body of knowledge on child-friendly formulations in South Africa. Looking forward, the evidence from this study on safety, acceptability, tolerability, and lessons learned from the South African experience will help catalyse greater interest in local manufacturing or bulk importation of child-friendly formulations.

Hyaluronic acid-Silybin conjugate as a multifunctional, biomimetic vancomycin-nanocarrier against bacterial sepsis

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Introduction: Bacterial sepsis is a life-threatening condition that, if not detected and treated early, can progress to septic shock, multiple organ failure, and death. To effectively manage sepsis, it is crucial to target various molecular and cellular pathways involved in the pathogenesis of the condition. The application of biomimetic materials in the nano delivery of antibiotics can provide avenues to target various sepsis pathways. Hyaluronic acid (HA) is a well-known Toll-like receptor (TLR) ligand, which decreases its expression and limits the infection-induced increase of inflammatory mediators. Silybin (SIL) is a flavonolignan with potent anti-inflammatory and antioxidant activities. A novel HA-SIL conjugate might represent a potential self-assembling nanocarrier of antibiotics to target multiple sepsis pathways and improve clinical outcomes.

Objective: This work was intended to develop a multifunctional, biomimetic nanosystem based on the novel HA-SIL for vancomycin (VCM) delivery (VCM-HA-SIL-NPs) to target bacterial infections and sepsis.

Method: HA-SIL was synthesised and characterised using FTIR and NMR. VCM-HA-SIL-NPs were formulated using a solvent evaporation technique and characterised in terms of particle size, polydispersity index (PDI), zeta potential (ZP), entrapment efficiency (EE%), in vitro drug release, physical stability, and biocompatibility. VCM-HA-SIL-NPs were also assessed for in vitro antibacterial activity, antioxidant activity (DPPH assay), and anti-inflammatory potential (Toll-like receptor-2 binding affinity using microscale thermophoresis (MST)).

Results: HA-SIL synthesis was confirmed. The optimised VCM-HA-SIL-NPs had 262.8 ± 1.662 nm particle size, 0.190 ± 0.010 PDI, -18.5 ± 1.63 mV ZP, and 66.03 ± 2.34% EE%. VCM-HA-SIL-NPs were proven to be physically stable and biocompatible. VCM-HA-SIL-NPs showed a sustained release, with 73.48 ± 1.53 % of VCM released throughout 48 hours, compared to 100% of bare-VCM release in 24 hours. VCM-HA-SIL-NPs showed enhanced and sustained antibacterial activity against methicillin-resistant Staphylococcus aureus (MRSA), which was retained for 96 hours, compared to bare VCM, which was maintained for only 24 hours. HA-SIL and VCM-HA-SIL-NPs also demonstrated good free radical scavenging and antioxidant properties. The MST studies showed lower dissociation constant (Kd) values of HA-SIL and VCM-HA-SIL-NPs compared to peptidoglycan (MRSA toxin) when bound to TLR2, indicating their promising anti-inflammatory effect for sepsis management.

Conclusion: These findings show VCM-HA-SIL-NPs as a promising multifunctional biomimetic nanosystem for improved bacterial sepsis management. The project continues, and the in vivo activity on the animal sepsis model will soon be done.

Assessing the ability of polyelectrolyte coatings to stabilise lopinavir and ritonavir in the amorphous state

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Introduction: Lopinavir/Ritonavir (LPV/RTV) is a fixed-dose combination (FDC) used in the treatment of HIV/AIDS. Commercially, LPV/RTV is available as an amorphous solid dispersion (ASD). The reason for this is that both LPV and RTV display poor aqueous solubility, and amorphisation is used to address this problem. However, the high polymer-to-drug ratio of this ASD results in large tablets and high frequencies of dosing.

Objective: The purpose of this study is to assess the ability of layer-by-layer (LbL) self-assembled polymer coatings to stabilise glassy LPV and RTV in the amorphous state. This innovative approach holds the potential to stabilise amorphous LPV and RTV in a form that has a higher drug-to-polymer content, potentially reducing tablet sizes and enhancing patient adherence.

Method: Glasses of LPV and RTV were prepared individually using the quench cooling method. The resulting glasses were ground and characterised using powder X-ray diffraction (PXRD), Fourier-transform infrared spectroscopy (FTIR), simultaneous thermal analysis (STA), and differential scanning calorimetry (DSC). After the amorphous nature of the glasses was confirmed, their zeta-potentials were measured, and based on the signs of their zeta-potentials, a polyelectrolyte with an opposite charge was used to coat the glasses. Coating was done using the layer-by-layer (LbL) self-assembling method. This LbL coating step was repeated up to six times with polyelectrolytes of alternating charges. The

inhibition of molecular mobility brought about by the polyelectrolyte coating was measured using thermal analysis techniques. Stability studies were conducted on both coated and uncoated glasses, and solubility and dissolution studies were conducted using individual raw materials as controls.

Results: Both LPV and RTV were amicable to forming glasses using the quench cooling method. Stability studies suggested that the polyelectrolyte coatings were successful in inhibiting crystallisation in both the LPV and RTV glasses. The extent of stabilisation increased with the number of polyelectrolyte coatings. The data obtained from DSC studies suggested that the polyelectrolyte coatings were also successful in extending the mean relaxation times and, therefore, able to inhibit the molecular mobility of the LPV and RTV glasses. Collating the data suggests that there were correlations between the number of polyelectrolyte coatings, the degree of relaxation time extension, and the extent of crystallisation delay in the coated glasses.

Conclusion: By integrating the quench cooling method with polyelectrolytes-based layer-by-layer self-assembly, a promising strategy for stabilising LPV and RTV in the solid state has been developed. This approach has the potential to improve therapeutic outcomes, reducing the frequency of dosing and enhancing patient compliance.

Tampon-like xerogel device for non-hormonal contraception

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Introduction: Over the past decade, the number of women desiring to use contraceptive methods for family planning has significantly increased. Unfortunately, marketed products provide limited choices for women to protect against unintended pregnancy, and concerns about undesirable side effects remain a significant barrier to greater uptake and continued use of existing methods. Moreover, women in low-resource settings who do not desire pregnancy often find themselves without viable options.

Objective: The main objective of this research is to develop a low-cost, tampon-like device suitable for on-demand, female-initiated contraception without the use of hormones.

Method: Xerogel devices were fabricated by lyophilisation of a hydrogel comprised of 2% (w/v) Carbopol® 974P, 4% (w/v) hydroxypropyl methylcellulose, and 3% (w/v) mannitol using conventional sol-to-gel transformation. The total pore volume contained within a xerogel device was estimated by the fluid displacement method using n-hexane as a non-polar solvent. The rate at which vaginal fluid simulant pH 4.2 (VFS) penetrates the xerogel after surface exposure was quantified gravimetrically. Contraceptive efficacy in vivo was assessed using the rabbit model. After a vaginal douche with VFS, female animals in each treatment group (n=10) received either a small (L = 5 mm) or large (L = 10 mm) xerogel device via the vaginal route. The spermicidal VCF® Gel containing 4% (w/v) nonoxynol-9 was used as a positive control, and animals exposed to an empty applicator were used as a sham control group. Artificial insemination of female rabbits in each treatment group was performed 15 min after vaginal administration of test or control formulations using 0.25 mL of pooled semen obtained from male breeder rabbits. Animals were euthanised 12 days later, and pregnancy status was assessed by counting embryos within the uterine horns.

Results: The porosity of tampon-like xerogel devices fabricated by lyophilisation was, on average, 85.5 ± 3.0% of the total device volume, which allowed a VFS hydration rate of 13.9 ± 0.7 mg/s×cm2. In comparison to animals in the sham control group, the small xerogel device reduced the pregnancy rate after artificial insemination by 40% but only by 20% after vaginal administration of the large device. In comparison, the prevention of pregnancy in animals that received the VCF® Gel was 80%.

Conclusion: Drug-free, tampon-like xerogel devices fabricated by lyophilisation can prevent pregnancy in vivo. However, contraceptive efficacy appears dependent on favourable hydration within a limited volume of vaginal fluid. Further optimisation of the hydration capabilities of these xerogel devices will be required before advancing this novel female-controlled, on-demand contraceptive technology towards clinical evaluation.

Targeted delivery and apoptosis induction of palbociclib loaded 4-carboxy phenyl boronic acid conjugated hybrid nanoparticles in breast cancer cells

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Introduction: Many anti-cancer therapies suffer from off-targeting and lack of specificity; this problem can be overcome by delivering the drug to a specific site. Targeted drug delivery is an advanced strategy for actively targeting the tumour, which can increase the amount of drug at the specific site and decrease the off-target toxicity and non-specific effects of the drug. Researchers have been identifying various receptors that are overexpressed in cancer tissues and are targeting cancer tissues.

Method: In the current work, we have fabricated a novel pH-responsive phenylboronic acid conjugated hybrid nanoparticle. We had conjugated chitosan with phenylboronic acid by carbodiimide chemistry and the formation of conjugation was confirmed by spectroscopic techniques. Hybrid nanoparticles were prepared using the ionic gelation method.

Results: Particle size, PDI, and zeta potential were found to be 226.5 ± 4.3 nm, 0.271± 0.014, and 5.03 ± 0.42 mV. The presence of pH-sensitive biological macromolecule, i.e., chitosan in the carrier system, imparts pH-responsiveness to PPCL and sustainedly releases the palbociclib up to 144 h. The hybrid nanoparticles showed nearly 7.2, 6.6, and 5-fold higher cytotoxicity than pure drugs in MCF-7, MDA-MB-231, and 4T1 cells. A receptor-blocking assay confirmed that the hybrid nanoparticles were internalised through sialic acid-mediated endocytosis in the breast cancer cells. Hybrid nanoparticles exhibited enhanced ROS generation, mitochondrial depolarisation, qualitative and quantitative apoptosis, and decreased % cell migration than pure drugs.

Conclusion: Thus, it reported that delivering palbociclib by phenylboronic acid conjugated hybrid nanoparticles provides a novel approach to the treatment of breast cancer.

Insight to Nanoliposomes as a smart radiopharmaceuticals' delivery tool for imaging Atherosclerotic plaque: Positron emission tomography applications

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Introduction: Atherosclerosis is a chronic progressive disease which is known to cause acute cardiovascular events as well as cerebrovascular events with high mortality. Unlike many other diseases, atherosclerosis is often diagnosed only after an acute or fatal event. At present, the clinical problems of atherosclerosis mainly consist of the difficulty in confirming the plaques or identifying the stability of the plaques in the early phase. In recent years, the development of nanotechnology has come with various advantages, among which include non-invasive imaging enhancement, which can be studied for the imaging of atherosclerosis.

Method: This research focuses on the advances in the development of tailored liposomal nano-radiopharmaceuticals -based techniques and their applications to atherosclerotic plaque diagnosis. Furthermore, it highlights liposomal nano-radiopharmaceuticals localisation and biodistribution key processes in the pathophysiology of atherosclerosis. Lastly, the direction and future of liposomal nano-radiopharmaceuticals as a potential clinical tool for the assessment and diagnosis of atherosclerotic plaque are discussed.

Results: The use of liposomal nano-radiopharmaceuticals in PET imaging offers several advantages over conventional imaging techniques. Moreover, by incorporating targeting ligands on the surface of liposomes, such as antibodies or peptides that recognise specific markers associated with atherosclerosis, the imaging agent can be further enhanced for selective plaque imaging. This targeted approach improves the sensitivity and specificity of PET imaging, enabling the detection of early-stage plaques and potentially identifying high-risk plaques prone to rupture.

Conclusion: These imaging agents hold great potential for clinical translation, as they can aid in the early detection, risk stratification, and monitoring of atherosclerosis, ultimately leading to improved patient management and personalised treatment strategies. However, further research and clinical trials are needed to validate their efficacy and safety in human subjects.

The development and validation of a RP-HPLC method for the quantitation of ethionamide in pharmaceutical dosage forms

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Introduction: Multi-drug-resistant tuberculosis (MDR-TB) is treated with second-line tuberculosis (TB) medicines. Ethionamide (ETH), a potent second-line TB compound, is a prodrug indicated for treating MDR-TB and TB meningitis. ETH is structurally related to isoniazid (INH); however, due to gastrointestinal irritation, it is not considered a first-line TB treatment option. The drawbacks of conventional TB therapy, such as drug toxicity, prolonged treatment, and patient non-compliance, result from poor aqueous solubility, stability, and bioavailability of TB drugs. Nanomedicine drug delivery systems for TB drugs that have shown good results in pre-clinical trials are polymeric nanoparticles, solid lipid nanoparticles, liposomes and niosomes. Encapsulation of ETH in lipid-polymeric hybrid nanoparticles will be beneficial in overcoming the challenges of the commercially available ETH dosage forms, viz. 250 mg film-coated tablets (registered in South Africa) and 125 mg dispersible tablets (not registered in South Africa).

Objective: To develop and validate a simple, rapid, precise, accurate and sensitive RP-HPLC for the estimation of ETH in pharmaceutical dosage forms.

Method: The development and optimisation of the RP-HPLC method was facilitated using a Central Composite Design generated by Design Expert® software. A Thermoscientific Ultimate-3000 HPLC system was used to develop an isocratic RP-HPLC method. A Phenomex® 250 × 4.6 mm i.d., 5 µm C18 column and a mobile phase consisting of phosphate buffer and acetonitrile (69:31) were successfully applied to the separation of INH (internal standard) and ETH. The chromatographic separation was achieved using a flow rate of 1ml/min at a temperature of 30 °C with detection at 275 nm. The injection volume was 20 µl. The RP-HPLC method was validated according to International Council on Harmonisation guidelines.

Results: The optimised RP-HPLC method produced well-resolved peaks with retention times of 2.43 and 6.3 minutes for INH and ETH, respectively. The method was linear over the concentration range 0.02 – 150 µg/ml with R^2 = 0.999. Precision investigations yielded % RSD values < 2%, while accuracy results had % Bias < 2% at the concentrations studied. The limits of quantitation and detection for ETH were 0.02 µg/ml and 0.006 µg/ml, respectively. Successful estimation of ETH in commercially available tablets was achieved, and 99.69% of ETH was recovered.

Conclusion: The RP-HPLC method that has been developed is simple, rapid, accurate, precise, and sensitive. It has been successfully applied to the analysis of ETH in bulk and tablets. The developed method is suitable for the analysis of ETH in other dosage forms, such as polymeric and lipid nanoparticles in which ETH may be incorporated.

Physicochemical and microbiological stability of compounded bethanechol chloride oral suspensions in PCCA Base, SuspendIt®

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Objective: To study the stability of extemporaneously compounded bethanechol chloride suspensions from two generic brands of commercial tablets in the contemporary vehicle PCCA Base, SuspendIt. SuspendIt is a sugar-free, paraben-free, dye-free and gluten-free thixotropic suspending agent containing a natural sweetener obtained from the monk fruit. It thickens upon standing to minimise the settling of any insoluble drug particles and becomes fluid upon shaking to allow convenient pouring during administration to the patient. The study design included two concentrations to provide stability documentation over a bracketed range for eventual use by compounding pharmacists.

Method: A stability-indicating ultra-high-performance liquid chromatographic assay for the determination of the chemical stability of bethanechol chloride in PCCA SuspendIt was validated. Suspensions of bethanechol chloride were prepared from the tablets in PCCA SuspendIt at 1 mg/mL and 5 mg/mL concentrations, selected to represent a range within which the drug is commonly dosed. Samples were stored in amber plastic prescription bottles at room temperature (25°C). Samples were assayed initially and on the following time points (days): 14, 30, 60, 90, and 180. Physical data such as pH and appearance were also noted. Microbiological stability was tested.

Results: A stable extemporaneous product is defined as one that retains at least 90% of the initial drug concentration throughout the sampling period. Bethanechol hydrochloride tablets were stable for 180 days in SuspendIt at room temperature. Drug concentrations were at or above 93% of initial values for both brands of commercially available tablets, Amneal and Upsher-Smith. No microbial growth was observed. pH values remained fairly constant.

Conclusion: A robust stability-indicating UPLC assay method for the determination of bethanechol chloride in PCCA SuspendIt was validated. This assay was used to determine the chemical stability of the 1-mg/mL and 5-mg/mL concentrations of commercially available bethanechol chloride tablets compounded in PCCA SuspendIt at a controlled room temperature of 25°C. Drug concentrations did not go below 93% of the label claim (initial drug concentration). pH values remained fairly constant. The preservative system in PCCA SuspendIt successfully protected the suspensions from the growth of challenging microorganisms. This study demonstrates that bethanechol chloride tablets are physically, chemically, and microbiologically stable in PCCA SuspendIt for 180 days at room temperature at both concentrations studied, thus providing a viable, compounded alternative for bethanechol chloride in a liquid dosage form, with an extended BUD to meet patient needs.

The formulation of a chloroquine-benzothiazole-urea amorphous solid dispersion for improved bioavailability

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Introduction: Malaria remains a critical health challenge globally, necessitating the exploration of novel therapeutic agents with improved efficacy and bioavailability. This study involves the formulation of a novel amorphous solid dispersion (ASD) of a chloroquine-benzothiazole-urea (CBU) hybrid molecule aimed at enhancing the compound's bioavailability so that it can fulfil its therapeutic potential in vivo. Given the compound's poor solubility and uncertain membrane permeability, it could potentially be categorised as a BCS class II or class IV drug, making its bioavailability suboptimal for therapeutic use. This research employs the abovementioned formulation strategy to surmount these limitations, thereby improving bioavailability.

Objective: This study aims to investigate the formulation and permeation characteristics of a novel CBU hybrid, employing ASDs to enhance its bioavailability which will address the knowledge gap around its low solubility and permeability yet high therapeutic potential. Given the limited research on CBU's formulation, this work aims to bridge this gap by comprehensively analysing its formulation and permeation characteristics.

Method: The study employed a comprehensive formulation strategy involving solvent evaporation to create the ASD. Screening for compatible polymers was followed by the formulation process and thorough characterisation using Differential Scanning Calorimetry (DSC) for miscibility assessment, Fourier Transform-Infrared Spectroscopy (FT-IR) for interaction analysis, and other planned methods such as X-ray Powder Diffraction (XRPD) and Polarised Light Microscopy (PLM), though some were constrained by equipment availability currently. Solubility enhancements were evaluated through supersaturated ASD solutions, with in vitro dissolution assessed via the dialysis bag method. Additionally, method development and validation for UV spectroscopy is underway to quantify solubility and dissolution accurately. Ex vivo permeability will be examined using a porcine intestinal model as the last part of the study.

Results: Preliminary findings demonstrated significant solubility improvements, with FT-IR analyses indicating favourable interactions between the CBU hybrid and the polymer polyvinylpyrrolidone K25 (PVP) in a 1:4 ratio, confirming the formation of an ASD. DSC results supported good miscibility between the drug and polymer, evidenced by appropriate glass transition temperatures. However, some characterisation methods like XRPD and PLM were not completed due to equipment issues but will be completed promptly, and UV spectroscopy method validation is still in progress. The solubility and dissolution studies, as well as the ex vivo permeability study, will soon follow the development of the method.

Conclusion: The initial results affirm the potential of the CBU hybrid in ASD form as an efficacious solution to the bioavailability challenges of antimalarial drugs. The study's findings contribute valuable insights into using ASD formulations to enhance the bioavailability of novel therapeutic compounds. Future work will focus on completing the remaining characterisation methods, refining the formulation process, and exploring the implications of these findings for broader therapeutic applications.

Improving drug release and permeability of furosemide in self-micro emulsifying drug delivery systems

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Introduction: BCS class IV drugs are characterised by poor and variable solubility and permeability. Self-micro emulsifying drug delivery systems (SMEDDS) and other lipid-based systems have gained attention recently as promising solutions to the low solubility and oral bioavailability of active pharmaceutical ingredients. The improvement of BCS class IV drug bioavailability will contribute to improved treatment and therapeutic outcomes.

Objective: A SMEDDS dosage form was formulated and characterised to improve the solubility and intestinal permeability of the BCS class IV drug, furosemide.

Method: Different combinations of surfactants and natural oils were tested to assess their emulsification capabilities. Subsequently, pseudo-ternary diagrams were generated to determine the optimal mass ratios at which micro/nano-emulsions formed. Successful micro/nano-emulsion formulations were loaded with 20 mg furosemide and characterised based on droplet size and zeta potential. An optimised formulation was selected and encapsulated into hard gelatine capsules to obtain a solid dosage form. It was also evaluated in terms of drug release and intestinal permeability. The drug release profile of the dosage form was assessed at pH 1.2 (0.1 M HCl) and pH 4.6 (0.1 M citate buffer) to simulate conditions of site-specific absorption of furosemide. The permeability of furosemide from the

SMEDDS formulation was evaluated using an ex vivo study using an ovine gastrointestinal model. Abomasum and duodenum tissue were mounted in Sweetana-Grass diffusion chambers, and the percentage of transport of furosemide was determined at pH 1.2 and 4.6, respectively. Drug release and permeation were evaluated against a commercially available product.

Results: The most effective SMEDDS combination consisted of sesame oil, Tween® 80, and PEG 400 at a mass ratio of 1:4.5:4.5. This SMEDDS formulation produced satisfactory spherical micro-droplets with a mean droplet size of 0.78 µm, (Span = 0.320) and a zeta potential of -23.5±3.84 mV. The drug release profiles of the SMEDDS in gelatine capsules in the pH 1.2 media were significantly ($p < 0.05$) better in terms of the initial dissolution rate (DRi), the area under the curve (AUC) and the mean dissolution time (MDT), compared to the commercial reference product, and at the pH 4.6, the DRi was significantly faster than the commercial reference product. Moore and Flanner's similarity (f1) and difference (f2) factor values indicated that the drug release profile of the SMEDDS formulation was not similar to the commercial reference product. The SMEDDS formulation significantly improved the permeability of furosemide by 2-fold compared to the commercially available product, as assessed with the ex vivo transport model representing its narrow in situ absorption window.

Conclusion: The results of the study indicate that SMEDDS could be a promising alternative for improving the solubility and permeability of BCS class IV drugs and possibly their oral bioavailability.

Ex vivo evaluation of selected nootropics in thermosensitive gel formulations for prediction of nose-to-brain delivery

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Introduction: Cognitive disorders are a category of mental health disorders that affect a patient's learning ability, perception, memory, and problem-solving capabilities. The pharmacological treatment of these disorders usually consists of nootropics. The intranasal route of administration harbours the potential to deliver drugs directly into the brain from the olfactory region, referred to as "nose-to-brain delivery", which bypasses the blood-brain barrier.

Objective: The aim of this study was to formulate thermosensitive gels to effectively deliver nootropic drugs across excised nasal epithelial tissue and to predict nose-to-brain delivery.

Method: Selected nootropics (caffeine, donepezil, rivastigmine, and sunifiram) were formulated into thermosensitive gel systems. The ex vivo permeation of the selected nootropics was evaluated across excised sheep nasal epithelial tissue from both the respiratory and olfactory regions following the application of the gel delivery systems, as well as solutions. For purpose of reference, the permeation was also measured across synthetic dialysis membranes. The %transport over time of each of the model compounds was determined, and the coefficient of apparent permeability (Papp) was calculated.

Results: The permeation studies showed that the selected nootropics exhibited medium (Papp values between 2 – 20 x 10-6 cm/s) to high (Papp values > 20 x 10-6 cm/s) permeability across the olfactory and respiratory nasal epithelial tissues, while the permeation across the synthetic dialysis membrane was in general lower. This indicated that active transport mechanisms may have been involved in addition to the passive diffusion of the selected nootropics across the excised nasal epithelial tissues. Of all the nootropics, sunifiram showed the highest potential to be effectively delivered across the respiratory and olfactory nasal epithelial tissues.

Conclusion: In general, the selected nootropics showed high potential for nose-to-brain delivery after intranasal administration for the rapid treatment of cognitive disorders. Future studies should investigate the rate and extent of delivery of the nootropics in the brain tissue after intranasal administration by means of advanced in vitro models, as well as in vivo animal models.

Nootropic permeation across excised sheep respiratory and olfactory epithelium

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Introduction: Over the past few decades, interest in intranasal delivery has grown as a non-invasive route of drug administration. The nasal cavity offers several benefits as a target site for drug delivery. A wide variety of therapeutic compounds may be administrated intranasally to achieve topical, systemic and/or central nervous system effects. Effective treatment of neurodegenerative disorders via oral drug administration is challenging due to several complicating

factors, such as limited and/or variable bioavailability, limited transfer of drugs across the blood-brain-barrier (BBB), rapid first-pass metabolism, and unwanted side effects due to the higher drug doses required. Nose-to-brain delivery bypasses the BBB and the blood-cerebrospinal fluid barrier via neural connections among the olfactory epithelium, olfactory bulb, and trigeminal nerve. Nootropics, known as cognition-enhancers or neuroenhancers, can stimulate cognitive processes. These compounds are useful for the treatment of various cognitive dysfunctions and neurodegenerative disorders such as age-related memory deficits, Alzheimer's or Parkinson's disease and multiple sclerosis.

Objective: The potential of direct nose-to-brain delivery was investigated by using an ex vivo permeation study with the model nootropic compounds, caffeine, sunifiram and rivastigmine. Comparisons were made between the extent of permeation across excised sheep nasal respiratory and olfactory epithelium.

Method: Ex vivo permeation studies were done using a Sweetana-Grass diffusion chamber apparatus and excised sheep nasal respiratory and olfactory epithelium. Two sampling conditions were used to determine the extent of nootropic permeation. First was the collection of small-volume samples (200 uL) from the basolateral chamber over time, with the addition of fresh pre-heated Krebs-Ringer bicarbonate buffer (KRB) to maintain the initial volume. The second was aimed at mimicking sink conditions by sampling the total volume (7 mL) of the basolateral chamber at each time point and replenishing it with fresh pre-heated KRB. The percentage transport over time of each of the model compounds was determined, and the coefficient of apparent permeability (Papp) was calculated.

Results: The comparison of the percentage permeation and Papp values obtained across the two regions showed that the percentage permeation, as well as the average Papp values, across sheep olfactory epithelium were, in general, higher than across respiratory epithelium, irrespective of the sampling method, that was used. Additionally, the results also showed that the extent of permeation was significantly ($p < 0.05$) higher when the artificial sink conditions were simulated during the ex vivo evaluation.

Conclusion: The ex vivo permeation studies results showed that the selected nootropics could potentially be administered intranasally to achieve direct nose-to-brain delivery, with greater permeation across olfactory epithelium compared to respiratory epithelium.

Curcumin-Loaded Vitamin E-TPGS-Polyquercetin Nanoparticles as a synergistic anti-inflammatory nanomedicine

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Introduction: Curcumin (CUR), the bioactive component of Curcuma longa rhizome, has a wide range of well-documented bioactivities, including antioxidant, anti-inflammatory, immunoregulatory, hepatoprotective, neuroprotective, antidiabetic, and anticancer activities. Unfortunately, CUR suffers from low water solubility, poor bioavailability, and rapid metabolism in vivo, which has hindered its clinical use, creating a need for more effective formulation approaches to enhance its biopharmaceutical properties. A novel nanoscale drug delivery platform based on the plant polyphenol quercetin has been recently developed by relying on its propensity to undergo oxidative self-polymerisation reactions, resulting in the formation of discrete nanoparticles (NPs). The NPs could be loaded with various drug molecules and co-assembled with other polymers to modify their surface properties.

Objective: The purpose of this study was to evaluate polyquercetin NPs co-assembled with vitamin E-TPGS as a delivery platform for CUR and investigate their anti-inflammatory activity compared to free CUR as a potential anti-inflammatory nanomedicine.

Method: The NPs were prepared by nanoprecipitation and characterised by dynamic light scattering to determine their particle size and polydispersity, UV-Vis spectroscopy to measure drug loading efficiency, and in vitro release testing. The formulation's anti-inflammatory activity was evaluated in vitro using lipopolysaccharide (LPS)--stimulated RAW 264.7 macrophages by measuring intracellular reactive oxygen species (ROS) and pro-inflammatory cytokines.

Results: The NPs had an average diameter of 71 nm, a polydispersity index of 0.23, a loading efficiency of 83%, and sustained release up to 96 h. In LPS-stimulated macrophages, CUR NPs significantly quenched intracellular ROS compared to free CUR. Notably, CUR NPs exhibited a pronounced attenuation of the pro-inflammatory cytokines tumour necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β) compared to free CUR, whereas the NPs and the free drug showed comparable effects on the reduction of IL-6 levels. The results were attributed to the antioxidant activity of the NP vehicle, as the drug-free NPs were also associated with significant ROS quenching and inhibitory activity against the pro-inflammatory cytokines.

Conclusion: These findings strongly indicate that vitamin E-TPGS-modified polyquercetin NPs can not only serve as a novel nanocarrier platform for CUR but also boost its anti-

inflammatory activity, making it a promising nanomedicine candidate for various inflammatory conditions.

Innovative multipurpose prevention technologies against HIV infection in high-risk underserved populations

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Introduction: High rates of HIV infection and other infectious diseases against a background of low access to preventive methods and diagnostic devices are major concerns in sub–Saharan Africa. Addressing these challenges requires embracing natural products in scientific trials and new innovative diagnostic methods.

Objective: This multi-disciplinary research consortium developed an anti-HIV herbal nanomedicine and a multiplexed 3D-printed point-of-care testing (PoC) device to address the resource gaps in access to HIV preventive methods and testing devices in the African setting. This goal was informed by the outcomes of a situational analysis that was conducted among undergraduate pharmacy students in Lesotho and South Africa – a study which indicated that new affordable diagnostic devices, as well as herbal-based anti-HIV preventive methods, could make a difference in addressing the problem of high HIV infection in sub–Saharan Africa.

Method: The anti-HIV herbal nanomedicine trials were conducted on plant species identified in a literature search based on a standard bibliometric approach aimed at identifying plant species with reported activity (in-vitro and in-vivo) against HIV infection. The PoC diagnostic device was developed following an in-house protocol designed by the researchers, with the POC device having the advantages of simultaneously detecting HIV and HCV, a concept adaptable to other infectious diseases. The protocol also optimised an innovative 3D printing method for manufacturing the cassette for the PoC device.

Results: In the preventive herbal nanomedicines study, trials based on some selected solvents exhibited strong inhibition (>50%) of HIV-1 gp120/CD4 binding and HIV-1 protease. The PoC diagnostic device trials successfully optimised the protocol for manufacturing the multi-test PoC diagnostic device and produced a prototype whose cassette can be manufactured using 3D printing.

Conclusion: Trials on HIV-preventive herbal nanomedicines have shown positive signs of being effective and, therefore, need further investigations. Innovative devices that can detect multiple infectious agents, including HIV, HCV and others, can make a difference in addressing the problem of infectious diseases in the African setting.

Comparative study of physicochemical properties of paracetamol injection and infusion marketed in Southeast Nigeria

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Introduction: Substandard medicines are widespread and represent a threat to health because they can lead to healthcare failures, such as antibiotic resistance and prolonged stay in hospital, as well as death. The estimated overall prevalence of poor-quality medicines was found to be 13.6 %. The average prevalence of substandard medicines was 19.1 % for anti-malaria and 12.4% for antibiotics. Because of this, physicians encounter problems with the selection of quality brands of drugs when prescribing.

Objective: To determine the quality of paracetamol injection and infusion brands marketed in Southeast Nigeria.

Method: Eight brands of paracetamol injections and four brands of infusion were analysed. Physicochemical properties were evaluated, including physical examination for the presence of foreign matter and pH determination. Each infusion pack was firmly squeezed to check for minor leakage. pH values for various injections and infusions were determined by using a calibrated pH meter. Drug content was assayed using the ultraviolet spectrophotometer method according to British Pharmacopoeia (BP) and the High-performance liquid chromatography technique. Ultraviolet spectrophotometer analysis was carried out by using 0.1N sodium hydroxide as the solvent. The absorbance was measured at a maximum wavelength of 257 nm. Drug content was confirmed using a high-performance liquid chromatography method. The column used was C18 dimension with a solvent mixture of methanol and water in the ratio of 1:3(v/v). The assay was done at a wavelength of 243 and at a flow rate of 1.5 ml/min. Qualitative determination of bacterial endotoxin test was also carried out

with gel clot technique by using Limulus amoebocyte lysate (LAL).

Results: A physical examination of all injection and infusion generics showed no presence of particles, and the results were colourless. All infusion paracetamols had no leakage. pH of all the brands ranged from pH 4.67 to 5.89. Five of the injection brands were outside official specifications, while two of the infusions failed tests. pH values of injection brands that failed the test were 4.83, 5.01, 4.62,5.13 and 4.85. Drug assay showed only three brands of paracetamol injection, and two of the infusions complied with the British pharmacopoeia standard of 90– 110% content. Drug content of Brand D – H of injection paracetamol, which failed the assay, were 89.2, 82.6, 85.0, 69.9 and 79.6%, respectively. Bacterial endotoxin results of all the injections and infusions comply with the standard specification since all the injections and infusions did not form gel clots as they contained less than 0.5 EU/ml release limit for paracetamol.

Conclusion: Based on these results, 37.5% of Paracetamol injections and 50% of infusions complied with quality specifications. The deviation from the range may depict poor production or deterioration from poor storage. Brands A, B and C of paracetamol injection and Brands I and J of paracetamol infusion can be used interchangeably. This study clearly demonstrated that there is still circulation of substandard paracetamol injection and infusion in Southeast Nigeria. This will pose a threat to the clinical outcome when used on patients, especially paediatrics with high fever, thereby creating undue anxiety in their parents.

Formulation and evaluation of effervescent metformin HCL tablets: A focus on enhanced dissolution and palatability

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Introduction: Oral medication is the most popular form of taking medicine. However, it has some disadvantages, like the risk of slow absorption, which can be overcome by administering the drug in liquid form, but many drugs are unstable in this form, which limits their use. The effervescent technique can be used as an alternative to developing a dosage form that accelerates drug disintegration and dissolution.

Objective: The main goal of this study is to develop an effervescent tablet to enhance patient compliance regarding the intake of Metformin HCl tablets (used to control high blood sugar in patients with type 2 diabetes). It was selected as a model drug because of the high drug content of 500 mg/dose, which may sometimes be difficult for patients to swallow (Approx. 422 million people worldwide have diabetes).

Method: Formulations will be prepared with a different molar ratio of Citric Acid, Anhydrous, & Sodium Bicarbonate as independent variables by using a 32 Factorial design. A systematic approach will be used to compress the tablet in controlled temperature and humidity and primarily packed in a closed container to preserve it from atmospheric conditions. Before compression, the effervescent granules will be evaluated for their flow properties, moisture content, and particle size distribution. Responses (dependent variable) will be evaluated by determining effervescence time and pH value along with other quality parameters like drug content and carbon dioxide (CO2) content.

Results: The best effervescent system will be selected based on appropriate pre- and post-compression parameters. Tablets will be kept at accelerated humidity and temperature for three months in normal packing and evaluated by testing their pharmaceutical quality attributes; results will be estimated at ANOVA $P < 0.01$. Different sweeteners, colours, and flavouring agents will be added to optimise the formulation and improve patient compliance. To improve the taste, the different combinations of flavour with FD&C colour and sucralose as a sweetening agent will be checked to get good acceptability.

Conclusion: The above-mentioned approach of developing effervescent formulation is supposed to be workable under room temperature & humidity and will play a vital role in the cost reduction of effervescent products.

Formulation of a self-emulsifying drug delivery system containing a fixed-dose rifampicin-isoniazid combination

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Objective: To formulate various topical self-emulsifying drug delivery systems (SEDDSs) comprising a fixed-dose combination (FDC) of rifampicin (highly lipophilic) and isoniazid (hydrophilic). This selected FDC is part of the first-line treatment of tuberculosis. The feasibility and appropriateness of each formulation to enhance this FDC dermal diffusion ability will be determined using a quality-by-design approach to determine whether improved cutaneous tuberculosis treatment is possible.

Method: Various formulations were prepared by combining selected natural oils (frankincense oil, lemon oil, olive oil, tea tree oil and rose blend fragrance), a surfactant (Tween 83®) and a co-surfactant (Span 60®). First, isothermal microcalorimetry was used to determine excipient compatibility, and then drug and FDC solubility in the different oils were established. Water titration experiments were subsequently conducted to ascertain the spontaneous self-emulsification ability of different FDC-excipient combinations. Pseudo-ternary phase diagrams were constructed to identify the self-emulsification region, and checkpoint formulations were selected after reviewing the formulation properties necessary for optimised topical drug delivery. SEDDSs that were considered stable after 24 h (no phase separation detected) were characterised in terms of (i) drug concentration, (ii) encapsulation efficiency, (iii) droplet size, (iv) size distribution, (v) zeta potential, (vi) self-emulsification ability, (vii) cloud point, (viii) thermodynamic stability, (ix) robustness to dilution, (x) viscosity, and (xi) pH. The SEDDS with the most acceptable characteristics were further exposed to membrane release and skin diffusion studies.

Results: Preformulation studies did not show interactions between the selected excipients. Following the characterisation experiments, SEDDSs showing the most acceptable properties for dermal drug delivery were identified for further assessment. Membrane release experiments indicated that both rifampicin and isoniazid could be effectively released from the selected SEDDSs. Additionally, promising results were obtained regarding in-vitro topical delivery of this FDC.

Conclusion: The use of natural oils in the formulation of SEDDSs containing a rifampicin-isoniazid FDC has the potential to improve skin penetration and enhance the dermal bioavailability of the said FDC following topical administration. Dermal formulations containing rifampicin and isoniazid will most probably decrease side effects and drug interactions typically experienced when used orally to treat cutaneous tuberculosis.

Bridging personal care and therapeutics: Development of shea nut cosmeceutical scrubs for enhanced dermatological health

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Introduction: The intersection of cosmetology and pharmaceutical science introduces innovative therapeutic skincare solutions called cosmeceuticals, which blend cosmetic and therapeutic benefits to address the growing demand for personal care products that are aesthetic with healing properties.

Objective: This study focused on determining the potential use of shea kernels as a source of bioactive ingredients in the formulation of mechanical scrubs and their effectiveness for dermatological use.

Method: Two types of scrubs were formulated — facial and body — utilising shea kernels as the active ingredient. Following the International Nomenclature of Cosmetic Ingredients (INCI) guidelines, formulations were developed to ensure therapeutic efficacy and safety as part of pre-formulation studies, and organoleptic and physicochemical tests were carried out. Multiple trial formulations were evaluated based on consistency, spreadability, and sensory attributes to select the best formulations for further evaluation.

Results: The selected formulations, characterised by their nutty odour, brown colour, and appropriate consistency, demonstrated significant potential in skin exfoliation without causing irritation. The body scrub exhibited good spreadability and a gritty texture suitable for exfoliating dead skin cells, while the facial scrub, which was designed for gentler application, was smoother with slight grittiness. Both formulations showed no foaming ability, indicating their focus on physical exfoliation and nourishment. Organoleptic and physicochemical evaluations affirmed their effectiveness in improving skin texture and radiance, underscoring the therapeutic potential of shea-based cosmeceuticals.

Conclusion: The development of shea kernel cosmeceutical scrubs demonstrates the convergence of cosmetic appeal and dermatological efficacy, offering a novel approach to dermatological health care. This study not only highlights the potential of natural ingredients in the formulation of therapeutic personal care products but also underscores the critical role of pharmacists in facilitating access to innovative skincare solutions. These findings suggest further exploration into cosmeceuticals as a sustainable and effective strategy for enhancing dermatological health and wellness.

Traditional medicines in South Africa: quality control lessons from the Pepper bark tree

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Introduction: South Africa has more than 23000 species of plants and is the most plant species-rich country on the African continent. Coupled with this, it has been estimated that approximately 70% of the population uses alternative or complementary medicines, sometimes alone or together with allopathic medicines. Historically, trees such as Warburgia species have played an important role in traditional medicines being used for their anti-infective and antimicrobial activity. The pepper bark tree (*Warburgia salutaris*) further cemented its place in South African history by being planted by the late former president Nelson Mandela because they were thought to provide "health-giving properties to the nation".

Objective: To determine the phytochemical variation using ultra-high-performance liquid chromatography coupled to mass spectroscopy (UHPLC-MS) and high-performance thin-layer chromatography (HPTLC) of *Warburgia salutaris* bark and leaf samples obtained from different geographical locations or provinces in South Africa, were harvested from the wild or cultivated populations, harvested during different seasons or were harvested at different ages.

Method: A total of 241 specimens of fresh leaf and bark material of W. *salutaris* from both wild-harvested and cultivated populations were collected from three provinces in South Africa, namely, Limpopo (wild specimens), Mpumalanga (wild specimens), and KwaZulu-Natal (cultivated specimens). The dried, powdered bark and leaves were prepared for UHPLC-MS according to standardised methods. In addition, the phytochemical fingerprints of the various samples using the same variables were determined by HPTLC according to standardised methods.

Results: The phytochemical fingerprints of the leaf and bark material revealed variation, while the bark also demonstrated variation between wild-harvested and cultivated specimens. The within-population variation of the wild-harvested bark of W. salutaris showed no clear variation, which was confirmed by the phytochemical fingerprints. Furthermore, phytochemical variation was observed between bark samples harvested in different seasons. Higher yields of various compounds were observed in bark compared to leaves across the seasons.

Conclusion: Analytical methods (UHPLC-MS) are useful in showing variation but the use of HPTLC offers a phytochemical fingerprint that can visually show both qualitative and quantitative differences. This method is also easier to use, fewer resources are needed, and highly skilled staff are not required to perform or interpret the results. Furthermore, the source of the material, geographical location, seasons, and different plant parts all played a role in phytochemical variation in W. *salutaris*. All these factors could affect the quality, safety and efficacy of natural medicines developed in the future. Compounds (besides polygodial) are responsible for bioactivity, and thus, the widespread use by traditional medicinal healers could be justified. These compounds should be further explored for both antimicrobial and anti-infective properties.

Formulation of metformin-gliclazide nano cocrystals for the management of type-2 diabetes mellitus

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Introduction: Pharmaceutical Nano cocrystals (NCC) are aimed at improving drug properties such as stability, mechanical properties, and bioavailability. The formulation of an NCC is an advanced strategy that uses top-down and bottom-up formulation techniques. They have the potential to enhance the physicochemical properties of the drugs. NCCs are nanometre-scale pharmaceutical cocrystals that exhibit properties that are superior to those of co-crystals and nanocrystals. NCC combination of nano sizing and co-crystallisation is utilised in their formation, further enhancing bioavailability, solubility, hygroscopicity, and dissolution kinetics. In this study, we report the results obtained from the formulation of metformin-gliclazide nano cocrystals by top-down and bottom-up methods.

Objective: The aim of the study is to synthesise a novel metformin-sulfonylurea NCC-loaded microneedle array for the management of T2DM.

Method: The metformin base was extracted from metformin HCL by reacting metformin HCL and sodium hydroxide. Metformin-gliclazide nano cocrystals were developed using a pseudo one solvent bottom-up method. Equimolar amounts of metformin were dissolved in deionised water, and gliclazide in acetone was injected rapidly into a precooled

polytube and sonicated at temperatures between 3-5°. The nano cocrystal suspension was first characterised using a zeta sizer. The particle size, polydispersity index and zeta potential were determined. The suspension was dried and subsequently characterised using powder X-ray diffraction, differential scanning calorimetry, scanning electron microscopy, and Fourier transform infrared spectroscopy. Surfactants that include tween 80, span 80, poloxamer 188, p407, pluronic 127 and TPGS were utilised as stabilisers for the formulation.

Results: The results indicated the presence of a possibility of a nano-cocrystal with metformin- gliclazide. The metformin-gliclazide nano-co-crystal analysis with the XRD exhibited the disappearance of characteristic peaks of gliclazide and metformin and the appearance of novel characteristic peaks. The FTIR spectrum indicated bond shifts in -OH groups and -NH groups, indicating the probability of hydrogen bond formation and enhancement of the conjugative effect. The DSC data reflected changes in melting point onset, enthalpy energies and the existence of single melting points.

Conclusion: The screening results of the study showed that gliclazide exhibited a nano cocrystal profile that could potentially be utilised in drug-drug pharmaceutical nano cocrystal combinations.

A novel 3D printed multi-component scaffold for targeted bone tuberculosis therapy

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Introduction: Bone tuberculosis (TB) is a common form of extrapulmonary TB and accounts for 1 to 3% of all TB cases. Effective management relies on a combination of chemotherapy and prompt detection. However, the regimen of anti-TB medications frequently yields suboptimal outcomes attributable to inadequate adherence and the emergence of drug resistance. Additionally, bacterial proliferation in bones leads to structural damage necessitating surgical intervention, resulting in bone loss and defects. Addressing these challenges necessitates innovative therapeutic strategies. Leveraging 3D-printing technology opens avenues for tailored scaffold design in biomedical engineering. Parameters such as mechanical strength, porosity, and biodegradability are crucial for scaffold success in bone TB therapy. While individual biomaterials have limitations, the multi-component approach offers distinct advantages over single-material scaffolds. The implementation of this pioneering approach holds transformative potential in bone TB treatment, promising improved patient outcomes, reduced surgical interventions, and enhanced quality of life.

Objective: The research explored the design, fabrication, and evaluation of the multi-component scaffold, focusing on its mechanical strength, porosity, and biodegradability.

Method: The 4th generation 3D BioplotterTM (EnvisionTEC, Germany) was used to fabricate multi-component scaffolds. The scaffold was developed using four solutions containing polycaprolactone, sodium alginate, polyvinyl alcohol, and varying concentrations of bioactive glass titanium. The solutions were mixed and homogenised to form a bio-ink suitable for 3D printing. The parameters for 3D printing were determined using a computer-aided design (CAD) and involved nozzle size, printing speed, temperature, waiting period, and printing pressure. The scaffolds were printed into a solidifying solution of propanol. The multi-component scaffolds were characterised using a Scanning Electron Microscope (SEM), Fourier Transform Infrared Spectroscopy (FTIR), X-ray Diffraction (XRD), Energy-Dispersive X-ray Spectroscopy (EDX), as well as degradation.

Results: The microstructural analysis and BET surface area measurements of the composite revealed that the predominant pore size fell within the micro-size range, spanning from 434 ± 4.58µm to 562 ± 10.87µm. Notably, pores larger than 50 µm are conducive to cell infiltration and bone mineralisation, indicating suitability for tissue regeneration. In the initial 7-day period, the scaffold exhibited a notable 55% mass reduction attributed to the presence of bioactive glass-titanium. Subsequently, from day 8 to day 28, the scaffold's mass remained stable, indicating a cessation or deceleration of the degradation process. Incorporating bioactive glass-titanium into the PCL-PVA-Sodium Alginate scaffold enhanced compressive strength through robust bonding with the polymer matrix. FTIR and XRD data suggested an interaction between the scaffold and simulated body fluid. EDX analysis revealed the scaffold's elemental composition, including Cl, Ca, Na, Si, and P peaks, which are essential for bone healing and regeneration.

Conclusion: This study utilised 3D printing to develop a multi-component biocomposite scaffold with interconnected pores, improving mechanical strength and biodegradation. Adjusting the bioactive glass-titanium content allowed for controlled scaffold biodegradation and mechanical properties.