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THE 2ND UNIVERSITI KUALA LUMPUR ROYAL COLLEGE OF MEDICINE PERAK (UNIKL RCMP)

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23 September 2024, UniKL RCMP

Committee

CONTENTS

01

Ciprofloxacin Loaded Gold Nanoparticles (Cipro-AuNP) – a Combinatorial Therapy against *Pseudomonas aeruginosa* Lung Infection

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Abstract

Background: Hospital acquired lung infection, mainly caused by *Pseudomonas aeruginosa* is well known to be multi-drug resistant and has drawn attention to researchers for finding a solution. To apprehend the *P. aeruginosa* infection, biofilm formation by the bacteria must first be dispersed and eradicated. Thus, the antibiofilm and antibacterial ability of conjugated ciprofloxacin-loaded gold nanoparticles against *P. aeruginosa* PAO1 have been studied. **Objective:** In this study, the conjugated nano-formulation was nebulised and the effect against *P. aeruginosa* PAO1 biofilm has been studied. **Methods:** P. aeruginosa PAO1 overnight culture was grown on 24-wells transwell for 3 days, while changing to fresh Luria Bertani broth each day. A twin-stage impinger (TSI) was set up with the biofilm transwell attached at the bottom, connecting to the nebuliser. Once the biofilm was nebulised for 2 mins with Cipro-AuNP, Cipro HCl and AuNPs subsequently, viable cell studies and SEM were carried out to determine the antibacterial properties. **Results:** The nebulised AuNPs penetrated the biofilm layers as observed in the SEM images, while destruction of the rod-shaped *P. aeruginosa* was observed after treated with Cipro-AuNPs. SEM images showed that treating with AuNP alone did not reduce the amount of *P. aeruginosa* significantly. *P. aeruginosa* PAO1 treated with Cipro HCL was found to eliminate planktonic cells, however the biofilm formed was not eradicated. Thus, the conjugated Cipro-AuNP exhibit excellent antibacterial and antibiofilm properties against *P. aeruginosa* PAO1. **Conclusion:** AuNPs was shown to be effective towards dispersing the biofilm, allowing ciprofloxacin to kill the dispersed planktonic *P. aeruginosa* PAO1. Thus, the Cipro-AuNPs could be a potential solution to cure multi-drug-resistant bacterial infection.

Keywords: *nebuliser, PAO1, cipro-AuNPs, nanoparticles, p. aeruginosa*.

02

Cytotoxicity of Karanjin and Curcumin Nanoparticles towards Hela Cervical Cancer Cells

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Abstract

Background: Phytochemicals such as karanjin and curcumin are known for their anticancer properties. Owing to their poor solubility in aqueous conditions, both karanjin and curcumin have been converted into nanoparticulate form to overcome the solubility issue and retain their anticancer activities. **Objective:** This study aimed to evaluate and compare the cytotoxic effects of karanjin nanoparticle and curcumin nanoparticles on HeLa cancer cells. **Methods:** HeLa cells were treated with varying concentrations of karanjin nanoparticles and curcumin nanoparticles for 24 hours. The MTS assay was employed to assess cell viability by measuring the absorbance of the formazan product, which correlates with the number of viable cells. IC50 values for each compound were calculated from dose-response curves to determine their cytotoxic potency. **Results:** The IC50 for karanjin nanoparticle was determined to be 148.1 µM, while curcumin nanoparticle exhibited an IC50 of 68.96 µM. These results indicate that curcumin nanoparticle is slightly more effective than karanjin nanoparticle in reducing HeLa cell viability within the tested concentration range. Karanjin showed limited efficacy against Hela cells. **Conclusions:** Curcumin nanoparticles exhibit higher cytotoxicity against HeLa cells compared to karanjin nanoparticles, indicating its greater potential as a therapeutic agent. Karanjin nanoparticles, while showing some cytotoxic effects, do not significantly impact HeLa cell viability when used alone. These findings suggest the need for further studies to explore potential synergistic effects or alternative combinations with karanjin nanoparticles to enhance its efficacy.

Keywords: *phytochemicals, antioxidant, cytotoxicity, HeLa cells, MTS assay*

03

Combination Therapy of Paclitaxel Nanoparticle and Curcumin Nanoparticle against Colon Cancer

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Abstract

Background: Colon cancer remains a leading cause of cancer-related mortality, demanding innovative approaches to improve treatment efficacy. Curcumin (CUR), a natural compound with known anticancer properties, and paclitaxel (PTX), a well-known chemotherapeutic agent, both have the potential to kill cancer cells, but also encounter difficulties in achieving optimal therapeutic effects due to their low water solubility and limited physicochemical stability. However, nanoparticle (NP)-based combination chemotherapy has been proposed as a potent strategy for colon cancer treatment. **Objective:** Therefore, this study employs nanotechnology to deliver CUR and PTX to increase the efficacy of colon cancer treatment. CUR and PTX NPs were developed via encapsulation into Pluronic F127 (PF127) nanocarrier. **Methods**: The efficacy of CUR-NPs and PTX-NPs as sole agent and in combination was assessed using MTS cytotoxicity assay against HCT116 cells. **Results**: The combination of CUR-NPs and PTX-NPs appears to have synergistic effects on HCT116 cells compared to the effects of CUR-NPs and PTX-NPs alone. The IC_50 values of CUR-NPs and PTX-NPs alone were 70.9 µM and 74.16 µM, respectively. In contrast, the combination of CUR-NPs and PTX-NPs resulted in a lower overall IC_50 values of 61.89 µM and 60.86 µM at a concentration of 10 µM. Additionally, the combination index (CI) values for CUR-NPs and PTX-NPs were less than 1, indicating a synergistic interaction between the two drugs. **Conclusions**: These findings offer valuable insights into improving the therapeutic efficacy of the combination formulations of CUR-NPs and PTX-NPs expending the possibilities for more effective and targeted treatment options for colon cancer.

Keywords: *cellular uptake, curcumin, paclitaxel, colon cancer, nanoparticles*

04

Engineered Nickel Nanoparticle Beads as a Superior Catalyst for Accelerated Breakdown of Theophylline Residue in Aqueous Solution

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Abstract

Background: A significant rise in environmental pollution is attributed to the escalating demand for pharmaceuticals, whose residues are now found in worldwide water sources, including lakes, rivers, and groundwater. These toxins pose potential risks to human health and marine ecosystems because of their persistence and bioactivity, facilitating their entry into the environment through industrial wastewater, hospital effluent, and incorrect medication disposal. Certain drugs deteriorate swiftly, but others remain in the environment, and their degradation byproducts are difficult to remove with conventional treatment methods. Photocatalysis represents a promising method for mitigating pharmaceutical contamination. This environmentally sustainable method efficiently breaks down pharmaceuticals into harmless substances like water and carbon dioxide. **Objectives:** This work intends to decompose the pharmaceutical substance which is theophylline with a photocatalytic method that leverages nickel beads as the photocatalyst. **Methodology:** The Ni bead catalyst was synthesized by casting alginate with nickel nanoparticle powder in calcium chloride. The beads were subsequently crosslinked with epichlorohydrin to improve their mechanical strength and chemical stability, followed by freeze-drying. The catalyst was analyzed to determine its physicochemical properties. The efficacy of the Ni bead catalyst was evaluated by the photocatalytic degradation of theophylline in a basic batch photoreactor. Samples were collected at intervals and evaluated with a UV-Vis Spectrophotometer to determine concentration and compute the degradation rate. Three critical factors were examined during the reaction: pH, catalyst dosage, and starting concentration. **Result:** Theophylline breaks down best when the pH is 5, the catalyst dose is 40 g/L, and the initial concentration is 10 ppm. **Conclusion:** Thus, it can be inferred that the photocatalytic process utilizing Ni beads demonstrates significant efficacy in the removal of medicinal compounds from aqueous solutions, serving as a practical and cost-effective operating technique.

Keywords: *photocatalytic, pharmaceutical, Ni bead catalyst*

05

Exploring Time Banking and Community Integration for the Ageing Population in Perak

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Abstract

Background: Malaysia's ageing population is projected to reach 14% by 2040, potentially making the country an "Old Country" by 2030. This demographic shift presents challenges, including increased healthcare needs and economic burdens. Time banking, a community-based system where participants earn time credits for providing services, offers potential benefits in enhancing social interactions and meeting healthcare and social needs. **Objective:** To investigate the interest and feasibility of time banking among elderly individuals in Bagan Serai, Perak. **Methods**: This mixed-methods study, conducted from March to April 2024, surveyed 34 elderly individuals in Bagan Serai, Perak. Participants aged 60 and above were selected based on residency and willingness to participate. Quantitative tools included structured surveys assessing socio-demographic data, healthcare and social needs, perceptions of time banking, and activity preferences. Qualitative data were gathered through focus group discussions. **Results**: Participants were predominantly aged 60-75, with a slight female majority. Most had primary education and no monthly income. Common health issues included hypertension and diabetes, with 67.6% reporting accessible health services and 70.6% satisfied with health service delivery. Initially, 97% were unfamiliar with time banking, and 82% of participants expressed interest after learning about it, noting benefits like improved service access and enhanced social connections. However, they identified challenges such as technological barriers and privacy concerns. Participants preferred safety, health, daily life requirements, and transportation-related activities. **Conclusion**: The study suggests significant interest in time banking among the elderly in Perak. Time banking could address healthcare access challenges and promote community integration. Effective implementation requires comprehensive education, user-friendly platforms, and personalized instructional methods. Collaboration between community organizations and healthcare providers is essential to create an inclusive and supportive environment for the elderly in Perak.

Keywords: *ageing population, elderly care, healthcare needs, social needs, time banking*

06

The Presence of Sun Tzu in Outbreak Control: a Literature Search and Review

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Abstract

Background: Infectious disease outbreaks are threats to national security, but rarely are military tactics used on them. Considering this, whether the military mindset, as outlined in Sun Tzu's "The Art of War," has any influence or presence in the approach to outbreak control. **Objective:** To determine the presence of military mindset in general, and Sun Tzu's Art of War in particular, in outbreak control by literature search and review. **Methods:** Google Scholar and PubMed were used. For Google Scholar, these search terms were used: 'military mindset" "outbreak"; "military mindset" "Sun Tzu" (or "Sun Zi" or "Sunzi"); "Sun Tzu" (or "Sun Zi" or "Sunzi") "infectious outbreak"; "Sun Tzu" "covid" "outbreak response"; and "Sun Tzu" "coronavirus". Where possible, the Google Scholar results were filtered to only include review articles. Results were shortlisted by title relevance, followed by in – depth individual reviews of shortlisted articles. **Result:** All Google Scholar searched combined yielded 59 results, reduced to 6 after evaluating for title relevance, and finally 2 after in – depth review. A third relevant article not listed in either Google Scholar was located through the references of one of these two. Only one paper out of the 3 directly applies Sun Tzu to outbreak control. Another one describes his principles but does not quote him; the third generally notes a generic increase of transferability of military mindset components including terminology into outbreak control. **Conclusion:** There is a dearth of literature regarding military mindsets in general, and Sun Tzu in particular, with respect to outbreak control, a knowledge gap that should be exploited.

Keywords: *Sun Tzu, military mindset, outbreak control*.

07

Socio-Demographic Characteristics and its Association with Perceived Mental Healthcare Services among Pharmacists in Malaysia: a Preliminary Study

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Abstract

Background: Mental healthcare services (MHS) is extended to community, inclusive of pharmacists in the provision of the mental healthcare needs. Thus, this pre-liminary study aimed to explore the association between socio-demographic characteristics and perceived MHS among pharmacists in Malaysia. **Objective:** 1. To identify the socio-demographic characteristics among Malaysian pharmacists in perceiving MHS in Malaysia. 2. To explore the socio-demographic characteristics that are associated with perceived MHS among pharmacists in Malaysia. **Methods**: A cross-sectional data of 40 Malaysian pharmacists gathered through distributed online questionnaires, were analysed. Descriptive analysis and Chi-Square test by SPSS were used to study the associations between socio-demographic characteristics and perceived MHS among Malaysian pharmacists. **Results**: Most respondents were aged between 25-34 years old (82.5%, n=33): majority were female (67.5%, n=27) and Malays (80%, n=32). The years of working experiences within less than 10 years (82.5%, n=33) were dominantly seen. The three most popular type of practice among them were pharmacists working in hospital (37.5%, n=15), community (27.5%, n=11) and health clinic (17.5%, n=3). Only 30% (n=12) of the respondents ever provided MHS, merely 33.3% (n=4) of them received MHS training ($p>0.168$). Types of MHS provision were screening, advice/ counselling, medications/ supplements, and referral/ encourage access to other MHS. Medications/ supplements were the highest type of MHS provided. While amidst respondents who never provide MHS, advice/ counselling (35.6%, n=21) is the most popular to be provided. There were no association between the gender, ethnicity, educational levels as well as type of practice with providing MHS ($p>0.05$). In contrast, the MHS provision were significantly decreased with increase of age and years of working experiences ($p<0.05$). All sociodemographic characteristics findings had no significant differences with neither the type of MHS provided nor the type of MHS intended to be provided ($p>0.05$). **Conclusions**: The pharmacists' socio-demographics seems not influence their perceptions towards providing the MHS.

Keywords: *mental health services, provide, pharmacists, Malaysia*

08

A Randomised Control Trial to investigate the Vitamin D Supplementation and its Improvement on Insomnia Symptoms among Vitamin D Deficient Malaysian Women: a Clinical Trial Protocol

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Abstract

Background: Vitamin D deficiency (VDD) is common among women and has been associated with various health issues, including sleep disturbances. Some studies suggested that VDD is associated with poor sleep quality and an increased risk of insomnia. Supplementing with vitamin D may offer a promising approach to improve sleep quality in women suffering from both insomnia and vitamin D deficiency. **Objective:** The primary objective of this study is to investigate the effectiveness of vitamin D_3 supplementation in improving insomnia parameters. The secondary objective is to evaluate the efficacy of vitamin D_3 supplementation in enhancing functional outcomes of daily activities and quality of life in women with low serum 25(OH)D level. **Methods**: This double-blind, randomized, placebo-controlled trial employs a parallel group design and is conducted in community settings. Eligible participants, women with insomnia symptoms and low 25(OH)D levels, will take 50,000 IU of vitamin D3 or a placebo weekly for nine weeks. The effect of vitamin D_3 on insomnia symptoms and daily functioning will be measured subjectively using questionnaires, while sleep parameters will be objectively assessed using an Actigraph, both before and after the intervention over the nine-week period. **Results**: This study was approved by the Universiti Kuala Lumpur Research Ethics Committee. Participants recruitment began in January 2023 and is expected to conclude in December 2025. Data collection is ongoing across all time points, with participants completing the 10-month follow-up, which includes baseline data at week 0 and post-intervention data at week 9. **Conclusions**: If vitamin D_3 supplementation proves effective in improving insomnia symptoms, it may be recommended as an adjunct treatment alongside cognitive behavioral therapy (CBT) for insomnia. Testing serum 25(OH)D levels could also be advised for individuals experiencing insomnia before considering medication.

Keywords: *vitamin d, vitamin d deficiency, insomnia, women*

09

Synthesis and Evaluation of Starch Aldehyde-Embelin Conjugate: Conjugation Ratio and Antioxidant Activity

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Abstract

Background: Embelin, a naturally occurring compound with potent therapeutic properties, is limited by poor solubility and bioavailability. Conjugation with starch aldehyde (SA) offers a potential solution by improving these pharmacological properties. **Objective:** This study aimed to determine the conjugation ratio and antioxidant activity of the synthesized starch aldehyde-embelin conjugate (SAEC). **Methods:** The conjugation was performed through acid-catalyzed condensation. The conjugation ratio was determined using Ultraviolet-Visible (UV-Vis) spectroscopy, while Fourier Transform Infrared (FTIR) spectroscopy was employed to identify the characteristic functional groups and electronic transitions. The antioxidant activity was assessed using ABTS and hydrogen peroxide (H_2O_2) assays, while the total phenolic content (TPC) and total flavonoid content (TFC) were determined by Folin-Ciocalteu and aluminium chloride methods, respectively. **Results:** The high degree of SAEC conjugation was observed at 100 mgEE/g. The FTIR confirmed the successful conjugation between embelin and starch aldehyde by looking at the expansion of O-H bond, the shift in the carbonyl (C=O) and new bonding of ether (C-O). SAEC showed the highest total flavonoid content compared with total phenolic content at 244.11 ± 0.096 µg/mL and 28.69 ± 0.018 µg/mL, respectively. SAEC possessed better antioxidant activity in ABTS assay compared to H_2O_2 assays through consistency in percentage inhibition among different concentrations. **Conclusions:** The findings demonstrate that the synthesized SAEC exhibits improved stability and has the potential to serve as a natural source of antioxidants. Future research should focus on optimizing the conjugation ratio and exploring the pharmaceutical effects of SAEC.

Keywords: *starch aldehyde-embelin conjugate, polysaccharides, conjugate, antioxidant*

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The Relationship between Autophagy and Glycolysis towards Lung Cancer Resistance

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Abstract

Background: The leading cause of cancer which contributed to the highest mortality rate worldwide is neoplasms of the lungs accounting for around 1.80 million deaths. Epidemiologically, there were significant variations between countries in lung cancer incidence, influenced by two different factors, including tobacco smoking rates and economic stage development. For lung cancer (LC) cells to survive dynamic conditions such as hypoxia, oxidative stress, or pathological changes, metabolic changes (glucose metabolism) for the cells are required. Besides that, autophagy, a lysosomal-dependent, evolutionary conserved degrading system can assist in clearing the tumor by segregating defective components (anti-cancer). At the same time, another theory believes that autophagy helps cancer survival by apoptotic regulations. Through both mechanisms, LC cells can increase their survivability and proliferate and can resist any apoptotic pathway. Therefore, LC resistance must first be overcome before formulating any possible anti-cancer substances. **Objective:** To investigate the crosstalk mechanisms (such as glucose metabolism, autophagy, and inflammation) that are involved in lung cancer resistance. **Methods**: Literature search from Scopus, PubMed, Directory of Open Access Journals. **Results**: There are data recorded from previous studies indicating the cooperative nature between glycolysis and autophagy which contributed to the lung cancer resistance, thus limiting the sensitivity of the lung cancer cells towards the treatment. **Conclusions**: A comprehensive and details experiment are needed to be conducted to elucidate the mechanisms involved in LC resistance can be carried out to provide a specific mechanism-targeting pathway to re-sensitize LC cells towards chemotherapy or chemoradiation treatments.

Keywords: *glycolysis, autophagy, lung cancer resistance, anti-cancer*

11

Quercetin attenuates Activation of Microglia through Anti-Inflammatory Reprogramming

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Abstract

Background: In the central nervous system (CNS), microglia regulate homeostasis and plays a role in nervous system inflammation. Activated microglia emits pro- and anti-inflammatory cytokines and shows significant morphological and functional alterations. Quercetin on the other hand, promotes neuronal regeneration processes, inhibits pro-inflammatory cytokines to regulate neuroinflammation processes, and lessens toxicity in neuronal cells due to oxidative stress. **Objective**: This study used the MTT assay to investigate how quercetin inhibits neurodegeneration through the viability of the cells. **Method**: 96 well plates were seeded with control BV2 microglia, stimulated-LPS BV2 microglia, and treated-quercetin BV2 microglia. After 24 hours incubation, 20 µL of a 5 mg/ml MTT solution was added to the cells and incubated for 4 hours. Then, MTT solution was removed and 200 µL of DMSO was added. The absorbance values were measured using ELISA plate reader at wavelength of 570 nm. **Results**: The viability of the cells in stimulated-LPS BV2 microglia was lower than the control and quercetin-treated BV2 microglia. Thus, it was shown that there was an activation of microglia using LPS as a stimulator. Meanwhile, in the quercetin-treated BV2 microglia, the viability of the cells was the same when treated with 1µM and 5µM concentrations of quercetin. **Conclusion**: Quercetin in both 1µM and 5µM concentrations acts as an anti-inflammatory agent through its protective effect on cell viability.

Keywords: *microglia, quercetin, neuroinflammation, cell viability, MTT assay*

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Synthesis, Characterization and Molecular Simulation of Potential TLR4 Antagonist against Triple-Negative Breast Cancer

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Abstract

Background: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer characterized by the absence of estrogen, progesterone and HER2 receptors that are commonly found in other breast cancers, which often leads to limited treatment options and poor prognosis. Blocking Toll-like receptor 4 (TLR4) activation has been linked to the inhibition of growth and metastasis of TNBC. **Methods:** In this study, we report the synthesis of a series of new compounds that potentially act as TLR4 antagonists. The structural validation is confirmed by using Nuclear Magnetic Resonance (NMR) and Infrared (IR) spectroscopy. A molecular docking was performed using AutoDock Vina-based CB-Dock server. **Results:** Ten potential TLR4 antagonists **(**KI01-KI10) bearing a heterocycle center linker and p-nitro aryl ring were successfully synthesized. Synthesized compounds revealed a strong and stable binding interaction with TLR4 (-10.7 to -15.0 kcal/mol). **Conclusion:** Compound KI01-KI10 potentially act as a TLR4 antagonist**.** The antagonism effects will be tested against TNBC cells in future studies.

Keywords: *Toll-like receptor 4, triple negative breast cancer, antagonists*

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The Effect of Gaseous Ozone Concentration, Exposure Time and Relative Humidity on *Pseudomonas aeruginosa* Biofilm

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Abstract

Background: *Pseudomonas aeruginosa* is a prevalent gram-negative bacterium frequently associated with nosocomial infections. Gaseous ozone has been recognized as a promising environmentally friendly disinfectant that could eliminate *P. aeruginosa* biofilm from hospital surfaces. Nevertheless, the efficacy of gaseous ozone disinfection treatment is not well comprehended due to the multitude of factors that influence it. **Objective:** This study aimed to investigate the effect of ozone concentration, relative humidity (RH) and time on the disinfection of P. aeruginosa biofilm using response surface methodology (RSM). **Methods**: *P. aeruginosa* biofilms were cultivated on stainless steel chips for 24 hours. The chips were then subjected to ozone treatment at different levels of dosage, duration of exposure, and RH, as instructed by the RSM model. The decrease in viable bacteria was evaluated using the drop plate technique and measured by determining the colony-forming units per square centimeter (CFU/cm^2). **Results**: The results indicate that the use of gaseous ozone alone did not effectively achieve disinfection, with the maximum decrease being a 2-log reduction. The model showed that ozone concentration and contact duration have a substantial influence on the disinfection of *P. aeruginosa*. The study found that there were positive and statistically significant impacts on bacterial decrease from both ozone concentration and contact duration ($p<0.05$). The correlation between the concentration of ozone and the duration of contact also exhibited a notable impact ($p<0.05$). Nevertheless, RH did not show a substantial influence and neither did the quadratic terms or other interaction factors ($p>0.05$). **Conclusions**: The decrease in *P. aeruginosa* was considerably affected by the concentration of ozone and the duration of contact. However, the treatment did not fulfill the necessary standards for disinfection. Future studies could explore enhancing the effectiveness of the treatment by combining ozone with other disinfectants.

Keywords: *gaseous ozone, Pseudomonas aeruginosa, biofilm, disinfection, response surface methodology.*

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The Effect of IGFBP2 on HeLa Cervical Cancer Cell Line Proliferation in Low and High Glucose Environments

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Abstract

Background: Cervical cancer ranks as the second most prevalent cancer among females between the ages of 15 and 44 in Malaysia. Recent findings indicated an intricate relationship between high blood sugar levels and cancer progression, in addition to its known connection to diabetes and its consequences. Insulin growth factor binding protein 2 (IGFBP2) is one of the known IGFBPs that binds to growth factors IGF-1 and IGF-2 expressed on cervical cancer cell. The IGFBP2 is known to exert a crucial impact on various fundamental processes related to the development of cancer and plays a prominent role in cancer development including the proliferation of cervical cancer cells. **Objective:** The primary aim is to investigate the effect of IGFBP2 on the proliferation of HeLa cervical cancer cell line cultured in low and high glucose environments. **Methodology:** HeLa cell line was treated with 250 ng/mL of IGFBP2 under low glucose (5 mM) and high glucose (25 mM) microenvironments. Control HeLa cell without treatment was prepared in 6-well plate. The effect of IGFBP2 treatment on cell proliferation was estimated using trypan blue staining and hemacytometer-based cell counting. **Results:** Preliminary analysis revealed that the treatment of HeLa cell with IGFBP2 increased the cell proliferation by 47.9±1.7% in low glucose, while 43.0±5.2% in high glucose. **Conclusion:** It was suggested that the treatment of IGFBP2 supports significance ($p<0.05$) proliferation of the cervical cancer cell line in both glucose concentrations.

Keywords: *hyperglycaemia, cervical cancer, IGFBP2, HeLa cell line, cancer progression.*

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In Silico Molecular Docking of Phytocompounds Isolated from *Christia vespertilionis* Leaves Extract as Potential ACE2 Inhibitors for Novel Anti-Sars-Cov-2 Agents

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Abstract

Background: Coronavirus disease (COVID-19) is a respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The entry of SARS-CoV-2 into host cells occurs through the binding of the SARS-CoV-2 spike protein to the ACE2 receptors located in the respiratory epithelium of host cells. Therefore, targeting ACE2 receptor in the host cells provides viable strategy to block the initial stage of infection and transmission. *Christia vespertilionis* has been reported to have medicinal properties and it is traditionally used in treating microbial infections. The traditional claim has garnered an attention in the search for new anti-SARS-CoV-2 agents from natural sources. **Objective:** In the present study, the molecular docking analysis was conducted to assess the potential of phytocompounds present in *Christia vespertilionis* in inhibiting the angiotensin-converting enzyme-2 (ACE2) receptor. **Methods:** *Christia vespertilionis* leaves were extracted and fractionated using vacuum liquid chromatography. The phytochemical compounds present in methanol fractions was identified using liquid chromatography-mass spectrometry (LC/MS) analysis. The dereplicated phytocompounds identified in methanol fractions were then docked against ACE2. **Results:** LC/MS-based phytochemical profiling of *C. vespertilionis* revealed the presence of 6 phenols and 11 flavonoids. These phenols and flavonoids were docked with ACE2 to identify the possible effective inhibitors. The outcomes of molecular docking analysis revealed that isovitexin (C1), isovitexin 2"-O-arabinoside (C2), and apigenin (C3) have the highest binding interaction energies against ACE2, with docking scores of -95.1 kJ/mol, -94.9 kJ/mol and -84.5 kJ/mol, respectively. In comparison, the reference compound, MLN-4760, exhibited a binding interaction energy of -78.4 kJ/mol. These findings suggest that the phytocompounds identified from methanol fraction of *C. vespertilionis* possess great potential as ACE2 inhibitors. **Conclusions:** In conclusion, the results provide useful insights as potential ACE2 inhibitors for the treatment of SARS-CoV-2 infection.

Keywords: *ACE2 inhibitors, Christia vespertilionis, molecular docking, SARS-CoV-2, phytocompounds*

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Hyperglycaemia Induces Chemoresistance in HeLa Cervical Cancer Cells

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Abstract

Background: Cervical cancer ranks as the second most prevalent cancer in Malaysia. In 2020, the World Health Organisation estimated about 604,237 new cases of cervical cancer worldwide. Research has indicated that individuals with cervical cancer who also have pre-existing diabetes tend to have a poorer prognosis compared to those without diabetes. The spread of cancer cells is a crucial stage in the advancement of cancer. A significant majority of cancer-related deaths are caused by the spread of cancer cells to other parts of the body. Chemotherapy remains the primary treatment for advanced or inoperable postoperative cervical cancer. However, the glucose conditions of the patient greatly impact the effectiveness of chemotherapy drugs in treating cervical cancer. In patients with uncontrolled diabetes, cervical cancer shows increased resistance to chemotherapy drugs compared to those without diabetes, leading to a poorer prognosis for cancer patients. **Objective**: The objective of this study is to examine the impact of high blood sugar levels on the behaviour of cervical cancer cells react to chemotherapy. **Method**: Using HeLa cells, we investigated the effect of different glucose concentration 5 mM, 9 mM and 25 mM on cells' response to chemotherapy drug cisplastin at concentration of 20 µM and 60 µM. Trypan Blue dye-exclusion assay was used to determine the percentage of cell death. **Results**: We observed a significant decrease in the ability of cisplastin to induce cell death in HeLa cells grown in 9 mM and 25 mM glucose conditions, in comparison to HeLa cells grown in the normal glucose condition (5mM). **Conclusion:** It is proposed that hyperglycaemia may lead to reduced effectiveness of chemotherapy drugs in cervical cancer cells. The results of this study could have significant implications for optimizing therapeutic strategies for cervical cancer patients with pre-existing diabetes.

Keywords: *hyperglycaemia, cervical cancer, chemotherapy drug, chemosensitivity, cisplatin, epithelial to mesenchymal transition.*

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Knowledge of Time Banking among Seniors

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Abstract

Background: Time banking has been used as a community currency in various countries. Countries like Japan (Hayashi, 2012) and UK (Naughton-Doe et al., 2020) has used it to elevate the lives of their senior citizen as part of their senior plan. It encourages elderly's involvement with the community as they would actively reciprocate time for services. Despite their low mobility, it reduces their chances from being excluded from the community. Evidence suggests that time banking helps individuals in transitional phases by offering psychological support, problem solving guidance, and resources (Kakar, 2020). It is important to establish the level of knowledge on time banking among the local elderly to have a better understanding about their insight on time banking. This study utilized the KAP (Knowledge, Attitude and Practices) Theory, and focusing on the Knowledge part. A "Knowledge on Time Banking" survey was created and used to establish the level of knowledge. The statements in the survey were derived from various literature regarding time banking. Correct answers were scored as 1, while incorrect answers were given a score of 0. Close to 65% of the participants had low knowledge about time banking while the remaining had moderate to high level of knowledge. It should be highlighted that most of the elderly are not even aware of the basic mechanisms in a time banking system. The findings of the study show that the elderly in the local area have a low level of knowledge about time banking. This lack of awareness points to the need for more informational campaigns on time banking. Educating the community about how time banking function could lead to better acceptance and provide benefits for both the elderly and the wider community. Nevertheless, time banking is seen as a promising tool for positively impacting the lives of senior citizens.

Keywords: *community, senior citizen, time bank*

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Uncovering Evidence of Overlooked Sources of Exposure to Major Heavy Metals in Malaysia

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Abstract

Background: Arsenic (As), lead (Pb), and cadmium (Cd) are listed among the top toxic heavy metals frequently identified as environmental contaminants. Several pieces of evidence of contamination with these heavy metals have been reported in Malaysia. A cross-sectional nationwide study by the Ministry of Health, Malaysia, also demonstrated the high prevalence of these metals in urinary samples of Malaysians. Globally, arsenic (As) is mainly transmitted through water sources whereas lead (Pb) is primarily introduced to humans via lead-based paint, and cadmium (Cd) through industrial emissions. However, in Malaysia, current data have highlighted that these metals are frequently reported as contaminants in water and marine sources. Notably, the general population is usually aware of the risk of heavy metal contamination in drinking water. Nevertheless, there is less knowledge among communities about the consequences of consuming vegetables and aquatic animals from areas heavily contaminated with these heavy metals, which can negatively impact health among Malaysians. Contamination with these toxic metals (As, Pb, Cd) was observed in some types of leafy vegetables in the Pahang region of Malaysia, and potential health risk analyses have highlighted the risk of health hazards to consumers of these vegetables. Similarly, it is suggested that tobacco plants grown in areas contaminated with heavy metals can pose a hazard through the smoking of these tobacco-containing cigarettes; evidence was demonstrated in the Selangor region. Moreover, at two lakes in Kuala Lumpur, considerable levels of heavy metals (Pb, Cd) were detected in the muscles of tilapia fish, although the range is still within the maximum allowable limit of Malaysian Food Regulations. These current data call attention to Malaysian communities to be aware of the threat of heavy metal exposure through aquatic animals living in this toxic metal-contaminated water and vegetables grown in soil irrigated with this impure water as a source.

Keywords: *toxic metals, vegetable, aquatic animal, water, contamination*

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Systematic Sampling Approach for Detection of *Burkholderia pseudomallei* from Soil in Terengganu

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Abstract

Introduction: Melioidosis, caused by the bacterium *Burkholderia pseudomallei*, is a severe infectious disease that poses significant public health challenges in tropical and subtropical regions. In Malaysia, melioidosis is recognised as an emerging infectious disease with sporadic cases reported across the country. However, the distribution patterns of melioidosis and the environmental factors influencing the prevalence of *B. pseudomallei* in different regions of Malaysia, particularly in Northeastern Peninsular Malaysia, remain poorly understood. **Objectives**: This research aims to propose systematic sampling to elucidate how environmental factors, including climate variables such as rainfall, temperature, humidity, and soil characteristics, influence the survival and dispersal of *B. pseudomallei* in the environment, ultimately affecting human exposure and infection rates. **Methodology**: In this study, systematic sampling approach will be employed to ensure representative data collection. The collection of samples will be conducted in 2 phases: before and after monsoon season in Terengganu. Samples will be collected from the flood-prone area and non-flood prone area to assess the relatedness. Additionally, meteorological data, land use information and other environmental parameters such as rainfall, temperature, humidity, and soil characteristics will be recorded. Environmental sampling will involve collecting soil samples from different sites within the study area such as agriculture, residential, and recreational/tourism areas. Soil samples will undergo appropriate laboratory procedures for pathogen detection including culture of *B. pseudomallei* on selective agar and genotypic molecular detection using portable RT – PCR thermocycler. **Result**: The finding of this study will investigate the relationship between climate factors and the occurrence of melioidosis. **Conclusion**: This proposed systematic sampling approach will be able to address the climate-related influences on *B. pseudomallei* in Terengganu.

Keywords: *B. pseudomallei, systematic sampling, environment factor; soil*