

The Latest Development in Liposomal Formulations for the Detection, Prevention, and Treatment of Coronavirus Disease (COVID-19)

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Abstract

The unprecedented outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) worldwide has rendered it one of the most notorious pandemics ever documented in human history. As of November 2022, nearly 626 million cases of infection and over 6.6 million deaths have been reported globally. The scientific community has made significant progress in therapeutics and prevention for the management of coronavirus disease 2019 (COVID-19), including the development of vaccines and antiviral agents such as monoclonal antibodies and antiviral drugs. Although many advancements and a plethora of positive results have been obtained and global restrictions are being uplifted, obstacles in efficiently delivering these therapies, such as their rapid clearance, suboptimal biodistribution, and toxicity to organs, have yet to be addressed. To address these drawbacks, researchers have attempted to apply nanotechnology-based formulations. Here, we summarize the recent data about COVID-19, its emergence, pathophysiology and life cycle, diagnosis, and currently available medications. Subsequently, we will discuss the progress in lipid nanocarriers, such as liposomes in infection detection and control. This presentation provides critical insights into the design of the latest liposomal-based formulations for tackling the barriers to detecting, preventing, and treating SARS-CoV-2.

Keywords: Liposomes; COVID-19; Nanocarriers

Functional Foods from Tropical Seaweeds: A Blue Economy Opportunity

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Abstract

Seaweeds or marine macroalgae, are used by coastal and island communities, as source of food, feed, medicine, food additives, fertiliser and industrial materials. In recent years, algal resources including seaweeds have shown potential for the sustainable production of biofuel. The use of seaweeds for its medicinal value has been documented in various medical treatises; eg. The Pen Ts'ao by Emperor Shen Nung circa 2800 BC which lists 366 herbs and 1000 herbal formulations. Porphyra or nori has been used by the Japanese for more than 1500 years. In China, in the year 600 AD, Sze Teu wrote "algae are a delicious delicacy for the most representative guests, even for the king himself". The "Economic Products of the Malay Peninsula" was first published by I H Burkill in 1935, and reprinted in 1966. Several species of seaweeds and their uses are included in this invaluable document of Malaya's indigenous natural resources. The global seaweed market reached a value of US\$ 6.73 Billion in 2021, and is expected to reach US\$ 12.85 Billion by 2027. Biomass produced from aquaculture has overtaken that from wild harvest. Seaweeds produce phycocolloids, namely agar, carrageenan and alginate, and together with high contents of minerals and bioactive compounds, find diversified applications in the food, feed, industrial materials, nutraceutical, cosmeceutical and agroindustries. Studies show that seaweeds possess functional and health benefits, which can lead to development of new functional foods, including providing a nutritious diet to vegans and vegetarians. Seaweed colloids can also be used to produce edible films for food packaging, as well as biodegradable plastic. Technologies for seaweed cultivation are well established, as are technologies for extraction of the colloids. The development of a Blue Economy industry based on functional foods from seaweeds, has potential for maritime nations, especially those within the Coral Triangle and the Asia-Pacific region. Malaysia has implemented the 10-10 Malaysian Science, Technology, Innovation and Economy (MySTIE) Framework that serves as an integrative tool for government, researchers, innovators, industries and communities to work together to transform Malaysia into a harmonious, progressive, prosperous and sustainable nation. This can provide a framework for development of this Blue Economy industry.

Keywords: Seaweeds, Functional food, Nutraceuticals, Blue Economy

Connecting Precision Medicine with Nano-Theranostics: A New Avenue of Research in Pharmacy and Medicine

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Abstract

Identification of biologically active small molecules for further optimization into candidate drugs has been challenging because of ethnic variations and hence could not capture full diversity of regulation seen in native cells. Biomarkers commonly utilized earlier in drug development and drug discovery included biochemical surrogate markers, enzymes, receptors and genes. Of late, application of stem cell research, novel biomarkers like microRNAs, extracellularRNAs, circulating tumour cells have emerged for non-invasive diagnostics as well as target identification in drug discovery. Translational research using precision medicine is one of the main strategies being evolved recently worldwide by the industry in the drug discovery. Precision medicine aims to integrate both clinical and molecular information and provides biomarkers to better understand the biological basis of disease and therefore select them as better disease targets. The 21st century will be remembered for coronavirus disease 2019 (COVID-19) pandemic although over 80 years are yet to come. Just two years of the COVID-19 have brought a number of transitions. For pharmaceutical companies there are number of opportunities emerging. There is now a wave of innovation and launching of generation of entrepreneurs. The 'Biopharma Revolution' is one of the major transformation that is in the forefront for the medical and pharmaceutical world in the form of Biomolecules, Biosystems, Biomachines, and Biocomputing. Coupled with these, many new strategies have evolved in the drug discovery and Diagnostics like Gene Therapy; Precision Medicine based on biomarkers; Stem cell Therapy, Crisper Technology, and Molecular Diagnostics. Currently in the Pharmaceutical sciences especially Pharmaceutics most common area of research is the nanotechnology, Fourth Industrial Revolution is combination of first three industrial revolutions in the world that has given robotics or automation. Theranostics is one such revolution that integrates therapywith diagnosis in one systemto achieve accurate treatment of disease like cancer.It has attracted tremendous interest, and has been recognized as a potential breakthrough in overcoming the challenges of conventional oncotherapy. Nanotheranostics is yet anothersort of novel and revolutionary strategies that has emergedfor accurate diagnosis of the site of cancer and the treatment to the right and accurate site in the body. It started with the biomarker based drug precision medicine but the same principles are utilized Nanopharmaceutical Scientists could realize that Nanoparticles are ideal candidates as carriers for theranostic agents,which is attributed to their extraordinary physicochemical properties, including nanoscale sizes, functional properties, prolonged blood circulation, active or passivetumor targeting, specific cellular uptake, and in some cases,excellent optical properties that ideally meet the needs of phototherapy and imaging at the same time. The development of nanotechnology based diagnostics and therapeutics, now known as Nanotheranostics has become a reality, and is now in the transition stage of "bench to bedside." Significant progress has been made in this nanotheranostics and has greatly assisted traditional therapies to provide therapeutic optionsas like "cocktail" mixingvarious nanotechnology, diagnostics and treatment modalities openingan exciting field of research in pharmaceutical sciences.

Keywords: Precision Medicine; Theranostics; Nanotechnology; Biomarkers; Covid-19

Immune Responses Induced During Dengue Virus Infection of Microvascular Endothelial Cells

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Abstract

The Malaysia Ministry of Health has reported that the number of dengue fever cases in 2022 has doubled as compared to the same period in 2021. Dengue is a very rapidly growing public health problem faced by 40% of the global population. It is a viral disease, caused by four types of dengue viruses, transmitted by mosquitoes. Vector control has not been successful and current diagnostic tests are far from optimal and there is no drug or vaccine to combat this disease. But the heightened awareness of its magnitude and its potential to spread beyond the tropical world, has put dengue on the list of neglected diseases. In recent years, new interest in this disease has drawn scientists from multiple disciplines into the dengue arena. This has resulted in novel insights into several aspects of dengue virus and its effect on the vascular endothelium. Research in dengue is at a critical juncture and it is hoped that existing knowledge and advanced technology supplemented by a better understanding of pathogenesis will make a tangible impact in the combat against dengue in the coming years. This study shows that high dengue virus (DENV) load differentially modulates human microvascular endothelial barrier function with organ-specific cytokine production and were activated differentially as soon as the virus was introduced exhibiting enhanced permeability. The activated cells produced inflammatory cytokines, chemokines and adhesion molecules that further disrupted the endothelial barrier. Inter-endothelial junctional proteins were differentially expressed as a response to DENV infection leading to vascular leakage. Study also revealed that dengue non-structural protein 1 (NS1) protein was able to induce the loss of barrier function in a dose dependent manner but levels of NS1 did not correlate with the extent of vascular leakage. This finding suggested the presence of other host factors that might overshadow the direct effect of NS1 in inducing vascular leakage during dengue virus infection. Study further showed that increased cytokine production deregulated the expression of junctional proteins with loss of barrier function. Gene expression and metabolomics indicated altered lipid metabolism in dengue patients, where severe manifestations were observed in patients with severe dengue and this might be associated with phospholipid metabolism that affect the membrane permeability of cells of endothelial cells. Insulin pathway and cytoskeleton pathway involving the expression of Tropomyosin 1 (TPM-1) protein were also identified to potentially play an important role in the pathogenesis of severe dengue.

Keywords: Dengue; Microvascular endothelial barrier; Junctional proteins; phospholipid metabolism, Cytoskeleton

Challenges and Encouragement Encountered on Starting a Bachelor of Pharmacy Programme in 1995 in Universiti Malaya from My Lab Office

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Abstract

In 1993-1994, as the Head of the Department Of Pharmacology, Faculty of Medicine, University of Malaya, I was invited by the Faculty Dean to start the Bachelor of Pharmacy (Honours) course under a new Department of Pharmacy within the Faculty of Medicine, as the Head. The first batch of 40 students were to enroll in June 1995. The new Department of Pharmacy operated from my research laboratory which doubled as my office. My research laboratory technologist joined me as a staff in the new Department. Within the 1 year we had the Board of Studies Meeting, to consider the curriculum, created, based on studying the strengths and weaknesses of the Pharmacy curriculum of Universiti Sains Malaysia (USM) and that of University of Singapore. The Director of Pharmaceutical Services Division has advised that we should ensure that the students develop good command in English to facilitate their access to new knowledge on medicines. For many months, we borrowed stationery, equipment and space from my previous Department, whose new Head was very supportive. In 1995 we welcomed the first batch of students with 4 lecturers and 1 laboratory technologist; their job establishment were all borrowed from vacancies in the Faculty of Medicine. We used lecture rooms and laboratories in the Faculty where time-tabling of teaching and laboratory sessions were a great challenge. For certain laboratory sessions, students needed to help find their own chairs. However, I was encouraged by the supportive response from the Director Of Pharmaceutical Services who offered pharmaceutical technology equipment from one of Ministry of Health's hospital pharmacies in Sabah. We borrowed pestle and mortar from Northern Consortium (Universiti Teknologi MRA through Dr Chua SS) and the Universiti Hospital Pharmacy to conduct the first laboratory session on making calamine lotion by the students. There was an offer of manufacturing equipment from Glaxo Smith Kline which was moving manufacturing activities from Petaling Jaya to Singapore. There were visits from foreign pharmacy academics to explore joint partnership programs. Although very encouraging, we could not accept as the program was just starting and we did not have space. Much later 2 storeys of a 4 storey building was approved for the Department of Pharmacy. Planning for the staff offices, laboratories took a lot of time.

Keywords: Pharmacy, Medicines, Pharmaceutical Services

Pharmacists' Role in Promoting Halal Lifestyle Principles in Daily Activities in Halal Cosmetics and Pharmaceuticals

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Abstract

Living in the new millennium forces people to engage in a variety of daily activities that emphasise technology, health and beauty. The majority of the society will consume and utilise cosmetic and pharmaceutical items on a daily basis for various purposes. Consumers in the majority of Muslim nations assume that all goods are produced using halal ingredients, so there aren't many concerns about whether or not any cosmetics or pharmaceuticals are halal. According to reports and observations, many of these items, even those produced in other countries, are discovered to include significant amounts of non-halal ingredients or even only traces of such substances. This implies that everything a person uses should be acceptable in accordance with Islamic beliefs. Halal lifestyle will therefore cover a variety of areas, including, but not limited to, banking and finance, tourism, communication and marketing, employment, cosmetics, technology and travel. Sometimes, what you think is acceptable in your country might not be in another. When discussing various halal lifestyle elements, most individuals prefer to use the phrase "halal friendly". It is true that when the halal lifestyle issue first gained attention, only Muslims were the main focus. Nevertheless, this has changed with time and nowadays, everyone is aware of what a halal lifestyle entails. Halal living attempts to encourage moral cohabitation and combat societal moral decline. A halal lifestyle offers a solution to the majority of injustices now roiling society. There are no uniform rules for living a halal lifestyle in some areas, so just find what works for you. Ingredients used in halal pharmaceuticals and cosmetics are manufactured in these products. Halal can also establish itself as a standard of acceptable quality and compliance in business transactions with Muslims for non-Muslims. Based on such significant difficulties, pharmacists should concentrate and come up with innovative approaches to make halal pharmaceuticals and cosmetics for everyday use and to educate consumers about them.

Keywords: Halal pharmaceutical, Halal cosmetics, Halalan toyyiban, Built in Halal

Unani Medicine - Status and Perspectives

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Abstract

Today the world is witnessing a rise in incidence of diseases and the demand for affordable health care has increased manifold. An effective and robust public health system is the need of the hour to improve the health and wellbeing of people across the globe. Unani Medicine is a holistic system of medicine, which offers indigenous and effective therapies, which are already helping millions of people across the globe in living a healthy life. Unani medicine gained momentum as an effective alternative to conventional medicine due to its systematic approach towards diagnosis and treatment of diseases, effective management of lifestyle disorders and primary focus on prevention of ailments. This system of medicine, which has its origin from Greece, today has a presence in many parts of the globe. Besides India, it is practiced in several countries like Bangladesh, South Africa, Pakistan, Iran, United Arab Emirates and Sri Lanka etc. The Government of India facilitated the growth and development of Unani medicine by recognizing its utility and scope and integrated it into healthcare delivery system. With its wide network of quality educational institutions, comprehensive healthcare facilities, state of the art research institutions and quality drug manufacturing industries and on account of its utilization by a large number of people for their healthcare needs, India has emerged as the global leader in Unani medicine. Concerted efforts are being made to carry out high quality, evidence based research and to make the system more accessible and affordable. Unani medicine can contribute a wealth of knowledge and experience for the benefit of human kind and has the potential to be one of the major contributors in health care delivery in other parts of the globe.

Keywords: Unani medicine, Healthcare, Drug

Benefits of Medicinal Plants Toward Sustainable One-Health Research

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Abstract

One-health is an integrated approach to balance and optimize the health of people, animals, plants and their shared environment. In this regard, plants with medicinal properties have been used in healthcare for thousands of years and documented in the history of mankind. Globally, there are numerous studies investigated to verify the efficacy and some of these findings have eventually led to plant-based medicines. The benefits of these medicinal plants have been reported in disease prevention of both humans and animals. *Acanthamoeba* spp., waterborne protozoan parasites, are ubiquitous free-living amoebae found in nature such as water and soil. This organism has two main forms: the trophozoite, an invasive stage; and cyst, a highly resistant stage in very harsh conditions. The protozoa are causative agents of amebic keratitis (AK) and granulomatous amebic encephalitis (GAE). Till date, selected Asian medicinal plants (e.g., *Curcuma longa*, *Garcinia mangostana*, *Annona muricata*, *Combretum trifoliatum*, *Knema retusa*, and Propolis) have been focused to treat *Acanthamoeba* infections in our studies. These Asian medicinal plant extracts have shown its synergistic efficacy/interaction against *Acanthamoeba triangularis* (WU19001-T4) using combination assay with chlorhexidine as the standard drug used for the current treatment. Of this, scanning electron microscope (SEM) has been performed to determine its morphological appearance before and after treatment. Moreover, molecular docking and dynamic simulation as well as advanced nanotechnology (e.g., GME-loaded niosomes) have also been performed. Our studies revealed the potentials of these selected medicinal plants which have played a vital role with growing interest and future promising anti-*Acanthamoeba* activity that can be used as alternative therapies and therapeutic uses of plants against *Acanthamoeba* infections in sustainable one-health management.

Keywords: Medicinal Plants, Benefits, *Acanthamoeba* sp., Sustainable, One-health, Research

Exploring Medicinal Benefits of *Acanthus ilicifolius*: The Coast and Health Guardian?

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Abstract

Acanthus ilicifolius, known internationally as Holly Mangrove/Spiny Mangrove and locally described as *Jeruju* or *Daruju* or *Jeruju Putih* (Indonesia/Malaysia), and *Sahachara* (India). *Acanthus ilicifolius* habitat is in the mangrove forest, so it contributes to protect the coastline erosion from storm surges, currents, waves and tides. Interestingly, this true mangrove plant species is more widely grown in the area of destructed mangrove forest. They can be found also in pure freshwater or waterlogged areas, and on dry land. Thus, exploration for its medicinal use become promising and having no harm on its environmental benefits. The traditional medicinal use of *Acanthus ilifolius* are found to be very diverse from preventing snake bites to prevent alopecia. Pharmacological activities of *Acanthus ilicifolius* are reported for its anti-inflammatory, anti-leishmanial, anti-osteoporotic, hepatoprotective, anti-ulcer, anti-microbial, and anti-cancer activity. Here, we also discuss the potential medicinal use of *Acanthus ilicifolius* based on our pharmacological activities investigation result i.e., estrogenic activity. Different fractions of *Acanthus ilicifolius* leaves showed estrogenic activity with IC₅₀ ~ 500 ppm. Though it is low, its estrogenic activity might relate to the ability of the compounds contained in *Acanthus ilicifolius* to establish interaction with estrogen receptors alfa and beta based on *in silico* analysis.

Keywords: *Acanthus ilicifolius*, Medicinal plant, Estrogenic activity

Critical Clinical Gaps in Cancer Precision Nanomedicine Development

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Abstract

The personalised perspective of precision medicine involves patient's health/omics analysis and customization of therapy in accordance with the individual health requirements which could encompass more than one drug to be delivered in variable doses of specific delivery kinetics to different intended target sites of action. On this note, an ideal dosage form is preferably can be dispensed flexibly with the required drug dose. It is able to carry two or more drugs in a single dosage form, deliver the drugs with the desired kinetics, can possess same or different drug release kinetics, and may engage different drug-specific delivery strategies. The dosage form should ideally be characterized by 100 % drug bioavailability. This presentation highlights the recent drug delivery innovations from nano-to-macroscales for skin, lung and oral applications from the perspectives of material design, dosage form development, and technology device application to realize the true meaning of personalized therapy. Specifically, critical clinical gaps in cancer omics analysis for precision medicine development will be highlighted with reference to nanomedicine design against the profiles of cancer cell target and metabolizing enzyme.

Keywords: Precision medicine, Nanomedicine, Cancer

Novel Approaches - Therapeutic Options for Treating Human Immunodeficiency Virus and Acquired Immune Deficiency Syndrome

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Abstract

As per the Joint United Nations Programme on Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (UNAIDS) 2021 global report, an estimate of 37.6 million people is living with Human Immunodeficiency Virus (PLHIV). In contrast to the earlier reports that the epidemic was most prevalent in female sex workers (FSWs) and truck drivers, currently the higher prevalence of Human Immunodeficiency Virus (HIV) infection has been reported among Men Sex with Men (MSM) and Injection Drug Users (IDUs) across the globe. The development of effective antiretroviral therapy (ART) in response to HIV is considered as one of the most remarkable achievements of modern medicine. Current antiviral drugs provide sustained virologic suppression, restore the immune system and still have side effects though limited. However, they do not eradicate the virus from the infected individuals and further they are burdened by taking drugs life-long. Early generation of antiretroviral agents have provided substantial evidence that viral suppression and immune restoration can be achieved. However, those earlier and recent antiviral agents have disadvantages of being a large pill burden, daily dosing, as well as intolerable side effects. Dramatic decline in morbidity and mortality due to HIV disease has been observed with the currently available or recommended antiretroviral drugs even in resource-limited settings like India as newer combination drug regimens have ever-increasing efficacy and decreasing toxicity, most importantly affordable. As a result, life expectancy and quality of life are close to normal for PLHIV with access to these medications. Moreover, patients with continuously undetectable viral load on ART pose virtually no risk of transmitting infection through sexual contact; thereby the HIV treatment has become a prevention tool also. Moreover, early treatment of HIV infected individuals also has potential public health implications. The question of when to initiate antiretroviral therapy has been a difficult one, but the recent studies have well documented that very strong supportive evidence suggesting a benefit for early therapy and limiting reservoir size; people living with HIV who initiate ART in primary infection maintain smaller reservoirs on suppressive ART than those who initiate treatment during chronic phase of the infection. Currently the focus and interest are using long-acting formulations of antiretroviral drugs as it has the potential to reshape the treatment paradigm for HIV infection. However, potential secondary drug resistance threats are always associated with the ART and some of our earlier studies documented it in India also. In recent years newer approaches have been recognized as an alternative treatment modality that include anti-HIV-1 microRNA (miRNA) and use of broadly neutralizing antibody (NAb). HIV patients with varied disease progression rates, with and without ART provide a powerful alternative wherein the levels of several anti-HIV-1 miRNAs and also broadly NAb has been shown to be protective against HIV-1 infection.

Keywords: HIV/AIDS, Cure, Novel therapeutic approach, miRNA

Development of SARS-CoV-2 Therapeutics

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Abstract

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, has been an infection with heterogenous clinical outcomes involving multiple disease stages and long-COVID symptoms. Patients admitted to the hospital with COVID-19 had significantly higher rates of death, cardiovascular disease, neurological and mental health disorders, fatigue, and coagulation disorders than those admitted with other respiratory infections. Evidence also suggests that long-COVID is more severe than other post-viral syndromes. Early treatment of COVID-19 before hospitalization substantially reduces the severity of the disease, long-term morbidity, and mortality. One challenge with drug development for COVID-19 has been tailoring therapies to different disease stages and treating long-COVID. A major challenge has been the emergence of SARS-CoV-2 variants, leading to heterogenous drug efficacy and clinical outcomes. With a good safety profile, the ideal antiviral agent would be efficacious against current and future variants. Ongoing drug development efforts focus on developing direct-acting antivirals that target viral proteins and host-targeting agents that affect the human host cells. Drugs targeting the human angiotensin-converting enzyme 2 (ACE2)-viral Spike protein interface reduce viral load and severity of the disease by lowering viral entry into host cells. Other viral targets include the main protease 3-chymotrypsin like protease (3CLpro), RNA-dependent RNA polymerase (RdRp), papain-like protease, helicase, and viral replication transcription complexes (RTC) responsible for viral RNA synthesis, proofreading, and 5'-capping. Although pathogenic mechanisms underlying long-COVID are not well understood, potential therapeutic strategies include antifibrotics, anticoagulants, statins, and anti-inflammatory agents. We will discuss our efforts in developing drugs that target the ACE2-Spike protein interface and RdRp as antivirals and long-COVID therapeutics.

Keywords: ACE2, RdRp, and Spike Protein

Computer Aided Drug Design in Drug Discovery and Drug Delivery. Application in Anti-infective Discovery and Anti-Cancer Drug Delivery

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Abstract

The utilisation of computer aided drug design in studying drug-target interaction have made significant contributions in improving our understanding of the drug action's mechanism at the atomic level. This approach has been widely used to study the dynamics behavior of targeted protein or drug receptor which was then further incorporated in our drug discovery and drug delivery research. Using molecular dynamics (MD) simulation, mutational effects on oseltamivir resistance in neuraminidase of Influenza virus was studied from a total of 140 nanosecond simulation time. The analysis reflected that the mutation was capable in altering the binding pathway of oseltamivir. In collaboration with Chulalongkorn University, we performed MD simulations of NS2B/NS3 protease complexes with six substrates of dengue virus type 2 with the aim to compare the specificity of protein-substrate binding recognition. Interestingly, we noted that although all substrates were in the active conformation for cleavage reaction by NS2B/NS3 protease, their binding strength was somewhat different and the arginine residues at the two subsites were found to be specific for preferential binding at the active site. Using the information on the mechanistic of drug interaction obtained from these simulations, we designed and synthesized new molecules which potentially inhibit the enzymes implicated in the replication of influenza and dengue. In anti-cancer drug delivery, the binding affinity of folic acid (FA) to the folate receptor-alpha (FR α) active site has been studied using MD simulation to understand the basis for recognition of FR α . Root mean square deviation (RMSD), root mean square fluctuation (RMSF), and radius gyration (Rg) demonstrated that FA and FA- β CD created more dynamically stable systems with FR α than apo-FR α system. The conjugation with β CD improved the stability and decreased the mobility for all the residues (except the residues 149-151) compared to FA-FR α and apo-FR α systems indicating that these residues might have a direct role in increasing the stability of holo systems.

Keywords: Computer aided drug design, Molecular dynamics, Anti-cancer drug delivery

An Amalgamation of Chemistry, Biology and Computation to Understand Drug-Protein Interaction

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Abstract

Studies on drug-protein interaction are essential in determining the drug's absorption, distribution, metabolism, excretion, and toxicity. This interaction is critical in the bloodstream in ascertaining the fate of a drug upon entry into circulation. Serum albumin is the leading drug carrier in blood circulation, with three well-defined ligand binding sites, namely Site I, Site II and Site III, confined in subdomains IIA, IIIA and IB, respectively. The drug binding to protein can be envisaged as beneficial to solubilize the hydrophobic drugs. On the other hand, competitive and allosteric binding of two drugs or a drug and an endogenous ligand for the same protein may lead to drug displacement and drug-drug interaction. These attributes must be known to pharmaceutical and clinical chemists to gain knowledge about the binding and modulation of a pharmaceutical agent to a protein in circulation. Here we summarize how various spectroscopic techniques, such as ultraviolet absorption, fluorescence and circular dichroism, atomic force microscopy and molecular docking, have helped study drug-protein and drug-drug interactions and how such binding affects protein conformation. Examples of drugs have been selected from natural sources (phytochemicals) and synthetic molecules.

Keywords: Human serum albumin; Drug-protein interaction, Drug displacement

Acute Pharyngitis and Private Primary Care: The Rise of Antibiotic Resistance in the Community

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Abstract

Acute pharyngitis (AP) is a common reason for private primary care consultations, thus providing an avenue for widespread antibiotic intake among the community. However, although there is systematic reporting of antibiotic resistance in the clinical setting, there is limited data from the Malaysian private primary care setting, especially in the investigation of the prevalence of isolated viruses and bacteria, antibiotic resistance patterns, antibiotic prescription patterns and appropriateness by general practitioners (GPs) and factors affecting antibiotic resistance and antibiotic prescription patterns. Antibiotic resistance is more prevalent than previously thought in Malaysia, with even pathogens of concern with multidrug resistance being carried by patients visiting private primary care. A multitude of factors contribute to this phenomenon, where prescription of antibiotics for common afflictions such as AP of viral origin is common and widespread among private primary care practitioners. What are these factors and how might this phenomenon be curbed?

Keywords: Acute pharyngitis, Antibiotic resistance, Private primary care, Community

Multicellular Three-dimensional Tumor Spheroid as Potential *in vitro* Model for Nasopharyngeal Carcinoma Research and Its Application

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Abstract

Nasopharyngeal carcinoma (NPC) is one of the major public health problems in its endemic countries. Metastasis and treatment resistance are the major causes of mortality in NPC. There is urgent need to develop effective therapeutic agents and biomarkers for early diagnosis through thorough understanding of the underlying pathogenesis in NPC. Although most of the NPC studies were relayed on two-dimensional model, but the tumor microenvironment involving cancer progression and metastasis are not recapitulated, hence the emergence of a more realistic three-dimensional (3D) cell culture model, that allows mimicry of physiological and pharmacological properties of *in vivo* human solid tumor. In present study, we focus on how 3D model recapitulating *in vivo* tumor microenvironment (TME) including heterotypic cell-cell and extracellular matrix cross-talk and also provided comprehensive overview of its advantages, opportunities and applications in metastasis study, as well as its challenges in NPC cancer research. The potential of patient-derived 3D spheroid culture in heterogeneity studies and personalized medicine development were also discussed here. 3D co-culture spheroid is holding a great promise as next generation standard of *in vitro* pre-clinical model for biomarkers discovery, accelerating drug screening process, and achieving a more precise personalized treatment for cancer patients.

Keywords: Nasopharyngeal carcinoma, Multicellular Tumor Spheroid, Tumor microenvironment

Strategy for Marker-Based Bioactivity Guided Fractionation of Botanical Extracts for the Targeted Receptors

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Abstract

In the development of new medications herbal remedies are frequently used as lead chemicals or candidate drugs. The pharmaceutical industry has primarily employed libraries of synthetic chemicals as a source for medication development throughout the past few decades. They have strong interoperability with conventional high throughput screening (HTS) technologies and are comparatively simple to create and restock. The amount of new pharmaceuticals entering the market, however, has declined recently, which has rekindled scientific interest in the development of drugs from natural sources despite the challenges involved. Medicinal plants with a long history of ethanopharmacological use have been a valuable source of effective phytochemicals that provide beneficial effects against numerous diseases. Medicinal plants are often utilized in the form of concoctions or concentrated extracts. Modern medicine however requires the separation and purification of one or two active compounds that elicit the activity. The bioactivity fractionation method is considered the most effective strategy for screening metabolites, particularly when the active compound is unknown. Typically, extracts with potential bioactivity are subjected to bioassay-guided isolation, which entails: 1) Extracting metabolites using the proper solvents, 2) Fractionating the resulting extract using chromatography, 3) Screening each fraction with a bioassay, 4) Isolating the molecule(s) from the bioactive fractions, and 5) Identifying the isolated molecules and assessing their bioactivity. Each fractionation step is guided by a bioassay result systematically, reducing the entire processing time and cost of drug discovery.

Keywords: Botanical extracts, Bioactive fractions, Bioassays

Evaluation of Antioxidant and Antimicrobial Activities of *Cassia alata* Leaf Extract in the Management of Skin Disorders

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Abstract

Cassia alata is traditionally used for managing certain skin disorders. *C. alata* leaves are rich in phytochemicals that confer antioxidant and antimicrobial properties. The aim of this study is to evaluate the antioxidant and antimicrobial properties of *C. alata* leaf extract. *C. alata* leaves were extracted with methanol. The antioxidant activity was assessed using: Folin-Ciocalteu assay (to quantify the total phenolic content), aluminium chloride colorimetric method (to quantify the total flavonoid content), ferric reducing power assay (to determine the ability to reduce ferric (III) iron to ferrous (II) iron) and 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay (to determine free radical quenching capacity). The antimicrobial activity was assessed using the agar well diffusion method and microbroth dilution method. The extraction yield obtained was 38.52%. *C. alata* leaves contained high total phenolic content (TPC) and lower total flavonoid content (TFC) of 7130 ± 0.0171 mg GAE/100g of extract and 190 ± 0.00660 mg RE/100g of extract, respectively. The DPPH radical scavenging ability determined was IC₅₀ of 0.651 ± 0.0308 mg/mL and AEAC of 627 ± 0.0308 mg AA/100g extract. The ferric reducing power determined was 0.145 ± 0.0243 mg GAE/g of extract. Among the bacterial and fungal strains, the extract showed antimicrobial activity against *Staphylococcus aureus* at MIC of 1.25 mg/mL and MBC of 5 mg/mL, as well as against *Malassezia furfur* at MIC of 60 mg/mL and MFC of > 60 mg/mL. *C. alata* leaf extract has prominent antioxidant activities and reasonable antimicrobial activity against *S. aureus* and *M. furfur*. These preliminary results showed that it could be used as a complementary and alternative therapy in the management of skin disorders.

Keywords: *Cassia alata*, Leaf Extract, Antioxidant Activity, Antimicrobial Activity, Skin Disorders

Antihyperglycemic Activity of *Drymaria cordata* Methanolic Extract in High Fat Diet and Streptozotocin Induced Diabetic Rats

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Abstract

Diabetes mellitus (DM) is a metabolic disorder characterized by the hyperglycaemia and glucose intolerance due to abnormal insulin secretion. Type 1 diabetes usually has an auto-immunological background with 10% cases while type 2 diabetes accounts for 90% of all cases and characterized by defective insulin secretion and resistance. *Drymaria cordata* (L.) Wild. (Caryophyllaceae) is a creeper plant, widely distributed in the Indian Himalayan region and has valuable uses as a folklore medicine against diabetes. The present study was designed to investigate the antihyperglycemic effects of the methanol extract of *D. cordata* leaves (DCME) and its ethyl acetate fraction (EAF) in high fat diet and streptozotocin induced diabetic rat model. Gas chromatography-mass spectrometry (GC-MS) profiling was performed to identify the compounds present in EAF. After that the DCME and EAF was subjected to *in-vitro* determination of α -amylase and α -glucosidase inhibitory potential. Male Wistar rats of 160-180g body weight (b.w.) were fed with high fat diet for 8 weeks to induce obesity and after that streptozotocin (30 mg/kg, b.w.; i.p.) were administered to evaluate the antihyperglycemic and antioxidative stress potentials. GC-MS analysis revealed the abundant presence of fatty acid compounds eg. (Z)9-Pentadecadien-1-ol, 7-Tetradecanal, n-hexadecanoic, pentadecanoic and tridecanoic acid. The *in-vitro* antihyperglycemic activity showed that EAF at 104 and 110 μ g/ml exerted highest inhibitions against both the enzyme, respectively than DCME. Administration of DCME at 200 mg/kg and 400 mg/kg and EAF at 25 mg/kg and 50 mg/kg b.w. for 28 days significantly lowered the FBG level, compared to metformin treated diabetic control rats. DCME and EAF also showed a significant reduction in glycosylated haemoglobin, plasma ALP, ALT, urea, cholesterol, triglyceride, LDL-C, and lipid peroxide levels and an increase in plasma insulin level and also the antioxidant parameters were restored in normal levels. An Immunohistopathological observation of EAF treated diabetic rat indicates significant development of β -cell density at cellular level. Collectively, the results from this study confirmed the beneficial effects of *D. cordata* leaf extract in controlling the dysregulated serum parameters in streptozotocin induced diabetes rats and may be helpful to develop novel therapeutic agent for the control of DM.

Keywords: Diabetes Mellitus, *Drymaria cordata*, High fat diet, Streptozotocin.

Anti-cholinesterase and Memory Improving Effects of North-East India's Ginger Varieties

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Abstract

Ginger constitutes the rhizome part of the plant *Zingiber officinale* from the Zingiberaceae family. A large number of ginger varieties with high functional quality are found in the Northeast India. Phytochemical screening of different ginger varieties is essential to develop high-end product and improve economical margins. Ginger has long been used as a type of folk medicine for the treatment of Alzheimer's disease (AD), associated with memory loss and impairments. The present study sought to determine the antioxidant activities and 6-Gingerol contents of nine different ginger varieties collected from Northeast India and to investigate the inhibitory effects of the most potent ginger on scopolamine (SCO) induced AD mice. Antioxidant activities were measured using 2,2-diphenyl-1-picrylhydrazyl (DPPH) and hydroxyl radical scavenging assays, while reversed-phase high performance liquid chromatography (RP-HPLC) analysis was utilized for quantitative determination of 6-Gingerol content. Y maze and Morris water maze tests were performed to assess anxiety-like behaviours and learning and memory processes in mice pre-treated with scopolamine. In addition, specific enzyme reaction tests were used to detect the activities of acetylcholinesterase (AChE), butyrylcholinesterase (BChE) and the brain oxidative stress parameters were also evaluated by measuring SOD, CAT and GSH level. The result revealed that the highest 6-gingerol content (8.69 % w/w) was present in ginger variety 6 (GV6) which showed maximum antioxidant activity with an IC₅₀ value of 31.24±1.08 and 44.52±1.14 for DPPH and hydroxyl radical scavenging activity, respectively. Single administration of GV6 (200 and 400 mg/kg) reversed the anxiety-like behaviours, and learning impairment effects of scopolamine in the experimental models studied and significantly reduced the activities of AChE, BChE and enhanced the activities of SOD, CAT and GSH in the brain of AD mice compared to SCO treated mice. Our findings demonstrated that the scopolamine-induced impairment of learning and memory was reversed by the administration of GV6. The antioxidant potential of GV6 implies benefit for the oxidative stress hypothesis of AD. Potency of the 6-Gingerol present in the extract to treat neurological complications has already been established. Thus it can be concluded that GV6 would be a useful source for further investigation against AD.

Keywords: Ginger, Quality evaluation, Alzheimer's, North-East India, Cholinesterase.

Preventative Effect of Vitamin E in Stress Dysregulation Related Depression in Systemic Inflammation-Induced Mice

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Abstract

Depression is a mood disorder accompanied by symptoms such as social withdrawal and decrease motor activity. Interferon is an endogenous cytokine produced upon stimulation by various stimuli, foreign bacteria, or viruses. Depression is considered one of the most prominent adverse effects following IFN therapy and the underlying mechanism involves HPA-axis dysregulation, the release of proinflammatory cytokines and stimulation of μ opioid receptor. Vitamin E is a potent anti-inflammation and antioxidant which prevent lipid peroxidation which believed to play a role in improving IFN-induced depressive symptom. The aim of this study is to investigate the ameliorative effect of vitamin E on systemic inflammation-induced stress dysregulation by repetitive IFN- α treatment. 50 adult male ICR strain mice were distributed into 5 cages of ten each: vehicle only, vitamin E (100mg/kg) only, IFN- α with vehicle, IFN- α with vitamin E (50mg/kg) and IFN- α with vitamin E (100mg/kg). Behavioural test is recorded and analyzed with ANY-MAZE software. Statistical Analysis with one-way ANOVA followed by Dunnett. In OFT, mice with IFN- α treatment show the least distance travelled while 100mg/kg vitamin E supplement significantly improve the distance travelled by the mice. In SI, mice with IFN- α treatment show the least interaction time while 100mg/kg vitamin E shows an improving trend in the interaction time. For TST, mice with IFN- α treatment show the highest immobile time and 100mg/kg vitamin E significantly decrease the immobile time of the mice. There is a significant improvement by vitamin E in OFT and TST and a trend of improvement in SIT. Hence, vitamin E is capable to treat anxiety and depression through its antioxidant and anti-inflammatory action.

Keywords: IFN- α ; interferon-alpha, α -tocopherol; vitamin E, HPA-axis

Identification of New Dual PDE1B and PDE10A Inhibitors using Ligand-Based Pharmacophore Modelling and Virtual Screening

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Abstract

Schizophrenia is a chronic neuropsychiatric disorder affecting over 1% of the world population, associated with the dysfunction in basal ganglia-cortical networks of the dopamine system and alterations in cyclic nucleotide signalling. To date, the current antipsychotic therapy shows inadequacy in mitigating the negative and cognitive symptoms, besides causing undesirable extrapyramidal side effects. Dual PDE1B and PDE10A inhibition has been considered as a potential therapeutic approach to alleviate positive, cognitive, and negative symptoms in schizophrenia as a whole, attributing to both D1 potentiation and D2 blockade. This study aims to identify new dual PDE1B and PDE10A inhibitors with high binding affinity from the natural products database using ligand-based pharmacophore modelling, virtual screening, and molecular docking. Ligand-based pharmacophore models for PDE1B and PDE10A were generated, validated, refined, and employed for sequential virtual screening of the Universal Natural Products Database (UNPD). Molecular docking and visualization of the dual hits with PDE1B and PDE10A were performed for binding and interaction analysis, followed by structural modifications via functional group substitution to improve interaction affinity. Pharmacophore validation of the PDE1B pharmacophore model produced a GH score of 0.83 while that of the PDE10A pharmacophore model produced a GH score of 0.71. Sequential virtual screening of UNPD yielded 4 filtered dual hits. UNPD167314 was identified as the lead compound with the lowest binding energy for PDE1B (-8.4 kcal/mol) and PDE10A (-9.7 kcal/mol). 51 novel inhibitors were designed via structural modifications. Compound 18 exhibited the highest binding affinity for both PDE1B and PDE10A, with R1-tertbutyl, R2-hydroxyl and R3-carboxyl substitution, at -10.6 kcal/mol and -11.7 kcal/mol respectively. Thus, ligand-based pharmacophore modelling, virtual screening, and molecular docking resulted in the identification of new dual PDE1B and PDE10A inhibitors with enhanced binding affinity upon desirable structural modifications. Key binding interactions include hydrophobic interactions with P-clamp and hydrogen bonding with invariant glutamine. In essence, there was an increase in binding affinity of 26.2% and 16.5% for PDE1B as well as 20.6% and 30% for PDE10A in comparison with the lead molecule UNPD167314 and the standard compounds DSR-141562 and TAK-063.

Keywords: Schizophrenia, PDE1B, PDE10A, Dual Inhibitors, Ligand-Based Pharmacophore Modelling and Virtual Screening

Phytochemical Screening and Evaluation of Antioxidant Interaction in A New Polyherbal Formulation TC-16: When 1+1 ≠ 2

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Abstract

Free radicals have been associated with the aetiology of many chronic illnesses. Thus, there is an increased need to identify potent antioxidants which can significantly destroy the free radicals. Combination of multiple herbs in polyherbal formulations (PHF) is often associated with greater therapeutic efficacy due to synergism. However, antagonism can occur in natural product mixtures and the resultant antioxidant potential might not always be the additive value of antioxidant properties of each component. The study aimed to evaluate the antioxidant capacity and interaction among the herbs in TC-16, a new PHF comprising *Curcuma longa* L., *Zingiber officinale* var. Bentong, *Piper nigrum* L., *Citrofortunella microcarpa* (Bunge) Wijnands and *Apis dorsata* honey. TC-16 was tested for the presence of phytochemicals followed by the determination of phenolic and flavonoid contents. The antioxidant properties of TC-16 and its ingredients were assessed using *in vitro* antioxidant assays (ABTS, DPPH, FRAP, ORAC, and β -carotene bleaching (BCB) assays). The difference in antioxidant activity and combination index were calculated to study the interactions among the herbs. Alkaloids, flavonoids, steroids, saponins, and glycosides were present in TC-16. TC-16 possessed the highest contents of phenolics (46.14 ± 1.40 mg GAE/g) and flavonoids (132.69 ± 1.43 mg CE/g) after *C. longa*. Phenolics and flavonoids are well-known antioxidant components that have been reported for their potential health benefits and prevention of diseases. The antioxidant mechanism of TC-16 was mainly by hydrogen atom transfer (HAT), a concerted movement of a proton and an electron in a single kinetic step. Synergism was reported in the antioxidant activity of TC-16 evaluated by ORAC and BCB assays while other assays have demonstrated antagonism. TC-16, a PHF comprising five herbs revealed that HAT is the main mechanism contributing to its antioxidant activity. Free radicals damage is associated with the development of many chronic health disorders. Hence, the antioxidant potential demonstrated by TC-16 could be beneficial in addressing this situation. A future study investigating the interaction of these herbs in combating cancer-related diseases is highly warranted, due to the multifactorial pathogenesis of cancer, which can be addressed by PHF that can act through multiple pathways.

Keywords: Polyherbal, Antioxidant Activity, Interaction, Phytochemicals

Antioxidant Potential of a Novel Polyherbal Formulation: DM-15

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Abstract

The study aimed to investigate the phytochemical screening and antioxidant potential of a novel polyherbal formulation DM-15, comprising *Cucumis sativus* L., *Momordica charantia* and *Azadirachta indica*. *C. sativus*, *M. charantia* and *A. indica* were blended together and preserved under -80°C for 24 hours. The crystallized DM-15 was obtained from freeze-drying. DM-15 was subjected to phytochemical screening and was tested *in vitro* antioxidant contents using total phenolics content (TPC) and total flavonoids content (TFC). Its antioxidant activities were also assessed using 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ferric ion reducing antioxidant power (FRAP) radical scavenging assays. All determinations of antioxidant activities were performed in triplicates. All data were presented as mean ± SD. Analysis of variance and significant difference among means were tested by one-way ANOVA followed by Tukey's multiple comparison test. Statistical significance was accepted with (P < 0.05), indicating significant difference and 95% of confidence intervals. Statistical analysis was performed using Prism software. Preliminary phytochemical screening showed the presence of alkaloids, flavonoids, saponins, sterols and cardiac glycosides. According to ABTS, the half maximal inhibitory concentration (IC₅₀) values of ascorbic acid (AA), trolox and DM-15 were 1.50 ± 1.15 µg/ml, 0.78 ± 0.06 µg/ml and 92.46 ± 1.78 µg/ml respectively. For DPPH, the IC₅₀ values were 2.57 ± 1.02 µg/ml, 6.85 ± 2.32 µg/ml and 1007.33 ± 4.04 µg/ml for AA, trolox and DM-15 respectively. The FRAP values equivalent to 1 µM FeSO₄ of AA, trolox and DM-15 were 52.76 ± 6.46 µg/ml, 53.28 ± 1.28 µg/ml and 22125.07 ± 41.88 µg/ml respectively. TFC of DM-15 was 2.56 ± 0.39 mg of RU/g whereas the TPC value was 10.23 ± 0.20 mg GAE/g. The antioxidant capabilities of the polyherbal DM-15 were ascertained. Knowing the antioxidant properties DM-15, further investigation suggested to investigate its roles in various ailments including cancer and diabetes mellitus.

Keywords: *Cucumis sativus*; *Momordica charantia*; *Azadirachta indica*; Free Radicals; Antioxidant.

Therapeutic Effect of a Polyherbal Formulation in Chronic Dysmenorrhea-Induced Mood Disorders

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Abstract

Dysmenorrhea is often being neglected among women with the mindset that it is not life-threatening, treatment is sought only when present signs/symptoms. Previous studies have proven that women with dysmenorrhea are more susceptible to depression and anxiety as a result of menstrual pain. This research aims to study the potential therapeutic effect of MM-15 polyherbal formulation on chronic dysmenorrhea-associated mood disorders. Adult female ICR mice were employed in this study. Sixty non-pregnant mice were randomly grouped into six groups: estrogen + normal saline group; estrogen + oxytocin group; estrogen + oxytocin + purified water group; estrogen + oxytocin + MM-15 group (50mg/kg *p.o.*); estrogen + oxytocin + MM-15 group (100mg/kg *p.o.*); estrogen + oxytocin + MM-15 group (200mg/kg *p.o.*). Open field test (OFT), social interaction test (SIT) and tail suspension test (TST) were employed to measure the effect of MM-15 formulation on chronic dysmenorrhea-induced mood disorders. From the analyzed result, high dose of MM-15 formulation (200mg/kg, *p.o.*) increased the total distance travelled in OFT which indicated significantly reduction in anxiety-like response. In TST, the same dose of MM-15 formulation significantly showed potential antidepressant response by reducing immobility time. In SIT, all dose of MM-15 formulation does not improve social-withdrawal behavior in mice with chronic dysmenorrhea. Overall, MM-15 polyherbal formulation has a significant result in reducing chronic dysmenorrhea-induced mood disorders in mice, including depressive and anxiety-like behaviours.

Keywords: Primary Dysmenorrhea; Polyherbal Formulation; Depression; Anxiety; mice

Economic Burden of Alzheimer's Disease: A Systematic Review

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Abstract

The growth of elderly population is estimated to rise abruptly to 1.5 billion by 2050. Alzheimer's disease has become one of the most prevalent neurodegenerative disorders among the elderly. The global cost of dementia is expected to reach US\$2 trillion in 2030. In this systematic review, we appraise the existing evidence on the cost of dementia specific to Alzheimer's disease. A comprehensive search was done on three databases, namely PubMed, ScienceDirect and Web of Science to identify original cost-of-illness studies that only evaluate the economic burden of AD. The protocol was registered in the International Prospective Register of Systematic Reviews database with registration number CRD42022363532. The cost inflation index utilized was adapted to 2021 World Bank values using country-specific consumer price index (CPI) data. The risk of bias in the studies was assessed using CHEERS criteria 2022. We screened 5536 studies, and 12 studies met the inclusion criteria. The total annual cost of AD per capita ranged from US\$468.28 in mild AD to US\$171283.80 in severe AD. Generally, the cost of care raised non-linearly with disease severity. Shifting of cost occurs between community dwelling patients and residential care patients. Direct non-medical cost became the major cost component in annual total cost of AD when special accommodation care was considered in country specific data. Overall, indirect cost comprises 32.7% of the annual cost of AD per capita while direct cost occupies a proportion of 67.3% where special accommodation contributes over 50% of direct cost. In conclusion, AD still exerts a huge economic burden on patients and caregivers. Indirect cost is the dominant cost component among community dwelling AD patients in assessing actual economic burden of the disease. Special accommodation provision results in shifting costs from indirect to direct non-medical care costs. As unpaid caregiving services are replaced by residential care with trained personnel, informal care cost decline along with less productivity loss from societal perspective. When disease progresses to severe stages, overall rise of each cost component could be anticipated. Caregiver's needs in healthcare and social support should be addressed to enhance HRQoL outcomes of both patients and caregivers.

Keywords: Alzheimer's disease, dementia, economic burden, expenditure, cost-of-illness

Formulation and In-Vitro Evaluation of Mangosteen Peel Extract Herbal Shampoo for Anti-Dandruff Properties

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Abstract

In this modern era, shampooing has become a prominent routine in our daily life. However, synthetic chemicals are present in most commercial shampoo. Their adverse effects on health and environment have been well-documented. These side effects are causing the consumers to opt for a plant-based, and sustainable personal care products. Mangosteen, or scientifically known as *Garcinia mangostana* in which the peel is usually discarded as agricultural waste. The objective of our study is to formulate the shampoo standardized with mangosteen peel extract and evaluate the antifungal activity towards *Malassezia furfur*. The mangosteen shampoo was prepared using natural-derived ingredients. Physicochemical tests including visual inspection, pH, surface tension, percentage solid contents, wetting time, foam ability and stability, and dirt dispersion were performed and compared with a commercial shampoo. Its antifungal activity towards *M. furfur* was also examined and compared with the commercial shampoo using agar well diffusion and microbroth dilution methods. An accelerated stability study (40°C, 75% Relative Humidity) was performed for 3 months consecutively. The formulated shampoo remained physically stable without phase separation. The physicochemical characteristics of the formulated shampoo passed the standard range. The pH, surface tension, wetting time, dirt dispersion, percentage of solid content and foaming stability of the formulated shampoo were 5.71, 34.1 dynes/cm, 18.44 seconds, light, 33.05% and 140 mL, respectively. Hair scalp microscopic examination after washing revealed its effective cleansing effect. The shampoo with 0.25% peel extract exhibited the best antifungal activity with the lowest minimum inhibitory concentration (MIC 0.039 mg/mL) and minimum fungicidal concentration (MFC 0.156 mg/mL). In conclusion, the formulated shampoo with 0.25% mangosteen peel extract is useful in inhibiting dandruff causing fungal.

Keywords: Mangosteen, Herbal shampoo, Formulation, Anti-dandruff, *Malassezia furfur*

Formulation and Physicochemical Evaluation of Green Cosmeceutical Herbal Face Cream Containing Standardized Mangosteen Peel Extract

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Abstract

The widely reported adverse effects of synthetic ingredients encourage the development of green cosmeceuticals to achieve Sustainable Development Goal (SDG) 3. The waste product of mangosteen (mangosteen peel) was utilized in the formulation to reduce waste production corresponding to SDG 12, in addition to its anti-aging and pigmentation control effects. This study aimed to formulate and evaluate novel herbal face creams containing standardized mangosteen peel extract. The mangosteen creams were formulated using natural ingredients and were evaluated for their organoleptic characteristics, rheology, spreadability and pH. Furthermore, an accelerated stability study, freeze-thaw stability study and centrifugation test were conducted. In addition, 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical scavenging assays were conducted to assess its antioxidant effects, whereas tyrosinase inhibitory assay was conducted to determine its anti-tyrosinase activity. The formulated creams appeared light yellowish-brown and homogenous without phase separation. The creams displayed shear-thinning behavior and optimal pH which was ideal for topical application. The creams were stable after being subjected to various stability tests and were shown to have antioxidant and anti-tyrosinase activity. In conclusion, the development of mangosteen-based green cosmeceutical face cream is in line with SDG 3 and 12. It is expected to be used as a safe and effective alternative to synthetic products.

Keywords: mangosteen, *Garcinia mangostana*, cream, anti-aging, whitening, pigmentation control

Delivery of Favipiravir Mucoadhesive Nanoparticle by Dry Powder Inhaler (DPI) for the Treatment of Covid-19: Formulation and Characterization

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Abstract

Favipiravir is an antiviral drug that has been approved during the Covid-19 pandemic for emergency purposes only. It has been administered via intravenous route as a solution form. In order to solubilize Favipiravir, sulfobutylether-beta-cyclodextrin (SBECD) is used as a solubility enhancer in IV injection. Since SBECB is excreted by the kidneys and it is contradicted in patients with several renal impairments. To avoid the severe side effect, it could be administered as a mucoadhesive nanoparticle by DPI. The nanoparticle has been prepared by the nanoprecipitation method using PLGA and Chitosan and the prepared nanoparticles are characterized by physiochemical parameters and in-vitro drug release. In vitro epithelial integrity and dispersion, studies are done and the nanoparticle has particle size and zeta potential of 104.6nm & -4.05mV respectively. The spherical-shaped nanoparticles exhibit sustained release over a period of time. The mucoadhesive nanoparticle showed negligible damage in epithelial integrity with DPI emitted dose of 87.02 % and MMAD of 2.90 μm . The prepared mucoadhesive nanoparticles showed significant mucoadhesive strength of 77.10 % in lung mucous. Based on the above studies, we concluded that delivery of mucoadhesive nanoparticles of Favipiravir through DPI, could be the best alternative route of administration of Favipiravir and this method could be able to treat COVID-19 patients at homecare.

Keywords: Favipiravir, Mucoadhesive nanoparticle, Dry powder inhalation, Integrity of lung epithelial, Binding efficiency

Medicinal Herbs for Uterine Fibroids: A Mechanistic Review

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Abstract

Uterine fibroids (UFs) are a common benign gynecological tumor that affect 70-80% of women over their lifetime. Several pharmacological agents are available to reduce the size of fibroids and ameliorate the symptoms of UF. However, these drugs are expensive and are usually associated with profound side effects. Thus, medicinal herbs are gaining attention in this era due to their cost effectiveness with a comparable or more potent therapeutic efficacy while demonstrating lesser adverse effects. Previous studies have extensively explored on the benefits and risks of using medicinal herbs in the treatment of uterine fibroid. However, a detailed review on the mechanism of medicinal herb extracts and polyherbal preparation have not been conducted. The objective of this review is therefore to summarize the available information on the mechanism of various medicinal herbs and polyherbal formulations with anti-uterine fibroid activity. A systematic search was performed using several search engines such as PubMed, Google Scholar, and Science Direct to identify medicinal herbs with anti-uterine fibroid activity. Based on the literatures identified, a total of five medicinal herbs and three polyherbal formulations were included and discussed in this review, which yields useful information regarding the mechanism of different medicinal herbs and polyherbal formulations in exerting anti- uterine fibroid activity for its potential use as an alternative treatment choice for uterine fibroids.

Keywords: Medicinal herbs, Polyherbal, Uterine fibroids, Leiomyoma, Mechanism

Nanotechnology-Tailored Drops of Brinzolamide and Curcumin for Glaucoma: Combined Attribution of Neuroprotection and Improved Oculo-Antihypertensive Effect

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Abstract

Glaucoma is a progressive ocular neuropathy characterized by the degeneration of ganglion cells and irreversible vision loss. An increase in intraocular pressure is associated with obstruction of outflow drainage pathways (uveoscleral or trabecular), which was considered to be the reason for such neuropathy in glaucoma. Brinzolamide (BZ) reduces elevated eye pressure by reducing the formation of aqueous humor. Regardless of its potency, using a high dose concentration for an extended period of time may cause unwanted side effects and necessitate adjunctive therapy to effectively manage glaucoma. Recent investigations suggest the role of oxidative stress in trabecular meshwork plays a crucial role in the pathogenesis of impaired outflow facilities. Curcumin (CU) is a natural polyphenolic compound that possesses antioxidant and anti-inflammatory properties. In this study, BZ (0.25% w/v) and CU (0.1% w/v) were combined in a nanostructured lipid carrier (NLC) with the intention of improving IOP lowering efficiency and neuroprotection in glaucoma. The nanoparticulate fabrication was carried out by the combined melt emulsification-ultrasonication method. The optimized formulations showed particle sizes in the nanoscale (136.83 ± 8.59 nm), good entrapment efficiency ($85.37 \pm 0.22\%$ and $79.30 \pm 1.68\%$, BZ and CU, respectively), and also exhibited a narrow particle size distribution (0.473 ± 0.024). Zeta potential of the optimized formulations was found to be -5.14 ± 1.28 mV. The analytical data of Fourier transform infrared spectroscopy (FTIR) and transmission electron microscopy (TEM) confirm the entrapment of the drug and the nanosize range of the formulation, respectively. The *in vitro* transcorneal permeability of the NLC formulation was 3.7 times greater than that of the commercial formulation. The combined formulations were well tolerated in rabbit eyes, exhibited antioxidant properties, and demonstrated greater IOP lowering potential for 12 hours (in glaucomatous rabbit eyes) than BZ nanoformulations and commercial eye drops. These results reveal that a dual drug delivery approach might enhance trabecular outflow as well as decrease aqueous outflow. Thus, combined nano-formulations (BZ-CU) could be the choice to manage ocular hypotension and neuroprotection in the glaucomatous eye in near future.

Keywords: Glaucoma, nanostructured lipid carrier, antioxidant, neuroprotection, ocular drug delivery

Rationally Engineered Phosphatidylcholine/Cyclodextrin Mediated Conjugate for Drug Delivery

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Abstract

Major membrane lipids like phospholipids which are made up of lipid bilayers has potential application in drug delivery. More crucially, this fundamental cellular element makes it possible for several cellular activities to take place in subcellular compartments while also acting as a barrier to guard the cell against different environmental insults. Initially the ratio of drug and phospholipid was determined rationally with Jobs plot. Drug loaded phosphatidylcholine mediated conjugate was prepared by methanol refluxing and subsequently solvent evaporation method. The prepared conjugate was characterized by DSC, FT-IR, and XRD analysis. The crystallographic analysis revealed formation of conjugate suggesting the phase conversion from the crystalline to amorphous form. Similarly, the DSC analysis showed no peaks, representing the conversion from crystalline form to amorphous. The developed conjugate was evaluated for permeability analysis with the help of confocal microscopy revealing 2.78 times higher drug penetration compared to control group. The developed complex was loaded into nanoparticles revealing 95.43 % drug entrapment concluding high drug loading and potential of the conjugate for the prevention of diseases.

Keywords: β -Cyclodextrin, conjugate, drug delivery, permeability, phospholipid

Preparation of Chitosan Particles as a Delivery System for Tetrahydrocurcumin: β -cyclodextrin Inclusive Compound for Colorectal Carcinoma

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Abstract

Chitosan particle has been famously known to its drug delivery ability due to its unique property, such as high biocompatibility and biodegradability. Its delivery of the various drug has been proven to improve or enhance the activity of the pharmaceutical drug. To further enhance the loading ability of the chitosan particle, a β - cyclodextrin containing a hydrophobic inner and an outer hydrophilic surface has been used. It is known to enhance the aqueous solubility of the various agents after the insertion of the agents into the hydrophobic inner of the β - cyclodextrin. This enhanced aqueous solubility can ease the ability of the hydrophobic drug to be loaded into the chitosan particle. Therefore, a chitosan composite loaded with β - cyclodextrin/ tetrahydrocurcumin inclusive complex was proposed in this research. Its brief characterization and its cytotoxic activity on the cancer cell were studied.

Keywords: Chitosan, β -cyclodextrin, Tetrahydrocurcumin

Cationic B-Cyclodextrin-Insulin Loaded Alginate Nanoparticles for Oral Delivery

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Abstract

The only effective treatment for type 1 and advanced insulin-dependent type 2 diabetes mellitus is frequent subcutaneous insulin injections, which are physiologically different from endogenous insulin secretion and can result in hyperinsulinemia, pain, infection and patients' low compliance. Thus, efforts were devoted to changing the management of insulin-dependent diabetes through oral insulin delivery. Although the oral route is the most convenient way of drug delivery, insulin is vulnerable to rapid degradation in the stomach. Polymeric nanocarriers have recently attracted considerable attention as oral delivery vehicles that can be used to protect insulin from degradation and facilitate insulin absorption. This study aims to fabricate cationic β -cyclodextrin (C β CD)-insulin-loaded alginate nanoparticles and evaluate their potential as an oral insulin delivery system. C β CD were prepared from β -cyclodextrin (β -CD) through a one-step polycondensation using choline chloride (CC) to provide an ammonium group and epichlorohydrin (EP) to form polymeric chains. Insulin was complexed with C β CD to enhance the release profile, then encapsulated into calcium alginate nanoparticles via the ionic gelation method. The size, zeta potential, encapsulation efficiency (EE), surface morphology and cumulative drug release of the nanoparticles were recorded. *In-vitro* cytotoxicity of the nanoparticles against HT-29 cells was evaluated by MTT assay. C β CD-insulin-loaded alginate nanoparticles were characterized by reduced particle size, improved encapsulation efficiency and controlled insulin release in the simulated gastric fluid (SGF). The optimised nanoparticles exhibited a suitable particle size, with high encapsulation efficiency >80% and a controlled cumulative insulin release profile in simulated gastric fluid. MTT assay revealed that all formulations were non-toxic. The present study advocates that C β CD-insulin-loaded alginate nanoparticles is a promising system for enhancing oral insulin delivery.

Keywords: β -cyclodextrin, Oral insulin, Alginate, Nanoparticles

Aptamer-Based Biosensor for Dengue Virus Detection

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Abstract

Aptamers are short RNA or single-stranded DNA comprise 20 - 80 nucleotides that can fold into unique three-dimensional conformation to specifically bind to targets. Compared to RNA aptamers, DNA aptamers are much more stable and therefore are widely used in several applications especially in diagnostics. Aptamers can specifically recognize molecular targets and modulate their biological activities, which allow aptamers to be used for diagnostic purposes. In this study, two aptamers targeting the EDIII and NS1 protein of dengue virus were designed and cross checked with Zika virus and Japanese encephalitis virus through in silico methods to prevent the cross-reactivity among flaviviruses. The aptamer sequence was first obtained from a random tRNA sequence, modified then follow by predicting their 2D and 3D structure. The AutoDock Vina software was used for molecular docking to find out the binding affinity. The designed aptamers which successfully binds to the target protein is selected for wet lab validation. Western-blotting and ELISA assay were used for the validation of aptamers. Aptamers which showed high-affinity and high-sensitivity towards dengue virus can be further used in the aptamer-based biosensor, which also known as the aptasensor for early detection of dengue virus infection.

Keywords: Aptamer, In silico design, DENV

Formulation and Development of Poly-Herbal Anti-ageing Cream

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Abstract

Skin ageing is a complicated biological process that is affected by both intrinsic and extrinsic factors. UV rays produce free radicals that can impair the collagen and elastin networks. Consequently, the cell regeneration process is impeded, resulting in hyperpigmentation and rough, wrinkled skin. As a result, the research advances in natural cosmetics that contribute to restoring a certain level of rejuvenation and delaying or reversing the ageing process are the focus of the study. The purpose of this research is to determine the percentage of radical scavenging activity of aqueous extract of Tremella fuciformis (TF) using the DPPH technique, as well as to develop a polyherbal anti-ageing cream containing TF, sea buckthorn, grape seed, rosehip seed, rose water, and natural excipients. The maceration technique was employed in the preparation of the TF extract. Hot water bath equipment was used to prepare oil-in-water emulsions by heating the aqueous phase and oil phase components separately at 75 °C. Subsequently, mixing both phases with the use of a homogenizer set at 1000 rpm for 5 minutes and reduced to 500 rpm until the emulsion cooled down to room temperature was necessary. Following that, the emulsion cream-based was levigated with TF extract to produce a smooth small amount of herbal cream, which was gradually incorporated with a large portion of the cream base until forming a homogenous polyherbal cream. At 2 mg/ml concentration, the TF extract demonstrated 80% radical scavenging activity. The polyherbal cream appeared light yellow with a smooth texture and was homogenous without phase separation. With the test, the formulation showed excellent stability across the 3 months of testing in different temperatures and different packaging materials, including plastic and glass containers. From the above results, it is concluded that the formulation containing TF could be the best formulation to rejuvenate the skin and reduce age-related wrinkles.

Keywords: Anti-ageing, Tremella Fuciformis, DPPH test, Polyherbal, Facial cream

Antioxidant Properties and Interaction Effects of a Novel Polyherbal Formula

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Abstract

A novel polyherbal formula was developed from crude drugs of *Andrographis paniculata* (Burm.f.) Wall., *Tinospora crispa* (L.) Hook.f. & Thomson, *Curcuma longa* L., *Curcuma comosa* Roxb., and *Phyllanthus niruri* L. The powdered crude drugs were combined in the ratio of 5-5-3-3-3, respectively. The determination of total phenolic content (TPC), the 2,2-diphenyl,1-picrylhydrazyl (DPPH) scavenging activity, and ferric reducing antioxidant power (FRAP) of the polyherbal formula and the individual constituents were conducted as per standard methods. The interaction effect of the components in the polyherbal formula toward antioxidant activities was statistically predicted. *Curcuma longa* contained the highest TPC at 625.35±28.39 mg Gallic acid equivalent (GAE)/g dry weight (DW) crude drugs and showed the strongest DPPH scavenging activity and FRAP at 1546.18±88.16 and 1292.92±43.42 mM Trolox equivalent (TE)/g DW, respectively. The polyherbal formula was in the median range of the component's value, with TPC, DPPH scavenging activity, and FRAP of 83.52±0.93 mg GAE/g DW, 652.63±28.84 mM TE/g DW, and 401.77±9.42 mM TE/g DW. TPC of all samples positively correlated to DPPH scavenging activity and FRAP. The combination of *Andrographis paniculata*, *Tinospora crispa*, *Curcuma longa*, *Curcuma comosa*, and *Phyllanthus niruri* generated interaction effects of additive and antagonist towards DPPH scavenging activity and FRAP, respectively.

Keywords: Antioxidant, Crude drugs, Phenolic compounds, Polyherbal formula

Immunomodulatory Effects of *Mitragyna Speciosa* Korth. on Macrophage Immune Responses

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Abstract

Mitragyna Speciosa Korth., or kratom is an Asian tropical plant that exhibited medicinal benefits including antioxidant, antibacterial, and antinociceptive effects. However, the effects of *Mitragyna Speciosa* on the modulation of innate immune response especially in macrophages remain to be elucidated. This study aimed to evaluate the immunomodulatory effect of *Mitragyna Speciosa* Methanolic Extract (MSME) on peritoneal-isolated primary macrophages (pM ϕ) and murine-derived macrophages RAW264.7 cell line. The pM ϕ were isolated aseptically from specific pathogen-free (SPF) Balb/c mice via induction with intraperitoneal Thioglycollate medium. The cytotoxicity effect of MSME on both RAW264 cells and pM ϕ was determined by a cell viability test using a cell-titer blue assay. Furthermore, the effects of MSME on the production and expression of immune mediators including nitric oxide (NO) and cytokines in macrophages were evaluated by Griess assay and qRT-PCR, respectively. In addition, the phagocytosis rate of lipopolysaccharide (LPS)-stimulated macrophages in the presence of MSME was measured by neutral red uptake assay. The cytotoxicity analysis on both types of macrophages shows a stable cell viability when treated up to 100 μ g/ml of MSME. MSME has exhibited anti-inflammatory effects in LPS-stimulated macrophages which determined by a significant inhibition of NO production ($p < 0.05$) in a concentration-dependent manner (0 μ g/ml to 100 μ g/ml). Moreover, the extract also significantly reduced the phagocytosis capacity in LPS-stimulated RAW264.7 cells ($39\% \pm 9.7$; MSME 100 μ g/mL; $p < 0.05$) and pM ϕ ($43\% \pm 15.8$; MSME 10 μ g/mL; $p < 0.05$). Interestingly, a significant ($p < 0.05$) inhibition was shown in the expression of inducible NO synthase (*iNOS*) and cytokines including *TNF- α* , *IL-1 β* , and IL-6 in the LPS-stimulated RAW264.7 cells treated with MSME in a concentration-dependent manner. In conclusion, our results suggest that MSME has potential immunomodulatory effects on macrophage immune responses induced by LPS through the downregulation of phagocytosis activity, the expression of *iNOS*, and proinflammatory cytokines.

Keywords: *Mitragyna speciosa* Korth, Kratom; Macrophages, Immunomodulatory, Anti-inflammatory, Immune response.

Thymoquinone Extract Loaded Pectin Beads for Colorectal Cancer Targeting

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Abstract

This study aimed to formulate an oral dosage form targeting colorectal cancer, consisting of thymoquinone-loaded calcium pectinate beads prepared by the ionic gelation method. Pectin was used to synthesize the hydrogel beads as it can undergo complete degradation in the colon while remaining resistant to the gastric and intestinal enzymes in the upper gastrointestinal tract. Thymoquinone, an anticancer substance, was included in this formulation as it exhibits great anticancer properties while remaining safe to use. The pectin beads were synthesized via the ionic gelation method. The prepared beads were then characterised depending on their particle size, swelling, erosion and water uptake. The optimisation of the thymoquinone-loaded pectin beads was done based on formulation parameters, including pectin and calcium chloride concentrations and processing parameters such as hardening time after beads fall into the hardening solution. The prepared beads were characterised in terms of size, sphericity, swelling, erosion and water uptake by means of an image analysis system (ImageJ). At the same time, entrapment efficiency was quantified using a spectrophotometer at a wavelength of 232 nm. MTT assay was conducted to evaluate the cytotoxicity of the formulated beads on colon cancer (HT-29) cell lines. The optimised thymoquinone-loaded pectin beads with a high entrapment efficiency (91.25%) were successfully prepared through the ionic gelation method. The size and sphericity of the optimized beads were at 1.561 ± 0.04 mm and at 0.012 ± 0.01 mm, respectively. The beads also demonstrated desirable swelling (SGF: 10.461 ± 0.05 %, SIF 18.854 ± 0.05 %, SCF 23.715 ± 0.08 %), erosion (SGF 41.566 ± 1.07 %, SIF 65.854 ± 1.47 %, SCF 68.293 ± 1.41 %) and water uptake (SGF 193.814 ± 1.09 %, SIF 169.643 ± 0.98 %, SCF 286.538 ± 1.97 %). MTT assay demonstrated that thymoquinone-loaded pectin beads showed anti-cancer effects against the human colorectal adenocarcinoma cell line (HT-29) as it decreased the viability of the cancer cells from ~65% to 0% as the number of beads was increased. The results suggested that thymoquinone-loaded pectin beads are a promising oral drug delivery system for colorectal cancer targeting.

Keywords: Thymoquinone, Pectin, Gel beads, Colorectal cancer, Colon targeting, Particle size.

Optimization of Antipollutant Cream Formulation with Purple Passion Fruit Seed Extract (*Passiflora edulis Sims*)

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Abstract

Pollution causes several adverse effects on skin. Purple passion fruit seeds contain piceatannol which acts as an anti-pollution agent. In this research, purple passion fruit seed extract cream was optimized by varying the concentrations of a stiffening agent (SA), a hydrophilic surfactant (HS), and a lipophilic surfactant (LS). Purple passion fruit seed extract was made into a cream preparation and tested for viscosity, pH, and dispersion. Optimization was carried out using the simplex lattice design method in Design Expert® software version 13. The optimum preparation was tested for its stability by cycling test method. The optimum formula was obtained, LS of 3%, HS of 2.6%, and SA of 2.4% with an average response yield of optimum viscosity of 5153.3 cps, pH 6.23, and power spread 6.04 cm². The cycling test showed no change in color, odor and dosage form so that this cream met the stability test standards. Optimization using the simplex lattice design with variations of SA, LS, and HS showed that viscosity and spreadability had a significant effect, while pH had less significant effect. Variation of concentrations of SA and HS increased the viscosity, pH, and spreadability of the cream. However, increasing the concentration of HS decreased the viscosity of the cream.

Keywords : Cream, Purple passion fruit seed extract, Piceatannol, Optimization, Irritation test.

Bioscintigraphy as an Imperative Tool for Efficacy, Safety and Branding of Pharmaceutical Formulations

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Abstract

The marketing of prescription medicines is constrained by regulatory restrictions on promotion, short product life cycles and product complexity. Pharmaceutical branding through scientific evidence including assessment of safety and efficacy is viewed as an effective communicator to the clinicians. Gamma-scintigraphy or Bioscintigraphy is a non-invasive, image-guided technique, which could be utilized to visualize real-time in vivo performance and behavior of the drug or drug product. Bioscintigraphy could be applied at all the phases of drug product development and results in development of evidence based drug product. Bioscintigraphy is expected to generate product claims, scientific merit over a competitor, product's differentiation data and real-time product performance in human subjects, all of which are prerequisites for pharmaceutical branding. In a nutshell, Bioscintigraphy has the potential to extend the life cycle of drug products through brand positioning and creating brand equity.

Keywords: Bioscintigraphy, Gamma-scintigraphy, Safety, Efficacy, Branding, Nano-formulation, Technetium.

Sensitive, Simple, and Quick Method for Simultaneous Quantification of Clozapine and Amlodipine using Reverse Phase HPLC

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Abstract

Hypertension is one of the most prevalent non-communicable diseases in the Malaysian population. In addition, it is associated with various mood and psychiatric disorders such as schizophrenia. Recent studies have shown that hypertension leads to worse clinical outcomes in psychiatric patients. Diverse psychosocial factors caused by schizophrenia also impact hypertension and its clinical care. Clozapine and amlodipine are the hallmark drugs for the treatment of schizophrenia and hypertension, respectively. To date, there is no analytical assay that can simultaneously determine the concentrations of these two drugs in human matrices. An Aquasil C₁₈ column was used in the analysis, with the mobile phase consisting of acetonitrile:water (40:60 v/v) adjusted to pH 4.5 with phosphate buffer. Detection with UV spectrometer was done at 240nm. The method was validated according to the International Council for Harmonization (ICH) guidelines. The calibration curves of clozapine and amlodipine were linear in the range of 100-600 ng/mL and 2-12 ng/mL, respectively ($r^2 > 0.99$). Clozapine limit of detection (LOD) and limit of quantification (LOQ) were 129.5 ng/mL and 392.4 ng/mL, respectively. Meanwhile, amlodipine achieved LOD of 0.25 ng/mL, and LOQ of 0.75 ng/mL. Overall, the study describes quick, precise and sensitive HPLC-UV method for the simultaneous determination of clozapine and amlodipine in human plasma.

Keywords: Amlodipine, Clozapine, HPLC, Quantification, Plasma

Design and Development of Novel Biopolymeric Nanoparticles Based Film Forming Spray for Effective Drug Delivery of Curcumin for Treatment of Wound Infection

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Abstract

Skin being the most exposed human organ susceptible of getting injured and thus leading to wound infections is one of the most prevalent disorder seen worldwide, and the increasing cases of bacteria building resistance to present available antibiotics, brings the need to investigate and research new antibacterial agents. The present research focus on valorizing lignin by using it as drug carrier as well as a therapeutic agent in a nanoparticulate system. In this work, attempts were made to synthesize and develop a new formulation of an antibacterial wound dressing. To meet the goal curcumin-loaded lignin nanoparticles were successfully synthesized using solvent displacement and dialysis method. Final optimized CLLNPs show a particle size within the range of 100- 200nm, which can vary with the concentration of drug and polymeric compound and showed systemic drug release with enhanced drug permeation and drug efficacy. The presence of drug and lignin within the nano-system was confirmed using UV/Vis spectrophotometry, FTIR, DSC, TEM images and particle size. Besides the various wound dressings available in the market for managing wound infections like hydrogel, films, forms, bandage etc, they own certain drawbacks majorly the secondary danged caused in wound while reapplication that can be combated with the present research. The synthesised fast-drying FFS solution formed a thin adhesive barrier between the wound and environment, which is non-toxic, water washable, non-sticky, and sustained release formulation. Antibacterial assay for the final formulation showed that the selected bacteria didn't show bacterial resistance to the formulated nano-systems, while it showed enhanced antibacterial action as compared to the blank lignin nanoparticles and comparable action to the marketed formulation (Neosporin & streptomycin), however, the formulation showed higher antibacterial action against gram-positive bacteria as compared to gram-negative bacteria. The final formulation showed its enhanced antioxidant action which was comparable to free drugs EC50 value i.e. 62.24 µg/ml. Thus the antibacterial action of developed CLLNPs loaded FFS makes it suitable to treat bacterial action, the enhanced antioxidant effect makes the formulation suitable to reduce oxidative stress, inhibit the inflammatory response and avoid rupture of vascular endothelial cells, therefore accelerate wound healing process.

Keywords: Curcumin, Wound healing, Dialysis, Antibacterial, Film former

Investigation of Anti-inflammatory Activity and Metabolite Content of Methanolic *Aquilaria Malaccensis* Leaves Extract

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Abstract

Aquilaria or agarwood leaves has gained a proactive interest among researchers due to its variety of secondary metabolites contents which reported to be effective as alternative treatment in many diseases. Even while agarwood leaf research is moving forward at a rapid pace, there is still a lack of empirical data to support the stated pharmacological effects, notably the anti-inflammatory effects. Therefore, this study aims to investigate the anti-inflammatory potential of *Aquilaria Malaccensis* leaf extract. Leaves were extracted in methanol by maceration. Both *in vitro* and *in vivo* tests were performed by BSA denaturation inhibition method and in mice paw edema model respectively. The phytochemical profiling for volatile compounds was conducted by GCMS while the non-volatile compounds was screened using UPLC-QToF/MS. The *in vitro* study revealed that the extracts exhibited concentration-dependent inhibition of protein (albumin) denaturation across the concentration range of 31.25-1000 µg/ml examined. The *in vivo* result revealed that the extract reduced the paw edema significantly (0.406 ± 0.054 mL, $p < 0.05$) after 4 hr pre-treatment observation as compared to the disease group (0.542 ± 0.031 mL). The phytochemical analysis of the bioactive extract by GCMS identified 48 compounds were identified and n-hexadecanoic acid (27.06%) was the major compounds present in the extract. Furthermore, the presence of phenolic compounds including xanthenes, benzophenone and flavones from UPLC-QToF/MS analysis may inspire further investigation on anti-inflammation mechanism, as well as its toxicity regarding its potential as an alternative therapeutic source for medicinal purposes.

Keywords: Agarwood; *Aquilaria Malaccensis*; Anti-Inflammatory; LCMS; GCMS

Formulation and Development of *Tremella Fuciformis* Whitening Gel

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Abstract

Cosmetics found in the market are frequently labelled as plant-based or 'chemical-free,' highlighting the absence of any potentially dangerous excipients such as paraben. However, most of them contain synthetic excipients in it, only the herbals were natural. As such, hydroquinone is used as a skin lightening agent in most whitening products whereby it may cause undesirable side effects. Skin hyperpigmentation is a dermatological condition in which the skin's color darkens due to an increase in melanin production. In this innovation, the natural formulation of gel was developed and characterized for the treatment of hyperpigmentation. Natural excipients and preservatives were used to improve the stability of the innovation. *Tremella Fuciformis* (TF) is a species of fungus that is often used in food preparation in Chinese cuisine. TF has great skin brightening properties and can be used to replace hydroquinone. The maceration extraction process was used to produce TF aqueous extract. The anti-tyrosinase activity of the aqueous extract was determined using the tyrosinase inhibition test and it showed 86.04% inhibition at 10 mg/ml concentration. Besides, the gel formulation showed maintained its integrity after 3 months of stability testing at various temperatures. Therefore, a novel polyherbal gel was successfully developed. The TF showed great anti-tyrosinase activity and this formulation could be a safer alternative to synthetic whiteners.

Keywords: *Tremella Fuciformis*, Whitening gel, Hyperpigmentation, Tyrosinase inhibition

Non-Catalytic Synthesis of N-(isoquinolin-3-yl) benzenesulfonamide: Optimization of Reaction Parameters, Product Monitoring, Isolation and Characterization

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Abstract

In the present situation, researchers have achieved important advances and contributions to chemical science and technology. As a crucial component of green chemistry, catalyst-free organic synthesis has been rapidly developed and widely adopted because it is a simple, low-cost, and practical separation and purification method. Therefore, the invention and application of chemical processes that do not require a catalyst are of crucial importance. This proposed project attempted to synthesise a sulfonamide derivative in the absence of a catalyst. Sulfonamide play a crucial role due to the presence of sulfa group which are very important in medicinal as it is the first antibiotics drug that had been developed and also vital synthetic organic chemistry. Sulfonamides derivatives classified as famous pharmacological agents because of the primary functional component found in majority of medication strictures have high stability and tolerability for human. Recently various methodologies have been developed to synthesis series of sulfonamides derivatives especially via green synthesis such as catalyst-free reaction. In research project, catalyst-free synthesis of a series of sulfonamide derivatives was carried out. Products can be observed through thin layer chromatography plate, and also through the determination of melting point. Besides, ultra-violet spectra was collected between 200nm-300nm, and the functional group of sulfonamide was detected through FT-IR spectroscopy. However, the yield obtained were less than 10% due to the little amount of starting materials were used for the pre-synthesis process.

Keywords: Sulfonamide derivative, Catalyst-free, Green chemistry

Are Malaysians Ready to Adopt the Tele-Pharmacy Services during the New Norm: A Cross-Sectional Survey?

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Abstract

Remote Healthcare services have grabbed much attention during the coronavirus disease 2019 (COVID-19) outbreak by bridging the gap between healthcare professionals and the general public while reducing the risk of transmission. This study aimed to investigate the knowledge, attitude, and practices (KAP) towards tele-pharmacy services during COVID-19 among individuals living in Malaysia. Method: A descriptive cross-sectional study was conducted among the general population living in Malaysia from July 2021 to Sept 2021 between the third wave of COVID-19. The data was collected through the convenience sampling method from the respondents, via different social networking websites such as telegram, course networking, Facebook, and WhatsApp. A self-administered questionnaire was utilized to assess their knowledge, attitude, and practices towards tele-pharmacy. Descriptive statistics Measure of central tendency and measure of variability were used to report demographic characteristics, inferential statistics were used to report the differentiation, association, and correlations of the variables. Result: Entire of 384 respondents participated in this survey. Nearly half of the participants had poor knowledge (49.0%), negative attitudes (44.5%), and poor practices (46.4%) of tele-pharmacy services during the pandemic. There was a significant association between the level of knowledge and practice of tele-pharmacy ($p < 0.001$). The majority of the participants (67.45%) with poor knowledge of tele-pharmacy were less likely to use tele-pharmacy services. Although 55.7% of the respondents found that tele-pharmacy services are feasible and convenient but only 18.5% of the participants have received any health services via tele-pharmacy during a pandemic. Conclusion: In brief, this study was able to provide an understanding of the knowledge, attitude, and practice among the individuals living in Malaysia towards tele-pharmacy services during covid-19 epidemic. The application of the tele-pharmacy opens a different as well as new stance of healthcare facilities for the patients and it can restrict the problem of less attainability of pharmacists.

Keywords: Tele-Pharmacy, Pandemic: COVID-19.

Neuroprotective Effects of *Vaccinium corymbosum* on Amyloid-Beta Peptide-Induced Amnesia in Mice

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Abstract

Neurodegeneration associated with short term memory loss is designated as Alzheimer's Disease (AD) and is due to the accumulation of neurotoxic amyloid beta (A β) peptide. Stress with hypothalamic-pituitary-adrenal (HPA) axis affects the cognition and emotion leading to AD. The present investigation was designed to evaluate the neuroprotection by ethanolic extracts of *Vaccinium corymbosum* (EEVC) and its fractions (VCF). The VCF were n-hexane, chloroform fraction, ethylacetate fraction and aqueous residue. For pharmacological evaluations male ICR Mice (aged 4 weeks) were treated with low dose (200 mg/kg) and high dose (400 mg/kg) of VCF. On the 15th day of treatment the mice were injected with A β ₍₂₅₋₃₅₎, intracerebroventricularly (icv) to induce the neurotoxicity and the VCF treatment was continued until 21st day. Water maze test was conducted to determine the behavioural memory. Brain derived neurotrophic factor (BDNF) and acetylcholinesterase enzyme were estimated in brain homogenate. The preeminent neuroprotective effect was exhibited by EEVC, ethyl acetate, chloroform fraction and aqueous residue which contains the active pharmacological compounds. The EEVC & VCF treated animals indicated the neuroprotective effect on AChE enzyme with significant reduction ($p < 0.01$) when compared to the disease induced group. In behavioural parameters (water maze) there was a significant ($p < 0.05$ & $p < 0.01$) improvement in EEVC & VCF respectively. There was a significant ($p < 0.01$) improvement in BDNF concentrations. In conclusion, this study indicates that *Vaccinium corymbosum* exhibits neuroprotection against Alzheimer's neurodegeneration and exerts neuroimmune-neuroendocrine regulation.

Keywords: *Vaccinium corymbosum*, Alzheimer's Disease, Cognitive Boost, Brain Derived Neurotropic factor, Acetylcholinesterase.

Extraction of Extracellular Membrane Vesicles from *Streptococcus pneumoniae* using Ultracentrifugation, Ultrafiltration and Iodixanol Gradient Fractionation

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Abstract

Extracellular membrane vesicles (EMVs) are membranous structures that are excreted by gram-positive bacteria. These vesicles are involved in a multitude of biological functions, essential for adaptability to the environment, cellular component exchange, antigen and virulence factor distribution, and infection transmission. Recently, bacterial EMVs have gained attention due to their potential as highly effective vaccine targets. However, extraction of EMVs from bacterial cells has been difficult. Briefly, in this study, the extracellular membrane vesicles (EMVs) of *Streptococcus pneumoniae* were extracted from its common serotypes of (6A, 14, 19A, 19F, and 23F) by using ultracentrifugation, ultrafiltration and iodixanol gradient fractionation. The extracted EMVs was validated by viewing its morphology by transmission electron microscope (TEM). In this study, the six serotypes used showed to released extracellular vesicles, albeit in varying numbers and sizes. (22 nm -250 nm). The extracellular vesicles measure 20–250 nm in diameter and contain various biologically active proteins that are required for bacterial nutrient acquisition, biofilm formation, and pathogenesis. Bacterial EMVs are non-viable component of the bacteria that acts as an antigen, hence able to induce host immune response. This suggests it to be a potential vaccine candidate for this bacterium. In this study, the success of extracting EMVs from *S. pneumoniae* using the modified method has now opened a path to study better drug targets for *S. pneumoniae*.

Keywords: *Streptococcus pneumoniae*, Extracellular membrane vesicle, Ultracentrifugation

Nanoemulsion Incorporated Gel of *Callistemon viminalis* Essential Oil for Acne Management

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Abstract

The essential oils of natural origin possess antimicrobial activity. These oils are formulated in different nanocarriers in order to improve bioavailability and antimicrobial efficacy in several topical ailments. Essential oils have been used in acne therapy. This study aims to extract *Callistemon viminalis* leaf oil, their constituent's identification and preparation of nanoemulsion loaded gel. Essential oil extraction was carried out using Clevenger apparatus (hydro-distillation method). The identification of different components of oil was done by Gas Chromatography–Mass Spectrometry. Nanoemulsion was prepared by spontaneous emulsification method using Tween 80 and Chremphor EL. The prepared nanoemulsion formulations were evaluated for globule size, polydispersity index using Zetasizer (Malvern). The optimized nanoemulsion formulations were further loaded in Carbopol gel and evaluated for rheological behaviour (Modular Compact Rheometer, MCR 102e, Anton Paar) and antimicrobial activity. The optimized nanoemulsion of essential oil (*Callistemon viminalis*) was found in the nano-range (21.46 ± 2.23 nm) with narrow polydispersity index (0.282 ± 0.052). The nanoemulsion loaded gel possesses good rheological properties for topical application. *Callistemon viminalis* oil nanoemulsion-loaded gel possesses antimicrobial potential against acne bacteria's and hence it would be better choice in acne management.

Keywords: Bottle brush, Essential oil, *Callistemon viminalis*, Acne, Carbopol gel.

Evaluation of the Local Protocol of Vancomycin-Therapy based on Targeted Trough Level and Extrapolated Area Under the Curve in Tengku Ampuan Rahimah General Hospital

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Abstract

The aim of this study was to evaluate the suitability and target concentration achievement of the local protocol of vancomycin-therapy based on targeted trough level and extrapolated area under the curve in TAR hospital, Selangor, Malaysia. A retrospective case series was carried out among the inpatient cases of vancomycin therapy who aged 18 years and above using TDM reports and a validated Bayesian software; PrecisePK®. The collected data were analyzed using the SPSS tool to study the association between trough levels, AUC_{24}/MIC and other investigating factors. This study showed that 87.3% of study participants have $AUC_{24}/MIC \geq 800$ mg.h/L which is beyond the recommended AUC_{24}/MIC . Only 2.7% of the trough readings have achieved the targeted AUC_{24}/MIC 400-600 mg.h/L. The findings indicated that AUC_{24}/MIC was significantly correlated with trough concentration and inversely with the MIC. The observed high AUC_{24}/MIC could be primarily attributed to the low MIC values in HTAR. The variation of MRSA MIC due to the different test methods and other technical concerns causes AUC_{24}/MIC interpretation to be arguable. Current study emphasizes the limitations of trough-guided dosage, as well as the complexity of the interpretation of the obtained high values of AUC_{24}/MIC . The abnormally low locally reported MRSA MICs ended up with very high AUC_{24}/MIC s which needs the MIC tests to be relooked, technically. On the other hand, the vancomycin dose adjustment guidelines need to consider this between and within variations of MIC with its great impact on AUC_{24}/MIC .

Keywords: Vancomycin; Area under curve; Minimum inhibitory concentration; Bayesian analysis

Consumption of Different Brands of Milk and Eggs Available in Sultanate of Oman: A Survey Study

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Abstract

In the production of milk and eggs, some producers have used antibiotics for diseases prevention, treatment and as growth enhancers. The purpose of this study was to measure the consumption of milk and eggs, compare it between different imported and locally available brands and knowledge of people about the usage of antibiotics in the animal farms. A questionnaire listing these points was circulated by mails and social media. The results showed that more than 50% of the studied population was using fresh and ultra-heated milk (UHT). Mazoon and Almarai were the most popular brands being used compared to others. Around 80% of people consumed at least 1 egg per a day. Around 25% of the studied population didn't know that farmers used antibiotics in animal farms. Moreover, 43% people didn't have knowledge about the presence of antibiotic residues in milk and eggs. Around 9% and 8% of the studied population got intolerance or unwanted effects after the consumption of milk and eggs, respectively. In conclusion, this survey highlighted the importance of studying the antibiotic residues in milk and eggs and will help in the sample collection for the ongoing research on investigating the antibiotic residues in milk and eggs.

Keywords: Milk, Egg, Consumption

Formula Optimization and In Vitro Evaluation of Purified Extract of *Azolla Microphylla* and *Moringa oleifera* Cream Using D-Optimal Mixture Design

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Abstract

Premature aging occurs due extremely the aging process. Continuous exposure of reactive oxygen species (ROS) and ultraviolet (UV) rays from sunlight trigger skin aging through several enzymes activation that contribute to skin aging, such as collagenase, elastase and hyaluronidase. These enzymes lead skin wrinkle, stiff, lose elasticity and hyperpigmentation. The aim of this study was to determine the total flavonoid and phenolic content of purified extract of *Azolla microphylla* and *Moringa oleifera* and to determine the optimum formula for the novel anti-aging formulation for these extracts using D-optimal mixture design, design expert software 13 version. Then proceed with determining the antioxidant activity, sun protection factor (SPF) value and inhibition of enzymes associated with anti-aging (collagenase and elastase). The optimal formula was then tested for stability by centrifugation and cycling test using the one sample t test. The total flavonoid content of the purified extract of *Azolla microphylla* was higher than that of *Moringa oleifera* (12.68 ± 0.24 mgQE/g and 7.88 ± 0.05 mgQE/g respectively), while the total phenolic content of both extracts was almost the same (7.29 ± 0.03 mgGAE/g and 7.99 ± 0.03 mgGAE/g). The in vitro antioxidant activities of *A. microphylla* and *M. oleifera* were tested using DPPH assays, resulting in extremely high antioxidant activity ($IC_{50} < 50$ ppm). The combination between both extracts yielded UV rays ultra protection (SPF > 15). The inhibitory effect of combinations extracts (500+500 and 1000+1000 g/mL) is almost equal with phenanthroline as anti collagenase inhibitor (>90%). The combination extracts generated synergism activity as a collagenase inhibitor. The combinations extracts particularly resulted in inhibitory effect on elastase and tyrosinase. Formula optimization was carried out by varying the composition of Span 80 and Tween 80 in nine formulas then were analyzed for organoleptic response, homogeneity, spreadability, pH, and viscosity. Parameters of spreadability and viscosity were determined as significance parameters for determining the optimum formula. Optimization was carried out with an importance level of 3 (+++) for both parameters with a spreading power range of 4.26 - 6.9 cm and a viscosity of 5073-6973 cPs. The optimal formula is determined with a desirability value of 1,000, namely a formula with a ratio of Span 80 and Tween 80 with ratio 1:1 (Formula 3). The results of the four cycles of the cycling test and centrifugation showed good stability, with a shelf life conversion of one year. If the cycling test is extended, it is still possible to get results with a longer shelf life. In conclusion, these findings could be a good baseline for further exploration of novel anti-aging agents from natural resources, especially *Azolla microphylla* and *Moringa oleifera*.

Keywords: *Azolla microphylla*, *Moringa oleifera*, anti-aging, D-Optimal mixture, Antioxidant, SPF

Morphometric and Molecular Analyses of Mahseer Fish (Torinae: Cyprinidae) in Progo River, Central Java, Indonesia

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Abstract

Mahseer fish (Torinae: Cyprinidae) is a group of native organisms in the upstream ecosystem in South Asia and Southeast Asia. The genera of Mahseer fish were recognized in Indonesia only *Tor* and *Neolissochilus*. Among those genera, Mahseer fish *Neolissochilus* only recorded in the North Sumatera, while *Tor* Mahseer has wide distribution in Sumatera, Borneo and Java. Taxonomic status of Mahseer in Java has recognized only *Tor* genus which consist of four species *Tor douronensis*, *T. tambra*, *T. tambroides* and *T. soro*. Whereas *T. soro* still doubted their valid name on the genus level. This study aimed to examine the taxonomic status of Mahseer fish in Progo River and Cipunegara river by comparing the morphometric characters and molecular marker of Cytochrome oxidase B (Cytb). The morphometric analysis shows both Mahseer populations mostly in one group of PCA quadrants. Meanwhile, the phylogenetic construction showed different sister clades of both Mahseer populations. The Cytb sequence of SB 10 sample from Cipunegara river grouped in clade sister with *T. tambroides*. Meanwhile, the SB 27 sequence Progo sequence shows a monophyletic group with *Osteochilus*, *Rasbora*, *Barbodes* and *Hampala* clade groups. The discrimination of phylogenetic analysis from both Mahseer populations indicate cryptic species of Mahseer in the Progo river population due to demographic history and intergeneric hybridization events. According to the morphometric and molecular analysis of both populations, the Mahseer fish from Progo river belong to the *Tor* genus.

Keywords: Mahseer, Cytb, Morphometric, Torinae

Review: Exploring the Potential of Designed Multiple Ligands (DML) Strategy with Quinolones for Targeting Multiple Ligands in Cancer Therapy

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Abstract

Quinolones are a group of medications that were initially created as antibiotics but have since been found to have anti-cancer capabilities. The pyridin-4-one-3-carboxylic acid serves as the building block for the chemical structure of quinolones and is connected to another six-membered ring at positions 5, 6, and 7. A few examples of slightly different ring systems on which quinolone derivatives are constructed include cinnolines, pyrido-pyrimidine, and bio isosteres cores. Notably, the majority of quinolone derivatives function as topoisomerase inhibitors, whose primary targets in the fight against cancer are type I (TOP1) and type II (TOP2 and TOP2 enzymes). Multi-target-directed ligands (MTDL) use a single chemical substance to affect several ligands or targets connected to a disease in order to boost efficacy or safety. In recent studies, many novel quinolones have adapted this strategy by targeting many cancer ligands, including topoisomerase, tyrosine kinase, tubulin polymerisation, and formation of G-quadruplex. Moreover, improvement of the effectiveness of anticancer quinolones also have been observed by conjugation of the compounds with metal complexes such ruthenium (III), boron, and copper (II). In the case of dual inhibitors, most of the substances target topoisomerases along with additional targets such as histone deacetylases (HDAC), telomerase, topoisomerases I, microtubules, kinases, Hsp90, and proteasome. Some of these hybrids, such as CX-5461, Q84441, and A-74441, have been shown to be successful against solid tumours and have an improved safety profile. Interestingly, there is also an increase in hybrids of quinolones in the form of antibody-drug conjugates (ADCs) therapy. In this review, the current quinolone hybrids and DML strategy against a range of targets will be examined with the hope that the insights obtained will aid in the development of novel quinolone derivatives for the treatment of cancer.

Keywords: Quinolones, Anticancer, Topoisomerase inhibitors, Tyrosine kinases, MTDL, Hybrids, Cancer therapy

Assessing Medication Adherence and Cardiovascular Outcomes Among Patients After Acute Coronary Syndrome Hospitalization

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Abstract

Adherence to a medication regimen in postmyocardial infarction patients is one of the most significant challenges of secondary prevention in cardiovascular medicine. Acute Coronary Syndrome (ACS) is a heart disorder with high morbidity. This study aims to collect comprehensive and detailed information about the relationship between medication adherence (adherence to guideline-recommended preventive medications and patient adherence) and clinical outcome. This cross-sectional study was conducted in the cardiac clinics at two hospitals in Indonesia. A random sample of ACS patients who were discharged on a regimen of secondary preventive medications was included in this study. Drug adherence was assessed as PDC (proportion of days covered calculated with drug use of one DDD) for different drug groups. Statistical analysis was used to quantify the relationship between medication adherence and cardiovascular outcomes. The highest level of patient adherence was in the high category, as much as 82,7%, and adherence to guideline-recommended preventive medications was 95%. There is no significant relationship between the level of adherence to medication use and the appropriateness of therapy on the therapeutic outcome of MAP, HR, and complications/ADR ($p > 0.05$). Medication adherence is still a therapeutic problem in patients, so it needs to be a concern to increase the efficacy and safety of drug use among patients after acute coronary syndrome hospitalization.

Keywords: Acute Coronary Syndrome, Cardiovascular Outcome, Guideline-recommended Preventive Medications, Patient Adherence

***Schizostachyum caudatum* Backer Ex Heyne: A Sacred Bamboo from the Foothills of Mt. Pesagi, West Lampung, Indonesia**

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Abstract

An ethnobotanical study was undertaken to inventory indigenous knowledge related to the use of wild bamboo belonging to the genus of *Schizostachyum* by the locals in the foothills of mount Pesagi, West Lampung, Sumatra, Indonesia. The methods used in this research were descriptive exploratory with qualitative and quantitative methods. Data collection was conducted with a semi-structured interview with local informants, followed by field observation and bamboo materials collection. The informants were people who have knowledge about bamboo and were selected by purposive snowball sampling. The data were analyzed using quantitative ethnobotanical analysis. The finding revealed that there are three species of bamboo used by locals in the foothills of Mount Pesagi, namely *Schizostachyum caudatum*, *S. bamban*, and *S. brachycladum*. According to the finding, *S. caudatum* had the most usages (URs) and obtained the highest indexes of Cultural Significance (CIs = 4.786), while *S. brachycladum* and *S. bamban* obtained 0.786 and 0.643 respectively. It indicates *S. caudatum*, well-known as Kawoh Bingkok by the locals, is most related to and engaged with the sociocultural. The culms of this bamboo were used to make a stick pole and used for a traditional ceremony (Sekugha). Local people considered this bamboo sacred and offered protection against evil influences. Furthermore, they believe anyone who retained it would be endowed with dignity, a strong body, and a calm face. The bad spirit appears to be associated with the body's response to oxidative chemicals. Hence, Kawoh Bingkok may contain chemical compounds that act as an antioxidant, and it will serve as a basis for future studies to discover high-potency antioxidants in bamboo.

Keywords: Antioxidant Source, Bambusoideae, Ethnobotany, *Schizostachyum*, Wild Bamboo.

Concomitant Exposure to EMF from Mobile Phones, Fructose Drinking and 7,12-Dimethylbenz [A] Anthracene Coalesce for Early Onset and Higher Incidence of Mammary Tumors in Adolescent and Young Adult Female Rats with Development of Insulin Resistance

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Abstract

EMF from mobile phones (IARC Group 2B) and 7,12-Dimethylbenz[a]anthracene (DMBA; IARC Group 1) are known inducers of mammary carcinogenesis adult females, but their cumulative role in fructose (15%) drinking growing females is not established. This study aims to investigate the cumulative role of fructose drinking, EMF and DMBA on mammary carcinogenesis in growing female rats. Weaned female Wistar rats, were randomly divided into five groups-NOR, DMC, DFC, DEC and FED and exposed to (i) normal drinking water and chow diet ii) DMBA (5 mg/rat/week x 6 weeks, po) iii) DMBA (5 mg/rat/week x 6 weeks, po) and fructose drinking solution (15%)+chow diet, *ad libitum*, (iv) DMBA (5 mg/rat/week x 6 weeks, po) and EMF from mobile phones (1600 MHz, 2 Hours/day/rat), and (iii) DMBA (5 mg/rat/week x 6 weeks, po) and EMF from mobile phones (1600 MHz, 2 Hours/day/rat) and fructose drinking solution (15%)+chow diet, *ad libitum*. Animals were assessed for tumor characteristics (latency, incidence), preterm mortality, physiological parameters (body weight, food intake, water/fructose consumption), insulin resistance parameters. At the end of eighteen-week study, the tumor tissues were processed to study ultrastructure via TEM, mitochondrial energetics and health markers were studied in serum. Tumor incidence was highest in FED (75%) vs DMC (61.54%). DEC and FED had reduced latency vs DMC ($P < 0.05$). The mortality was 50% in DEC and 42.85% in FED vs DMC (23%). No significant difference in tumor burden and volume seen in DMC vs FED. Significant development of insulin resistance and suppressed mitochondrial enzyme activity was observed in FED group vs DMC. FED group presented with significant degeneration of mitochondria along with vacuolated space and edematous changes in tumor ultrastructural analysis. To conclude, unhindered fructose drinking (15%) and EMF from mobile phones cumulatively with 7,12-Dimethylbenz[a]anthracene led to early onset and higher incidence of mammary gland tumorigenesis with perturbations in mitochondrial and metabolic markers.

Keywords: Mobile phone, Fructose, Breast cancer, Insulin resistance, Emf

Antibacterial Activity Clay Liquid Soap of Combination Bentonite and Pineapple Peel Ethanolic Extract (*Ananas Comosus* (L.) Merr.) against *Pseudomonas Aeruginosa* and *Bacillus Subtilis*

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Abstract

In modern life, cleaning najis by using clay, is not practical. It is necessary to formulate clay liquid soap with pineapple peel extract (*Ananas comosus* (L.) Merr.) as an antibacterial for cleaning mughallazah najis. Bentonite is one of clay that has antibacterial properties. Pineapple peel extracts contain antibacterial compounds, there were flavonoids, tannins, and bromelain enzymes. The bromelain enzyme has antibacterial activity in all bacterial strains, both aerobic and anaerobic. This study aims to determine the physical quality, stability and antibacterial activity of the clay liquid soap with pineapple peel extract (*Ananas comosus* (L.) Merr.) against *Bacillus subtilis* and *Pseudomonas aeruginosa*. Pineapple peel extracts was made by maceration and then formulated into clay liquid soap. Clay liquid soap was made using pineapple peel extract in four formulas 0%, 1,56%, 3,12%, and 6,24% (F1, F2, F3, F4). The physical characteristics of the formula were observed through organoleptic and homogeneity, specific gravity, pH, viscosity, foam stability, and cycling tests. Antibacterial activity was determined using disk diffusion against samples of gram-positive bacteria *Bacillus subtilis* and gram-negative bacteria *Pseudomonas aeruginosa*. The physical properties of the clay liquid soap combination bentonite and pineapple peel ethanoic extract have the organoleptic, homogeneity, pH (7.48±0.02, 7.12±0.0, 6.95±0.03, 6.65±0.01), specific gravity (1.07±0, 1.07±0, 1.06±0, 1.06±0.01, 1.06±0.01), viscosity (2066±15, 2500±17, 2843±21, 3827±6) meet the requirements, while the foam stability test do not meet the requirements. The results of the cycling test showed that there were changes before and after the fourth cycle (one cycle of 24 hours), however, the pH and viscosity data obtained after the test showed that they were still included in the SNI 2588:2017 and SNI 4085:2017 criteria. Clay liquid soap with pineapple peel extract has antibacterial activity against *Bacillus subtilis* and *Pseudomonas aeruginosa* bacteria with the inhibition zone included in the strong-very strong category.

Keywords: Clay liquid soap, Pineapple peel extract, Antibacterial, Mughallazah najis, Bentonite .

Identification of Dual PDE4/5 Inhibitors using Pharmacophore Based Virtual Screening

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) is a progressive airway obstruction due to inflammation of the mucosa layer. SABA is the first-line treatment while LAMA+ LABA is a maintenance therapy. A combination of LABA+ ICS is commonly used in treating COPD patients to reduce the mucosa layer inflammation. In order to obtain a desirable result, the training set were collected from literature review. All the compounds were drawn using ChemDraw Pro 12.0. All the ligands were converted into 3D structure using Ligand Scout 4.4. Ligands were clustered according to their similar pharmacophore properties. Pharmacophore models were developed from each cluster. Optimization of pharmacophore models were made to obtain the best pharmacophore model. Pharmacophore models were validated using test sets and decoy set. The validated pharmacophore models were then screened using Universal Natural Products Database (UNPD). The result of the PDE 4 inhibitor pharmacophore model has a sensitivity of 0.71 and specificity of 0.78. GH score is 0.19. ROC curve is 0.78. Meanwhile, PDE 5 inhibitor pharmacophore model has shown a sensitivity of 0.88 and specificity of 0.49. GH score is 0.13. ROC curve is 0.73. In short, these two models shared the same features i.e., hydrogen bond acceptors and aromatic rings, which indicate these two features were important in inhibiting PDE4/5 enzyme simultaneously.

Keywords: Dual inhibitors, Pharmacophore-based, Virtual screening, COPD, Inflammation of mucosal layer.

Possible Therapeutic Effects of Polyherbal Formulation on Primary Dysmenorrhea through Leukotriene E4 Pathway

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Abstract

The present study aimed to identify whether the polyherbal formulation MM-15 exerts possible therapeutic effects on primary dysmenorrhea through LTE4 pathway. Thirty non-pregnant female mice were employed in this study. They were randomly assigned into five groups: negative control, MM-15 (50mg/kg), MM-15 (100mg/kg), MM-15 (200mg/kg) and positive control group. After completing the treatment on fourth day, the blood was collected from the mice and undergo centrifugation to obtain the blood plasma for ELISA test. During the test period, LTE4 ELISA kit were used to quantitatively determine the concentration of LTE4. Besides, SPSS ANOVA test and Tukey Post-Hoc test were used to determine the statistical significance difference of LTE4 concentration in each group. Through this, the effect of polyherbal formulation MM-15 on primary dysmenorrhea via LTE4 pathway can be determined. Based on the findings in ANOVA test, there is no significant difference in the mean blood plasma LTE4 concentration between the control and treatment groups because the p-value is greater than 0.05. Besides, the findings in Tukey Post-Hoc test shows that none of the groups is significantly different from the other groups as all the p-value are greater than 0.05. It can be stated that the concentration of LTE4 and primary dysmenorrhea is not significant. It can be stated that primary dysmenorrhea is not mainly demonstrated via the LTE4 pathway. Hence, the used of polyherbal formulation MM-15 has no significant therapeutic effects on primary dysmenorrhea via the LTE4 pathway.

Keywords: Primary dysmenorrhea, Polyherbal formulation MM-15, LTE4 pathway

Identification of Dual PDE4/7 Inhibitors using Pharmacophore Based Virtual Screening

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Abstract

Autoimmune diseases and chronic inflammatory diseases, such as chronic obstructive pulmonary disease (COPD), are becoming more prevalent worldwide, posing significant challenges to global health. Phosphodiesterase 4 (PDE4) inhibitors that can be used to treat COPD present withdrawal symptoms such as emesis, nausea, and gastrointestinal disturbance. Recent studies have demonstrated that the simultaneous inhibition of PDE4 and phosphodiesterase 7 (PDE7) can regulate both pro-inflammatory and immune T-cell function, which is advantageous for treating various inflammatory diseases. The three-dimensional structure of compounds with inhibitory activity on the PDE4 and PDE7 enzymes were generated by LigandScout 4.4.9. Then, training sets and test sets were assigned at random. For PDE4 inhibitors, 13 compounds were chosen for the training set, and 7 compounds were selected for the test set. In contrast to PDE7 inhibitors, a training set of 16 compounds and a test set of 4 compounds were chosen. Two pharmacophore models were generated using the training set and the test set. Validation of pharmacophore models were carried out by using decoy sets. Virtual screening of the pharmacophore model was performed using the UNPD database to identify the active molecules that can bind to a specific target. The identified molecules were docked against the PDE4 and PDE7 enzymes. Visualisation of the binding interactions was performed, and the best-performing compound was chosen for further modification to increase its binding affinity. The pharmacophore validation resulted in a GH score of 0.19 for the PDE4 inhibitor pharmacophore model and 0.27 for the PDE7 inhibitor pharmacophore model. After Molecular docking, it was discovered that UNPD98199 had the highest binding affinity for both protein structures and structural modifications were made to enhance the interaction. Compared to UNPD98199, the modified compound, compound 16, exhibited a 15.2% binding affinity for the PDE4 enzyme and a 1% binding affinity for the PDE7 enzyme. Future research could be executed based on compound 16 such as synthesising and testing their biological activities through experimental validation. In drug discovery, applying ligand-based pharmacophore modeling can generate a good pharmacophore model to identify a novel ligand capable of binding to dual PDE4/7 enzyme.

Keywords: Phosphodiesterase 4, Phosphodiesterase 7, Pharmacophore Based Virtual Screening, Dual PDE4/7, COPD

Comparison of Different Extraction Methods to Determine Thymoquinone Contents in the Seed of *Nigella sativa* L. and Evaluation of its DPPH Radical Scavenging Activity

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Abstract

This study aimed to investigate the effects of different extraction methods on the content of thymoquinone using HPLC and UV-Vis spectroscopy. To investigate the antioxidant activities of thymoquinone by measuring the free radical scavenging activity. To identify the functional groups of thymoquinone using FTIR analysis. One gram of powdered black seed was added to 20 mL of solvents (hexane and methanol) into a conical flask and mixed. The mixtures were extracted by different methods which were maceration, percolation, and ultrasonic-assisted extraction. In the percolation method, the mixtures were placed in a water bath of 40 °C for 4 hours whereas, for maceration, the mixtures were left at room temperature for 4 hours. On the other hand, the mixtures were placed in an ultrasonic bath at room temperature for 2 hours in ultrasonic-assisted extraction. The extracts were centrifuged at 4000 rpm at 4 °C for 10 minutes and filtered. The extracts were then analyzed qualitatively and quantitatively by a validated method which was HPLC and UV-Vis spectroscopy. The standard thymoquinone was scanned to identify the functional groups present in the chemical structure. On the other hand, the antioxidant activity was measured by DPPH radical scavenging. In HPLC analysis, the maceration method with hexane extracted the most content (1.5299mg) of thymoquinone. On the other hand, in the UV method, the percolation method with methanol extracted the most content (9.1019mg) of thymoquinone. The free radical scavenging activity was observed highest (95.6891%) in methanol extracts from the percolation method. The results in the present study show that hexane extract from the maceration method is the best method to extract the main bioactive component, thymoquinone from *N. sativa* L. seed. Furthermore, the *N. sativa* seed extracts exhibit antioxidant activity.

Keywords: *Nigella sativa* L., Thymoquinone, Extraction methods, DPPH Radical Scavenging Activity.

Effect of Different Extraction Solvents on Thymoquinone Contents of *Nigella Sativa L.* Seeds and Evaluation of the Free Radical Scavenging Activity

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Abstract

The study aims to develop and validate HPLC and UV-visible spectroscopy methods for the determination of Thymoquinone (TMQ) content in different solvent extracts of *N.sativa L.* seed. Evaluation of free radical scavenging effect of different solvent extracts of TMQ was investigated. Extraction of solvent was done by adding 20 ml of the following solvent (hexane, methanol, ethanol, ethyl acetate and water) to one gram of blackseed and in a conical flask, respectively. The mixtures were then incubated on a water bath at 40 °C for 2 and 4 hours, respectively. The mixtures were then centrifuged at 4000 rpm for 10 minutes at 4 °C. The extracts were then quantitatively analyzed using HPLC and UV-visible spectrophotometry. The free radical scavenging activity of TMQ extracts was studied using 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay. The results obtained from HPLC indicate that TMQ extracted using hexane at 4 hours (0.075 mg/ml, $p < 0.05$) was significantly higher compared to other extraction solvents used. The results obtained from UV-vis spectroscopy analysis indicate that the methanol extract at 4 hours (0.00957 mg/ml, $p < 0.05$) was significantly higher compared to other extraction solvents used. Methanol extracts at 2 hours showed the highest free radical scavenging activity (95.8 %) compared to other extraction solvents. The results obtained show that hexane extracted the most TMQ at 4 hours. Methanol extract demonstrated the highest free radical scavenging activity.

Keywords: Thymoquinone, HPLC, UV-vis spectroscopy, Extraction solvent, DPPH

Depression, Anxiety, and Quality of Life (QoL) in Women with and Without Polycystic Ovary Syndrome (PCOS): A Community-Based Study

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Abstract

The study aimed to determine the prevalence of depression and anxiety symptoms among women with and without PCOS in Klang Valley, Malaysia, and focused on determining the association between depression, anxiety, and health-related QoL. A descriptive cross-sectional study was conducted with women from Klang Valley, Malaysia using a self-completion questionnaire. Respondents were selected by a convenience sampling method in public areas and outside of shopping malls. Study tools include clinical evaluation-related questions, established HADs, and MPCOSQ. Respondents were classified as undiagnosed PCOS with fewer than four symptoms, suspicions with four to eight symptoms, and diagnosed with more than eight symptoms. A score range of 0 to 3 in both anxiety and depression sub-scales in the HADs tool. Higher scores represent higher symptom levels for both sub-scales. Respondents with a score equal to or above 11 are considered to have abnormal levels of depression and anxiety. The MPCOSQ consists of 30 items with a 7-point Likert scale ranging from 1 = "maximum impairment" to 7 = "no impairment". Domain with lower mean scores represents worse QoL. A total of 550 people were polled for this study. 81 (14.8%) of respondents had been diagnosed with PCOS, 73 (13.3%) were suspected of PCOS and 396 (72%) of respondents were not diagnosed with PCOS. The finding of the study revealed that 50 (68.5%) of the respondents with PCOS were having a higher level of anxiety compared to 6 (1.3%) of the respondents without PCOS. Also, 21 (28.8%) of the respondents with PCOS reported a higher level of depression compared to 17 (3.6%) of the respondents without PCOS. The study finding revealed a significant association between PCOS and the level of anxiety and depression (p-value <0.001). The mean scores of the six domains in the MPCOSQ were reported lower in respondents with PCOS than respondents without PCOS. Abnormal weight gain was the most impacted domain among respondents with PCOS. Study findings will be beneficial in the early detection and management of psychological distress whilst improving health-related QoL among PCOS women. Future studies should be considered in the aetiology assessment and management of PCOS-related psychological distress.

Keywords: Polycystic ovary syndrome; prevalence; anxiety, depression; quality-of-life

Preventive Effect of Vitamin E on Stress Dysregulation in Acute Alcohol-Withdrawn Mice

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Abstract

According to World Health Organisation (WHO), 3 million people lose their lives as a result of the dangerous use of alcohol every year. There are 230 distinct diseases that alcohol contributes to. However, the detrimental effects of alcohol on human health are still underestimated by society. Alcohol use disorder (AUD) causes decreased capability to regulate alcohol use regardless of negative social, professional or health effects. Acute alcohol withdrawal syndrome occurs when alcohol is withdrawn in chronic alcoholics including stress dysregulation and depression. Even though the precise pathway is still unknown, oxidative stress is believed to be the cause of these detrimental consequences. Therefore, numerous researches have been done to discover whether antioxidants help to minimise mood disorders once ethanol is withdrawn. This study is designed to examine the neuroprotective effect of vitamin E, a well-known strong antioxidant in the form of alpha-tocopherol against ethanol withdrawal-induced mood disorders in mice. Male ICR mice were administered with repeated ethanol treatment (2g/kg, i.p.) either alone or together with vitamin E (50mg/kg or 100mg/kg, p.o.) for 10 repeated sessions prior to behavioural tests, i.e. in open field test (OFT), social interaction test (SIT) and tail suspension test (TST) for investigation of depressive and anxiety-like behaviours. Acute withdrawal from repeated alcohol intake resulted in decreased exploratory behaviour in OFT, decreased interaction with stranger mice in SIT and increased immobile time in TST. Co-treatment with vitamin E at 100 mg/kg significantly ameliorated these phenotypes. Vitamin E decreases ethanol withdrawal-induced stress-dysregulation in mice.

Keywords: Vitamin E, Stress dysregulation, Depression, Alcohol withdrawal, Alcohol use disorder

Course Satisfaction and Perception of Malaysian Provisionally Registered Pharmacists Towards their Training: A Nationwide Study

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Abstract

In Malaysia, all pharmacy graduates are required to undergo a one-year Provisionally Registered Pharmacist (PRP) training in either private or public premises. Due to lack of a comprehensive, nationwide study that covers both public and private of training for the PRP, including government hospital, private hospital, government health clinic, community pharmacy, manufacturing pharmaceutical industry, non-manufacturing pharmaceutical industry, research, and development (academia), a nationwide study is conducted. This study aims to assess the course satisfaction and perception of Malaysian Provisionally Registered Pharmacist towards their training in different settings. A cross-sectional nationwide study was conducted among Malaysian PRP who started their PRP training at least 6 months ago and those who finished their PRP training within the past 2 years using a self-administered questionnaire. A total of 255 PRPs participated in the survey. On the basis of the response received, most of the respondents felt that the one-year training period was sufficient. More than 30% of the respondents from government sectors opined that the logbook is too complicated and some logbook requirements are hard to achieve. Most of the respondents are required to do extended hours except for the pharmaceutical industry. In conclusion, most of the respondents were satisfied with the PRP training in Malaysia. However, there is still some inconsistency of quality in PRP training programs in different settings such as the lack of important facilities on certain premises. The findings of this study indicate some suggestions and factors that affect PRP's job satisfaction. Hence, this can be used as an indicator for further improvement of current PRP training.

Keywords: Provisionally Registered Pharmacists (PRP); PRP Training; Pharmacist; Malaysia; Pharmacy

Development of Gold Nanoparticles for Phytochemical Delivery

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Abstract

The phytochemical tetrahydrocurcumin (THC), a major metabolite of curcumin, demonstrates higher anticancer activity, systemic bioavailability, and stability than curcumin itself. However, the poor aqueous solubility of THC causes it to be susceptible to oxygen and is poorly absorbed in the gastrointestinal tract. Therefore, a delivery system is needed to address the delivery issues of THC. The gold-copper nanocomposite (Au-CuNP) is a good candidate in drug delivery, it has been shown to have anticancer and antibacterial effects with the advantages to decrease the cost of gold and enhance the stability of copper. In this study, the nanocomposite composed of gold and copper alloy was used to design a THC delivery system. The Turkevich method was used to create a bioengineered Au-CuNP system for delivering the herbal phytochemical THC. A UV spectroscopy, FTIR analysis, drug entrapment efficiency, and zeta sizer were used to characterise the prepared bioengineered nanocomposite system. To confirm the biological property, xCELLigence real-time monitoring of Caco-2 cell cytotoxic activity of THC loaded gold-copper nanocomposites (THC Au-CuNPs) was performed. Au-CuNPs in 1:1 ratio was selected to prepare the THC delivery system. The amount of THC loaded was optimised by selecting 2 mg THC due to the highest possible amount of drug loading with optimum nanoparticles size character. FTIR analysis showed the THC was successfully loaded in the delivery system. The mean particle diameter of THC Au-CuNPs was 248.8 nm, indicating the formation of nanocomposites successfully. The cell culture studies showed that the THC Au-CuNPs have significant cytotoxic activity on Caco-2 cell lines. In conclusion, the anticancer activity of the THC Au-CuNPs was confirmed in this study.

Keywords: Gold nanoparticle, Copper nanoparticle, Tetrahydrocurcumin, Nanocomposite

Cosolvency of Green Solvents for Solubilizing for Polyphenol and Flavanone

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Abstract

Green chemistry has made considerable advancements in recent decades, garnering a lot of academic interests as viable alternatives to hazardous chemicals. Pharmaceutical and chemical industries started to take a step for green chemistry due to its advantages such as decreasing waste and cost. The most straightforward and direct way to apply green chemistry in pharmaceuticals is to use environmentally friendly, nonhazardous, reproducible, and efficient solvents in drug synthetic chemistry research. The main objective of this fundamental research is to identify the best green solvent for the Polyphenol and Flavanone formulation. Solubility test was conducted to identify the most suitable green solvent. Green solvents include polyethylene glycol 200, polyethylene glycol 400, C12-15 alkyl benzoate, tween 20, poloxamer 188, and dimethyl isosorbide. Among the selected green solvents, polyethylene glycol 200, 400, and dimethyl isosorbide were found to be suitable for dissolving polyphenol and flavanone to prepare oral formulations. At the same time, we found that the amount of polyphenol and flavanone dissolved in the selected solvents varied based on the functional groups present in the polyphenol and flavanone derivatives. The solubilized phytochemicals in the green solvent were tested in Caco-2 cells to find their suitability to prepare oral supplementary solutions. In conclusion, the suitable green solvent for polyphenol and flavanone was identified for preparation of an oral supplementary solution to improve their bioavailability.

Keywords: Green solvents, Polyphenol, Flavanone, Cosolvency, Solubility

Design and Evaluate the Impact of an Online Educational Game on Breast Cancer Awareness

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Abstract

Breast cancer is one of the world's most prevalent cancer and the most common type of cancer in Malaysia. Interestingly, breast cancer in young women is more aggressive compared to older women and the survival rate among these groups of individuals is poor. Thus, breast cancer awareness is essential among young women as early detection is possible and treatment will be effective during which the disease is curable. Hence, the purpose of this study is to design and evaluate the impact of an educational game on breast cancer awareness among female university students in Malaysia. This is a one-group pre-and post-intervention study design trial. It was conducted in Private and public higher education institutions around Malaysia. An online education game was created and used as the intervention. A self-administered questionnaire was administered to the participants during the pre-and post-intervention test to evaluate the online educational game on breast cancer awareness. A total of 52 responses were collected. The mean age of the participants were 21.98 (SD = 1.896) years. The findings shown that there is a statistically significant median increase ($p < 0.05$) in breast cancer knowledge scores among participants in the post-intervention. A median increase in breast cancer knowledge score of 6 was shown when participants were exposed to the online education game (24.00) compared to before they were exposed to it (17.00). The use of online educational games was effective in raising awareness of breast cancer among university students. Online games can be used as a health educational tool to promote awareness of a topic of interest, as digital games can be accessed with ease, game content can be tailored made or updated, and improve participant engagement in learning.

Keywords: Breast cancer awareness, Online educational game, Serious game, Female university student

Scintigraphic Evaluation of Topical Therapeutic Interventions, Using ^{99m}Tc -Sulfur Colloid as 'Mock Venom' Agent, in Preclinical Model of Peripheral Snakebite Envenoming

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Abstract

Snakebite envenoming is one of the major public health concerns across many tropical and subtropical countries, accounts for significant mortality (~138,000 deaths/year). Nearly 75% snakebite fatalities occur far from primary hospital settings leading to delay before antivenom can be administered, particularly in rural areas and for military personnel deputed in remote combat-areas. First-aid measures like pressure bandage immobilisation is a tenuous procedure and has suboptimal efficacy in managing snakebite casualties. Present study is based on the fact that majority of venom components are high molecular weight toxins, which enter the bloodstream through lymphatic system. We have therefore prepared a topical formulation consisting of a combination of lymphatic modulators and evaluated its efficacy in delaying lymphatic transit time (LTT) using lymphoscintigraphy. Topical gel formulation(s) were prepared in suitable vehicle containing varying conc. of Nifedipine, Lidocaine and Sodium nitroprusside using Carbopol®940 as a gelling agent. The test formulations were characterized by *in-vitro* parameters like viscosity, homogeneity, extrudability, spreadability, melting point, FTIR and stability studies. Thermostability was assessed by TGA and DSC analysis, while surface morphology was studied using SEM. Efficacy of test formulations was assessed using lymphoscintigraphy by applying the test gel (3g) over rats lower body immediately within 20sec of administering intradermal injection of the 'mock-venom' agent into the tail of rats. Any modulation in LTT from periphery to systemic circulation after gel application was assessed by taking dynamic gamma-scintigraphy images of 60sec each till 1h post-injection of the mock-venom. The pH of different test formulations was in range of 5.1±0.2 to 6.2±0.1, while viscosity was between 15696±2.5 to 69870±1.1(cp). Spreadability values ranged between 5.2±0.3 to 7.2±0.3 (gcm/s). All combinations exhibited good stability behavior and homogeneity. Lymphoscintigraphy studies showed significant retardation in LTT (~20-50min) post-application of test formulations, as seen by reduced uptake of ^{99m}Tc -SC by the lymphatic system in comparison to control ($P<0.05$). The findings suggest that topical application of lymphatic modulators could potentially be used as an adjunct first aid measure in snakebite envenoming. Study also indicates that lymphoscintigraphy could be a useful tool in evaluation of such therapeutic strategies in preclinical models.

Keywords: Peripheral snake envenomation; preclinical models; lymphoscintigraphy; ^{99m}Tc -sulfur colloid; lymphatic transit time.

Formulation And Characterization of Melatonin Based Nanoemulgel for Management of Radiation Dermatitis

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Abstract

About 95% of head and neck cancer patients eventually develop radiation-induced dermatitis (RID) during or after treatment. Chronic RID develops in one out of three patients and can appear up to 10 years after the completion of Radiotherapy (RT). Due to their poor transcutaneous permeation and associated side effects, conventional formulations do not display optimum efficacy, requiring the development of novel nano-preparations exhibiting improved efficacy and effectively managing skin damage. Melatonin based nanoemulgel was prepared by using probe sonicator method containing carbopol®934 as gelling agent. By using pseudo-ternary phase diagrams during preformulation development by varying concentration of oil (olive oil), surfactant (tween 80) and co-surfactant (transcutol HP), thus screening best suitable combination which is effective for radiation dermatitis. The optimized formulation was assessed by *in vitro* characterization namely, FTIR, droplet size, polydispersity index (PDI), viscosity, zeta potential. Further, *in vitro* drug release profile was analysed by UV-spectrophotometer method and release kinetics was evaluated. Mean droplet size of developed formulation was found 178.8nm, whereas Polydispersity index (PDI) showed 0.175. The formulation was thermodynamically stable, compatible to pH of skin and viscosity was found to be in the range of 9100cps. We measured globule size by the zeta potential and found it to be 23.47mv, signify stability of nanoemulsion. Further, *in vitro* release studies showed 98.71±0.99% cumulative release of melatonin (MLT) from nanoemulgel over a period of 24 h. Moreover, drug release profile demonstrated that developed formulation follows Higuchi and Korsmeyer-Peppas model, which indicates non-Fickian drug release from matrix system. An optimized melatonin nanoemulgel preparation was evaluated, with all properties indicating that it would be effective and safe for treating damaged skin following radiotherapy.

Keywords: Radiation, Dermatitis, Nanoemulgel, Radiotherapy, Skin damages

Complementary and Alternative Medicine Usage During COVID-19 Pandemic

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Abstract

Several studies in different countries have looked at their public interest in using Complementary and alternative medicine (CAM) during the COVID-19 outbreak but there is no study conducted in Malaysia. Overall, most populations are interested in taking or have taken CAM during the COVID-19 outbreak as a way to boost their immunity and get rid of the infections. This study was aimed to identify the types and patterns of CAM usage during the COVID-19 pandemic among the general public in Klang Valley and to assess the knowledge, attitude, and practice of CAM during COVID-19 pandemic. A cross-sectional study was conducted using a self-administered questionnaire adapted from a previous study was utilised for data collection. A total of 384 participants were recruited to participate in this study using convenience sampling using the online Raosoft Software. Malaysians aged 18 years old and above, staying in Klang Valley and able to understand English/Malay/Chinese were included in the study; while non-Malaysian, participants aged below 18 years old and who were unable to understand English/Malay/Chinese were excluded from the study participation. Statistical analyses were performed using the IBM SPSS Statistics Version 26. Data was analysed using descriptive and inferential analysis. The prevalence of CAM usage during COVID-19 was found to be 89.3%. where the majority of the responded were aged between 18-30 years old. More than half respondents showed poor knowledge (n=196, 51%), negative attitudes (n=204, 53.1%), and bad practice (n=215, 56%) towards CAM usage. A significant association was found between knowledge and practice (p-value < 0.001). Respondents who had poor knowledge of CAM were more likely to have poor CAM practice. Biologically based therapies are the most frequently used CAM approach during the COVID-19 pandemic. High prevalence of CAM usage was reported during COVID-19. The study findings identified the common CAM utilised during the pandemic. Participants' low knowledge and negative perception may play an important role to influence their poor practices. Thus, these are vulnerable groups, and strategies should be made to educate them through proper counselling and education.

Keywords: Complementary and alternative medicines, COVID-19, Knowledge, Attitude, Practice

Clinical Studies of Traditional Japanese Herbal Medicines (Kampo) in Japan

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Abstract

Japanese Kampo medicine is a traditional medicine with roots in ancient Chinese medicine. Because traditional physicians had been abolished in Japan, the present mainstream of Kampo treatment is that physicians who learned modern Western medicine prescribe Kampo extract products based on Western medical diagnosis. This situation is different from that in other east Asian countries, and the physicians require scientific clinical evidence. Clinical studies were searched from literature databases, clinical trial registry sites, and “Evidence Reports of Kampo Treatment (EKAT)” published by the Japan Society for Oriental Medicine. At the approval of Kampo products, scientific clinical evidence was not required because they have a long-period experience as a decoction. However, in the 1990s, Kampo products became a subject for national reevaluation; double-blind and placebo-controlled clinical trials. At the time, a methodological foundation for conducting clinical assessments of Kampo medicines was established. From 2000 onwards, with the evidence-based medicine era, the field of Kampo medicine also saw many randomized controlled trials, and their evidence was collected and published as EKAT. In the 2010s, post-marketing clinical trials of Kampo products also had to be conducted in this environment due to the need for ethical and scientific assurance. Currently, there are numerous clinical trials of Kampo products being conducted with high-grade trial designs. The situation of Kampo clinical studies reflects the unique history and position of Kampo medical system and Kampo products in Japan.

Keywords: Clinical study, Clinical trial registry, Traditional Japanese herbal medicines, Randomized controlled trial, Reevaluation

Synthesis and Evaluation of In Vitro Bioactivity for Polysubstituted *N*-Arylpyrazole Derivatives

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Abstract

Pyrazole-containing compounds have often offered the flexibility for design and construction of the structural analogs of biomedical interest and also are considered as the attractive targets for organic synthesis. The goal of this work is to prepare a series of polysubstituted *N*-arylpyrazole derivatives utilizing thiophenyl and benzothiophene as bioisostere for investigating the attractive structural targets. Based on the structure-activity study and the biological assay, modified pyrazole compounds were examined the significant inhibitory activity using nasopharyngeal carcinoma (NPC-TW01), human non-small cell lung carcinoma (NCI-H226) and T-cell leukemia (Jurkat) cancer cells by modified MTT method. Scheme 1 shows the synthetic routes and results for the fused thiophenyl/phenylpyrazole and benzothiophene/phenylpyrazole derivatives 5a-d, 6a-d and 7a-d. A series of polysubstituted *N*-arylpyrazole derivatives were synthesized from *N*1-arylsydnone with acetylene and boronic acid via 1,3-dipolar cycloaddition and Suzuki coupling reaction. 2-Thiophenyl, 3-thiophenyl, 2-benzo[*b*]thiophenyl, and dibenzothiophenyl groups were introduced into the *N*-arylpyrazole core as the bioisosteres. Following the structure-activity relationship study, 4-dibenzothiophenyl group was regarded as the best active bioisostere for the improvement of the inhibitory activity. Furthermore, compounds 5d and 7d with dibenzothiophenyl moiety possessed the significant inhibitory activity for NPC-TW01 (32 μ M and 16 μ M) and NCI-H226 (16 μ M and 8.9 μ M) two cancer cells, respectively.

Keywords: Thiophene, Benzothiophene, Pyrazole, Suzuki coupling reaction, Bioactivity study

Contemporary Role of Technetium-99m labelled Dimercaptosuccinic Acid (99mTc DMSA) in Childhood Kidney Conditions – Review and Case Series of Static Planar Renal Scintigraphy

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Abstract

Nuclear medicine scan performed using pharmaceutical compounds tagged with small amount of radioactive tracer has contributed towards improvement of diagnostic imaging services in Malaysia. Dimercaptosuccinic acid labelled with technetium-99m (99mTc DMSA) binds to cortical proximal tubules in the kidneys. Inhouse strict labelling procedure is maintained with percentage of bound 99mTc DMSA kept at least 95%. It provides stable target for high-quality imaging with gamma camera machine at 2-3 hours after intravenous injection. 99mTc DMSA has high sensitivity (90%) for renal parenchymal injury detection and superior resolution compared to other radiopharmaceuticals. DMSA static planar renal scintigraphy is indicated for morphological and functional evaluation of individual kidney and localisation of ectopic kidney. A review of DMSA scintigraphy performed in our centre between 2020 and 2021 was done. Several cases were selected to depict and highlight normal scintigraphy image as well as several other childhood kidney conditions. Usual injected paediatric dose for 99mTc DMSA is 0.05 mCi/kg with typical administered activity at our institution approximately 1.0-2.5 mCi in toddlers. A normal scan shows physiological tracer uptake with homogenous distribution throughout both kidneys in bilateral flank. A case of horseshoe kidney which is a normal variant demonstrates tracer uptake in the midline of abdomen with the lower poles of both kidneys appearing to be connected. In ectopic kidney, there will be no accumulation of tracer at the involved renal fossa associated with ectopic tracer uptake seen commonly in the pelvic region. Other possibilities of absent tracer accumulation in a renal fossa are congenital absent, atrophic, or multicystic dysplastic kidney. Paediatric patients with prior history of febrile or recurrent urinary tract infection may show irregular or wedge-shaped cortical perfusion defects affecting single or both kidneys. In conclusion, we have discussed the contemporary role of 99mTc DMSA in several childhood kidney conditions and their static planar renal scintigraphy findings. 99mTc DMSA will continue to be one of the important investigations for morphological and functional evaluation of the kidneys in paediatric population.

Keywords: DMSA, Scintigraphy, Childhood kidney conditions

Fabrication and Characterization: Natural-Based Caffeine Fast Melting Tablets

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Abstract

The current study aimed to formulate cocoa butter based fast melting tablets (FMTs) using caffeine as an active pharmaceutical ingredient and to perform suitable physical characterization techniques for evaluation. The Caffeine FMTs were formulated using cocoa butter as the base, chitosan as a super-disintegrant, microcrystalline cellulose as a binder, stevia as a natural sweetener and caffeine as an active pharmaceutical ingredient (API). Before the formulation process, the raw cocoa butter was subjected to a series of heating and cooling procedures that aimed to convert it into a more stable polymorph (Form V). This process is known as "tempering". Other excipients were added part by part, including caffeine as an API. A simple freezing method was performed for tablet solidification purposes by storing the formulation in the refrigerator for around 2 hours until it was ready to be unmolded. To evaluate and validate the caffeine FMTs formulation, several characterization techniques were performed, including UV-visible spectrometry, Fourier transform infrared (FTIR) spectroscopy, *in-vitro* disintegration test, *in-vitro* dissolution test and stability studies. Upon a series of formulation optimizations, the F3 formulation showed the most superior characteristics, with a suitable hardness, a short *in-vitro* disintegration time, and an excellent drug-release profile. The F3 formulation also showed pale yellow colour with a shiny appearance, which could enhance the patient's preference. Besides, the λ max of caffeine was observed at 273nm using a UV-visible spectrometer, while the FTIR spectroscopic analysis results showed no incompatibility between drugs and excipients. For the *in-vitro* disintegration test, an average mean of 1.28 mins \pm 0.03512 was obtained. On the other hand, the percentages of cumulative drug release (%CDR) over time were observed using the *in-vitro* dissolution analysis. The results showed that 88.52% of the drug was released within 60 mins, whereas 94.08% of the drug released in 75 mins. In a nutshell, the main goal of naturally based caffeine FMTs is to bring the greatest convenience to all age groups while achieving desired therapeutic outcomes. The use of natural ingredients also able to ensure the maximum cost-effectiveness. All physiochemical evaluation test results fell within the pharmacopoeia specification.

Keywords: Caffeine, Cocoa butter, Fast melting tablets, *In-vitro* disintegration, *In-vitro* dissolution.

Elucidation of Mechanism of Anticancer Activity of Panax Japonicus Using Network Pharmacology and Computational Chemistry

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Abstract

Panax japonicus, one of the herbal medicines belongs to Panax species, has anti-gastric cancer effects, but the specific mechanism is unknown. This research was to identify the molecular targets of Panax japonicus responsible for the anti-gastric cancer activity constituents and to determine their binding activity. Network pharmacology and computational chemistry perspective to predict the combined effects of the constituents of Panax japonicus on gastric cancer, molecular docking to validate the mechanism of action. A total of 116 potential active chemical components of Panax japonicus were collected from TCMSP, HERB, SymMap, TCM@taiwan databases and literature. Targets were collected using TCMSP, PubChem databases, and predicting targets based on drug similarity, pharmacophore similarity and QSAR models on STITCH, SWISS, SEA, Super-Pred, PharmMapper and TargetNet platforms, with a total of 2938 targets. 5655 genes for gastric cancer were obtained in OMIM, Gene Cards and DisGeNET database. The intersection of disease targets and targets from 2 different data sources was regarded as potential targets for the treatment of gastric cancer by chemical components, a total of 286, which were introduced into the SRTING platform to build protein-protein interaction (PPI), network visualization in Cytoscape software, and performed the Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses, finding that TP53, CTNNB1, HSP90AA1, STAT3, TNF, EGFR, and ESR1 were potential targets, potential active ingredients including Ginsenoside Rg1, Ginsenoside Rb1, Ginsenoside Ro, Ginsenoside Rh1, Chikusetsusaponin Iva, Chikusetsusaponin IV, 20(S)-Ginsenoside Rg2, Notoginsenoside R2, Vinaginsenoside R1, Protopanaxadiol, and so on. The mechanism of Panax japonicus anti-gastric cancer may be involved in cancer-related biological functions and signaling pathways, such as nuclear receptors meta-pathway, cellular response to lipid, response to oxygen levels and TP53 signaling pathway. This research predicted the key anti-gastric cancer active components and targets of Panax japonicus through network pharmacology and computational chemistry methods.

Keywords: Network Pharmacology, Panax japonicus, Ginsenosides, TP53

Formulation and Optimization of Microbeads Pharmaceutical Formulation Incorporating Black Cumin Seed Oil (BSO)

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Abstract

Nigella sativa L. (black cumin) is one of the most important spices used in the treatment of respiratory and allergy illnesses. Pharmaceutical formulation incorporated with black seed oil (BSO) can be a promising therapy to manage respiratory inflammation. The present study aims to formulate and optimize BSO encapsulated formulation (microbeads) using natural polymers and their combination for effective delivery. The methodology involves the use of natural biopolymers gellan gum, alginate, and anionic surfactants. Special emphasis was given to formulation variables and pharmacokinetic profiling for the optimization procedure. BSO-loaded beads were prepared by the ionic gelation method. In this method pre gelation liquid of sodium alginate (2-4% w/v) and gellan gum solution (2-6% w/v) was prepared. BSO in different concentrations (10%-50%) was then added to the polymer solution. BSO beads were formulated and characterized using different parameters. The effect of the independent variables on the response variables was studied by response surface plots and contour plots generated by the Design-Expert software. The desirability function was used to optimize the response variables. From the results, the best formulations (the most optimized formulations F 12 and F15) were chosen as they possessed most of the required physicochemical characteristics and sustained drug release properties. Entrapment efficiency and drug release of the optimized batch were found to be above 70%. The optimization, drug entrapment efficiency, and drug release behavior of BSO beads were also done by applying design expertise. It also exhibited sustained drug release in simulated pH. The in vitro release data fitted with higher values in the matrix model and the release was found to be Non-Fickian diffusion (anomalous transport) as the n value is between 0.5 to 1.0. Findings of this study enable the scale-up production of loading BSO and similar bioactive compounds in gellan gum and alginate beads. Hence, the designed system could be advantageous in terms of prolonged release with enhanced bioavailability for a promising therapy.

Keywords: *Nigella sativa*, Black seed oil, Gellan gum, Alginate, Microbeads

Development and Physicochemical Characterization of Green Cosmeceutical Herbal Facial Gel-Cream Containing Green Tomato Locular Gel (GTLG)

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Abstract

Green cosmeceuticals are sustainable skincare products formulated using only biodegradable, naturally derived ingredients aiming to improve various skin conditions while concomitantly preserving the environment. Its rising demand is due to its generally better toxicological profiles with appreciable pharmacological effects as compared to synthetic-based cosmeceuticals with frequently reported adverse reactions. The locular gel extracted from the locular cavities of tomatoes (*Solanum lycopersicum* L.) is an excellent example of a plant-derived ingredient with cosmeceuticals benefits. The partially matured green tomatoes consist of locular gel (GTLG) with numerous bioactive compounds beneficial for skin health may be a potential alternative for chemical active ingredient in the formulation of green cosmeceuticals. This study was undertaken to evaluate the antioxidant and antimicrobial profiles of GTLG and to formulate a green cosmeceutical herbal facial gel-cream with claims of being colour-free, sulfide-free, alcohol-free, paraben-free and SLS-free utilizing GTLG as the active ingredient. The extracted GTLG was subjected to *in vitro* antioxidant assays including 2,2-Diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), antibacterial and antifungal assays. The formulated GTLG-containing facial gel-cream was evaluated for its physicochemical properties (e.g. organoleptic characteristics, pH, spreadability, washability, viscosity) and its stability under freeze-thaw and accelerated conditions. GTLG was found to possess moderate antioxidant capacities at IC₅₀ of 0.6405 ± 0.029mg/mL and 0.061 ± 0.013mg/mL for DPPH and ABTS assay respectively as compared to the positive control, Trolox (IC₅₀(DPPH) = 5.237 ± 0.938µg/mL; IC₅₀(ABTS) = 5.409 ± 0.612µg/mL). Besides, GTLG showed promising antibacterial and antifungal properties against *Staphylococcus aureus* and *Malassezia furfur* in agar well diffusion assay with zones of inhibition of 10.33±0.58mm and 16.00mm respectively. The formulation had vanishing cream properties with cosmetically appealing appearance, smooth texture, homogenous without any signs of phase separation, skin-friendly pH, and good spreadability. It possessed non-Newtonian, pseudoplastic behaviour that facilitates topical application. It was stable throughout the freeze-thaw test and under accelerated stability conditions (40 ± 2°C/75 ± 5% RH). GTLG-containing green cosmeceutical facial gel-cream with antioxidant and antimicrobial potential was successfully developed in line with SDG 3 and 12. Further pharmacological and clinical studies would be conducted to warrant them as clinically tested evidence-based formulations.

Keywords: Green Cosmeceutical Herbal Facial Gel-Cream, Green Tomato Locular Gel, *Solanum lycopersicum* L., Antioxidant, Antimicrobial

2-Benzoxazolinone as Breast Cancer Cells Inhibitor via Estrogen Receptor

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Abstract

Estrogen receptors alpha (ER α) and beta (ER β) is highly expressed in different cancer cells. Inhibition of ERs by small molecules is a promising approach to developing novel anticancer agents amidst increased endocrine therapy resistance. A heterocyclic molecule, 2-benzoxazolinone and its derivatives, found in *Acanthus ilicifolius* leaves, possesses anticancer on varied cancer cell types such as HeLa, MCF-7, A-549, and SW-480. However, the mechanism of its cancer cell growth inhibition is an enigma. This study aimed to unmask the activity of 2-benzoxazolinone to inhibit the growth of the MCF-7 breast cancer cell line via estrogen receptors. The modulation mechanism was predicted by docking molecular of 2-benzoxazolinone toward ER α (PDB ID: 2JF9) and ER β (PDB ID: 5TOA). Subsequently, the MCF-7 cell viability assay was performed to validate the *in-silico* prediction. We preliminary identified the presence of 2-benzoxazolinone in *Acanthus ilicifolius* leaves using high-performance liquid chromatography (HPLC). The binding energy of 2-benzoxazolinone on ER α and ER β exhibited a similar score (-6.3 kcal/mol). 2-Benzoxazolinone showed inhibition toward the MCF-7 breast cancer cell line with IC50 value 35.4 μ M. 2-Benzoxazolinone may be a potent small molecule inhibitor of the MCF-7 breast cancer cell growth via estrogen receptors.

Keywords: 2-Benzoxazolinone, Breast cancer, Estrogen receptor, ER α , ER β

Development of Regenerative Bio-Scaffolds for Periodontitis and Bone Regeneration

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Abstract

Periodontal diseases are the most frequently occurring inflammatory diseases which arises due to plaque or bio film formation in dental region and affects 30-40% population of adults and the elderly. Recently, non-biodegradable membranes are in market, made from polytetrafluoroethylene (PTFE) and titanium which appear to at high risk of postoperative infection and surgery is required to retrieve implants of the same. Therefore, to overcome the above associated problem, biodegradable materials could be highly desirable for the preparation of periodontal membranes to achieve regeneration of periodontal tissue loss. This study aim to develop regenerative and antibacterial bio-scaffolds by the blend of Poly lactic acid (PLA) and gelatin through electrospinning and results shows that acidic degradation of PLA controlled by magnesium oxide which neutralize the acidic degradation and easily absorb in body. The physiochemical characters are successfully achieved which includes water uptake capacity, thickness 100 to 150 micrometers and scanning electron microscopy image. Desired degradation rates were achieved by invitro degradation analysis which mimic regeneration. The above results shows that scaffold efficiently control application area pH and enhance periodontal regeneration capabilities by its porous structure.

Keywords: Bio-Scaffold, Electrospinning, Periodontal, Regeneration,

Role of Chrysin Nanoformulation in Cytotoxicity Study of Colon Cancer

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Abstract

The nano-formulation of chrysin is formulated, characterized and evaluated for the cytotoxic effect. The formulation is prepared by anti-solvent precipitation technique. The characterization of the prepared nano-formulation is done for particle size, polydispersity index, zeta potential, entrapment efficiency, SEM and FT-IR analysis. The cytotoxicity study of the nano-formulation is carried out on HT29 cell lines. The developed nano-formulation of the chrysin showed particle size <100nm and all the other parameters like polydispersity, zeta potential and entrapment efficiency also showed good results. The increased cytotoxic effect on HT-29 cell line was shown by the chrysin nano-formulation. The study performed shows confirmative indication for utilization of Chrysin nano-formulation. The results can be used as the background to further analyze the effect of the formulation on experimental animals.

Keywords: Chrysin, Colon cancer, Nanoformulation, Cytotoxicity.

Investigations on the Gingerols and Shogaols as Potential Selective PDE4B Inhibitors by Molecular Docking Screening

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Abstract

Inflammation is the natural way our bodies respond to infection or injury. However, if it fails to subside, inflammation can damage the body and contribute to several illnesses. Although non-resolving inflammation is not the primary factor, it is still considered to significantly contribute to several diseases such as chronic obstructive pulmonary disease (COPD), asthma, inflammatory bowel disease, rheumatoid arthritis, cancer, neurodegenerative disease, and so on. Phosphodiesterase 4 inhibitor is an established treatment to treat inflammation worldwide. However, the non-selective PDE4 was reported to exhibit adverse reactions such as nausea and diarrhoea. This study aims to identify compounds with higher selectivity for PDE4B over PDE4D and determine their binding mode and interaction through molecular docking. In this present study, three x-ray crystal structures representing PDE4B and PDE4D each were downloaded from Protein Data Bank and redock with their co-crystallized ligand to calculate the RMSD as the validation step for the docking procedure. The protein structures with the lowest RMSD (PDB ID: 3W5E for PDE4B and PDB ID: 3G58 for PDE4D) were docked with gingerols and shogaols. Binding energies were obtained and the ratios between the binding energy of PDE4B and PDE4D were calculated. 10-gingerol had been found to have the lowest binding energy and the highest selectivity of PDE4B compared to PDE4D among the compounds. Thus, the binding interaction was further investigated, and found that 10-gingerol form a hydrogen bond with invariant glutamine residue which is GLN 443 in PDE4B and GLN 535 in PDE4D. Besides, 10-gingerol also formed hydrophobic bonds between PHE 446 in PDE4B and PHE 538 in PDE4D while with isoleucine and phenylalanine residues (ILE410 and PHE414 in PDE4B and ILE502 and PHE506) on the other side. 10-gingerol also showed hydrophobic interaction with non-conserved residues in CR3 region, which is with LEU502 in PDE4B. This interaction was absent with the CR3 region in PDE4D which in turn determined the PDE4B selectivity of 10-gingerol. These results showed that 10-gingerol is a potential candidate as a selective PDE4B inhibitor as a new anti-inflammatory drug.

Keywords: Docking, Phosphodiesterase 4, Gingerol, Shogaol

Antibacterial Activity of Zinc Oxide Nanoparticles Against Gram-Positive and Gram-Negative Bacteria

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Abstract

Antibiotic resistance is a global health care threat. This phenomenon is one of the leading causes of morbidity and mortality worldwide. Therefore, this study aimed to determine the antibacterial activity of green fabricated zinc oxide nanoparticles (ZnO NPs) using ginger, *Zingiber officinale* (G-ZnO NPs) against commonly encountered bacteria, *Staphylococcus aureus*, *Staphylococcus epidermis* and *Pseudomonas aeruginosa*. In this study, G-ZnO NPs were studied along with chemically synthesised ZnO NPs and ginger extract. The growth inhibitory effects of G-ZnO NPs, ZnO NPs and ginger extract (10, 50 and 100 mg/ ml) on the three strains of bacteria were determined through the Kirby-Bauer test. The zone of inhibition was checked and measured after 24 hours of incubation at 37°C. G-ZnO NPs and ZnO NPs demonstrated a dose-dependent growth inhibitory effect on *S. aureus*. The zone of inhibition demonstrated by G-ZnO NPs and ZnO NPs increased from 8.7mm ± 0.6% to 13.7mm ± 0.6% and from 9.7mm ± 0.6% to 15.3mm ± 1.5% respectively, when given at a dose of 10 mg/ml to 100 mg/ ml. For *S. epidermis*, zone of inhibition of 10.3 mm ± 0.6% was only observed for G-ZnO NPs at 100 mg/ ml. *P.aeruginosa*, on the other hand, was insensitive to both G-ZnO NPs and ZnO NPs even at the highest concentration tested. Ginger extract had no growth inhibitory effect on any of the three bacteria strains tested at any of the three concentrations. From the present study, G-ZnO NPs demonstrated antibacterial properties against *S.aureus* and could potentially be the next choice of nanomedicine to treat bacterial infections.

Keywords: Zinc oxide nanoparticles, *Zingiber officinale*, *Staphylococcus aureus*, Antibacterial property, Growth inhibition

An Expedition Towards Formulating Natural Face Serum with *Garcinia mangostana* (Mangosteen)

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Abstract

The admiration for healthy skin has encouraged the cosmeceutical industry to develop quickly. The serum is a cosmeceutical formulation that rapidly absorbs and penetrates the deeper layers of skin with its non-greasy finish and an intensive formula with a very high concentration of active substances. However, several synthetic and harmful substances are used in many of those skin care products. The resulting skin irritations, redness, and itching leave the user with unpleasant experiences. These synthetic chemicals are even harmful to the environment. Hence, the need for an entirely natural formulation for skin health has influenced the researchers to acknowledge the positive impact of *Garcinia mangostana*. It is one of Asia's most well-known tropical fruits and has been the center of attention for many scientists for its anti-aging and anti-inflammatory properties. Based on these properties, this project is aimed to formulate anti-aging face serums using mangosteen herbal extracts and evaluate their physiochemical properties. A combination of magnetic stirring and homogenization techniques was used for the serum formulation at room temperature. The stability of the formulation was satisfactory based on redispersion and pH (4.71) stability results. The serum had 6-7 cm spreadability with around 48% occlusive properties. In addition, the *in-vitro* skin permeation results exhibited the highest absorption within the first 15 minutes of application. The face serum is 100% natural, and free of sulfide, alcohol, microplastics, and parabens. Therefore, this mangosteen face serum is much safer for the consumer and the environment than conventional ones.

Keywords: Face serum, *In-vitro* permeation, Mangosteen, Occlusivity, Spreadability

Possible Therapeutic Effect of Polyherbal Formulation on Primary Dysmenorrhea through Leukotriene D4 (LTD4) Pathway

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Abstract

The current study aims to investigate whether the polyherbal formulation MM-15 exerts possible therapeutic effects on primary dysmenorrhea through the LTD4 pathway. Thirty non-pregnant female mice were employed in this study. Mice were randomly divided into five groups, namely the negative control group (normal saline), low-, medium-, and high-dose treatment groups (50, 100, 200mg/kg) and the positive control group (mefenamic acid 100mg/kg). All mice were administered their treatment through the oral route from the second day to the fourth day. After the fourth day of treatment, blood samples were collected and centrifuged to obtain supernatant for ELISA. Levels of LTD4 from the samples were determined and one-way ANOVA was used to evaluate statistical significance. From this, the therapeutic effect of polyherbal formulation through the LTD4 pathway can be determined. Based on the results from the ANOVA test, there is no significant difference in the mean LTD4 plasma concentration between all groups as P is not less than 0.05. It can be stated that the treatment from polyherbal formulation MM-15 did not reduce mean concentrations of LTD4 plasma levels. It can be concluded that further studies on the therapeutic effects of polyherbal formulations can be investigated through the COX pathway.

Keywords: Primary dysmenorrhea, LTD4 pathway, Polyherbal formulation MM-15

Potential Effects of Tocotrienols on Perimenopausal-associated Depression – A Mini Review

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Abstract

Perimenopausal depression is a type of emotional impairment that affects women between the ages of 56 and 66 before or after menopause. In addition to perimenopause-related endocrine dysfunction, particularly hypogonadism and senescence, the chief symptoms of perimenopausal depression are emotional melancholy, anxiety and stress. Chemical antidepressant medications, such as tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), etc, and hormone replacement therapy are currently used to treat perimenopausal depression. However, these treatments only provide symptomatic relief to patients and have many side effects. While the development of conventional chemical antidepressant medicines for perimenopausal depression is generally slow, natural substances have recently emerged as research hotspots due to their potent therapeutic effects and relatively low risk of adverse effects. Tocotrienols, natural minor components form of vitamin E, are naturally present in many foods like wheat, rice bran oil, and palm oil, help treat perimenopausal depression in several ways, including by reducing oxidative stress damages and low-grade chronic inflammation. In this mini review, the potential antidepressant effects of tocotrienols are discussed from the perspectives of their anti-inflammatory, antioxidant and neurotransmitter regulatory abilities. Tocotrienols were investigated for their potential antidepressant properties utilising a variety of internet databases, including Pubmed and Google Scholar. To date, despite evidence from animal and in vitro studies indicating tocotrienols can reduce the severity of depressive symptoms by scavenging free radicals, reducing inflammation, and guarding against glutamate-induced neurotoxicity in cells, there has been no human clinical research to support this claim. Tocotrienols may be regarded as a potential antidepressant medication, however more clinical research is needed to confirm their impact and probable underlying mechanisms on perimenopausal depression.

Keywords: Vitamin E, Depression, Oxidative stress, Perimenopause, tocotrienols

Potential sensitization effect of kaempferol on ABT-199-resistant hepatoma cells

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Abstract

The first-in-class selective B-cell lymphoma 2 (Bcl-2) inhibitor, ABT-199 (venetoclax), is well-known for having no effect on liver cancer cells. Here, we looked into the effectiveness and underlying molecular mechanisms of kaempferol derived from persimmon leaves' (KPL) sensitization effect on ABT-199-resistant HepG2 cells. The proliferation of HepG2 cells and the H22 liver tumour bearing animal model were both studied, along with the underlying mechanisms, in relation to different dosages of KPL combined with ABT-199. According to our research, ABT-199 alone, as opposed to KPL, had no discernible effect on the development of hepatoma cells either in vitro or in vivo. It's interesting that the combined therapy shown noticeably greater anti-hepatoma effectiveness. In HepG2 cells, combining KPL and ABT-199 may increase both early and late apoptosis and lower the mitochondrial membrane potential, according to mechanistic investigations. ABT-199 and KPL dramatically decreased the expression of the anti-apoptotic proteins Bcl-2, Bcl-xL, and Mcl-1, increased the expression of Bax and cleaved caspase 3, and improved cytochrome C release and Bax translocation, according to a Western blot study. As a result, the combination of KPL and ABT-199 may one day be used to treat hepatocellular cancer.

Keywords: Hepatocarcinoma, Kaempferol, Persimmons leaves, ABT-199, Bcl-2

The Use of Cheap and Low Toxicity Carbon Dots as Reagent Ferric Reducing Antioxidant Power (Frap) Assay and Application to Plant Extracts

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Abstract

Antioxidants are compounds that inhibit the oxidation process. An interesting antioxidant assay is the ferric reducing antioxidant power (FRAP) method. FRAP is an antioxidant assay based on reducing of Fe^{3+} to Fe^{2+} due to the presence of antioxidant compounds. FRAP assay employ colorimetric detection with some reagent such as 2,4,6-Tripyridyl-s-Triazine (TPTZ), phenanthroline, batho-phenanthrolin, ferricyanide or ferrozine as a chromogenic ligand. Otherwise, the colorimetric detections have limitation in sensitivity and selectivity comparing with fluorometric detection. In this study we successfully employ carbon dots (CDs) as fluorescent probe to monitor the conversion of Fe^{3+} to Fe^{2+} in determining the antioxidant activity of the ethanol extract of a bay leaf by spectrofluorometry. The results showed that the modified FRAP method using CDs showed good linearity, with the intraday and interday precisions of 0.4% and 1.7 %RSD respectively. The modified FRAP using CDs method was successfully applied to determining the antioxidant activity of ethanolic bay leaf extract with IC_{50} value of 29.0 $\mu\text{g}/\text{mL}^{-1}$.

Keywords: Antioxidant, Modified FRAP, Carbon dots

Knowledge, Attitude, and Practice on Iodine Deficiency Disorders (IDD) Among the Population of Muscat, Oman

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Abstract

Iodine deficiency causes a spectrum of diseases called iodine deficiency disorders (IDD), which affect all stages of life from early pregnancy to adulthood. (WHO) considers iodine deficiency to be “the only most important avertible cause of brain impairment” worldwide. The purpose of this survey is to find out and assess the knowledge, attitude, and practice of iodine deficiency disorders among the Omani population in Muscat. A cross-sectional study was conducted. The total number of households surveyed was 70. A structured knowledge and practices questionnaire was used to collect data by using a Google Form, which was distributed online through social media to the local population. The statistics were combined with reference to information, mindset, and practices regarding IDD. Descriptive analysis and MS excel were used to present the data. In this study, most of the households were aware of the role of iodine in the body. The respondents' education details and age were strongly interrelated with knowledge and attitude, though, the practice was not significantly interrelated with age and education. 50% of respondents do not know iodine deficiency causes preventable mental disorders. More than half of respondents (66.7%) had known about the role of iodine in the body and 37.7% of respondents obtained the common source of information being television and 13% through family and friends. It was found that more than half of respondents never took a thyroid hormonal test. While 21.4% take it every year and 12.9% every six months, even though 81.4% of the respondents agreed thyroid hormones are vital to the body and 14.3% responded with a NO. Appropriate knowledge about iodized salt and IDDs should be familiarized to all public education locations points. Curricula can be framed to enhance knowledge, attitude, and practice at the family level so that the consumption of satisfactory iodized salt can be certified to reduce iodine deficiency complications. Health education conferences on IDD and the benefits of iodized salt should be approved out with special attention on illiterate individuals.

Keywords: Iodine Deficiency Disorder, Iodized Salt, Cross-sectional study.

Medicinal Implications of *Bombax ceiba*: A Narrative Review

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Abstract

Bombax ceiba (BC), red silk-cotton tree, is abundantly found in Asian tropical region and has ethnopharmacological significance. Its flowers and buds are used in Indian, Myanmar and Thai cuisine. This study reviewed the medicinal properties of different parts of *Bombax ceiba* (flowers, calyces, leaves, stem-barks and roots) indexed in PubMed database. BC flower extract (BCFE) increases the serum motilin and gastrin, substance P and decreases somatostatin. This results in increased faecal water, faecal quantity and gastrointestinal transit rate. Treatment with BCFE in mice significantly decreases both the body and liver weight, and improves the alcohol induced fatty changes histologically. Anti-inflammatory, anti-oxidant and anti-steatosis properties of BCFE offer potential for ameliorating alcohol-induced liver damage. Neuroprotection is a potential due to its anti-acetylcholine-esterase inhibition and free radical scavenging. High antiproliferative activity against human renal adenocarcinoma (ACHN) is also observed. Selenium nanoparticles, synthesised from BCFE, have antibacterial activities. Phenolic compounds from BCFE show anti-oxidant, and anti-viral activities. BC calyces are rich in vitamins, minerals and phytochemicals. Phytochemicals from BC calyx extract (BCCE) possesses insulin secretory and sensitization properties and displays antihyperglycemic activity. Free radicals scavenging and antioxidative activities of BCCE prevents free radicals induced erythrocytes lipid peroxidation and haemolysis. BC leaf extract (BCLE), having mangiferin as the main constituent, enhances insulin release, antihyperlipidemic and antioxidant. Its antihyperglycemic effect has potential for preventing diabetic nephropathy and neuropathy. Its anti-inflammatory activity is mediated through inhibition of nitric oxide production. BCLE significantly decreases the viability of human hepatocarcinoma (HepG2) cancer cells. BC-stem bark extract (BCSBE), containing flavonoids, lupeol, gallic acid and β -sitosterol, alleviates high-fat-diet induced obesity and ameliorates the bone fragility and fracture. BCSBE also have potential for anti-ulcerogenic, antisecretory, and cytoprotective actions for gastric ulcers as it decreases gastric juice amount and increases gastric pH. Hepatotoxicity of HepG2 cells, anti-bacterial and antioxidant activity is observed with BCSBE. The root extract of BC has inhibitory activity against HepG2 cells and HBsAg secretion. BC is a medicinal plant with its role in constipation, obesity, gastric ulcer, diabetes and liver cancer. BE calyces can be a promising functional food for diabetics due to its antioxidant and antiglycation activities.

Keywords: *Bombax ceiba*, anti-hyperglycaemia, anti-oxidant, HepG2 cytotoxicity, fatty liver

In Silico Molecular Docking on Chemical Constituent form *Garcinia Cambogia (Asam Gelugur)* as Anti – Colorectal Cancer

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Abstract

Colon cancer is one of the leading tumours in the world and it is considered among the big killers, together with lung, prostate and breast cancer. This study focused on discovering the substantial need for the development of anti-cancer compounds, particularly from natural sources such as medicinal plants and employing computational methods. The goal of the study was to ascertain the *Garcinia Cambogia (Asam Gelugur)* chemical constituents' potential as an inhibitor of the colon cancer-preventive protein enzyme 4UYA (*MLK4 kinase domain with ATPgammaS*). *Garcinia Cambogia (Asam Gelugur)* chemical compounds were used in this study's *in silico* molecular docking of the protein enzyme 4UYA (*MLK4 kinase domain with ATPgammaS*). By using Lipinski's Rule of Five (RO5), molinspiration software evaluated the physicochemical characteristics of the five compounds from *Asam Gelugur*. The results for the compounds garcinol, Capecitabine, isogarcinol, tartaric acid, citric acid, and hydroxycitric acid show that their respective binding affinities are -7.1, -6.4, -6.2, -5.6, -5.3, and -4.8. The study showed that garcinol have higher binding affinity than Capecitabine standard drug. However, only tartaric acid was able to bind to the active site of protein 4UYA (*MLK4 kinase domain with ATPgammaS*) without breaking Lipinski's rule of Five. Tartaric acid, a component in *Asam Gelugor's Garcinia Cambogia*, has the potential to be an anti-colorectal cancer 4UYA (*MLK4 kinase domain with ATPgammaS*) inhibitor.

Keywords :4UYA, *Garcinia Cambogia*, Molecular Docking, Anti-colorectal cancer, Lipinski's rule of Five.

***In Silico* Molecular Docking on Chemical Compounds Constituents from *Garcinia Cambogia* (Asam Gelugur) as Antimicrobial**

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Abstract

Antimicrobial Resistance (AMR) in bacterial pathogens is a global issue with major mortality and morbidity. The study applied computational approaches to discover the strong necessity of generating improved antimicrobial compounds sourced primarily from natural sources such as medicinal plants. The study aimed to evaluate the activity of Asam Gelugur (*Garcinia Cambogia*) chemical compounds against gram-negative bacteria using protein 2NLE (*Human Beta-Defensin-1*). *In silico* molecular docking of protein enzyme 2NLE (*Human Beta-Defensin-1*) with Asam Gelugur (*Garcinia Cambogia*) chemical compounds were used in this study. Molinspiration software was used to assess the physicochemical properties of 6 compounds using Lipinski's rule of five (RO5). The result for the binding affinity of garcinol, tartaric acid, malic acid, citric acid, hydroxycitric acid lactone, hydroxycitric acid, and included standard drug tetracycline is - 5.2; - 4.6; - 4.3; - 4.0; - 4.0; -3.5 and -6.1 respectively. The finding showed that the standard drugs tetracycline has higher binding affinity compared to 6 of the chemical compounds from Asam Gelugur (*Garcinia Cambogia*) (garcinol, tartaric acid, malic acid, citric acid, hydroxycitric acid lactone, and hydroxycitric acid). However, 2 compounds citric acid and hydroxycitric acid from Asam Gelugur (*Garcinia Cambogia*) achieved Lipinski's rule of five. These 2 compounds (citric acid and hydroxycitric acid) bind to the active site of the protein enzyme 2NLE at amino acid residues (Thr²¹, Pro¹⁸, Cys¹⁷). In conclusion, Asam Gelugur (*Garcinia Cambogia*) chemical compounds (citric acid and hydroxycitric acid) have the potential as antimicrobial drugs against gram-negative bacteria.

Keywords: Antimicrobial Resistance (AMR), 2NLE, Molecular Docking, Lipinski's Rule of Five, Molinspiration

***In silico* Molecular Docking of Potential Antifungal Phytochemicals from Akar Sintok (Entada Spiralis) Against Therapeutic Targets of Fungal Infection**

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Abstract

Fungal infection also known as mycosis are disease caused by fungi (yeast or mold). An antifungal agent is a drug that selectively eliminates fungal pathogens from a host with minimal toxicity to the host. Computational approaches, applied in this study to determine better antifungal compounds derived from natural sources such as medicinal plants. The purpose of the research to determine the activity of chemical compounds from Akar Sintok (Entada Spiralis) as a potential inhibitor of the protein enzymes of Escherichia coli, Trichophyton rubrum, /and Microsporum Canis. This research was carried out using in silico molecular docking of protein enzymes from Escherichia coli, Trichophyton rubrum, and Microsporum canis with Akar Sintok (Entada Spiralis) chemical compounds. The physiochemical properties of the 3 chemical compounds from Entada Spiralis and 1 standard drug based on Lipinski's rule of five (RO5) were evaluated by Molinspiration software. Kaempferol bind to amino acid active residue Microsporum canis and Trichophyton rubrum and the gallic acid bind to amino acid active site residue Escherichia coli. Nystatin possesses the highest bind affinity for all the result of protein interactions. However, the second highest for Escherichia coli is gallic acid and for Microsporum canis and Trichophyton rubrum is kaempferol. The binding affinity value for Nystatin, pachypodol, kaempferol and gallic acid for Microsporum canis is -4.7, -4.2, -4.6, and -4.1, for Escherichia coli is -6.6, -6.2, -6.1 and -5.9 and for Trichophyton rubrum is -6.7, -5.4, -5.6 and -5.5 respectively. Kaempferol, pachypodol and gallic acid have potential as antifungal agent.

Keywords: Antifungal, Molecular docking, Binding affinity, Active site

Drug Lag for Biosimilar Medicines in Malaysia: A Kaplan-Meier Survival Analysis

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Abstract

The availability of biosimilar medicines increases access to biological therapies at potentially lower costs. However, drug lag, defined as the delay between the global first approval and the approval from the national regulatory authority in each country, can minimise the cost-saving benefit of biosimilar medicines. This study assesses the drug lag from the first approval of a biosimilar medicine in Europe to the first approval of the corresponding biosimilar medicine in Malaysia as of December 31, 2022, and examines the difference in drug lag between the biosimilar medicines based on biological classification. The list of approved biosimilar medicines by their international non-proprietary names (INN) with their approval dates in Europe as of July 1, 2022, was obtained from the literature and the drug approval database of the European Medicines Agency. Data on approved biosimilar medicines (INN) in Malaysia was obtained from the approved biosimilar medicine database of the Malaysian national pharmaceutical regulatory authority. Drug lag (in median time) was assessed using Kaplan-Meier survival analysis. The difference in drug lag between the biosimilar medicines based on biological classification was assessed using the log-rank test. Statistically significant level was set at $p < 0.05$. All analyses were conducted using IBM SPSS version 25. A total of 18 biosimilar medicines (INN) were first approved in Europe as of July 1, 2022, of which 15 (83.3%) were approved in Malaysia as of December 31, 2022. The drug lag to the first approval of biosimilar medicine in Malaysia was 1572 days (95% CI = 503.25 - 2640.75). The log-rank test shows there was a statistically significant difference in drug lag between monoclonal antibody biological products (506 days) and non-monoclonal antibody biological products (2161) days, $\chi^2(1) = 11.924$, $p = 0.001$. On average, it took about 52 months for a biosimilar medicine to be approved in Malaysia after it was first approved in the global market. Monoclonal antibody biosimilar medicines experienced a significantly shorter drug lag compared to non-monoclonal antibody biosimilar medicines. Further research can examine the factors associated with drug lag for biosimilar medicines and the impact on access to biological therapies in Malaysia.

Keywords: Biological Products, Biosimilar Medicines, Entry, Drug Lag, Approval

***In silico* Design and Molecular Docking Studies of Metformin Derivatives as Dipeptidyl Peptidase IV (DPP-4) Inhibitor in Diabetes Type II**

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Abstract

The diverse nature of type 2 diabetes mellitus (T2DM) makes it challenging to achieve optimal treatment success with monotherapy. By increasing efficacy and lowering toxicity, active dipeptidyl peptidase IV (DPP-4) inhibitor is one novel strategy that has shown encouraging outcomes in the treatment of numerous complicated disorders. In this study, a computational framework was applied to discover potential drugs. Many researchers are launching new endeavors to create derivatives of metformin because it is known that they include the same parent metformin molecules but with side chain modifications. 14 different derivatives of metformin were chosen for the discovery of an antidiabetic agent with modification of various side chains and dipeptidyl peptidase IV (DPP-4) with code 3C45 was used as a diabetes-related target receptor. These 14 derivatives of metformin compounds were subjected to *in silico* studies to determine the best drug candidates. In comparison to metformin, 1- Piperidinamine, N, N-dimethyl- and 4-Butyl-3-thiosemicarbazide showed good binding affinity and interactions with the target receptor 3C45 with the binding affinity value is 5.1 kcal/mol. Further, the molecular interactions between 14 derivatives of metformin and the diabetes-related target protein 3C45 were established by analyzing the interactions with associated amino acids. *In silico* pharmacokinetics and toxicity profile of 14 derivatives metformin using ADME software predicted compounds non-carcinogenic and non-mutagenic. The drug-likeness was calculated using molinspiration software respecting Lipinski's rule of five. All of the 14 metformin derivatives were found to comply with Lipinski's rules of 5. The study suggested that 1- Piperidinamine, N, N-dimethyl- and 4-Butyl-3-thiosemicarbazide metformin derivatives could be a potential antidiabetic agent.

Keywords: Diabetes, Docking, Metformin Derivatives, In silico analysis, ADMET

Mental Health and Its Sociodemographic Determinants among Students at Selected Private Universities in Kuala Lumpur, Malaysia

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Abstract

Mental health issues come in light of the worrying rise in the number of Malaysians, especially the youth among university students. The aim of this project is 1) to screen the mental health status among students at selected private universities in Kuala Lumpur, 2) to identify the mental health categories among students at selected private universities in Kuala Lumpur in four domains of somatic symptoms, anxiety, social dysfunction, and depression, 3) to determine the relationship between sociodemographic and mental health status among students at selected private university in Kuala Lumpur. In this survey used primary data that were distributed to 403 respondent students at selected private universities in Kuala Lumpur using cluster sampling. The 28-item General Health Questionnaire was administrated to collect data. The factor of socio-demographic analysis such as gender, age, race, number of siblings, family income, living area, BMI, and CGPA was identified as a factor that may cause mental health problems. The result was analyzed using the Chi-square test to analyze the data. The result shows that the mental health status among students at selected private universities has mild symptom of mental illness through four domains of mental distress which 48.4% has somatic symptoms, 41.9% has anxiety, 57.3% has social dysfunction and 50.6% has depression among student universities. Students' mental health was significantly related to their low family income which will cause social dysfunction and depression among student university aged 24 and above. However, the result shows there is no significant difference relationship between somatic symptoms, social dysfunction, and anxiety with gender, living area, bmi, and CGPA among students at selected private universities. Students at selected private universities in Kuala Lumpur have mild symptoms of mental illness by screening using GHQ-28 questions. Low family income within the range of age 24 and above of universities student was identified as the risk factor for poor mental health. Precautions are needed to prevent the risk of mental health because the number is showing increasingly.

Keywords: Somatic, Anxiety, Social dysfunction, Depression, Sociodemographic

Comparative *in vitro* cytotoxicity study of Taxol and Aqueous Extract from Asam Gelugur (*Garcinia Cambogia*) against Vero cell line

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Abstract

Garcinia cambogia (known as Asam Gelugur) is a popular traditional herbal medicine and is one of the well-known folk medicines reported for the treatment of obesity and incorporated in several nutraceuticals worldwide. These effects are mediated by a myriad of bioactive compounds with most effects attributed to its hydroxy citric acid (HCA) content. This present study aimed to compare *in vitro* cytotoxicity of Taxol and aqueous extract from Asam Gelugur (*Garcinia Cambogia*) against the Vero cell line. The cell used for the test was Vero, which is a kidney-like cell line. Taxol is a cytotoxic drug used as a positive control. Cytotoxicity was assessed by 3-(4,5-dimethyl-2-thiazolyl)-2, 5-diphenyl-2H-tetrazolium bromide (MTT) assay. The assay is a colorimetric assay, based on mitochondrial succinate dehydrogenase potential to reduce MTT. Reduction of MTT can only occur in metabolically active cells, therefore the level of MTT reduction is an indication of cell viability. The finding from this study showed IC₅₀ value for the aqueous extract from Asam Gelugur (*Garcinia Cambogia*) is more than 500µg/mL compared to Taxol 0.0581µg/mL. A higher IC₅₀ value means that the Aqueous extract from Asam Gelugur (*Garcinia Cambogia*) is less toxic. In conclusion, the aqueous extract of Asam Gelugur (*Garcinia Cambogia*) possesses low toxicity and safe use in nutraceuticals and herbal supplements.

Keywords: MTT Assay, Vero Cell Line, Cell Viability, Cytotoxicity

Topical Anti-Inflammatory Activity of The Combination of Red Ginger Rhizome (*Zingiber officinale* var. *rubrum*), Red Betel Leaves (*Piper crocatum* Ruiz & Pav.), and Red Lemongrass (*Cymbopogon nardus* (L.) Rendle) Ethanolic Extracts

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Abstract

The rhizome extracts of red ginger (*Zingiber officinale* var. *rubrum*), red betel leaves (*Piper crocatum* Ruiz & Pav.), and red lemon grass (*Cymbopogon nardus* (L.) Rendle) are traditionally used by Kebumen (Central Java, Indonesia) people to treat inflammation in osteoarthritis. This research aims to determine the topical anti-inflammatory activity of a combination of ethanol extracts from these three plants. The plant materials of each species were collected from Kebumen and extracted using the maceration method. The topical anti-inflammatory activity was evaluated by the inflammation-associated edema method with a combination cream of 8% ethanol extract. The ratio of red ginger rhizome, red betel leaves, and red lemongrass were varied into four groups on a Biocream® basis. The thickness of the skin folds on the back of the mice was measured every 1 hour for up to 6 hours. The average percent decrease in inflammation from the positive control cream treatment groups 1, 2, 3, and 4 were 15.65%, -13.06%, 31.98%, -3.65%, and 31.29%. The data is not normally distributed with a p-value <0.05. Based on these results, it can be concluded that the combination of ethanol extract of red ginger rhizome, red betel leaf, and red lemon grass has the highest anti-inflammatory activity in group 2, with an average reduction in inflammation of 31.98% at the sixth hour.

Keywords: Anti-inflammatory, Red ginger, Red lemongrass, Red betel

The Effects of Low Temperature on Biochemical Properties and Bioactivity of Selected Malaysian Seaweed Species

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Abstract

Malaysian waters comprise a rich diversity of seaweeds which can be utilised for various applications, namely, functional food, feed, energy, pharmaceuticals and medicine. Seaweed is a potential source of macro- and micronutrients, high-quality proteins, soluble dietary fibre, vitamins, minerals, phytochemicals and fatty acids. Their growth conditions, especially temperature, specifically at the lower range, may play a very important role in improving the biochemical composition and quality of seaweeds. Our project is part of the SATREP Hybrid-OTEC system development in Malaysia. This is a step towards establishing the OTEC system for generation of renewable energy in Malaysia. OTEC (Ocean Thermal Energy Conversion) generates energy from the difference in temperature gradient between the cold nutrient-rich deep seawater and the warmer surface seawater. It generates an effluent of low temperature but rich in nutrients, thereby providing a rich culture medium for culture of edible seaweeds. Our study investigates the effects of temperature reduction on the biochemical properties (protein, amino acid, lipid, fatty acid, carbohydrate and moisture), metabolite profile and bioactivity (Anti-Alzheimer property using cholinesterase activity and cell viability) of selected Malaysian edible seaweed species (*Caulerpa lentillifera*, *Gracilaria changii* and *Ulva reticulata*). Preliminary investigations observed a reducing trend in seaweed biomass in colder temperatures where across the board, 20°C, 24°C exhibited best temperatures for culture. Regarding protein content, an increasing trend was recorded with an increase up to 333% between 28°C and 15°C for *C. lentillifera* and 98% in *G. changii*. Quantification of other parameters are on-going. Anti-Alzheimer property will be assessed using cholinesterase activity assay and cell viability assay.

Keywords: Nutritional properties, Bioactivity, Seaweed, Metabolite profiling, Anti-Alzheimer