

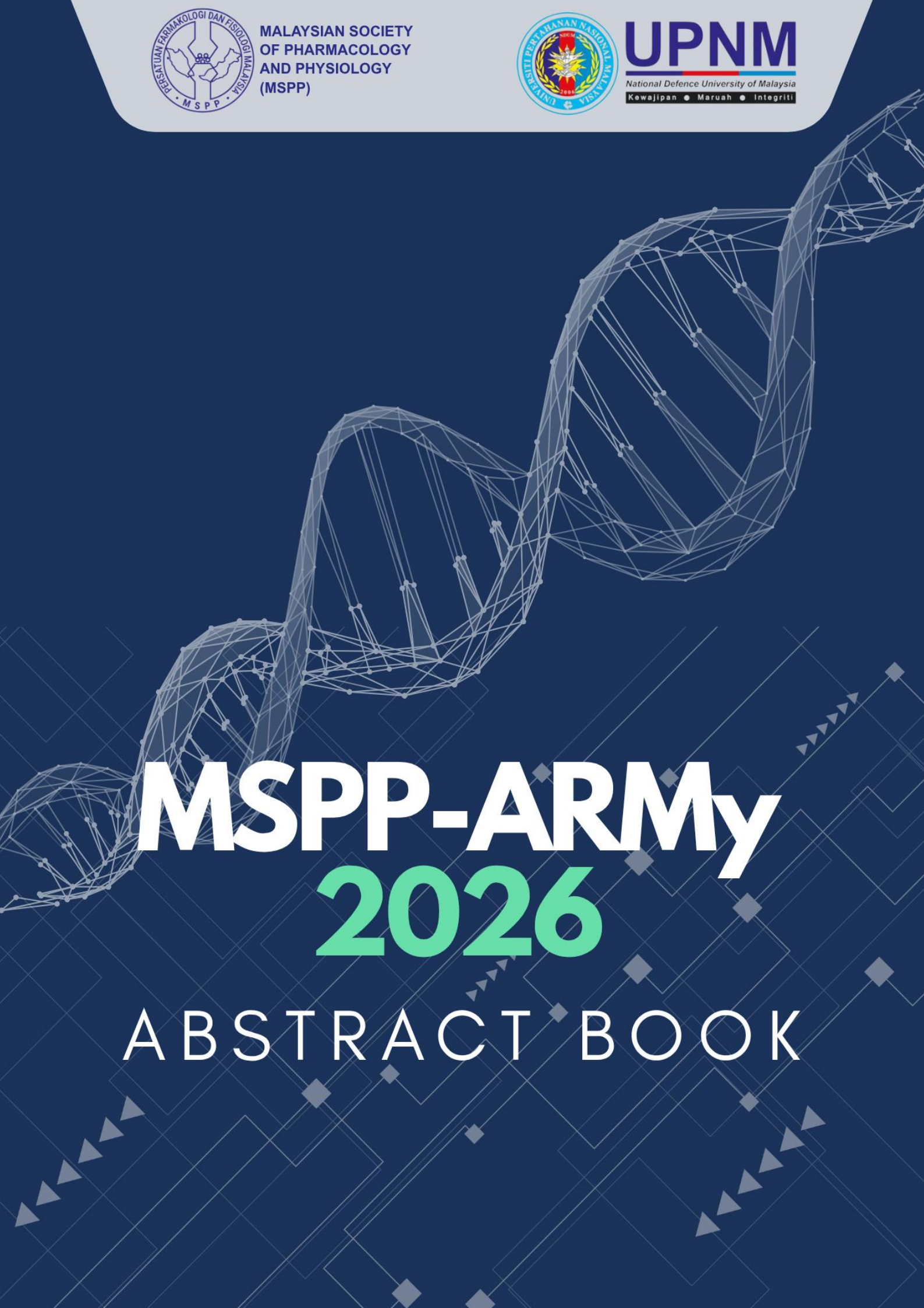


MALAYSIAN SOCIETY
OF PHARMACOLOGY
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ABSTRACT BOOK

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YOUNG INVESTIGATOR AWARD

Integrating Clinical Translation and Molecular Precision Medicine to Address the Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) Burden in Malaysia

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Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD), commonly referred to as fatty liver disease, represents an increasingly important health challenge in Malaysia, driven by the rising prevalence of obesity and type 2 diabetes. Addressing this burden requires approaches that enable early identification of individuals at risk of progressive liver disease while remaining accessible and applicable to the local healthcare setting. A translational research programme encompassing clinical, genetic, and molecular biomarkers has been developed to address this need. At the clinical level, accessible blood-based biomarkers have been investigated to improve risk stratification for advanced fibrosis. A simple approach combining the Fibrosis-4 (FIB-4) index with serum gamma-glutamyl transferase (GGT) demonstrated potential to improve identification of individuals at risk of advanced fibrosis, with subsequent translation into community-based liver health screening and contribution to national policy implementation. At the genetic level, genetic determinants of MASLD have been characterised, including variants in *PNPLA3* and *HSD17B13*, together with copy number variations. These findings provide a foundation for genetic risk stratification and precision medicine, particularly in the context of emerging therapies targeting fibrosis progression and reversal. At the molecular level, exportin-4 (XPO4) has been investigated as a potential biomarker across the MASLD disease spectrum. Ongoing mechanistic studies examining the XPO4/eIF5A pathway aim to elucidate its contribution to liver fibrogenesis and support the development of novel diagnostic and therapeutic strategies. Collectively, the integration of routine blood-based biomarkers, genetic epidemiology, and mechanistic molecular research provides a translational framework for advancing early detection and personalised risk stratification of MASLD. This approach has the potential to support scalable clinical implementation in Malaysia and contribute to precision medicine strategies for MASLD in broader regional populations.

Keywords: fatty liver; liver fibrosis; MASLD; precision medicine

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The background is a light blue gradient. On the left, a wireframe model of a DNA double helix is shown, composed of dark blue lines and dots. The helix curves upwards and to the right. In the lower right, there is a complex pattern of thin, light blue lines forming a circuit-like or grid-like structure. Small dark blue squares and triangles are scattered throughout this pattern, some acting as nodes or markers. The text 'Oral Presentation' is overlaid on the right side of the image, in a large, bold, dark blue font.

Oral Presentation

FLARe-UTI: An Augmented Reality Innovation for Learning Urinary Tract Infection

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Abstract

FLARe-UTI (Facilitated Learning with Augmented Reality on Urinary Tract Infection) is an interactive educational application (app) developed to enhance learning amongst pre-clinical medical students. FLARe-UTI aims to foster a dynamic and engaging learning experience through augmented reality (AR) technology to improve students' comprehension of urinary tract infection (UTI). Key features include three-dimensional (3D) AR anatomical kidney models, explanatory videos, structured notes, and interactive quizzes. Content is organised into seven sections: classification, clinical manifestations, risk factors, pathogenesis, investigations, treatment, and complications. The app was developed using a user-centred design approach, incorporating input from medical educators. User acceptance testing (UAT) was conducted amongst 12 pre-clinical medical students following informed consent, utilising an 11-item validated questionnaire assessing usability, functionality, educational impact, and user engagement. Quantitative data were analysed descriptively using a five-point Likert scale. Participants rated the app favourably across all domains, with mean scores of no less than 4.0 out of 5.0. Most students found the content accessible (91.7%) and navigation intuitive (83.3%). App performance was rated as smooth (83.3%), whilst 91.7% expressed high satisfaction with the 3D AR features. Multimedia elements enhanced learning for 75.0% of users, and 83.3% found the quiz section engaging. Overall satisfaction was reported by 91.7% of participants, of whom an equal proportion would recommend the app to peers. A notable limitation was the constrained timeframe available for UAT. In conclusion, FLARe-UTI with AR technology is an innovative and effective tool that is potentially useful for enhancing medical education and improving pre-clinical students' understanding of UTI.

Keywords: augmented reality (AR); effectiveness; FLARe-UTI; urinary tract infections; user acceptance testing (UAT).

Effectiveness of Instructor-led VR-Assisted Sessions Versus Prosected Cadaveric Models for System-Based Anatomy Practical Sessions Among First-Year Medical Students at UPNM

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Abstract

Cadaver-based learning is the traditional gold standard in anatomy education but presents ethical, cost, and hazard challenges. While Virtual Reality (VR) serves as a scalable 3D anatomical alternative, rigorous evaluations of its system-specific effectiveness remain limited. This study aimed to compare the effectiveness of VR-assisted 3D anatomy sessions with traditional prosected cadaveric models among preclinical medical students, and to determine whether this effectiveness differs across anatomical systems. A randomized crossover design was employed, where a total of 62 first-year medical students participated across the cardiovascular (CVS) and digestive (GI) systems. Group 1 utilized cadaveric models for CVS and VR for GI, whereas Group 2 used VR for CVS and cadaveric models for GI. Pre-test scores and immediate post-test scores were assessed to determine knowledge gain. For the CVS, the mean knowledge gain was 7.23 ± 5.40 for VR and 6.19 ± 4.84 for the cadaveric method ($p = 0.425$). For the GI system, VR yielded a mean knowledge gain of 6.00 ± 3.33 compared to 6.33 ± 4.06 for the cadaveric method ($p = 0.724$). Statistical comparisons between the two groups also showed no significant differences for the VR ($p = 0.281$) or the cadaveric model ($p = 0.902$). The results indicate that instructor-led VR-assisted sessions achieved learning outcomes comparable to traditional cadaveric sessions and the effectiveness does not differ across the CVS and GI systems. These findings contribute to the existing body of knowledge by supporting the integration of VR as a scalable complement to anatomy education, particularly for the CVS and GI systems.

Keywords: anatomy education; cadaveric learning; preclinical students; system-based anatomy; virtual reality

Emulating Randomised Trials from Disease Registries: Propensity Score Methods vs Conventional Regression for Acute Coronary Syndrome Pharmacotherapy

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Abstract

Randomised controlled trials (RCTs) remain the gold standard for evaluating cardiovascular therapies, yet they are frequently costly, slow, or impractical. Disease registries offer large, real-world datasets, but non-randomised treatment assignment introduces confounding by indication that can undermine the validity of conventional outcome estimates. Propensity score (PS) analytics address this by approximating an RCT framework within retrospective data. To evaluate PS-based covariate adjustment against conventional regression for estimating the survival effect of an evidence-based cardiovascular pharmacotherapy using registry data. A total of 18,910 consecutive patients from the Malaysian National Cardiovascular Disease–Acute Coronary Syndrome (NCVD-ACS) registry (2008–2017) prescribed renin-angiotensin-aldosterone system (RAAS) blockers on discharge were analysed, with one-year all-cause mortality as the primary outcome. The PS was estimated via multivariable logistic regression on baseline covariates. Four PS methods; matching, stratification, PS-as-covariate, and inverse probability weighting (IPW) were benchmarked against conventional Cox regression using the Bayesian Information Criterion (BIC). All approaches showed that on-discharge RAAS blockers significantly improved one-year survival. Conventional Cox regression estimated a 35% lower mortality hazard (HR = 0.65; 95% CI: 0.59–0.71), while the four PS methods averaged a 36% benefit (mean HR = 0.64). IPW yielded the highest estimated benefit (HR = 0.62; 95% CI: 0.56–0.69) and the lowest BIC (25,362.57), indicating the strongest model fit. When RCTs are unfeasible, PS methods, particularly using IPW provide a robust, trial-approximating framework that mitigates confounding in registry data. This data-driven approach offers a transferable template for reliable pharmacoepidemiological research across Malaysian disease registries.

Keywords: acute coronary syndrome; disease registry; inverse probability weighting; pharmacoepidemiology; propensity score

Exploring Student Engagement and Perceived Understanding Through an AI-Enhanced Interactive Web Application in Pharmacology Small Group Discussions

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Abstract

Despite the emphasis on active learning in medical education, Small Group Discussions (SGDs) often rely on static slides, potentially hindering clinical reasoning. This study evaluates student engagement and understanding following the implementation of an AI-enhanced interactive web application in undergraduate pharmacology SGDs. A prospective educational intervention was conducted across three modules among 65 Year 2 MBBS students. Traditional slides were replaced by a lecturer-led web application (Canva AI Code) integrating AI-generated resources (NotebookLM), visual scaffolds, and case-based prompts. Feedback was collected via Likert-scale questionnaires and thematic analysis of open-ended responses. Results demonstrated overwhelmingly positive perceptions, with 95.2% of responses agreeing that the platform was more engaging than traditional methods. In the Reproductive System module, 100% of respondents reported improved understanding. Thematic analysis identified three core mechanisms: visual scaffolding enhanced comprehension, guided questioning promoted active cognitive engagement, and facilitated collaborative learning repositioned the lecturer as a learning orchestrator. In conclusion, the AI-enhanced interactive web application notably enhanced student engagement and perceived conceptual understanding during pharmacology SGDs. By integrating AI-assisted development, visual storytelling, and lecturer-guided facilitation, this intervention fostered an active, collaborative learning environment, demonstrating the potential of generative AI to empower educators in designing scalable, learner-centered innovations that enhance clinical reasoning in medical education.

Keywords: active learning; clinical reasoning; generative AI; medical education; pharmacology

Systematic Review and Meta-Analysis of Apoptotic Markers in High-Fat Diet-Induced Metabolic Syndrome Animal Models

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Abstract

Animal models maintained on a high-fat diet (HFD) are widely used to replicate the metabolic and cognitive disturbances associated with metabolic syndrome (MetS). Research indicates that apoptosis plays a central role in neuronal loss and memory impairment under these conditions, with scattered and conflicting evidence across the literature. This review systematically evaluates and meta-analyses pre-clinical evidence on the hippocampal expression of pro-apoptotic and anti-apoptotic markers, as well as their associations with HFD-induced memory impairment according to PRISMA guideline (PROSPERO: CRD420250619473). A comprehensive search of PubMed and Scopus databases conducted from inception to March 2026 identified five eligible studies that measured apoptotic markers in rodents with HFD-induced memory impairment, assessed via the Morris water maze, Y-maze, novel object location, and novel object recognition tests. Random effects meta-analyses demonstrate that hippocampal pro-apoptotic markers (Bax and caspase-3) are significantly elevated in HFD compared to control groups (standardised mean difference, SMD = 1.75, 95% CI = 0.54 to 2.95, $p = 0.005$), with Bax identified as the main component significantly expressed in the pro-apoptotic cascade (SMD = 2.28, 95% CI = 1.07 to 3.50, $p < 0.001$). In contrast, the expression of anti-apoptotic marker Bcl-2 is similar between HFD and control groups (SMD = -1.24, 95% CI = -2.64 to 0.16, $p = 0.082$). These findings suggest that HFD intake triggers hippocampal neuronal apoptosis rather than failure of the anti-apoptotic mechanism. The present work underscores the detrimental impact of dietary fat on rodents' hippocampi, highlighting the potential for developing novel pharmacological or dietary strategies to mitigate HFD-induced neuronal damage.

Keywords: apoptosis; cognitive dysfunction; high-fat diet; metabolic syndrome; neuroinflammation

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National Culture and Individual AI Readiness: A Cross-National Study of Medical Students in Indonesia and Malaysia

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Abstract

Cross-national variation in technology adoption has often been linked to national culture, with country-level studies reporting associations between Hofstede's cultural dimensions and AI readiness. Whether these relationships apply at the individual level remains unclear. To compare cultural dimensions and AI readiness among medical students in Indonesia and Malaysia and determine whether individual cultural values predict AI readiness. A cross-sectional survey was conducted between November 2025 and January 2026 among 552 medical students (Indonesia, $n = 320$; Malaysia, $n = 232$). Cultural dimensions were measured using the Values Survey Module 2013, and AI readiness using the validated 22-item Medical Artificial Intelligence Readiness Scale for Medical Students (MAIRS-MS). Between-country differences were analysed using Mann-Whitney U tests, while associations were examined using Spearman's correlation and multiple linear regression. Indonesian students scored higher in uncertainty avoidance (11.33 ± 2.28 vs 9.66 ± 2.27) and long-term orientation (9.61 ± 2.43 vs 8.13 ± 2.90) (both $p < 0.001$). Malaysian students demonstrated higher ability (25.84 ± 4.14 vs 18.25 ± 7.05), vision (16.13 ± 2.86 vs 15.01 ± 4.61), ethics (15.94 ± 2.95 vs 14.94 ± 4.53), and the overall AI readiness (81.73 ± 10.08 vs 72.93 ± 14.66) (all $p < 0.01$), whereas Indonesian students scored higher in cognition (24.74 ± 4.69 vs 23.82 ± 4.56 ; $p = 0.032$). Correlations were absent in Indonesia and weak in Malaysia (overall $r_s = -0.130$, $p = 0.049$). Regression models explained little variance (adjusted $R^2 = 2.8\%$ in Indonesia; non-significant in Malaysia). Although cultural dimensions differed between countries, they showed limited influence on individual AI readiness. Differences in AI readiness, particularly practical ability, appear to reflect educational exposure and institutional context rather than cultural values, supporting targeted curricular interventions.

Keywords: artificial intelligence readiness; cross-national comparison; cultural dimensions; Hofstede; medical education.

Unmasking Black Dot Syndrome: Preserving Cell Culture Integrity for Reliable Drug Discovery and Therapeutics

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Abstract

Black dot-like particles observed in cervical cancer cell cultures frequently raise concerns of contamination, threatening the integrity of in vitro models essential for drug discovery and precision therapeutics. To prevent the unnecessary disposal of valuable samples and ensure reliable pharmacological screening, this study investigated the origin of these particles. The investigation was performed on complete media used for the SiHa cell line and unfiltered Fetal Bovine Serum (UF-FBS) in a cell-free environment, which were incubated and observed daily for five days. Throughout the observation period, no macroscopic changes occurred in the complete cell culture media; however, slight turbidity developed in the UF-FBS after four days. Microscopic examination revealed that the black dots multiplied in the UF-FBS but not in the complete media. In both samples, the particles exhibited a non-directional vibrating motion consistent with a Brownian movement rather than active microbial motility. After seven days of incubation, black dot particles were isolated from the flask containing UF-FBS (designated as UF-FBS7). To identify potential biological contaminants, three specimens (UF-FBS7, fresh filtered FBS, and fresh unfiltered FBS) were inoculated onto Nutrient agar, Potato Dextrose agar, and MacConkey agar. Following a 120-hour incubation of the agar plates, no visible microbial growth was observed across any of the samples. The multiplication of particles in the FBS, coupled with negative microbial cultures, suggests that these are non-biological serum protein precipitates. Resolving this artefact prevents resource waste and ensures the robust baseline integrity required for accurate downstream therapeutic evaluations.

Keywords: black dot syndrome; cell culture; cervical cancer cell; contamination; fetal bovine serum

Gamma-Oryzanol Attenuates Diabetic Cardiomyopathy by Suppressing Oxidative Stress and Inflammation in a Type 2 Diabetic Rat Model

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Abstract

Diabetic cardiomyopathy (DCM) is a diabetes-associated cardiac disorder characterised by myocardial remodelling and dysfunction independent of hypertension or coronary artery disease. Oxidative stress and chronic inflammation are key contributors to its pathogenesis. Gamma-oryzanol, a bioactive compound derived from rice bran oil, possesses antihyperglycaemic, antioxidant, and anti-inflammatory properties; however, its cardioprotective potential in DCM remains insufficiently investigated. This study evaluated the effects of gamma-oryzanol (100 mg/kg body weight) on hyperglycaemia, oxidative stress, inflammation, and myocardial histopathology in a rat model of type 2 diabetes. Forty-eight male Sprague–Dawley rats were randomly assigned to six groups: non-diabetic control, non-diabetic plus gamma-oryzanol, diabetic control, diabetic plus metformin, diabetic plus gamma-oryzanol, and diabetic plus metformin and gamma-oryzanol. Type 2 diabetes was induced by feeding rats a high-fat diet for six weeks, followed by a single intraperitoneal injection of streptozotocin (STZ) at 40 mg/kg body weight. Treatments were administered orally once daily for four weeks, and fasting blood glucose (FBG) was monitored weekly. Following sacrifice, oxidative stress markers, antioxidant enzyme activities, pro-inflammatory cytokines, and myocardial histopathology were evaluated. Gamma-oryzanol significantly reduced FBG ($p = 0.0285$), oxidative stress markers (MDA, AGE, and PCO; $p \leq 0.0008$), and pro-inflammatory cytokines (IL-1 β , IL-6, and TNF- α ; $p \leq 0.0150$), while significantly enhancing antioxidant enzyme activities (SOD, CAT, and GPx; $p \leq 0.0037$) compared with diabetic controls. Histological examination revealed marked preservation of myocardial architecture in gamma-oryzanol-treated diabetic rats. Combination therapy with metformin produced only modest, non-significant additional benefits. These findings indicate that gamma-oryzanol, as a nutraceutical, exerts cardioprotective effects against DCM by attenuating oxidative stress and inflammation.

Keywords: diabetic cardiomyopathy; gamma-oryzanol; hyperglycaemia; inflammation; oxidative stress

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Network Pharmacology Elucidation of Wound Healing Mechanisms of Standardised Synacinn™ Polyherbal Extract

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Abstract

Impaired wound healing in type 2 diabetes mellitus (T2DM) is driven by chronic hyperglycaemia, oxidative stress, sustained inflammation, and dysregulated extracellular matrix remodelling. Synacinn™ is a standardised polyherbal extract comprising *Cinnamomum zeylanicum*, *Curcuma xanthorrhiza*, *Syzygium polyanthum*, *Orthosiphon stamineus*, and *Andrographis paniculata*, characterised by five phytochemical markers: Rosmarinic acid, Gallic acid, Catechin, Andrographolide, and Curcumin. Preclinical studies demonstrate systemic anti-diabetic activity and wound-relevant bioactivities including TNF- α inhibition (IC₅₀: 3.74 mg/mL), MMP-1 inhibition (92%), pro-collagen synthesis (33.9%), HaCaT keratinocyte migration (18.6% at 72h), and *in vivo* complete wound resolution within 3 weeks. However, the molecular network underlying this activity remains uncharacterised. This study investigates the multi-target mechanisms of Synacinn™ through integrated network pharmacology and molecular docking, cross-validated against its existing preclinical dataset. Active compounds were retrieved from PubChem database. Molecular targets predicted via SwissTargetPrediction and PharmMapper were intersected with a merged T2DM and wound healing disease gene set from GeneCards, DisGeNET, and OMIM. Initial target mapping identified 33 overlapping targets spanning 9 wound healing, 12 anti-diabetic, and 3 bridge categories. High-frequency hub candidates included EGFR (4 compounds), MMP9 and SERPINE1 (3 compounds each), and MMP1, TNF, DPP4, and PPARG (2 compounds each). Rosmarinic acid demonstrated the highest prediction probability against MMP1 (probability = 0.809), concordant with 92% *in vitro* MMP-1 inhibition. TNF and SERPINE1 emerged as bridge targets shared across both disease axes. This represents the first preliminary network pharmacology characterisation of a polyherbal extract validated across the complete diabetic wound healing axis, supporting Synacinn™ advancement as an evidence-based botanical wound care product.

Keywords: diabetic wound healing; MMP1; network pharmacology; polyherbal; Synacinn™; TNF

Hydroxytyrosol Modulates Anabolic and Catabolic Pathways in Human Osteoarthritis Chondrocytes

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Abstract

Osteoarthritis (OA) is a progressive degenerative joint disease characterized by articular cartilage destruction, affecting over 240 million people worldwide. The pathogenesis of OA is driven by a chronic inflammatory environment in which pro-inflammatory cytokines such as interleukin-1 β (IL-1 β) trigger a metabolic imbalance that favours cartilage degradation over repair. Hydroxytyrosol (HT), a potent antioxidant phenolic compound derived from olive oil, has demonstrated significant anti-inflammatory properties. This study evaluates the efficacy of HT as a precision therapeutic approach to target chondrocyte health and restore molecular metabolic homeostasis in OA. Initially, an MTT assay across a concentration range (12.5–400.0 μ M) established cytotoxicity and metabolic profiles, selecting three optimal concentrations (12.5, 25.0, and 50.0 μ M) for investigation. Human OA chondrocytes were treated with these concentrations, and cell migration was evaluated using scratch and transwell assays. sGAG and PGE₂ production were measured, while RT-qPCR analysed anabolic genes (*COL2A1*, *ACAN*, *SOX9*) and catabolic markers (*MMP13*, *ADAMTS5*, *iNOS*) in IL-1 β -induced chondrocytes. Results revealed that HT significantly improved chondrocyte proliferation ($p < 0.0001$) and migration ($p < 0.03$). Notably, HT treatments markedly increased sGAG production ($p < 0.01$) and upregulated anabolic markers compared to controls, alongside a significant decrease in PGE₂ production and catabolic gene expression. These findings show that HT selectively modulates genes involved in cartilage repair and reduces inflammatory and catabolic mediators, thereby restoring metabolic balance in OA chondrocytes. Thus, HT emerges as a promising therapeutic candidate with strong potential to support targeted treatment and regeneration of osteoarthritic cartilage.

Keywords: cartilage regeneration; chondrocyte; hydroxytyrosol; inflammation; osteoarthritis.

Effects of Trans-resveratrol on ECM Remodelling in Dexamethasone-treated HTMCs via Renin-Angiotensin System (RAS)

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Abstract

Glaucoma is a progressive optic neuropathy leading to irreversible visual field loss. Elevated intraocular pressure (IOP) is a major modifiable risk factor, arising from impaired aqueous humour outflow stemming from excessive extracellular matrix (ECM) deposition in the trabecular meshwork. The renin-angiotensin system (RAS) and its dysregulation play significant roles in the pathological ECM remodelling. This study aimed to determine whether trans-resveratrol (TRV) attenuates ECM remodelling in dexamethasone-treated human trabecular meshwork cells (HTMCs) involving local ocular RAS components. HTMCs were treated with Dexa (Dexamethasone, 100 nM) with or without TRV (12.5 µM) or Losartan (AT1R inhibitor, 1 mM) for 7 days. Cell lysate and media samples were then collected for measurement of fibronectin, matrix metalloproteinase-9 (MMP-9) and its inhibitor, tissue inhibitors of metalloproteinase-1 (TIMP-1), and RAS components: ACE, AT1R, and AT2R using ELISA. Dexa significantly upregulated fibronectin and TIMP-1 while downregulating MMP-9, resulting in a high TIMP-1/MMP-9 ratio compared to untreated HTMCs ($p < 0.001$). Dexa also increased ACE activity and AT1R expression but lowered the AT2R expression compared to untreated HTMCs ($p < 0.0001$). This indicates that Dexa triggers pathological ECM remodelling via RAS signalling. TRV and Losartan co-treatment reduced fibronectin and TIMP-1 levels, with restored MMP-9 compared to Dexa-treated HTMCs ($p < 0.001$). Co-treatment with TRV also reduced ACE activity and AT1R expression, along with higher AT2R expression compared to Dexa-treated HTMCs ($p < 0.0001$). These findings indicate that the reduction of ECM remodelling by TRV may be mediated through modulation of RAS signalling.

Keywords: ECM remodelling; glaucoma; renin-angiotensin system; trabecular meshwork; trans-resveratrol

***Trans*-3-Hydroxycinnamic Acid Attenuates Metabolic Dysfunction, Cardiac Inflammation, and Myocardial Fibrotic Remodeling in High-Fat High-Fructose Diet-Induced Metabolic Disease Rats**

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Abstract

Metabolic disease (MD) is a major risk factor for cardiovascular complications, characterized by obesity, insulin resistance, and chronic inflammation. Although hydroxycinnamic acids show cardioprotective potential, their role in MD-associated cardiac dysfunction remains unclear. This study investigated the effects of *trans*-3-hydroxycinnamic acid (HCA) in a high-fat high-fructose (HFHF)-induced MD rat model. Male Sprague Dawley rats ($n = 20$) were fed a normal diet (Normal) or HFHF diet for 12 weeks. HFHF rats received either distilled water (MD), HCA (30 mg/kg/day), or metformin (100 mg/kg/day) ($n = 5$ per group). Metabolic parameters such as Lee obesity index, lipid profile, fasting glucose, insulin, homeostatic model assessment of insulin resistance (HOMA-IR), oral glucose tolerance test (OGTT) were measured, along with cardiac inflammatory markers interleukin-10 (IL-10) and tumour necrosis factor- α (TNF- α), as well as myocardial histopathology were evaluated. The MD group exhibited significant increases in body weight changes, Lee obesity index, total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), fasting glucose, insulin resistance (HOMA-IR, OGTT AUC), and TNF- α level, with reduced high-density lipoprotein (HDL) and IL-10 levels compared to the Normal group. Early myocardial fibrotic remodeling was evident in the MD group, characterized by significantly increased collagen deposition on Masson's Trichrome staining and upregulated Collagen I immunoexpression. HCA significantly improved metabolic parameters, suppressed cardiac inflammation, reduced myocardial collagen deposition, and downregulated Collagen I immunoexpression, suggesting protection against myocardial fibrotic remodeling. These findings demonstrate that HCA attenuates metabolic and cardioinflammatory disturbances while preserving myocardial integrity, suggesting its potential as a cardioprotective agent against metabolic disease-associated complications.

Keywords: cardioprotection; collagen; hydroxycinnamic acid; inflammation; metabolic disease

***Trans*-3-hydroxycinnamic Acid Attenuates Fibrogenesis via TGF- β /Smad3 Pathway Modulation in Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) Rats**

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Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) progresses from hepatic steatosis to fibrosis via profibrogenic pathways. This study aimed to investigate the anti-fibrogenic potential of *trans*-3-hydroxycinnamic acid (HCA) in high-fat high-fructose (HFHF)-induced MASLD rats through modulation of fibrogenic transforming growth factor-beta (TGF- β)/Smad3 signaling pathway. Twenty-four male Sprague Dawley rats ($n = 6/\text{group}$) were assigned to either a normal group or three HFHF diet groups. After a 6-week HFHF induction, the HFHF-fed rats received daily treatments of either normal saline (MD group), HCA (30 mg/kg/day), or metformin (100 mg/kg/day) for another 6 weeks while maintaining the diet. All treatments were orally administered, and assessments were done on anthropometric indices, lipid profile, and insulin levels. Key indices of inflammatory modulators and collagen deposition were assessed via colorimetric assay and immunohistochemical techniques. Across all parameters, the MD group exhibited significant deterioration compared to the normal group. Notably, HCA treatment effectively mitigated systemic metabolic disturbances, evidenced by significant reductions in body mass index, body weight changes, and the specific rate of body mass gain. Metabolic improvements were further evidenced by a decrease in total cholesterol and insulin levels. Both HCA and metformin attenuated inflammation by suppressing tumour necrosis factor-alpha while restoring interleukin-10 levels. Masson's trichrome staining demonstrated a marked reduction in hepatic collagen deposition in rats from both treatment groups. These histological findings were further supported by significantly reduced hepatic immunoexpression of TGF- β and Smad3 proteins. Our findings suggest that HCA attenuates early hepatic fibrogenesis by modulating the TGF- β /Smad3 signaling pathway, highlighting its potential as a natural therapeutic candidate for MASLD.

Keywords: fibrogenesis; MASLD; Smad3; TGF- β ; *trans*-3-hydroxycinnamic acid

Anti-Cancer Effects of Curcumin Diarylpentanoid Analogue (1,5-bis(4-hydroxy-3-methoxyphenyl)-1,4-pentadiene-3-one, MS13) on Gastric Cancer Cells with KRAS Mutation

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Abstract

Gastric cancer is among the top ten most frequently diagnosed cancers in men in Malaysia. Cetuximab is largely ineffective in gastric cancer patients with KRAS mutations. Therefore, alternative therapies are needed to overcome this chemoresistance. MS13 (1,5-bis(4-hydroxy-3-methoxyphenyl)-1,4-pentadiene-3-one), a chemically modified curcumin analogue, has shown more potent anti-cancer effects in several cancer models. Our study evaluated the anti-cancer effects of MS13 in human gastric adenocarcinoma AGS cells which harbour KRAS mutations. Cytotoxicity, apoptosis, mitochondrial membrane potential, and cell cycle analyses of curcumin- and MS13-treated AGS cells were performed using MTT, Annexin V/Propidium Iodide (Annexin V/PI), Tetramethylrhodamine ethyl ester (TMRE), and PI/RNase assays, respectively. MS13 exerted significantly greater cytotoxic effects than curcumin in a concentration- and time-dependent manner. MS13 treatment at the IC₅₀ resulted in a higher proportion of apoptotic cells relative to curcumin. Consistently, 24 hours of MS13 treatment at both IC₅₀ and IC₂₅ concentrations produced a more pronounced reduction in mitochondrial membrane potential in AGS cells than curcumin at equivalent doses, indicating stronger mitochondrial-mediated apoptotic activity. MS13 also induced G₂/M phase arrest more prominently after 24 hours of treatment. Overall, MS13 demonstrated greater cytotoxic, anti-proliferative, and pro-apoptotic effects than curcumin in a KRAS-mutated gastric cancer model, with enhanced induction of mitochondrial-mediated apoptosis and distinct cell-cycle arrest. Further transcriptomic analysis is anticipated to identify key genes and biological pathways associated with MS13 treatment, particularly those related to KRAS signalling, cell death, and cell-cycle control.

Keywords: curcumin; curcumin analogue; gastric cancer; KRAS; MS13

Therapeutic Efficacy of Methanolic Extract of *Abelmoschus esculentus* in Complete Freund's Adjuvant-Induced Rheumatoid Arthritis: Attenuation of Inflammation and Arthritic Biomarkers

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Abstract

Abelmoschus esculentus (L.), or okra, is a widely consumed functional food and traditionally used for its medicinal benefits. Despite its phytoconstituents' richness and diverse pharmacological activities, scientific evidence on its anti-arthritic potential in rheumatoid arthritis (RA) remains scarce. Present study aimed to evaluate the anti-arthritic effects of the methanolic extract of *A. esculentus* fruits (AEME) in a Complete Freund's Adjuvant (CFA)-induced arthritis model in Sprague-Dawley rats. Dried powdered *A. esculentus* fruits were extracted with 70% acidified methanol. Arthritis was induced by intra-plantar CFA injection (5 mg/kg) in the left hind paw on Day 1, with a booster on Day 7. CFA-induced arthritic rats were randomly allocated to treatment groups ($n = 5$ per group) and administered AEME (50, 100, or 200 mg/kg/day) or methotrexate (MTX, 0.5 mg/kg thrice weekly) orally for 21 days. Disease progression was assessed through body weight, paw oedema, locomotor activity, and paw pressure measurement throughout the study. Serum concentrations of RA biomarkers, C-reactive protein (CRP), rheumatoid factor IgM (RF-IgM), and anti-cyclic citrullinated peptide antibodies (ACPA) were also evaluated. Data were analysed using one-way ANOVA with significance set at $p < 0.05$. AEME (200 mg/kg) treatment significantly reduced paw oedema by 28% and decreased serum CRP, RF-IgM and ACPA levels by up to 56%, 58%, and 72%, respectively compared with the arthritic control ($p < 0.05$). These effects were accompanied by non-significant improvements in body weight and locomotor activity. Overall, AEME ameliorated experimental RA, supporting its potential as a natural anti-arthritic agent, and require further mechanistic studies.

Keywords: *Abelmoschus esculentus*, anti-arthritis, arthritic biomarkers, Complete Freund's Adjuvant (CFA), rheumatoid arthritis

Rocaglamide Sensitizes Nasopharyngeal Carcinoma to Standard Chemotherapy: A Randomized and Investigator-blinded Preclinical Trial in Middle-aged NSG Mice

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Abstract

Nasopharyngeal carcinoma (NPC) is highly prevalent in East and Southeast Asia, with a typical diagnostic age distribution of 40 to 75 years and limited treatment options. The current work sought to evaluate the efficacy of orally bioavailable rocaglamide combined with cisplatin + gemcitabine (standard chemotherapy) in NPC cell line-xenografted mice. The 52- to 56-week-old female and male NSG mice (equivalent to human age of 45 years) were subcutaneously inoculated with C666-1^{p53 wild-type} and NPC43^{p53 mutant} cell lines. Upon reaching tumor inclusion volume, mice were randomized into treatment cohorts (standard chemotherapy + rocaglamide *vs* standard chemotherapy + placebo). Following dose optimization, cisplatin (2 mg/kg) + gemcitabine (20 mg/kg), and gemcitabine alone were intravenously injected into the tail vein on Day 1 and Day 8, respectively. Rocaglamide was administered orally (six days/week) at 0.5 mg/kg (Day 1–10) and a maximum tolerated dose of 0.7 mg/kg (Day 11 to 21) for C666-1 or 28 days (NPC-43). Treatment, tumor volume (mm³), body weight, final tumor weight, and necropsy were conducted in a blinded manner according to ARRIVE guidelines and approved ACUC-IBBC protocols. Standard chemotherapy + rocaglamide significantly reduced C666-1 but not NPC43 tumor weight in both female (0.387 ± 0.055 g *vs* 0.793 ± 0.586 g; tumor reduction (%): 51.198; *p* = 0.049) and male (0.178 ± 0.064 g *vs* 0.463 ± 0.245 g; tumor reduction (%): 61.555; *p* = 0.048) mice, compared to standard chemotherapy + placebo, without significant impact on body weights. Rocaglamide enhanced chemotherapy efficacy in wild-type p53 NPC xenografts but not p53-mutant variants, supporting its use as a stratified treatment strategy.

Keywords: combination therapy, nasopharyngeal carcinoma, NSG mice, rocaglamide, standard chemotherapy

Comparative Transcriptomic Analysis of Curcumin and the Diarylpentanoid Analogue MS13 in Chronic Myeloid Leukemia K562 Cells

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Abstract

Chronic myeloid leukemia (CML) is the second most common leukemia in the elderly. Curcumin is a natural bioactive compound from turmeric with anticancer activities; however, its clinical translation is limited by poor bioavailability. MS13, a novel curcumin diarylpentanoid analogue with a modified keto-enol bridge, has demonstrated promising anticancer activities against several cancer cell lines, including CML K562 cells. Previously, we demonstrated that both compounds induced mitochondrial dysfunction and caspase-3 activation during apoptosis in K562 cells. Pan-caspase inhibition completely abrogated MS13-induced apoptosis but not curcumin-induced cell death. This study aimed to further identify the upstream apoptotic pathways through transcriptomic analysis. Briefly, total RNA, primarily mRNA, was extracted from treated cells using the Qiagen RNeasy Mini Kit. The purity, concentration, and quality of the RNA samples were evaluated prior to whole-transcriptome sequencing. The transcriptomic profiling demonstrated that curcumin induced caspase-independent cell death, with significant upregulation of endoplasmic reticulum stress (ERS), mitogen-activated protein kinase (MAPK), autophagic and lysosomal signaling pathways. In contrast, MS13 differentially upregulated caspase-3 transcription, with a similar activation profile of the ERS, MAPK, and autolysosomal pathways. Crucially, pharmacological inhibition of either the ERS or MAPK pathway significantly enhanced curcumin- and MS13-induced apoptosis, indicating that the upregulated ERS and MAPK pathways function as compensatory, pro-survival cellular defense mechanisms rather than primary drivers of cell death. In conclusion, chemical modification of the keto-enol bridge in MS13 alters curcumin's mechanism of action. Both agents activate protective ERS and MAPK signaling, highlighting selective ERS and/or MAPK inhibition as a potential synergistic therapeutic strategy for CML.

Keywords: apoptosis; chronic myeloid leukemia; curcumin; endoplasmic reticulum stress; transcriptomics

Early Harvest Extra Virgin Olive Oil Modulates Metabolic Disturbances, Oxidative Status, and Hepatic Alterations in High-Fat Diet-Induced Metabolic Syndrome

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Abstract

Metabolic syndrome (MetS) is a global health concern characterized by obesity, insulin resistance, dyslipidaemia, and chronic inflammation. Prolonged high-fat diet (HFD) consumption exacerbates these metabolic disturbances, increasing the risk of cardiovascular disease and type 2 diabetes. Early harvest extra virgin olive oil (EHEVOO), rich in polyphenols and healthy fats, has attracted interest due to its potential metabolic benefits; however, evidence regarding its effects on diet-induced metabolic disorders remains limited. This study investigated the effects of EHEVOO supplementation on metabolic alterations in an HFD-induced MetS rat model. Male Sprague-Dawley rats were randomly assigned into experimental groups ($n = 6$ per group). MetS was induced by HFD feeding (55% of total calories from fat) for 12 weeks, followed by streptozotocin injection (35 mg/kg, i.p.). Rats received oral EHEVOO supplementation (1.0 mL/kg/day) for six weeks. Serum lipid profiles, liver function markers, oxidative stress parameters (SOD and GSH), and liver histopathology were assessed. Data were analysed using one-way ANOVA with Tukey's post hoc test ($p < 0.05$). Compared with normal controls, HFD-fed rats exhibited increased total cholesterol, elevated ALT and AST levels, reduced GSH and SOD activities, and hepatic steatosis, indicating metabolic disturbances, oxidative stress, and liver injury. EHEVOO supplementation significantly reduced total cholesterol, ALT, and AST levels while increasing GSH and SOD activities compared with untreated HFD rats. Histopathological assessment further revealed significant attenuation of hepatic steatosis and improved liver architecture. These findings support the potential of EHEVOO as a functional dietary intervention for ameliorating MetS-associated metabolic disturbances, oxidative stress, and hepatic alterations.

Keywords: early harvest extra virgin olive oil; high-fat diet; liver injury; metabolic syndrome; oxidative stress

Nanoformulated Fisetin Ameliorates Oxidative Stress-Induced Neuroinflammation Through Regulation of Nrf2 and NLRP3 Signalling

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Abstract

Neuroinflammation, mediated by oxidative stress, plays a critical role in the pathogenesis and progression of Alzheimer's disease (AD). Plant-derived flavonoids, including fisetin, have gained increasing attention due to their diverse pharmacological activities and favourable safety profiles. However, its therapeutic potential is limited by poor oral bioavailability resulting from low aqueous solubility and rapid hepatic metabolism. This study investigated the potential of nanoformulated fisetin in ameliorating oxidative stress-induced neuroinflammation in a mouse model. Fisetin nanosuspension was prepared via nanoprecipitation and subsequently characterized for its physicochemical properties. Following optimization, mice were treated with fisetin (10 and 20 mg/kg) or fisetin nanosuspension (10 mg/kg) for 21 days. Neurotoxicity was induced through intracerebroventricular (ICV) administration of A β _(25–35), followed by biochemical analyses. The optimized fisetin nanosuspension exhibited a particle size of 212.6 ± 0.467 nm, polydispersity index (PDI) of 0.068, zeta potential of -18.3 ± 0.24 mV, entrapment efficiency of 79.1%, and drug loading of 14.5%. Treatment with fisetin nanosuspension significantly increased Nrf2 expression ($p < 0.01$) while markedly reducing NLRP3 expression ($p < 0.0001$). Collectively, these findings suggest that fisetin nanosuspension exerts neuroprotective effects through activation of antioxidant defence and suppression of neuroinflammation, highlighting its potential as a multitarget therapeutic strategy for AD.

Keywords: Alzheimer's disease; fisetin; nanosuspension; neuroinflammation; oxidative stress

Adjunctive Non-Contact Pulsed Electromagnetic Field Therapy for a Chronic Diabetic Thigh Wound: A Case Report

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Abstract

Delayed healing of chronic wounds in type 2 diabetes mellitus (T2D) patients is associated with reduced tissue perfusion, persistent inflammation, and impaired tissue repair. Despite standard wound care and adjunctive therapies, a substantial proportion of patients continue to experience poor healing outcomes, highlighting the need for additional safe and effective treatment options. We report a 66-year-old man with T2D and multiple comorbidities who presented with delayed healing of a traumatic open wound on the posterior aspect of the right calf. Initial assessment revealed a 10.0 cm × 4.0 cm wound with healthy granulation tissue but limited improvement following conventional wound management. In addition to routine dressing, pulsed electromagnetic field (PEMF) therapy using the CRAD ULCER X-01 device was initiated as an adjunct treatment. Similar to existing models, this device generates a 10 V/m electric field, a 10–22 kHz rectangular waveform, and a 0.2 µT magnetic field, but it is specially designed for contactless operation. PEMF therapy was administered for one hour per session, three times weekly, over a four-month period. The wound demonstrated gradual and consistent size reduction throughout treatment. Wound area decreased by 70.0% at week five and 88.8% at week 11, achieving a 99.5% reduction with near-complete closure by week 17. No local or systemic infections or treatment-related adverse effects were observed. The patient also reported significant pain relief and improved joint mobility. The contactless CRAD ULCER X-01 delivers comparable clinical benefits while offering easier administration for chronic diabetic wounds, supporting its value as an adjunct to standard wound care.

Keywords: case report; diabetes complications; diabetes mellitus; electromagnetic field; wound healing

Safeguarding Digital Medicines: Ethical and Regulatory Challenges in Malaysian E-Pharmacy Services

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Abstract

The growth of e-pharmacies has made medicines more accessible, particularly for individuals in remote locations or with mobility challenges, replacing traditional pharmacy visits with online purchases. However, treating e-pharmacies like a conventional e-commerce platform raises ethical and regulatory concerns. The objective of this study is to explore stakeholders' awareness of the Guideline for E-pharmacy in Online Health Service 2022, focusing on protecting patient safety, ensuring data security, and mitigating risks of illegal or non-compliant platforms. A qualitative multi-method approach was employed involving 12 key stakeholders, including regulators, e-pharmacy operators, telemedicine practitioners, and relevant NGOs, through in-depth interviews and focus-group discussions from November 2024 to May 2025. Data were analysed using thematic analysis and triangulated with Verified Internet Pharmacy Practice Sites (VIPPS) observation as an international benchmark and documentary analysis of relevant government guidelines. The results revealed four main issues: (1) There are no legal penalties specific to non-compliant platforms; (2) No public-facing registry to verify a legitimate e-pharmacy; (3) Low public awareness about the risks of illegal e-pharmacy platforms; (4) Unclear division of roles between telemedicine providers and e-pharmacy operators. In conclusion, this study recommends consolidating Malaysia's fragmented legislation into a unified act with mandatory platform licensing, establishing a certified national registry modelled after VIPPS to boost public awareness, and forming a multi-stakeholder joint task force to define telemedicine and e-pharmacy roles to elevate ethical standards in Malaysia's digital health sector.

Keywords: e-pharmacy; online pharmacy; stakeholder; telemedicine; VIPPS

Strengthening Regional Health Security: The ASEAN Drug Security and Self-Reliance (ADSSR) Initiative and Public Health Emergency Preparedness

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Abstract

The COVID-19 pandemic and subsequent public health emergencies, such as mpox, exposed critical vulnerabilities in global supply chains, severely impacting medicine sustainability across countries. As a regional organization, the Association of Southeast Asian Nations (ASEAN) promotes multilateral cooperation among its member states to mitigate health security risks. This policy review evaluates key ASEAN initiatives aimed at ensuring medicine security and improving regional management of public health emergencies. A targeted review of policy frameworks, situational reports and strategic agreements related to medicine security for the past ten years in the ASEAN region was conducted. Five ($n = 5$) initiatives were found and highlighted in this policy review. First, Malaysia, as the lead country of the ASEAN Drug Security and Self-Reliance (ADSSR) initiative, convened its inaugural workshop among Member States in Putrajaya, Malaysia in 2019. Second, a regional survey evaluating the pharmaceutical ecosystem revealed critical dependencies on imported finished products and active pharmaceutical ingredients. Third, during the outbreak of mpox in 2024, ASEAN successfully executed a joint pooled procurement of mpox vaccines, securing rapid vaccine access for the region. Recognizing drug security as a core component of health security, the ADSSR initiative successfully secured political commitment through the ASEAN Leaders' Declaration of Commitment in 2025. To transition political commitments into operational realities, the ADSSR initiative has developed a strategic action plan to be implemented from 2026 to 2030. In conclusion, these five initiatives highlighted the regional effort in enhancing collaboration among member states by leveraging their strengths and building long-term regional self-reliance against future public health emergencies.

Keywords: access to medicine; drug security; pandemic preparedness; self-reliance; sustainability

Evaluating the Impact of a Short-Course CBRNE Preparedness Workshop on Healthcare Responders in Malaysia: Quasi-experimental pretest–posttest study

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Abstract

Effective CBRNE response requires specialised competencies, yet structured training remains limited among Malaysian healthcare first responders. To inform curriculum refinement, this study evaluated knowledge gains from a one-day course conducted in Klang Valley (June–July 2026). This quasi-experimental pretest–posttest study evaluated a one-day multimodal teaching course (lectures, skills stations, demonstrations, and a tabletop exercise) among 183 healthcare responders. Of 183 participants, 111 completed matched pre- and post-course assessments. Knowledge across seven domains, including PPE, preparedness, chemical agents, and scene management, was evaluated pre- and post-training using a 20-item questionnaire. Matched data were analysed using paired t-tests, 95% CIs, Cohen's d, and exact McNemar tests. Kruskal-Wallis tests were used to evaluate differences in scores across five major professional categories ($n = 109$). A paired-samples t-test showed a significant increase in knowledge scores from pre-course ($M = 12.95$, $SD = 3.48$) to post-course ($M = 16.00$, $SD = 3.12$), $t(110) = 8.46$, $p < 0.001$, $d = 0.80$. All seven domains improved significantly, led by toxic industrial chemicals (+30.2%, $p < 0.001$) and PPE selection (+21.4%, $p < 0.001$). Fourteen of 20 items improved significantly. There was no difference across professional categories ($p = 0.377$). Evaluated against Kirkpatrick's Level 2 framework and adult learning theory, this problem-centred course showed high educational efficacy across diverse professionals. Non-significant items clustered around institutional/administrative protocols and nerve-agent pharmacology, with a ceiling effect for workplace-hazard knowledge (> 90% pre-course) and persistently low administrator-action scores. The course significantly improved responder knowledge. These findings support the institutionalisation of structured CBRNE training through scenario-based exercises, with longitudinal evaluation of knowledge retention and performance.

Keywords: disaster medicine; hazardous materials (HazMat); Kirkpatrick evaluation model; mass casualty incidents

Clinical Outcomes of Non-Contact Pulsed Electromagnetic Field Therapy in Diabetic Foot Ulcers: A Case Series

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Abstract

This case series aimed to evaluate the clinical benefit of non-contact pulsed electromagnetic field (PEMF) therapy as an adjunct treatment for delayed wound healing in patients with diabetic foot ulcers (DFU). Nine patients (five males and four females) with DFU receiving standard wound care at the Department of Hyperbaric Medicine, Tuanku Mizan Armed Forces Hospital, between October 2025 and March 2026 were included. All wounds were irrigated with Prontosan[®], patted dry, and subsequently treated with PEMF therapy using the CRAD ULCER X-01 device for 1–2 hours per session. Following PEMF treatment, wounds were cleaned and dressed according to standard dressing protocols. Wound progression was assessed at each treatment session using serial measurements of wound length, width, and surface area. All cases demonstrated progressive wound healing, characterised by epithelialisation, healthy granulation tissue formation, and improved wound bed quality. Serial measurements showed consistent reductions in wound size compared with baseline values, including median wound length (11.0 vs. 7.0 cm, $p = 0.012$) and surface area (66.0 vs. 22.5 cm², $p = 0.008$), while reductions in wound width were not statistically significant (6.0 vs. 3.0 cm, $p = 0.109$). This case series provides preliminary evidence supporting the use of non-contact PEMF therapy with the CRAD ULCER X-01 device as an adjunct to standard wound care in the management of chronic DFU. PEMF therapy may offer an additional therapeutic option to enhance delayed wound healing in patients with type 2 diabetes, potentially reducing complications and improving quality of life in affected patient populations.

Keywords: diabetes mellitus; diabetic foot; electromagnetic field; wound healing

Global Patterns of Sugar-Sweetened Beverage Consumption After Tax Implementation Across Income Groups

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Abstract

Sugar-sweetened beverage (SSB) taxes are increasingly adopted to reduce unhealthy dietary consumption and mitigate non-communicable diseases. This study evaluated changes in SSB consumption before and after national SSB tax implementation using a global event study framework stratified by income group. Country-level SSB intake estimates from the Institute for Health Metrics and Evaluation Global Burden of Disease 2021 Dietary Risk Factors dataset were linked with national tax implementation years from the WHO/WCRF SSB Tax Database (August 2023). Consumption was indexed to 1.0 at the tax implementation year (Y0) and analysed across a 21-year event window (Y-10 to Y+10) for 97 taxed countries. Country-specific counterfactual trajectories were extrapolated from pre-tax log-linear trends; untaxed countries ($n = 65$), aligned to group-specific reference years, served as secular comparators. Post-tax trajectories varied substantially by income group. In high-income countries, observed consumption increased above both projected and untaxed trajectories following implementation. Upper-middle-income countries demonstrated observed trends closely aligned with projected counterfactuals but below the rising untaxed comparator. Lower-middle-income countries initially tracked below projected trends before increasing sharply in later years, whereas low-income countries showed relatively stable observed consumption despite projections of continued growth. These findings suggest that the relationship between SSB taxation and long-term consumption trends is complex and strongly influenced by economic context. The divergence between observed and projected trajectories, particularly in low-income settings, highlights uncertainty in long-term extrapolation from pre-tax trends. Post-tax consumption patterns are likely shaped by both tax policies and broader economic and dietary transitions, emphasising the need for context-aware evaluation.

Keywords: event study; non-communicable disease; policy evaluation; sugar-sweetened beverages; taxation

Circulating miR-21 Levels and Essential Hypertension: A Systematic Review and Meta-Analysis

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Abstract

Essential hypertension (EH) is a leading cardiovascular risk factor lacking precise biomarkers for early risk stratification. While emerging studies implicate microRNA (miRNA) dysregulation, particularly miR-21, individual findings remain inconsistent. This systematic review and meta-analysis aimed to evaluate the association between circulating miR-21 expression and EH. A systematic search of five electronic databases from inception to April 2026 identified studies assessing circulating miR-21 expression in human adults with EH. Pooled standardized mean differences (SMD) were calculated using random-effects models. Heterogeneity was evaluated using I^2 statistics. The Joanna Briggs Institute critical appraisal tool (cross-sectional) and the Newcastle-Ottawa Scale (cohort) were used for quality assessment. Of 16 identified studies (14 cross-sectional, 2 cohort), 10 were included in meta-analyses. Cross-sectional studies demonstrated a high risk of bias, while cohort studies showed low risk and some concerns. The initial pooled SMD was non-significant (SMD: 0.51, 95% CI: -0.11 to 1.12; $p = 0.11$, $I^2 = 92\%$). A sensitivity analysis by excluding two outliers yielded a significant SMD of 0.64 (95% CI: 0.33 to 0.90; $p < 0.001$; $I^2 = 67\%$). Subgroup analysis identified normalization controls ($p < 0.0001$) and ethnicity ($p = 0.03$) as significant sources for methodological and statistical heterogeneity. Notably, the two outliers uniquely utilized external spikes (cel-miR-39/cel-miR-54), while the remaining studies relied on internal controls (U6/RNU6B). Circulating miR-21 is significantly upregulated in EH when controlling methodological outliers, highlighting its potential as a clinical biomarker. However, standardized miRNA normalization protocols and large-scale, diverse validation cohorts remain critical prerequisites to confirm its utility in risk stratification.

Keywords: essential hypertension; meta-analysis; microRNA-21; systematic review

Hyperbaric Oxygen Therapy in Management of Toxic Optic Neuropathy Secondary to Alcohol Intoxication

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Abstract

Toxic optic neuropathy (TON) is a rare, vision-threatening condition often associated with alcohol intoxication. Conventional management with corticosteroids may be insufficient, underscoring the need for adjunctive therapies such as hyperbaric oxygen therapy (HBOT). We report a 31-year-old female patient with delayed presentation of sudden bilateral visual loss seven days after alcohol consumption. The diagnosis of TON was established based on clinical findings (complete loss of light perception), ophthalmological examination (blurred optic disc margins, hyperemic color, pale retina around the optic nerve head), and exclusion of alternative causes through physical and laboratory evaluation (no evidence of trauma or systemic disease). The patient initially received high-dose corticosteroids for five days but showed no improvement. HBOT was subsequently initiated (100% oxygen at 2.4 ATA) for 30 sessions. After four HBOT sessions, she regained light perception and was able to walk independently. Following 17 sessions, she could read large-font text on her mobile phone. At 30 sessions, visual acuity improved to 0.7 in the right eye with no further improvement on pinhole testing, and 1/60 in the left eye. Fundoscopy revealed a normal optic disc in the right eye, and in the left eye, a round papilla with firm boundaries, pale color, attached retina, and reduced macular reflex were observed. HBOT was temporally associated with visual improvement in this patient with toxic optic neuropathy secondary to alcohol intoxication, despite delayed presentation. While causality cannot be established from a single case, this observation suggests HBOT may warrant further investigation as a potential adjunctive therapy in toxic optic neuropathies.

Keywords: alcohol intoxication; hyperbaric oxygen therapy; toxic optic neuropathy; visual loss

Metabolic Syndrome as a Risk Factor of Working Memory Impairment: A Systematic Review and Meta-Analysis of Longitudinal Studies

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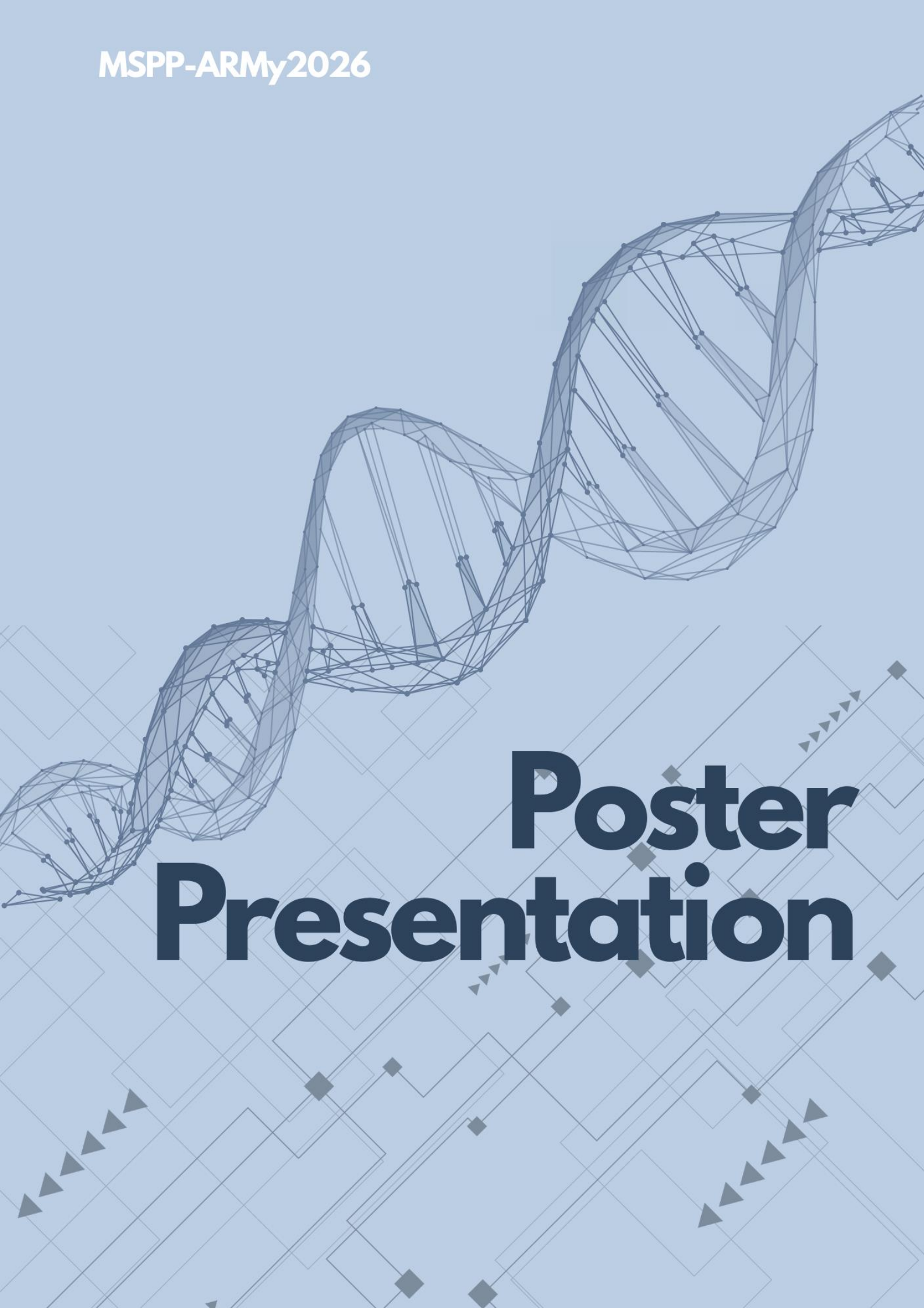
Abstract

Metabolic syndrome (MetS) is linked to cognitive decline, yet the evidence on its specific impact on working memory remains conflicting. This meta-analysis quantified the pooled longitudinal association between MetS and working memory performance. Five longitudinal cohort studies assessing MetS and working memory via Digit Span Backwards and Numerical Memory analysis were retrieved from the PubMed and Scopus databases. Quality assessments using the Newcastle-Ottawa Scale for Cohort Studies rated four papers as good quality and one paper as fair quality. Fixed-effects and random-effects models estimated the pooled correlation (r). Cochran's Q and I^2 statistics assessed heterogeneity, leave-one-out sensitivity analysis evaluated robustness, and both Egger's and Begg's tests evaluated publication bias. A total of 32,599 subjects were followed for cognitive assessments over 1–17 years. Meta-analysis results show that fixed-effects and random-effects models yielded identical pooled estimates, underscoring the stability and reliability of the findings. MetS was significantly associated with reduced working memory, with a small but highly significant negative pooled correlation ($r = -0.033$; 95% CI: -0.0438 to -0.0221 ; $p < 0.001$). No statistical heterogeneity was observed across the included studies (Cochran's Q : $p = 0.472$; $I^2 = 0.00\%$). Leave-one-out sensitivity analyses confirmed the stability of the primary effect across all iterations ($p < 0.05$). Furthermore, no evidence of publication bias was detected by Egger's ($p = 0.935$) or Begg's tests ($p = 0.817$). The present work demonstrates a significant longitudinal association between MetS and impaired working memory performance. The high degree of cross-study consistency strengthens the clinical importance of actively targeting modifiable metabolic risk factors to preserve this critical cognitive domain.

Keywords: cognitive dysfunction; meta-analysis; metabolic syndrome; short-term memory

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Poster Presentation

**Navigating Digital Healthcare Innovation in Hospital Systems:
A Systematic Review of System-Level Challenges and Strategic Responses**

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Abstract

This study presents a systematic literature review examining the implementation of digital healthcare innovation within hospital systems, with a particular focus on system-level challenges and strategic responses. Drawing on evidence from Scopus, Web of Science, and PubMed databases, the review follows the PRISMA protocol to synthesise recent empirical studies (2021–2026) that investigate integrated digital health systems in real-world hospital contexts. The findings reveal that digital healthcare innovation is shaped by a complex interplay of technological, organisational, and governance-related factors that collectively influence implementation outcomes. Key challenges identified include interoperability fragmentation across heterogeneous systems, data quality and cybersecurity vulnerabilities, limited digital competencies among healthcare professionals, resource and infrastructural constraints, and disruptions to clinical workflows. These challenges are not isolated but interdependent, often reinforcing system complexity and hindering effective integration and scalability. In response, the review highlights multidimensional strategies that extend beyond technical solutions, including the adoption of standardised interoperability frameworks, strengthened data governance structures, continuous workforce training, workflow redesign, and phased implementation supported by strong leadership and stakeholder engagement. Building on these insights, the study advances a conceptual contribution through an adaptive, system-level perspective that frames digital healthcare innovation as a dynamic and iterative process requiring continuous alignment across technological, human, and organisational dimensions. By shifting beyond fragmented and technology-centric approaches, this review provides a more coherent understanding of how digital innovations can be effectively implemented and sustained within complex hospital systems. The findings offer practical implications for healthcare administrators and policymakers seeking to achieve scalable, integrated, and sustainable digital transformation in healthcare environments.

Keywords: digital health; healthcare management; smart hospital transformation; system integration; system interoperability

Advancing Digital Healthcare Innovation: A Systematic Review of Predictive Analytics and Ethical Governance in Patient Outcomes

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Abstract

This study presents a systematic literature review examining how data science advances digital healthcare innovation in patient outcome prediction, with a particular focus on predictive analytics and ethical governance. Drawing on evidence from Scopus and Web of Science databases, the review follows the PRISMA framework to synthesise findings from 14 empirical studies published between 2021 and 2026. The results demonstrate that predictive analytics, including machine learning, deep learning, and multimodal modelling, significantly enhance prognostic accuracy across diverse clinical domains such as oncology, transplantation, critical care, and chronic disease management. Beyond performance improvement, data science increasingly supports real-time clinical decision-making, risk stratification, and personalised care delivery through integration with electronic health records and clinical decision support systems. However, the findings also reveal critical ethical challenges that accompany the adoption of predictive technologies. Key concerns include algorithmic bias, subgroup miscalibration, limited transparency of complex models, data privacy risks, and unclear accountability in high-stakes clinical decisions. These issues highlight that predictive systems operate as socio-technical infrastructures requiring robust governance mechanisms. Emerging approaches such as explainable artificial intelligence, fairness auditing, and privacy-preserving architectures (e.g., federated learning) are identified as essential strategies to ensure responsible implementation. This review advances a conceptual understanding of digital healthcare innovation by positioning predictive analytics as both a clinical performance enhancer and an ethically embedded system. It emphasises the need to balance technical optimisation with governance, clinician oversight, and patient-centred communication. The findings provide practical insights for healthcare practitioners, policymakers, and system developers seeking to achieve accurate, equitable, and accountable patient outcome prediction in increasingly data-driven healthcare environments.

Keywords: algorithmic fairness; clinical decision support systems; ethical AI in healthcare; machine learning in healthcare; patient outcome prediction

From COVID-19 Challenges to Digital Innovation: Digitalization of HAI Bundle Care Using the HCAI Shield Application

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Abstract

The COVID-19 pandemic placed unprecedented pressure on healthcare systems and increased concerns regarding hospital-acquired infections (HAIs) and infection prevention practices. These challenges highlighted the need for accessible digital health tools to support healthcare professionals (HCPs) in implementing evidence-based HAI bundle care. To evaluate the impact of COVID-19 on HAI rates and develop a mobile health (mHealth) application to support HAI prevention practices. A retrospective before-and-after study was conducted at Sultan Ahmad Shah Medical Centre among 578 admitted patients during April–October 2019 (pre-COVID-19) and April–October 2020 (during COVID-19), comparing HAI rates using chi-square analysis. A mobile application was developed based on national and international HAI bundle care guidelines and standard precaution measures. A pilot usability evaluation was conducted among HCPs using convenience sampling and the Mobile Application Usability Questionnaire (MAUQ). The overall HAI rate slightly decreased from 12.1% pre-COVID-19 to 11.3% during COVID-19 ($p = 0.70$). The HCAI Shield application was successfully developed with four main menus incorporating HAI bundle care, hand hygiene, personal protective equipment, and standard precautions. The application demonstrated good usability among HCPs, with a mean usability score of 5.28 ± 0.38 and high ratings for ease of use, interface and user satisfaction. Despite enhanced infection prevention measures during the pandemic, an insignificant reduction in HAI rates was observed during COVID-19, indicating persistent infection control challenges. The HCAI Shield application demonstrated good usability and may serve as a practical digital platform to support the implementation of HAI bundle care among HCPs. Further large-scale evaluation is recommended.

Keywords: COVID-19; digital health; hospital-acquired infections; infection prevention; mHealth

Beyond the Classroom: A Systematic Thematic Analysis of Medical Students' Reflections in an Anti-Drug Abuse Community Outreach Program

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Abstract

Medical students often lack authentic opportunities to translate complex pharmacological knowledge into accessible public health education. This study investigates how participating in an interactive, peer-delivered community engagement program shapes medical students' professional learning, personal growth, and identity as future medical doctors and public health advocates. An artificial intelligence (AI)-assisted systematic thematic analysis was conducted on 52 handwritten reflective essays by Year 2 medical students from Universiti Pertahanan Nasional Malaysia (UPNM) following the Program Eksplorasi & Realiti Isu Sains Anti-Dadah Interaktif (PERISAI). PERISAI was a community-engagement project undertaken as part of the "Substances of Abuse" topic within their Pharmacology course, involving approximately 200 secondary-school students at Maktab Tentera Diraja. Applying a six-step AI-assisted thematic analysis framework, the analysis identified four primary themes: "From apprehension to confidence", "Translating science into engaging education", "Interactive engagement as a pedagogical bridge", and "Forging the future medical educator". Students successfully navigated logistical pressures and translated technical science into relatable concepts using interactive methods such as live theatre performance, infographic booths, and live demonstrations, including intravenous drug administration and cardiopulmonary resuscitation (CPR) simulations. This experience facilitated the transition from initial nervousness to increased self-efficacy. The findings culminated in the "Reflective educator development cycle," a conceptual model illustrating how students develop "Experiential confidence" and "Preventive professionalism". In conclusion, authentic community teaching tasks bridge the gap between clinical pharmacology and public health. They are powerful tools that reinforce pharmacological concepts while building the communication skills, teamwork, and preventive-care values necessary to empower future medical doctors to educate their communities.

Keywords: community engagement; health education; medical students; pharmacology; thematic analysis

The Role of GSK-3 in HeLa Cervical Cancer Cells: A Scoping Review of *In Vitro* Studies

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Abstract

Glycogen synthase kinase-3 (GSK-3) plays a complex regulatory role in human papillomavirus (HPV)-driven malignancies, making it a highly compelling therapeutic target in cervical cancer. This scoping review synthesizes *in vitro* evidence evaluating the expression, activity, and regulatory roles of GSK-3 specifically within HPV-driven HeLa cervical cancer cells. Following the PRISMA-ScR guidelines, a structured search of PubMed, Scopus, and ScienceDirect was conducted to identify peer-reviewed, English-language primary studies presenting *in vitro* experimental data on GSK-3 in HeLa cells. Studies lacking mechanistic validation, utilizing non-HPV cell lines, or incorporating *in vivo* and clinical patient data were excluded. Six studies (five GSK-3 β , one GSK-3 α) met the inclusion criteria. Synthesized data reveal that targeted downregulation of GSK-3 α yields anti-cancer effects via p21-mediated cell-cycle arrest and the reversal of epithelial-mesenchymal transition (EMT). Baseline GSK-3 β activity suppresses PI3K/Akt survival signaling and induces apoptosis via MCL-1 degradation. Additionally, inhibiting upstream kinases to restore GSK-3 activity triggers anti-tumor responses. In conclusion, GSK-3 acts as a multifaceted regulator in HeLa cells. Both isoform-specific inhibition and restoration of GSK-3 baseline activity can effectively disrupt cervical cancer proliferation and induce apoptosis. These findings suggest potential therapeutic targets that warrant further investigation in preclinical models.

Keyword: cervical cancer cell; glycogen synthase kinase-3; HeLa, *in vitro*; scoping review

The KEPT App: A Theory-Driven mHealth Intervention for Antenatal Pelvic Floor Muscle Training

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Abstract

Pelvic floor muscle training (PFMT) effectively manages urinary incontinence (UI) during pregnancy, yet adherence remains low due to the challenge of visualizing non-visible pelvic muscles without structured guidance. To address this gap, this study systematically designed a theory-driven mobile health (mHealth) intervention that is the Kegel Exercise Pregnancy Training or KEPT app, using the Behaviour Change Wheel (BCW) framework and COM-B model to enhance PFMT adherence among antenatal primary care patients. Guided by a three-stage BCW methodology, we mapped targeted behaviors and adherence barriers to COM-B components, evaluated active intervention functions against Acceptability, Practicability, Effectiveness, Affordability, Side-effects, and Equity (APEASE) criteria, and translated them into specific digital Behavior Change Techniques. The resulting KEPT app framework systematically overcomes key psychological, physical, and environmental barriers through expert-led instructional videos for proper muscle contraction, automated daily reminders, gamified reward systems (points and star collections) to build self-efficacy, and digital peer-support modules to reduce stigma. Furthermore, the app integrates contextual prompts that anchor PFMT to daily activities, facilitating automatic habit formation. In conclusion, applying the BCW framework provides a robust, scalable digital intervention strategy that translates complex behavioral theory into practical primary care delivery. By bridging the gap between clinical recommendation and patient execution, the KEPT app provides primary care providers with an accessible tool to empower pregnant women, strengthen antenatal UI management, and serve as a scalable foundation for future digital health interventions across diverse obstetric and gynecological populations.

Keywords: Behaviour Change Wheel; COM-B model; mHealth; pelvic floor muscle training; urinary incontinence

Machine Learning for Pharmaceutical Demand Forecasting: A Narrative Review of Forecasting Evolution and Data-Driven Model Selection

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Abstract

Accurate pharmaceutical demand forecasting is essential for ensuring medicine availability, optimizing inventory management, and reducing waste across pharmaceutical supply chains. Recent advances in statistical, machine learning (ML), deep learning (DL), and hybrid models have expanded forecasting capabilities. However, existing reviews primarily compare forecasting algorithms while providing limited insight into how data characteristics influence model selection. This narrative review aims to synthesize the evolution of pharmaceutical demand forecasting methods and examine how dataset characteristics influence forecasting model selection. A comprehensive literature search was conducted using Web of Science, Scopus, and PubMed from inception to July 2026, supplemented by manual reference screening. The literature was thematically reviewed, identifying 21 key studies. The review synthesized literature concerning dataset characteristics, proposed forecasting models, additional input features, and comparator models. Studies were classified by number of observations as micro/small (< 10,000), moderate (10,000 to < 200,000), large (200,000 to < 1,000,000), and massive ($\geq$ 1,000,000). The findings indicate a clear progression from traditional statistical approaches to ML, DL, and hybrid models. More importantly, the review demonstrates that forecasting performance is influenced not only by algorithm selection but also by dataset size and additional input features. Conventional statistical and ML models remain effective for smaller and less complex datasets, whereas DL and hybrid models are better suited to larger datasets enriched with features such as seasonality and epidemiological data. Overall, this review contributes a data-driven perspective on forecasting model selection and provides practical guidance for developing effective pharmaceutical demand forecasting systems.

Keywords: artificial intelligence; machine learning; pharmaceutical demand forecasting; predictive modelling; supply chain

Digital Access as a Behavioural Insights Component in MyMediSAFE Implementation for Safe Medicine Disposal in Malaysia

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Abstract

Improper disposal of unused, expired or damaged medicines may contribute to environmental contamination and health risks. Uncertainty about where and how to return medicines creates barriers despite intentions to dispose of them safely. MyMediSAFE addresses these barriers through collection centres and a digital locator. This study evaluated digital access as a behavioural insights' component in MyMediSAFE implementation and examined digital engagement and medicine return. A retrospective longitudinal evaluation used programme records, Google Analytics data from October 2024 to June 2026, and semi-annual medicine collection data from July 2024 to June 2026. Descriptive statistics quantified growth in collection centres, patterns of locator utilisation and collection volumes. Linear regression assessed locator trends, Spearman's correlation examined the relationship between active users and locator utilisation, and the Friedman test evaluated collection volumes over time. Digital access was mapped to friction reduction, simplification, salience, reduced cognitive burden and choice architecture. Collection centres increased from 705 to 1,248. Locator utilisation increased by 23.3 uses per month ($p = 0.0009$) and correlated strongly with monthly active users ($\rho = 0.852$, $p < 0.001$), supporting its role in nudging users towards collection centres. Medicines collected and disposed of appropriately at Ministry of Health facilities increased by 341% from 3,948.98 kg (July–December 2024) to 17,413.00 kg (January–June 2026); volumes differed significantly across periods ($\chi^2(3)=33.20$, $p < 0.001$). Embedding digital access into behaviourally informed implementation may reduce search effort, simplify decision-making, and support safe medicine disposal at expanded collection centres.

Keywords: behavioural insights; digital access; healthcare innovation; medicine disposal; MyMediSAFE

Standardised *Tinospora crispa* Extract Reduces Atherosclerotic Plaque and Demonstrates Favourable Safety Profile in Preclinical Studies

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Abstract

Atherosclerosis, a leading cause of cardiovascular mortality worldwide, is characterised by chronic vascular inflammation and progressive arterial lipid deposition, necessitating multi-targeted therapeutic strategies. *Tinospora crispa* is a climbing shrub widely used as traditional medicine, recognised for its antioxidant, anti-inflammatory, and lipid-lowering properties. This study aimed to evaluate the genotoxic safety and anti-atherosclerotic efficacy of a standardised aqueous extract of *T. crispa* through validated preclinical assessments. Genotoxicity was determined via an in vivo micronucleus assay in bone marrow cells. Acute toxicity was conducted following OECD Guideline with a single oral dose up to 5,000 mg/kg, whilst subacute toxicity was assessed over 28 days in Sprague Dawley rats. Parameters evaluated included clinical observations, body weight progression, haematological indices, serum biochemistry, and histopathological examination of major organs. Anti-atherosclerotic efficacy was investigated using the apolipoprotein E-deficient (ApoE^{-/-}) mouse model, maintained on an atherogenic diet, with *T. crispa* extract administered orally for 57 days. *T. crispa* extract demonstrated no genotoxic activity and was well tolerated up to 5,000 mg/kg, with no adverse effects on organ function or tissue integrity. Treatment significantly reduced atherosclerotic plaque area and markedly improved lipid profiles, including reductions in LDL and total cholesterol in ApoE^{-/-} mice compared to untreated controls. These findings support *T. crispa* as a safe and promising botanical candidate for atherosclerosis prevention, warranting further clinical evaluation.

Keywords: ApoE^{-/-} mouse model; atherosclerosis; genotoxicity; lipid profile; *Tinospora crispa*

Anti-Angiogenic Effect of *Persicaria minor* Aqueous Extract in TNF- α -Induced HUVECs: An Integrated Network Pharmacology, Molecular Docking and In Vitro Study

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Abstract

Angiogenesis plays a critical role in the development of diseases such as atherosclerosis and cancer. *Persicaria minor* (Huds.) Opiz (sy. *Polygonum minus* Huds.), commonly known as *Kesum* in Malaysia, is traditionally valued for its anti-oxidative and anti-inflammatory properties. However, its anti-angiogenic potential remains unclear. This study aimed to evaluate the anti-angiogenic activity of aqueous extract of *P. minor* (AEPM). Network pharmacology identified molecular targets of AEPM bioactive compounds, quercitrin and quercetin-3-O-glucuronide (Q3G), revealing 119 angiogenesis-related genes enriched in biological processes and signaling pathways. Molecular docking further demonstrated strong binding affinities between these compounds and 10 hub angiogenesis genes, suggesting regulatory involvement. *In vitro* assays using human umbilical vein endothelial cells (HUVECs) showed that pretreatment with AEPM (300 μ g/mL for 18 hours) followed by tumor necrosis factor-alpha (TNF- α) induction (6 hours) significantly reduced endothelial migration, proliferation and tube formation. Dexamethasone (1 μ M) served as positive control in this study. AEPM also suppressed VEGF and bFGF mRNA expression and decreased VEGF protein levels in TNF- α -induced HUVECs. Collectively, these findings demonstrate that AEPM effectively inhibits angiogenesis by targeting key endothelial functions and angiogenic mediators. In conclusion, *P. minor* aqueous extract exhibits promising anti-angiogenic activity, highlighting its potential as a natural therapeutic agent for angiogenesis-related diseases.

Keywords: angiogenesis; endothelial cell; *Persicaria minor*; tumor necrosis factor-alpha, vascular endothelial growth factor (VEGF)

Bee Bread Attenuates Hepatic Steatosis and Insulin Resistance in MASLD Through Activation of AMPK Signaling

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Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) is characterized by excessive hepatic lipid accumulation and insulin resistance, with limited effective therapeutic options currently available. Bee bread, a fermented bee product rich in phenolic compounds and flavonoids, has demonstrated beneficial metabolic effects; however, its mechanisms against MASLD remain incompletely understood. This study investigated the hepatoprotective effects of bee bread on hepatic steatosis and insulin resistance in high-fat diet (HFD)-induced MASLD rats, with emphasis on AMP-activated protein kinase (AMPK) signaling. Forty male Sprague-Dawley rats were assigned to normal control, HFD, HFD supplemented with bee bread (0.5 g/kg/day), or HFD supplemented with orlistat (10 mg/kg/day) for 12 weeks. Hepatic histology, free fatty acid (FFA) levels, AMPK concentration, and the expression of genes involved in lipid metabolism and insulin signaling were evaluated. Bee bread significantly reduced liver weight and serum and hepatic FFA levels while improving hepatic architecture and glycogen accumulation compared with untreated HFD rats. These effects were associated with increased hepatic AMPK levels, downregulation of lipogenic mediators including sterol regulatory element-binding protein-1c (SREBP-1c) and fatty acid synthase (FAS), and enhanced expression of insulin signaling components, including GLUT2, IRS-2, and PI3K. Collectively, bee bread attenuated hepatic steatosis and improved hepatic insulin sensitivity through modulation of AMPK-mediated metabolic pathways. These findings highlight bee bread as a promising natural product candidate for precision-based therapeutic strategies targeting MASLD.

Keywords: AMPK signaling; bee bread; hepatic steatosis; insulin resistance; MASLD

Effects of Ifenprodil on Mobility Performance, Spinal Nociceptive Signalling, and Memory Function in Complete Freund's Adjuvant-Induced Chronic Polyarthritis Rats

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Abstract

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease characterised by persistent pain, impaired mobility, and reduced quality of life. Activation of the N-methyl-D-aspartate receptor subtype 2B (NMDAR-2B) contributes to central sensitization and chronic pain signalling. Ifenprodil, a selective NMDAR-2B antagonist, has demonstrated antinociceptive effects in experimental pain models. This study evaluated the therapeutic effects of ifenprodil on mobility performance, spinal nociceptive signalling, and memory function in a complete Freund's adjuvant (CFA)-induced chronic polyarthritis rat model. Arthritic rats received intrathecal administration of ifenprodil (0.5 or 1.0 µg/µL) or sodium diclofenac (6 µg; positive control), while arthritic and non-arthritic control groups received 0.9% normal saline for seven consecutive days (days 16–22 post-induction). Mobility performance was assessed using a mobility scoring scale, while memory function was evaluated using the Novel Object Recognition Test (NORT). Assessments were conducted at baseline (day 0), pre-intervention (day 15), and post-intervention (day 23). Lumbar spinal cord tissues (L4–L5) were collected for immunohistochemical and RT-qPCR analyses. Treatment with ifenprodil, particularly at 0.5 µg/µL, significantly improved mobility performance and enhanced memory function, as indicated by a higher discrimination index. Moreover, ifenprodil markedly reduced the protein and mRNA expression of total and phosphorylated NMDAR-2B, brain-derived neurotrophic factor (BDNF), ionised calcium-binding adapter molecule-1 (Iba-1), and P2X4 receptor (P2X4R). These effects were comparable to those observed with sodium diclofenac treatment. In conclusion, ifenprodil improved functional and cognitive outcomes while suppressing spinal nociceptive signalling in chronic polyarthritis rats, supporting its therapeutic potential for managing RA-associated pain and disability.

Keywords: brain-derived neurotrophic factor (BDNF); complete Freund's adjuvant; ifenprodil; N-methyl-D-aspartate receptor-2B (NMDAR-2B); rheumatoid arthritis

Bee Bread Ameliorates Cardiometabolic Parameters Through Modulation of Myocardial Fatty Acid Synthase Expression in Obese Rats

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Abstract

Bee bread has been widely used as a dietary supplement due to its potential health-promoting properties. This study evaluated the effects of bee bread supplementation on cardiometabolic parameters and myocardial histological changes in high-fat diet (HFD)-induced obese rats. Male Sprague Dawley rats were fed an HFD for six weeks to induce obesity. The obese rats were subsequently treated with 0.5 g/kg/day bee bread (Ob/Bb group), 10 mg/kg/day orlistat (Ob/Or group), or distilled water (Ob group) via oral gavage for an additional six weeks. Compared with normal diet-fed rats, the Ob group showed a significant increase in the Lee obesity index and significant adverse alterations in cardiometabolic parameters, including the Lee obesity index, total cholesterol, triglycerides, low-density lipoprotein, free fatty acids, glucose, and insulin levels. Histological examination revealed cardiomyocyte hypertrophy, while cardiac mRNA expression analysis demonstrated upregulation of fatty acid synthase (*FAS*). Compared with the Ob group, bee bread supplementation significantly improved the Lee obesity index, cardiometabolic parameters, and myocardial histological architecture. Furthermore, bee bread significantly downregulated myocardial *FAS* mRNA expression compared with untreated obese rats. These improvements were comparable to those observed in the orlistat-treated group. The findings suggest that bee bread exerts cardiometabolic protective effects in obesity, potentially through modulation of *FAS*, a key enzyme involved in *de novo* fatty acid synthesis. Therefore, bee bread may represent a promising natural intervention for obesity-associated cardiometabolic disturbances.

Keywords: bee bread, cardiometabolic, fatty acid synthase, heart, obesity.

Palm Tocotrienol-Rich Fraction Supplementation Counteract the Lipotoxicity Effect of High-Fat Diet on Oocyte Quality

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Abstract

Palm tocotrienol-rich fraction (TRF) possesses potent antioxidant and anti-obesity properties. High-fat diet (HFD)-induced obesity causes oxidative stress that negatively affects reproductive health. However, there are limited studies on whether TRF supplementation can alleviate the lipotoxicity-induced oxidative damage in the female reproductive system. Thirty-two, six-week-old female mice were divided into four groups, and treated for 12 weeks: Group 1: Normal control (given standard mouse chow diet; 10 g/100 g fat); Group 2: HFD (45 g/100 g fat)-induced obesity; Group 3: HFD-induced obesity (given palm olein as vehicle); Group 4: HFD-induced obesity + TRF supplementation. Mice were given TRF for 8 weeks via oral gavage daily (0.1 ml) at a dose of 150 mg/kg BW, 4 weeks after the induction of obesity. At the end of the treatment period, all mice underwent superovulation, were euthanized, and serum, ovaries, and oocytes were collected concurrently. Serum was analyzed for triglyceride (TG) levels, ovaries were examined for the expression of oxidative DNA damage response genes (*CHEK1/2*), and oocytes were assessed for quality. The HFD group showed significantly higher TG levels ($p < 0.05$), indicating lipotoxicity, and elevated *CHEK1* and *CHEK2* expression ($p < 0.001$) compared to controls. In contrast, TRF supplementation reduced TG levels and normalized the expression of these genes. Additionally, the percentage of normal oocytes in the HFD group was significantly lower ($p < 0.001$) than in the controls, but TRF supplementation restored oocyte quality. In summary, TRF effectively counteracts HFD-induced lipotoxicity, reduces oxidative damage in the ovaries, and improves oocyte quality.

Keywords: high-fat diet, lipotoxicity, oocyte, oxidative stress, tocotrienol-rich fraction

Effects of Early-Harvest Extra Virgin Olive Oil Supplementation on Serum Leptin and Adiponectin in High-Fat Diet-Induced Obese Rats

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Abstract

Obesity is a metabolic disorder characterised by excessive adipose tissue accumulation and adipokine dysregulation. Although extra virgin olive oil (EVOO) has shown beneficial metabolic effects, the impact of early harvest extra virgin olive oil (EHEVOO) remains unclear. Therefore, this study evaluated the effects of EHEVOO supplementation on body weight, food intake, Lee obesity index, and adipokine secretion in a high-fat diet (HFD)-induced obese rat model. Male Sprague Dawley rats were randomly assigned to six groups ($n = 6$): a normal control, an HFD control, and HFD-fed groups supplemented with EHEVOO (0.5, 1.0, and 3.0 mL/kg body weight) for six weeks. Food intake was recorded daily, and body weight recorded every six days. Following overnight fasting, rats were euthanised and blood samples collected for biochemical analysis. Serum leptin and adiponectin concentrations were measured using enzyme-linked immunosorbent assay (ELISA) kits. Data were analysed using GraphPad Prism, with significance set at $p < 0.05$. 3.0 mL/kg EHEVOO group exhibited significantly lower body weight gain compared with the HFD group. Food intake was significantly reduced in the 3.0 mL/kg EHEVOO group compared with all other groups. The Lee obesity index was significantly lower in all EHEVOO-treated groups than in the HFD group. Furthermore, serum leptin concentration was significantly reduced in the 1.0 mL/kg EHEVOO group, while serum adiponectin concentration was significantly increased in the 0.5 mL/kg and 1.0 mL/kg EHEVOO groups compared with the HFD group. EHEVOO supplementation improved obesity-related parameters and modulated adipokine secretion in HFD-induced obese rats, suggesting its potential as a dietary intervention against obesity-associated adipokine dysregulation.

Keywords: adiponectin; early harvest extra virgin olive oil; high-fat diet; leptin; obesity

Antihypertensive and Vasculoprotective Effects of *Etlingera elatior* (Kantan) Flower Aqueous Extract in a Hypertension Rat Model

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Abstract

Hypertension remains a leading risk factor for cardiovascular morbidity despite the availability of multiple antihypertensive agents, highlighting the need for novel therapies that provide both blood pressure control and vascular protection. *Etlingera elatior* (Kantan), a medicinal plant traditionally consumed in Southeast Asia, possesses antioxidant and anti-inflammatory properties, but its antihypertensive efficacy has yet to be comprehensively validated *in vivo*. This study aimed to evaluate the antihypertensive, safety, and vasculoprotective effects of aqueous *E. elatior* flower extract (EEAE) using a standardized preclinical validation framework. A standardized aqueous extract was prepared and characterized for phytochemical content. Acute oral toxicity was assessed according to OECD Guideline 425, while antihypertensive efficacy was investigated in nitric oxide-deficient hypertensive rats induced by N ω -nitro-L-arginine methyl ester (L-NAME). Animals received EEAE at 500 or 1,000 mg/kg for four weeks following hypertension induction. Blood pressure was monitored throughout the treatment period, and thoracic aortic tissues were subjected to histopathological examination. EEAE demonstrated a favourable safety profile with no mortality or significant toxicity at doses up to 2,000 mg/kg. Both treatment doses significantly reduced systolic blood pressure compared with untreated hypertensive rats, with the 1,000 mg/kg dose producing the greatest antihypertensive effect. Histological analysis revealed attenuation of vascular smooth muscle hypertrophy, reduced collagen deposition, and preservation of normal aortic architecture, indicating substantial vasculoprotective activity. These findings demonstrate that EEAE exerts dose-dependent antihypertensive and vascular protective effects while exhibiting a wide safety margin, supporting its potential as a promising natural therapeutic candidate for hypertension management and warranting further mechanistic and translational investigations.

Keywords: antihypertensive; *Etlingera elatior*; hypertension; medicinal plants; vasculoprotection

Hepatoprotective Effects of *Etlingera elatior* Flower (Bunga Kantan) Extract in a High-Fat, High-Cholesterol Diet-Induced NAFLD Rat Model

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Abstract

Non-alcoholic fatty liver disease (NAFLD) is the presence of hepatic steatosis detected by imaging techniques or histology. Hepatic steatosis is characterised by excessive lipid accumulation in hepatocytes driven by dyslipidaemia and oxidative stress. Although *Etlingera elatior* flower (bunga kantan) possesses antioxidant properties, its hepatoprotective effects in NAFLD remain poorly understood. This study aimed to evaluate the effects of *E. elatior* flower aqueous extract (AEEe) on hepatic steatosis in a high-fat, high-cholesterol diet (HFHCD)-induced NAFLD rat model. Twenty-eight male Sprague-Dawley rats were assigned to four groups (n=7/group): Control, HFHCD, HFHCD + AEEe (1000 mg/kg/day), and HFHCD + Atorvastatin (20 mg/kg/day). Rats were fed the HFHCD for 12 weeks, while AEEe or atorvastatin was administered during the final six weeks. Compared with the Control group, the HFHCD group demonstrated significantly higher lipid profiles (total cholesterol and LDL-cholesterol) and oxidative stress marker (oxidised-LDL). Furthermore, the HFHCD group showed significantly decreased antioxidant enzyme activities (superoxide dismutase and catalase) and demonstrated marked hepatic steatosis characterised by extensive lipid vacuole accumulation within hepatocytes as confirmed by haematoxylin & eosin (H&E) staining. Treatment with AEEe significantly improved lipid profiles, reduced oxidative stress, restored antioxidant enzyme activities, and attenuated hepatic steatosis, with effects comparable to those of atorvastatin treatment. In conclusion, AEEe protects against HFHCD-induced NAFLD by ameliorating dyslipidaemia, suppressing oxidative stress, enhancing endogenous antioxidant defence, and preserving hepatic architecture. These findings suggest that AEEe may serve as a promising natural antioxidant and hepatoprotective agent for the prevention or management of NAFLD.

Keywords: *Etlingera elatior*; hypercholesterolaemia; NAFLD; oxidative stress; oxidised-LDL

From Andrographolide to Precision Oncology Therapeutics: A Web of Science-indexed Bibliometric Mapping and Network Analysis

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Abstract

Andrographolide is a principal ingredient of *Andrographis paniculata* (Burm.f.) Wall. ex Nees (Acanthaceae), an abundant herb in Southeast Asia known as ‘*hempedu bumi*’. While prior studies have established its substantial anticancer properties, a comprehensive analysis of research trends and emerging themes remains elusive. This study addresses the gap in mapping global publication patterns by evaluating the top countries, authors, journals, institutions, articles and subjects, and analysing the research life cycle and co-occurrence network. The terms ‘andrographolide’ AND ‘anticancer’ were searched in the Web-of-Science (WOS) database, yielding 261 publications. ScientoPy and Biblioshiny were used for performance analysis and network mapping. Performance-wise, the annual growth rate is 12.33% spanning 2004 to 2025. China is the leading country (86 publications), while Ye Zhang is the most prolific author (5 publications). Bioorganic & Medicinal Chemistry Letters is the most productive journal (14 publications). The Institute of Pharmaceutical Education and Research, India, had the largest output (11 publications). Kumar et al. (2004) published the article with the most citations (367). ‘Pharmacology and Pharmacy’ is the most indexed subject (126 publications). Life cycle analysis estimates a cumulative publication approaching saturation close to 459 publications by 2050, reflecting a mature niche. The keyword co-occurrence map reveals three clusters: natural product aspects, anticancer mechanisms and chemical derivatives. The findings highlight trending topics and under-researched themes, mainly on preclinical studies, which could be attributed to dynamic research landscapes. Conclusively, andrographolide has attracted global interests due to its promising anticancer role. Nonetheless, its translational application in precision oncology requires in-depth exploration.

Keywords: andrographolide; bibliometric; cancer therapeutics; network analysis; research trend

Marantodes pumilum Selenium Nanoparticle-Fortified Nanocellulose Hydrogel Exhibits Biocompatibility, Selective Antibacterial Activity, and Controlled Particle Release for Diabetic Wound Care Applications

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Abstract

Diabetic wound healing remains clinically challenging due to prolonged inflammation, impaired fibroblast migration, and susceptibility to secondary bacterial infection, driving the search for alternative therapeutic dressings. This study evaluated the *in vitro* biocompatibility, antibacterial activity, and release behaviour of *Marantodes pumilum*-synthesised selenium nanoparticles (MP-SeNPs) incorporated into a nanocellulose hydrogel. Cytotoxicity was assessed via MTT assay on NIH-3T3 fibroblasts, migration via scratch assay, and antibacterial activity via disc diffusion against *Staphylococcus aureus*, MRSA, *Escherichia coli*, and *Pseudomonas aeruginosa* at 63 and 630 µg/mL MP-SeNP loading, alongside swelling, degradation, and release studies. MP-SeNPs exhibited an IC₅₀ of 243.30 µg/mL, indicating low cytotoxicity, with viability at lower concentrations exceeding the untreated control. At 6.3 µg/mL, MP-SeNPs produced an approximate 50% increase in fibroblast migration relative to control. The MP-SeNP-loaded hydrogel showed selective antibacterial activity, with clear inhibition zones against *S. aureus* (1.37 to 1.43 cm) and MRSA (1.00 to 1.03 cm), moderate activity against *E. coli*, and none against *P. aeruginosa*; the unloaded control hydrogel showed no inhibition against any strain, confirming the effect was attributable to MP-SeNPs. The hydrogel showed higher swelling in distilled water (106%) than phosphate-buffered saline (81%) at 6 hours, and degraded faster in phosphate-buffered saline, losing up to 79% mass within 24 hours. Cumulative MP-SeNP release plateaued at 15.3% by 24 hours, indicating a restrained, sustained-release profile. These findings support MP-SeNP-fortified nanocellulose hydrogel as a biocompatible, selectively antibacterial, controlled-release platform for diabetic wound care applications.

Keywords: antibacterial activity; biocompatibility; diabetic wound care; nanocellulose hydrogel; selenium nanoparticles

Response Surface Optimization of *Marantodes pumilum*-mediated Selenium Nanoparticles Biosynthesis for Sustainable Biomedical Applications

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Abstract

Selenium nanoparticles (SeNPs) have gained significant attention due to their remarkable antioxidant properties and broad applications in biomedicine, pharmaceuticals, and agriculture. However, conventional chemical synthesis relies on toxic reagents, raising environmental and safety concerns. Green synthesis using plant-derived precursors offers a sustainable alternative. This study investigated the biosynthesis of SeNPs using *Marantodes pumilum* (Kacip Fatimah) extract, optimized through response surface methodology with a Box-Behnken design. Process parameters, including precursor concentration (50 to 75 mM), incubation temperature (35 to 45°C), and incubation time (3 to 5 days), were optimized to improve nanoparticle yield, size control, and antioxidant capacity. The synthesized SeNPs were characterized using dynamic light scattering, high-resolution transmission electron (HRTEM) microscopy, energy dispersive X-ray (EDX) analysis, Raman spectroscopy, zeta potential analysis, and phytochemical analysis, while cytotoxicity was evaluated using fibroblast cells. Under the optimum conditions of 75 mM precursor concentration, 45°C, and 3 days, SeNPs exhibited a hydrodynamic size of 277 nm with a polydispersity index of 0.3. HRTEM revealed particle sizes ranging from 28 to 154 nm, with a mean diameter of 93 nm with EDX showed high purity elemental selenium formed. The synthesized SeNPs exhibited a zeta potential of −40 mV, and Raman spectroscopy confirmed their amorphous nature. Phytochemical analysis identified bioactive compounds that contribute to nanoparticle reduction and stabilization. Cytotoxicity analysis showed an IC₅₀ of 243.30 µg/mL against NIH/3T3 fibroblast cells, indicating promising biocompatibility. These findings demonstrate that *M. pumilum* is a sustainable source for producing biocompatible SeNPs with potential for wound healing applications.

Keywords: antioxidant activity, green synthesis, *Marantodes pumilum* (Kacip Fatimah), response surface methodology (RSM), selenium nanoparticles (SeNPs)

Anti-Inflammatory and Metabolic Modulatory Effects of *Andrographis paniculata* Extract in an HFD/DMH-Induced Colorectal Cancer Sprague-Dawley Rats

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Abstract

Colorectal cancer (CRC) ranks third in global cancer prevalence and is a leading cause of cancer mortality in Malaysia, with obesity a major modifiable risk factor promoting chronic inflammation and metabolic dysregulation. *Andrographis paniculata*, a medicinal herb widely used in Southeast Asian traditional medicine, has demonstrated anti-inflammatory and anticancer properties. This study evaluated the chemopreventive effects of *A. paniculata* ethanol extract (APEE) in a high-fat diet (HFD) and 1,2-dimethylhydrazine (DMH)-induced CRC rat model. Male Sprague-Dawley rats received HFD for 20 weeks with concurrent weekly DMH injections (40 mg/kg, i.p.) for the first 10 weeks. APEE was administered at 125, 250, and 500 mg/kg throughout. Serum inflammatory cytokines (TNF- α , IL-6, MCP-1, CXCL10), metabolic hormones (leptin, insulin), lipid profile, and colonic aberrant crypt foci (ACF) were assessed. APEE dose-dependently suppressed pro-inflammatory mediators in the HFD/DMH + APEE 500 mg/kg group (HCAP500), TNF- α , IL-6, and CXCL10 fell by 40.3%, 50.0%, and 34.9%, respectively, relative to the disease control group (HC) ($p < 0.05$). Insulin and leptin declined by 41% and 43% ($p < 0.05$), both returning to levels not significantly different from the normal control. HDL cholesterol rose by 73% while triglycerides fell by 46% ($p < 0.05$). Total ACF per colon was reduced by 32% in HCAP500 versus HC ($p < 0.05$), exceeding the 13% reduction in the 5-FU-treated group. These findings support *A. paniculata* as a promising botanical chemopreventive candidate for obesity-associated CRC.

Keywords: *Andrographis paniculata*; chemoprevention; colorectal cancer; high-fat diet; inflammation

Computational Analysis of the Anti-Apoptotic Mechanisms of 2,6-Dimethoxy-1,4-Benzoquinone

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Abstract

2,6-Dimethoxy-1,4-benzoquinone (DMBQ) is a natural bioactive phytochemical derived from fermented wheat germ with promising anticancer properties. However, its molecular interactions with anti-apoptotic proteins implicated in cancer cell survival remain uncharacterised at the atomic level. This study utilized molecular docking, molecular dynamics (MD) simulation and MM/PBSA binding free energy analysis to evaluate DMBQ's inhibitory potential against six anti-apoptotic targets: AKT-1, MCL-1, BCL-2, BCL-XL, XIAP and BCL-W. Molecular docking revealed binding affinity values from -4.31 to -5.41 kcal/mol, identifying MCL-1 (-5.41 kcal/mol) and AKT-1 (-5.40 kcal/mol) as the top targets. Triplicate MD simulations of the MCL-1—DMBQ complex showed consistent ligand dissociation across all replicates, indicating dynamic instability under physiological conditions. Conversely, the AKT-1—DMBQ complex demonstrated stable binding across two independent 200-ns MD replicates, supported by convergent RMSD values (0.25-0.40 nm), stable radii of gyration, low per-residue fluctuations at key binding site residues and consistent solvent-accessible surface area profiles. Hydrogen bond occupancy analysis identified ALA230 as the primary interaction residue (> 59% occupancy in both replicates), corroborated by MM/PBSA energy decomposition (-1.83 and -1.77 kcal/mol). Total MM/PBSA binding free energy were -9.76 ± 3.09 and -10.12 ± 3.10 kcal/mol, driven predominantly by van der Waals and electrostatic contributions. These findings suggest DMBQ is a promising natural lead compound for AKT-1 inhibition, warranting further experimental validation.

Keywords: 2,6-dimethoxy-1,4-benzoquinone; AKT-1; anti-apoptotic proteins; molecular docking; molecular dynamics simulation

Navigating Pharmacokinetic Collision: Extended Intravenous Artesunate Monotherapy for Submicroscopic *Plasmodium knowlesi* in a Patient on Rifampicin-Based Tuberculosis Therapy

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Abstract

Plasmodium knowlesi (*P. knowlesi*) is a severe malaria strain with a rapid 24-hour replication cycle, prevalent in Southeast Asia. Primary treatment with artemether/lumefantrine is contraindicated in patients co-infected with tuberculosis. Rifampicin is a potent CYP3A4 inducer that rapidly clears oral artemisinin-based combination therapy (ACT) and jeopardizes the drug concentration, leading to treatment failure. This case report aimed to evaluate the safety and effectiveness of prolonged intravenous (IV) artesunate monotherapy in patients with submicroscopic *P. knowlesi* infection receiving rifampicin-based tuberculosis treatment. We report a 42-year-old male with tuberculosis who developed a refractory fever. A diagnostic PCR test returned after a 14-day turnaround revealed a submicroscopic *P. knowlesi* infection. Since stepping down to standard oral ACT was unfeasible, a multidisciplinary team opted for an off-label, extended course of IV artesunate at a dose of 2.4 mg/kg at 0, 12, and 24 hours, followed by a daily maintenance dose for one week. Clinical parameters including liver function tests, direct and indirect bilirubin, coagulation profiles, and signs of severe malaria, were closely monitored. The patient's temperature improved shortly after artesunate initiation. He demonstrated complete clinical recovery without adverse events. This case demonstrates that extended IV artesunate monotherapy can be a feasible therapeutic option for selected patients with *P. knowlesi* infection who are receiving rifampicin-based therapy, warranting future validation cohort studies. This case contributes to the limited literature on malaria-tuberculosis co-infections, offering guidance for healthcare personnel navigating complex pharmacokinetic interactions.

Keywords: artesunate; malaria; pharmacokinetic interaction; rifampicin; tuberculosis

Comparative Evaluation of Pro-Apoptotic and Anti-Proliferative Mechanisms of Nisin ZP and Doxorubicin in Osteosarcoma

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Abstract

Osteosarcoma (OS) chemotherapy using doxorubicin (DOX) causes severe systemic toxicities, highlighting an urgent need for targeted therapies like Nisin ZP (NZP), whose comparative molecular mechanisms against OS remain unestablished. This study aimed to evaluate the selective cytotoxicity, apoptotic profile, calcium dynamics, calpain-1 (CAPN1) protein expression, and cell cycle modulations of NZP, DOX, and DOX + NZP co-treatment in MG-63 OS cells and normal hFOB1.19 osteoblasts. Cells were treated at IC₅₀ doses of NZP (543.8 µg/ml) and DOX (0.46 µg/ml), followed by MTS viability, Muse Annexin V & Dead Cell flow cytometry, Fluo-4 NW calcium, CAPN1 ELISA, and cell cycle assays. MTS assay showed that NZP selectively reduced MG-63 viability to 56.80% while preserving hFOB1.19 at 79.73%, whereas DOX reduced viability of both (49.29% and 58.94%), and DOX + NZP produced maximal cytotoxicity in MG-63 (32.23%). Annexin V assay revealed a significant induction of early apoptosis in NZP-treated MG-63 (38.73% vs 14.00% in hFOB1.19) and the lowest live cell fraction in DOX + NZP (30.82%). Both NZP and DOX significantly elevated intracellular calcium in MG-63 cells (48,885.20 RFU and 48,223.80 RFU, respectively vs 46,546.40 RFU in controls). DOX + NZP significantly upregulated pro-apoptotic CAPN1 protein in MG-63 (0.1244 OD; $p = 0.002$ vs control, $p = 0.005$ vs DOX). NZP induced targeted G₂/M cell cycle arrest in MG-63 (33.50%) vs hFOB1.19 (10.30%), whereas DOX caused G₂/M arrest (44.17% and 54.60%), and DOX + NZP compounded anti-proliferative stress. In conclusion, Annexin V analysis confirms that NZP selectively induces OS apoptosis via calcium-mediated CAPN1 activation and G₂/M arrest while enhancing DOX cytotoxicity, supporting NZP as a novel, tissue-sparing OS adjuvant.

Keywords: apoptosis; calcium; doxorubicin; nisin ZP; osteosarcoma

Elucidating the Extrinsic and Intrinsic Apoptotic Pathways Induced by 2,6-Dimethoxy-1,4-Benzoquinone (DMBQ) in Colorectal Cancer Cells: An *In Vitro* Study

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Abstract

Colorectal cancer (CRC) remains a leading cause of cancer-related death worldwide, with treatment often limited by the ability of tumor cells to evade apoptosis through dysregulation of intrinsic and extrinsic death pathways. 2,6-dimethoxy-1,4-benzoquinone (DMBQ), a naturally occurring quinone with documented antiproliferative activity in gastric and lung cancer models, has not yet been characterized in colorectal cancer, leaving its mechanism of action in this context unknown. This study aimed to evaluate the cytotoxic effect of DMBQ against colorectal cancer cells, SW620, as a preliminary step toward elucidating its apoptotic mechanisms. SW620 cells were treated with increasing concentrations of DMBQ, and cell viability was determined using the MTT assay. Cytotoxicity was further validated using the Trypan Blue exclusion assay. DMBQ reduced cell viability in a concentration-dependent manner, with an IC_{50} value of approximately 20 μ M. The Trypan Blue exclusion assay showed a cell viability of 51% following treatment with DMBQ, supporting its cytotoxic activity. These preliminary findings demonstrate that DMBQ effectively inhibits colorectal cancer cell growth and provide the basis for subsequent investigations into its effects on apoptosis, oxidative stress, mitochondrial dysfunction, and apoptosis-related signalling pathways. The study contributes to the growing evidence supporting DMBQ as a promising candidate for colorectal therapy.

Keywords: apoptosis; cytotoxicity; DMBQ; natural anticancer compound; SW620 cells

Genetic Susceptibility to Bortezomib-Induced Peripheral Neuropathy in Asian Patients with Multiple Myeloma

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Abstract

Bortezomib has revolutionized the treatment landscape of multiple myeloma (MM), substantially improving survival outcomes and redefining therapeutic standards. However, bortezomib-induced peripheral neuropathy (BiPN) remains a clinically significant dose-limiting toxicity that may necessitate dose reduction, treatment interruption, or discontinuation, potentially affecting treatment efficacy. The rs2839629 polymorphism, located within the 3' untranslated region (3'-UTR) of *PKNOX1*, has been proposed as a functional variant influencing individual vulnerability to bortezomib-related neurotoxicity. We prospectively enrolled 102 newly diagnosed Malaysian patients with MM receiving bortezomib-based therapy. Peripheral neuropathy was assessed and graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Genotyping of *PKNOX1* rs2839629 was performed using the Sequenom MassARRAY platform. Allelic and genotypic associations between patients with grade ≥ 2 BiPN and those with grade < 2 BiPN were evaluated using chi-square or Fisher's exact tests. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Subgroup analyses were performed according to major ethnic groups (Malay, Chinese, and Indian). Among 102 patients, 39 (38.2%) developed clinically significant BiPN (grade ≥ 2). The *PKNOX1* rs2839629 (A vs G: OR = 0.86, 95% CI: 0.43–1.52, $p = 0.74$) showed no significant association with BiPN, either in the pooled cohort or within Malay, Chinese, and Indian subgroups. The *PKNOX1* rs2839629 polymorphism was not significantly associated with susceptibility to bortezomib-induced peripheral neuropathy in Malaysian patients with multiple myeloma. These findings emphasize the multifactorial, polygenic nature of BiPN and highlight the need for genome-wide and integrative approaches to identify predictive biomarkers for risk stratification and personalized supportive care.

Keywords: bortezomib; genetic polymorphism; multiple myeloma; peripheral neuropathy; single nucleotide polymorphi

Astaxanthin as a Precision Therapeutic for Neurological Diseases: A Systematic Review of Antioxidant and Neuroprotective Mechanisms

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Abstract

Neurological diseases, including Alzheimer's disease, Parkinson's disease, and ischaemic stroke, are fundamentally driven by oxidative stress and neuroinflammation. Despite its recognized antioxidant potency, the targeted efficacy of the marine carotenoid astaxanthin as a precision therapeutic remains fragmented in current literature. This systematic review aims to comprehensively evaluate astaxanthin's neuroprotective mechanisms and its viability in precision medicine for neurological disorders. Adhering to PRISMA guidelines, a systematic literature search was conducted across PubMed, Scopus, and Web of Science to identify relevant preclinical and clinical studies. The synthesized data reveal that astaxanthin uniquely crosses the blood-brain barrier, exerting direct and potent neuroprotection within the central nervous system. Key findings indicate that astaxanthin significantly mitigates reactive oxygen species production, downregulates pro-inflammatory cytokines, and prevents neuronal apoptosis across multiple disease models. Consequently, astaxanthin demonstrates profound potential as a targeted, natural neuroprotective agent rather than a mere general supplement. These findings underscore its value in the transition from natural products to precision therapeutics, offering a robust mechanistic framework to guide future clinical trials and the development of targeted neurological therapies.

Keywords: astaxanthin; blood-brain barrier; neurodegenerative diseases; neuroinflammation; oxidative stress

Methodological Characteristics of Long-Term High-Fat Diet-Induced Obesity Models in Rats: A Systematic Review

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Abstract

High-fat diet (HFD)-induced obesity in rats is widely used preclinical models for investigating metabolic disorders. However, considerable variation in dietary composition, experimental protocols, and obesity assessment limits reproducibility and comparison across studies. This systematic review aimed to synthesise characteristics of long-term HFD-induced obesity models in rats, with emphasis on dietary composition, experimental protocols, obesity induction duration, and used outcome measures. A systematic literature search of Scopus, PubMed, and Web of Science identified 293 records. Following duplicate removal and screening according to predefined criteria, 13 original *in vivo* studies published between 2016 and 2025 were included. Data extracted comprised rat strain, sex, dietary composition, fat source, fat percentage, obesity induction duration, confirmation methods, and metabolic outcome measures. Sprague-Dawley and Wistar rats were the predominant models used. High-fat diets ranged from 38.8% to 65.3% of energy derived from fat and commonly incorporated lard, ghee, mixed fats, or commercial formulations. Obesity induction periods varied between 8 and 18 weeks, with longer protocols more consistently producing stable metabolic abnormalities. Body weight, adiposity indices, lipid profiles, glucose homeostasis, insulin resistance, and histological assessment were the most frequently reported indicators of successful obesity induction. Considerable heterogeneity was observed in dietary formulations, induction duration, and obesity assessment despite the widespread use of HFD models. Long-term HFD-induced obesity models remain indispensable for preclinical obesity research. Methodological variability limits reproducibility and translational comparability. Greater standardisation of dietary composition, induction protocols, and obesity assessment criteria is needed to improve consistency and strengthen the translational value of future experimental studies.

Keywords: dietary composition; diet-induced obesity; high-fat diet; long-term protocol; rat model

Neuroprotective Effects of Philanthotoxin-102 Against NMDA-Induced Retinal Excitotoxicity: Behavioural, Histological and In Silico Evidence

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Abstract

Glutamate-mediated excitotoxicity through excessive N-methyl-D-aspartate (NMDA) receptor activation contributes to retinal ganglion cell (RGC) and optic nerve degeneration in glaucoma. Philanthotoxin analogues are glutamate receptor antagonists with potential neuroprotective properties. This study evaluated the neuroprotective effects of philanthotoxin-102 (PhTX-102) against NMDA-induced retinal excitotoxicity using behavioural, histological and in silico approaches. PhTX-102 incorporates a bulky 1-naphthylacetyl lipophilic head group and a modified asymmetric 3-4-3 polyamine backbone capped with a guanidino group, modifications hypothesised to enhance interaction with glutamate receptor channels. Adult male Sprague-Dawley rats were divided into phosphate-buffered saline (PBS) control, NMDA-induced retinal injury, and PhTX-102 pre-treatment groups. PhTX-102 was administered 24 hours before NMDA induction. After seven days, behavioural and vision-related functions were assessed using the Open Field Test, Colour Recognition Test and Novel Object Recognition Test. Retinal and optic nerve morphology were evaluated histologically. Molecular docking assessed the predicted binding affinity of PhTX-102 towards GluN2A and GluN2B NMDA receptor subunits. PhTX-102 pre-treatment significantly attenuated NMDA-induced locomotor alterations ($p < 0.05$). NMDA exposure significantly reduced retinal ganglion cell layer (GCL) thickness compared with PBS controls ($p < 0.05$), while PhTX-102 significantly preserved GCL thickness compared with the NMDA group ($p < 0.05$). NMDA also produced significant optic nerve degeneration compared with PBS controls ($p < 0.05$). Molecular docking demonstrated favourable PhTX-102 interaction with NMDA receptors, with stronger predicted binding affinity towards GluN2B than GluN2A. In conclusion, PhTX-102 demonstrated neuroprotective potential against NMDA-induced retinal excitotoxicity by preserving retinal GCL morphology and attenuating behavioural alterations. Its preferential predicted interaction with GluN2B further supports its potential modulation of NMDA receptor-mediated excitotoxicity.

Keywords: glaucoma; neuroprotection; NMDA receptor; philanthotoxin; retinal excitotoxicity

***Acanthamoeba* spp. as an Environmental Reservoir for Opportunistic Pathogens in Hospital Infrastructure: A Scoping Review**

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Abstract

Acanthamoeba spp. are free-living amoebae increasingly recognised as environmental reservoirs of opportunistic bacteria within the hospital-built environment, where their resistant cysts survive routine disinfection. This scoping review maps the detection of *Acanthamoeba* spp. across hospital infrastructure and characterises reported genotypes, pathogenic potential, associated bacteria, endosymbionts, and disinfection-relevant findings through environmental and experimental studies. A comprehensive electronic search was performed using PubMed, Scopus, and Web of Science from January 2000 until May 2026 for studies published in English, following PRISMA-ScR and Joanna Briggs Institute guidance. Only primary studies reporting *Acanthamoeba*-specific detection in hospital air-conditioning systems, premise plumbing and water networks, or dust, surfaces and clinical instruments were included. Altogether, 24 studies from eight countries were included in this review. The evidence gathered indicated that *Acanthamoeba* was detected across all three niches, with positivity ranging from 4.2% to 77.8% and genotype T4 predominating, while co-detected or endosymbiotic organisms included *Legionella* spp., *Pseudomonas aeruginosa*, nontuberculous mycobacteria, *Staphylococcus aureus*, *Acinetobacter baumannii*, and *Campylobacter jejuni*. However, a direct link between environmental *Acanthamoeba* and patient infection remains unestablished due to a lack of longitudinal evidence. In conclusion, *Acanthamoeba* spp. are under-recognised protozoan reservoirs in hospital infrastructure. Yet, further research is essential to confirm intracellular viability and transmission, emphasising the need for prospective surveillance that combines culture and molecular methods. Other areas for future study include how well disinfection works against cysts, and whether the findings hold in other regions, since most current evidence comes from a single area.

Keywords: *Acanthamoeba*; amoeba-resistant bacteria; free-living amoebae; nosocomial infection; opportunistic pathogens

Chemiluminescent Multiplex Serological Profiling of Insecticide-Treated Uniforms and Spatial Repellents Against Mosquito Bites and Malaria Exposure Among Malaysian Army Personnel

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Abstract

Malaria and other mosquito-borne diseases remain significant threats to military personnel operating in endemic environments, compromising force health protection and operational readiness. This 12-week cluster-randomised field trial evaluated cumulative mosquito bite and malaria exposure among 180 active-duty Malaysian Army personnel in Johor, Malaysia. Participants were allocated into six intervention groups receiving different combinations of topical N,N-diethyl-3-methylbenzamide (DEET), permethrin (PM)-treated uniforms, etofenprox (ETOX)-treated uniforms and metofluthrin (MF) spatial repellent strips, alongside a control group receiving DEET and untreated uniforms. Serum samples collected at weeks 0, 6, and 12 were analysed using the Meso Scale Discovery (MSD) multiplex chemiluminescent assay targeting five mosquito salivary biomarkers and five *Plasmodium falciparum*/*P. vivax* exposure markers. Seropositivity was defined as a fold-ratio ≥ 2 relative to negative controls. The DEET+MF+ETOX group consistently demonstrated the lowest mosquito salivary-marker seropositivity throughout the study, declining from 13.5% at baseline to 11.8% at week 12, whereas the DEET+MF+PM group reached 26.5% positivity by study end. For malaria-specific markers, the DEET+ETOX combination exhibited the lowest week-12 seropositivity (36.9%) compared with 51.7% in the DEET-only control group, with significant longitudinal reductions observed for the malaria exposure markers NANP and PfMSP1. Generalised estimating equation modelling confirmed that participants wearing ETOX-treated uniforms had significantly lower odds of *Anopheles dirus* salivary-marker seropositivity (adjusted odds ratio, aOR = 0.34, $p = 0.008$) and NANP seropositivity (aOR = 0.43, $p = 0.011$) compared with participants wearing PM-treated uniforms. These findings suggest that ETOX-treated uniforms, when combined with metofluthrin and DEET, may provide superior protection against mosquito bites and malaria exposure under military operational conditions.

Keywords: chemiluminescent multiplex serology; etofenprox-treated uniforms; malaria; military personnel; mosquito exposure biomarkers

Impact of an Interactive Anti-Substance Abuse Program on the Knowledge, Attitude and Perception Regarding Illicit Drugs Among Military School Students

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Abstract

Substance abuse prevention among youths requires innovative educational approaches beyond conventional methods, which often lack the immersive engagement necessary to effectively improve youth behaviour and comprehension. This study evaluates the effectiveness of a novel, peer-led intervention involving hands-on STEM activities combined with a 30-minute stage performance in improving the knowledge, attitude, and perception regarding illicit drugs among 16-year-old military school students. The study utilised a 10-item pre- and post-intervention questionnaire designed to evaluate the cadets' baseline information sources, objective pharmacological knowledge, and psychological attitudes and perceptions regarding substance abuse. Baseline categorical data were analysed using frequency distributions; to measure the intervention's efficacy, paired- samples t-tests were applied to the continuous knowledge scores, while Wilcoxon signed-rank tests were used to analyse the ordinal Likert-scale attitude and perception data. Baseline data revealed the 158 participants predominantly sourced drug-related information from books (89%), social media (86%), and mass media (84%). Post-intervention results among 49 selected respondents demonstrated a highly significant increase in objective pharmacological knowledge, with mean scores rising from 3.00 to 3.55 out of 4.00 ($p < 0.001$). Moreover, psychological defence mechanisms improved significantly; respondents exhibited greater confidence in rejecting peer pressure ($p < 0.001$) and a stronger sense of responsibility to report substance use ($p < 0.001$). In conclusion, integrating theatrical storytelling with hands-on STEM activities significantly enhances scientific understanding, protective attitudes and perceptions of youths against drug abuse. This peer-led pedagogical model contributes an effective, evidence-based strategy to the existing body of public health interventions, complementing conventional methods.

Keywords: addiction; health education; peer education; STEM education; substance abuse

Advancing Healthcare Resilience and Health Security: A Clinical Pathway Framework for Menstrual Insecurity

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Abstract

Menstrual insecurity, defined as the inability to access safe and adequate menstrual materials, is associated with recurrent urinary tract infections, vulvovaginal candidiasis, and contact dermatitis. Yet, no standardised clinical pathway exists to guide diagnosis, treatment, and downstream social referral for these presentations, nor a model for estimating the associated institutional cost burden. This paper proposes a preliminary five-phase Clinical Pathway (CP) for managing the clinical sequelae of menstrual insecurity, together with a framework for future cost estimation. An online focus group discussion (FGD) was conducted with five experts, comprising three family medicine specialists, one obstetrics and gynaecology specialist, and one health policy maker, exploring the causes, symptoms, and complications of menstrual insecurity. FGD transcripts were thematically analysed and triangulated with a scoping review, conducted following the PRISMA-ScR framework, mapping existing evidence on menstrual insecurity-related morbidity, risk factors, and screening approaches. This synthesis informed a five-phase CP progressing from aetiology-focused screening for improvised absorbent use, through acute antimicrobial treatment, clinical stabilisation and health education, to multidisciplinary referral and longitudinal supply-security follow-up. The HITS tool, originally validated for intimate partner violence screening, is proposed as a candidate proxy measure for household-level deprivation associated with menstrual insecurity, with psychometric evaluation in this context identified as a priority for future work. Concurrently, a linear regression model drawing on institutional billing and utilisation data is proposed to identify key cost-determining CP phases, with screening and referral phases hypothesised as likely primary drivers. Findings are preliminary and hypothesis-generating; formal expert validation, empirical testing, and cost-data collection are needed.

Keywords: clinical pathway; cost estimation; health resilience; health security; menstrual insecurity

Effectiveness, Acceptability, and Safety of Insecticide-Treated Army Uniforms Among Malaysian Armed Forces: A Field Evaluation

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Abstract

Mosquito-borne diseases remain a critical threat to military personnel deployed in vector-rich environments. This study evaluated the effectiveness, acceptability, and tolerability of insecticide-treated army uniforms as a protective strategy during jungle operations. A randomized field evaluation was conducted among 187 soldiers assigned to six treatment groups. Outcomes included prevention behaviours, uniform care, perceived mosquito reduction, acceptability, and side effects. Analyses used Rao-Scott χ^2 , ordinal logistic regression, and Poisson regression with cluster-robust standard errors. Uniforms treated with N,N-Diethyl-meta-toluamide (DEET) + Metofluthrin + Permethrin (DEET+MF+PM) showed the highest protection, with adjusted probabilities of 74.2% reporting 'much fewer bites' and 71.8% reporting 'much fewer mosquitoes noticed'. Compared to DEET-only uniforms, this represented improvements of +17.3 and +24.5 percentage points, respectively ($p < 0.001$). Other combinations provided moderate improvements, while DEET+MF did not outperform DEET alone. Side effects were infrequent and mild, with $> 85\%$ of soldiers reporting no adverse effects. Insecticide-treated uniforms, especially DEET+MF+PM, significantly improve protection while maintaining high acceptability. They should be prioritized for operational deployment to reduce vector-borne disease risk in military and civilian populations.

Keywords: insecticide-treated clothing, military health, mosquito prevention, operational safety

Evaluating Healthcare Agency Preparedness and Medical Emergency Response in a National Field Training Exercise in Melaka, Malaysia: The EXCOMSEC 2024 Experience

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Abstract

Preparedness of healthcare agencies is essential to ensure effective response during large-scale emergencies. The aim of this simulation exercise is to assess command, control, coordination, communication, and clinical readiness across multiple response levels under the MKN Order No. 18 framework during complex, large-scale incidents. The simulation involved six cascading scenarios, ranging from cyberattacks and chemical leaks to mass evacuations, testing response levels from community to tertiary care. Performance was qualitatively assessed by designated controllers, evaluators, and observers using standardized checklists and After-Action Reviews (AAR) to document coordination, decision-making, and clinical management across multiple medical stations. Qualitative analysis derived four key themes as follows: (1) Strong Strategic Command: High-level committees (CMT, CRT, CPRC) demonstrated effective inter-agency coordination and timely reporting; (2) Operational Coordination Gaps: The district level (PKD) faced challenges with data accuracy and communication glitches with field responders; (3) Infrastructure and Protocol Limitations: Primary care facilities lacked standardized case management tools; and (4) Variable Community and Facility Leadership: Hospital teamwork was excellent, yet community evacuation centers showed critical weaknesses in leadership and protocol activation. This simulation exercise demonstrated effective emergency preparedness relies on coordinated performance across all levels of the healthcare system. While strategic command and hospital readiness were strong, gaps at the district and community levels highlight opportunities for strengthening communication, coordination, and operational preparedness. Regular multidisciplinary simulation exercises are essential to improve health system resilience and emergency response capacity.

Keywords: community resilience; disaster management; healthcare preparedness; inter-agency coordination; simulation exercise

Positioning as the First Mechanical Step of Emergency Front-of-Neck Access in the Field Hospital: A Translational Appraisal of the IComPBag Inflatable Positioning Device

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Abstract

Airway compromise accounts for approximately 8% of potentially survivable pre-medical-treatment-facility battlefield deaths, and emergency front-of-neck access (eFONA) is the terminal step of the difficult-airway algorithm. The 2025 Difficult Airway Society guidelines designate scalpel-bougie-tube cricothyroidotomy as Plan D and require maximal neck extension, yet conventional practice requires an apnoeic patient to be lifted manually onto a gel pad, consuming personnel and time when both are least available. This study examined whether a pre-emplaced inflatable device (IComPBag) can convert positioning into a single-operator, titratable action that requires no lifting, and its role in resource-limited facilities. Guidelines and anatomical studies of cricothyroid membrane (CTM) accessibility were synthesised alongside a prospective comparative observational study at Tuanku Mizan Armed Forces Hospital (May 2021 to May 2024), in which 60 adults undergoing elective head and neck surgery were positioned with the IComPBag ($n = 30$) or a silicone gel pad ($n = 30$); outcomes were positioning time and personnel required. Mean positioning time was 125.2 s versus 261.8 s ($p < 0.001$), a difference of 136.6 s, and one operator sufficed in 83.3% of cases versus 23.3% ($p < 0.001$). Unit cost was RM150, compared with approximately RM4,000, with no adverse events in either group. Ultrasound studies show that maximal neck extension is associated with a 10% to 30% increase in sagittal CTM height. Positioning is therefore a modifiable, measurable determinant of eFONA preparedness that has received little attention. The evidence remains extrapolated from elective positioning; ultrasound and simulation studies are required before any effect on eFONA performance can be claimed.

Keywords: cricothyroidotomy; difficult airway; emergency front-of-neck access; military medicine; patient positioning

Academic Stress and Its Associated Factors Among Preclinical Students of a Malaysian Military-Based Medical Programme

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Abstract

Medical education is inherently challenging, and high expectations from oneself, faculty, and family often contribute to stress among medical students. However, factors associated with various stressor domains among medical students attending a Malaysian military-based medical school remain unexplored. Hence, this study aimed to determine the levels of academic stress and factors associated with various stressor domains among first- and second-year undergraduate students at Universiti Pertahanan Nasional Malaysia. A cross-sectional study was conducted in January 2025 during the regular academic calendar following ethical approval by the university's ethics committee. Participants were requested to complete a self-administered questionnaire containing socio-demographic and students' characteristics. Self-perceived academic stress was assessed using the Medical Students Stressor Questionnaire (MSSQ). The results showed that medical students in this institution experienced an elevated level of moderate (45.3%) to high academic stress (48.1%). Domain-specific analyses revealed that military cadets exhibited lower odds of "Intrapersonal and Interpersonal Related Stress" (odds ratio, OR = 0.12, $p = 0.048$) and higher odds of "Drive and Desire Related Stress" (DRS) (OR = 3.82, $p = 0.043$). Year 2 students had increased odds of DRS (OR = 2.72, $p = 0.049$), and students aged ≥ 20 years had increased odds of "Group Activities Related Stress" (GARS) (OR = 3.13, $p = 0.007$). Meanwhile, Malay students exhibited increased odds for "Social Related Stress" (OR = 4.01, $p = 0.013$), GARS (OR = 2.87, $p = 0.039$), and Overall Academic Stress (OR = 3.00, $p = 0.031$). These findings highlight cadetship, increased age, later academic year, and ethnicity as significant factors influencing stress domains among medical students in a military-based institution, underscoring the urgent need for targeted interventions to enhance student well-being and academic outcomes.

Keywords: academic stress; medical students; military medical school; preclinical students; undergraduate

Acknowledgement: This study was registered under a self-funded research project (Registration No.: SF0164–UPNM/2024/SF/SKK/3) and the ethical clearance was approved by the UPNM Research Ethics Committee (Reference No. 24/2024).

Assessing Hypoxia Tolerance in Military Air Force Personnel Using Rapid Colourimetric Testing of Hypoxia Inducible Factor-1 (HIF-1): A Pilot Study

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Abstract

Hypoxia remains an important operational risk for military aircrew exposed to altitude, where reduced oxygen availability may impair performance and compromise flight safety. Hypoxia-inducible factor-1 alpha (HIF-1 α) is a key biomarker involved in the cellular response to low oxygen tension and may have potential value for early hypoxia detection. This pilot study aimed to evaluate the feasibility of a rapid colorimetric saliva-based test for detecting HIF-1 α in military air force personnel following simulated altitude exposure. Twenty-four healthy participants were recruited from the Institute of Aviation Medicine, Royal Malaysian Air Force (RMAF) Subang Air Base, which was divided into two groups: (1) a “sea-level” control, and (2) an “altitude-exposed” group exposed to a simulated altitude of 10,000 feet at 40 minutes. Participants were screened for fitness before enrolment. Saliva samples and oxygen saturation measurements were obtained after exposure. To reduce variability, participants underwent a standardised pre-test at rest period, and no prior altitude acclimatisation was permitted during the study period. HIF-1 α levels were assessed qualitatively using the rapid colorimetric test. A detectable colour change consistent with the presence of HIF-1 α was observed in the altitude-exposed group than in the control group. These findings suggest that simulated altitude exposure was associated with increased HIF-1 α detectability in saliva. In conclusion, the rapid colorimetric assay shows potential as a non-invasive screening approach for early physiological responses to hypoxia in aircrew.

Keywords: aircrew; HIF-1 α (hypoxia-inducible factor-1 alpha); high altitude; hypoxia; rapid colorimetric test

Acknowledgement: This study was supported by the FRGS-EC, Ministry of Higher Education Malaysia (Registration No.: FRGS/1/2024/SKK10/UPNM/02/2)

Breaking Point to Breakthrough: Restoring Protected Casualty Evacuation Under Fire Through Rapid Armoured Ambulance Innovation

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Abstract

Escalating regional hostilities in South Lebanon transformed the peacekeeping environment into a high-threat, resource-constrained theatre, placing significant strain on medical support systems. Failure of the ageing 43-year-old Armoured CONDOR ambulance fleet exposed a critical vulnerability in protected casualty evacuation under the United Nations 10–1–2 doctrine. To sustain protected casualty evacuation capability through rapid repurposing of a surplus GUARDIAN Armoured Personnel Carrier (APC) into a frontline armoured ambulance. A technical operational case study was conducted following a rapid 9-day conversion (7–15 April 2026). The intervention included interior reconfiguration for 360° clinical access, modular stretcher fabrication, dual-redundant DC/AC power integration for advanced life support equipment, and operational validation through high-speed manoeuvre and in-motion clinical simulations. The modified platform accommodated ≥ 3 stretcher-bound casualties within a multi-access treatment layout. The GUARDIAN platform demonstrated superior mobility, off-road capability, and operational reliability compared to legacy systems. Enhanced vibration isolation and acoustic dampening improved clinical precision and communication, while full 360° access enabled uninterrupted resuscitative intervention during transit. The intervention sustained 100% FMT deployability and maintained protected evacuation capability in high-threat operational zones. Rapid repurposing of an armoured platform effectively restored a critical operational capability at the most vulnerable point of the evacuation chain. This intervention reinforced operational medical resilience and provides a scalable, doctrine-aligned model for protected casualty evacuation in conflict-affected peacekeeping environments.

Keywords: armoured ambulance; CASEVAC; conflict medicine; medical resilience; peacekeeping

Forging Health Operational and Logistical Resilience in a Mandate-Strained Conflict Zone – A Strategic Evaluation of Malaysia’s Final Peacekeeping Battalion in Lebanon

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Abstract

Malaysia has been a proud member of the community of nations since 1960, resolutely advancing global peace through distinguished peacekeeping missions worldwide. The presence of the Malaysian Battalion (MALBATT) in Lebanon since 2007 signifies over two decades of sustained peacekeeping commitment. As the mission enters its final phase, MALBATT 850-13 operates within a mandate-strained environment marked by force reduction, logistical contraction and escalating regional instability. A convergent mixed-methods evaluation was conducted at Level 1 medical facilities in Marakah and Tibnine Camps. Quantitative analysis included 775 clinical encounters (Nov 2025–May 2026) and governance assessment of 970 medical assets valued at RM1.55 million. Qualitative assessment examined workflow strain, governance coordination and Forward Medical Team (FMT) preparedness against the United Nations 10-1-2 doctrine. Clinical continuity was sustained despite manpower contraction. Outpatient care accounted for 39.0% of encounters, Civilian-Military Cooperation (CIMIC)-related care was 31.6%, while referrals and admissions remained below 1.0%, indicating strong Level 1 containment without sentinel adverse outcomes. More than 60% of medical asset value was preserved through phased verification, repatriation, transfer and regulated disposal. Despite high FMT readiness, delays persisted in evacuation workflows, particularly in 9-liner fidelity and command authorisation. Operational medical resilience during mandate-strained drawdown is achievable through governance coherence, adaptive asset utilisation, and protection of core clinical capability.

Keywords: casualty evacuation; force reduction, medical logistics; operational resilience; peacekeeping medicine

Differential Effects of Microwave and Millimetre-Wave Frequencies in 5G Communication Technology on the Testosterone-to-Estradiol Ratio and Mounting Behaviour in Male Rats

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Abstract

As the deployment of 5G networks operating at 3.5 GHz and 24 GHz continues to expand, research on their potential effects on male reproductive hormonal balance is still in its early stages. This study investigated the differential effects of microwave (3.5 GHz) and millimetre-wave (24 GHz) exposure under 5G technology on the testosterone-to-estradiol (T/E) ratio and mounting frequency in male rats. Eighteen male Sprague Dawley rats were randomly assigned into Control, 3.5 GHz, or 24 GHz exposure groups ($n = 6/\text{group}$). Animals were exposed for 7 hours daily over 60 consecutive days. Serum testosterone levels were significantly increased in the 3.5 GHz group ($8.086 \pm 0.963 \text{ ng/mL}$, $p < 0.01$) compared with the Control group ($5.068 \pm 0.623 \text{ ng/mL}$). In contrast, testosterone levels in the 24 GHz group ($3.273 \pm 0.315 \text{ ng/mL}$, $p < 0.01$) were significantly lower than those in the 3.5 GHz group. Serum estradiol levels were significantly reduced in the 24 GHz group ($0.00058 \pm 0.00018 \text{ ng/mL}$, $p < 0.001$) compared with Controls ($0.0022 \pm 0.00066 \text{ ng/mL}$). The T/E ratio was significantly elevated in the 3.5 GHz group (2950 ± 270.03) compared with Controls (1764 ± 437.02), whereas the 24 GHz group (1321 ± 554.13) showed a significant reduction compared with the 3.5 GHz group. Mounting frequency was significantly reduced in the 24 GHz group compared with the 3.5 GHz group. In conclusion, 5G frequencies may differentially influence hormonal balance and sexual behaviour in male rats. These findings suggest the potential for millimetre-wave exposure to exert greater adverse reproductive effects compared with microwave exposure, highlighting the need for further investigation into its long-term biological safety profile.

Keywords: 5G frequencies; microwave; millimetre wave; sexual behaviour; T/E ratio

Subacute 2,3-Benzofuran Exposure Induces Hypospermatogenesis and Testicular Damage in Male Rats

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Abstract

The emergence of new psychoactive substances (NPS), particularly 2,3-benzofuran, poses significant public health concerns due to their poorly characterised toxicological profiles. Although their neurological effects resemble those of MDMA, their effects on male reproductive health remain largely unexplored. This study investigated the reproductive toxicity of subacute oral exposure to 2,3-benzofuran in 40 adult male Sprague-Dawley rats over 28 days. Animals were randomly assigned to a control group or to low-, medium-, and high-dose treatment groups receiving 0.1, 2.0, and 4.0 mg/kg/day of 2,3-benzofuran, respectively, via daily oral gavage. Following exposure, testicular tissues were examined histopathologically using haematoxylin and eosin staining, while spermatogenesis was evaluated using Johnsen's scoring criteria. Histopathological analysis demonstrated dose-dependent structural alterations in the testes. Rats exposed to high-dose 2,3-benzofuran showed a marked reduction in primary spermatocytes, decreased seminiferous tubule diameter, and increased basal membrane thickness compared with controls. Correspondingly, Johnsen scores were significantly reduced, indicating impaired spermatogenesis and disrupted germ cell maturation. All observed changes were statistically significant ($p < 0.05$). These findings demonstrate that subacute oral exposure to 2,3-benzofuran induces reproductive toxicity in male rats and highlight the potential systemic risks associated with benzofuran-based NPS exposure.

Keywords: 2,3-benzofuran; new psychoactive substance; testicular toxicity

The Prevalence and Factors Associated with Depression, Anxiety, and Stress Among Patients Attending a Private Primary Care Centre in Kuantan

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Abstract

Mental health disorders such as depression, anxiety, and stress are increasingly common but underreported in private healthcare settings. This study assessed the prevalence, severity, and associated factors among outpatients attending Klinik Putramedic, a private primary care clinic in Kuantan. A two-week cross-sectional study was conducted using the DASS-21 questionnaire. The prevalence rates of depression, anxiety, and stress were 34.9%, 53.2%, and 21.4%, respectively. Individuals < 30 years were more likely to experience all three mental health outcomes, being almost three times as likely to have depression (OR = 2.94, $p = 0.009$) and anxiety (OR = 2.82, $p = 0.006$), and about six times more likely to experience stress (OR = 6.67, $p = 0.001$), compared to those aged ≥ 30 years. Female respondents had a higher probability of experiencing depression (OR = 2.53, $p = 0.026$) and anxiety (OR = 3.59, $p = 0.001$) than males. Meanwhile, employment status was only associated with anxiety, where unemployed respondents were about twice as likely to experience it compared to employed counterparts (OR = 2.23, $p = 0.027$). In conclusion, depression, anxiety, and stress were common among outpatients in private healthcare, indicating a substantial mental health burden. Younger age, female sex, and unemployment were associated with a higher likelihood of these conditions. These findings suggest a substantial burden of depression, anxiety, and stress among private primary care outpatients. Population targeted screening may be useful to help early detection and effective management.

Keywords: anxiety; depression; mental health; private primary care; stress

ATAD1 Deficiency Promotes Hepatic Steatosis via SIRT1-Mediated Suppression of the mTORC1-PLIN3 Lipophagy Axis

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Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) is an escalating global health burden. Although GLP-1 receptor agonists show therapeutic benefit, effective treatment options remain limited, and mitochondrial dysfunction is recognized as a central driver of disease progression. ATPase family AAA domain-containing 1 (ATAD1), a mitochondrial outer-membrane protein essential for mitochondrial quality control, plays an undefined role in linking mitochondrial integrity to hepatic nutrient sensing and lipid metabolism. This study investigated how ATAD1 regulates hepatic steatosis through the SIRT1-mTORC1 axis. The ATAD1-knockout (KO) FL83B murine hepatocytes were generated using lentiCRISPR and single-cell cloning. Steatosis was induced with 400 μ M free fatty acids (oleic:palmitic, 1:1) versus 1% BSA and analyzed via bulk RNA sequencing, Western blotting, and Nile Red staining. ATAD1 deficiency markedly exacerbated fatty acid-induced lipid accumulation and upregulated the lipid-droplet proteins PLIN2 and PLIN3. Transcriptomic profiling revealed the suppression of mitochondrial fusion genes (*Mfn1/Mfn2*) alongside elevated *Sirt1* and *de novo* lipogenic genes (*Fasn*, *Scd1*, *Acacb*). Consistently, SIRT1 protein was significantly upregulated, suppressing mTORC1 signaling (reduced p-mTOR and p-p70S6K) and activating acetyl-CoA carboxylase (decreased p-ACC) to promote lipogenesis. Concurrently, lipophagy was impaired: LC3-II accumulated, autophagic flux was blocked, and PLIN3 phosphorylation significantly declined. These findings demonstrate that ATAD1 protects hepatocytes against steatosis. Its loss dysregulates the SIRT1-mTORC1-PLIN3 axis to simultaneously drive *de novo* lipogenesis and impair lipophagic clearance, establishing ATAD1 as a potential therapeutic target for MASLD.

Keywords: ATAD1; hepatic steatosis; lipophagy; MASLD; SIRT1-mTORC1

Prevalence and Comparison of Anxiety and Depression by Cumulative Sea Service Duration Among Indonesian Seafarers: A Study Protocol

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Abstract

Anxiety and depression, the most prevalent mental health disorders among the global working population causing an estimated loss of 12 billion working days annually, are linked to extreme occupational environments – social isolation, disrupted sleep, and limited healthcare access – inherent to seafaring. Global prevalence of depression and anxiety among seafarers is 25% and 17%, respectively; yet no prevalence data exist for Indonesian seafarers, nor do data exist regarding differences by cumulative sea service duration. This study aims to determine the prevalence of anxiety and depression and examine differences across cumulative sea service durations among Indonesian seafarers. This cross-sectional study will recruit active, certified Indonesian seafarers across all vessel types and ranks via an online questionnaire distributed through INSA, the Directorate General of Sea Transportation, and affiliated seafarer networks, using consecutive sampling ($n = 163$). Cadets, seafarers currently undergoing psychiatric treatment, and participants with incomplete responses will be excluded. Anxiety and depression will be assessed using validated Indonesian versions of the GAD-7 and PHQ-9 (cutoff ≥ 10) and will be compared across two groups (< 3 months vs ≥ 3 months cumulative sea service) using the chi-square test. Seafarers with < 3 months sea service are hypothesized to have a higher prevalence of anxiety and depression than those with ≥ 3 months, a difference potentially related to the biological adaptation phase (4–12 weeks). This study is the first to map the prevalence and differences of anxiety and depression by cumulative sea service duration among Indonesian seafarers, serving as a reference for policy development, particularly screening and intervention programs tailored to sea service duration.

Keywords: anxiety; cumulative sea service duration; depression; occupational health; seafarers

Paediatric Fulminant Myocarditis Masquerading as Acute Gastroenteritis: A Case Report

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Abstract

Fulminant myocarditis in children is a rare, potentially fatal condition that is often challenging to diagnose due to non-specific symptoms. We report a case of a four-year-old boy who presented with a two-day history of fever, intermittent non-specific abdominal pain, non-bilious vomiting and reduced oral intake, whose underlying diagnosis was obscured by prominent gastrointestinal symptoms and apparent clinical improvement. Initial laboratory investigations were unremarkable, and he was admitted and managed as presumed early acute gastroenteritis with poor oral intake. Within the first 24 hours of admission, fever and vomiting resolved, oral intake improved, and he appeared to recover clinically. Although intermittent abdominal pain persisted, he remained alert, interactive, ambulant, and played in the ward playroom. On the second day of admission, he developed recurrent vomiting with worsening intermittent abdominal pain and severe hypoglycaemia (1.9 mmol/L). During attempted intravenous access, he collapsed. Rigorous resuscitation, including endotracheal intubation, intraosseous access, adrenaline administration, and metabolic correction, continued for 80 minutes without return of spontaneous circulation. Autopsy was performed and revealed extensive lymphocytic infiltration and myocytolysis in the heart tissue, confirming the cause of death as fulminant myocarditis. No significant intestinal inflammation was identified at autopsy. This case highlights how fulminant myocarditis can masquerade as a gastrointestinal illness, show transient clinical improvement, before causing rapid cardiovascular collapse. Early consideration of myocarditis remains difficult but crucial in atypical paediatric presentations. Furthermore, it demonstrates the indispensable role of thorough post-mortem examination in establishing the definitive diagnosis and advancing clinical understanding of sudden unexpected paediatric deaths.

Keywords: acute gastroenteritis; fulminant myocarditis; sudden unexpected paediatric deaths; viral myocarditis

Transforming Stress into Resilience: Psychological Effects of COVID-19 on Defence University Students and Their Coping Mechanisms

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Abstract

Mental health is a key part of human well-being, influencing overall behaviour, coping mechanisms and executive function. The COVID-19 pandemic disrupted daily life, impacting university students and raising concerns about their mental health. This study examines the coping style of undergraduate university students and its association with demographic factors and psychological distress. A cross-sectional online survey was conducted among undergraduate students of the National Defence University of Malaysia during the period of the Conditional Movement Control Order (CMCO). Coping Orientation to Problems Experienced (BRIEF-COPE) was used to assess coping style, while the Depression, Anxiety and Stress Scale (DASS-21) was used to measure the level of stress, anxiety and depression. Descriptive analysis was performed for sociodemographic data, and regression analysis examined associations between coping styles, demographic factors, and levels of depression, stress, and anxiety. A total of 603 students (mean age: 21.06 ± 1.75 years) completed the survey. Depression, anxiety, and stress were reported in 42%, 45%, and 13% of respondents, respectively. Religion was the most frequently used adaptive coping strategy, while substance abuse was the least utilised maladaptive coping behaviour. Ethnicity was the only significant predictor of adaptive coping ($\beta = 5.586, p < 0.001$). Maladaptive coping was positively correlated with depression ($r = 0.60, p < 0.001$), anxiety ($r = 0.56, p < 0.001$), and stress ($r = 0.62, p < 0.001$). This study demonstrates the range of coping strategies employed by students during the pandemic. Concern should be directed toward those engaging in maladaptive coping, which may negatively impact psychological well-being. Targeted interventions are needed to reduce maladaptive behaviours while reinforcing adaptive coping mechanisms.

Keywords: coping style; COVID-19 pandemic; mental health; psychological distress; university students

Bridging Life's Mechanics and Health Security: A Sixty-Year Bibliometric Trajectory of Environmental Health Research in Military Medicine

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Abstract

Military environmental health research has historically focused on legacy, reactive paradigms of localized post-conflict tracking, creating a knowledge gap regarding how broader global policy frameworks shape long-term health security. This study maps the 60-year global scientific trajectory of environmental health research within military medicine to establish a data-driven model for systemic threat resilience. Following PRISMA guidelines, 7,125 high-quality records from 1964 to 2026 were extracted from Scopus and analyzed using Bibliometrix in R, evaluating scholarly dispersion via Bradford's and Lotka's laws. Quantitative modeling reveals that annual publication output entered rapid exponential growth post-2010, peaking sharply in 2024–2025. Geographically, the United States leads with 871 documents, while Malaysia (60 articles) and Thailand (58 articles) dominate Southeast Asia. Military Medicine serves as the premier global publishing channel with 145 documents. Longitudinal keyword network modeling identifies a profound thematic evolution, transitioning from combat toxicology (1964–2005: "persian gulf war") to chronic psychological and biological stressors (2006–2015: "ptsd", "oxidative stress"), broad ecological frameworks (2016–2024: "climate change", "one health"), and current multi-omics precision mechanics (2025–2026: "gut microbiota", "inflammation"). We establish that the discipline has transitioned from descriptive casualty tracking into an integrated systems-biology framework. These insights expand existing knowledge by demonstrating how bridging micro-level molecular physiology with macro-level environmental surveillance under amended international frameworks optimizes future force readiness and global biothreat response.

Keywords: bibliometric analysis; environmental health; global health security; military medicine; systems biology

Toxic Epidermal Necrolysis Mimicking Kawasaki Disease in a 6-Year-Old Girl: A Diagnostic Challenge in a Febrile Mucocutaneous Syndrome

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Abstract

Toxic epidermal necrolysis (TEN) is a rare, life-threatening mucocutaneous reaction in children, and early diagnosis may be difficult because its initial features overlap with common febrile exanthems and inflammatory conditions such as Kawasaki disease. This case report aims to highlight the diagnostic challenges of paediatric TEN and identify clinical features that may support earlier recognition. A previously healthy 6-year-old girl presented with persistent high-grade fever, bilateral conjunctivitis, oral ulceration, cervical lymphadenopathy, and a progressive painful rash. Her clinical course, laboratory findings, infectious investigations, treatment, and outcomes were reviewed. Initial diagnoses of scarlet fever and Kawasaki disease were considered, and she received intravenous antibiotics, intravenous immunoglobulin, and aspirin. However, progressive mucosal sloughing, purpuric macules, vesiculobullous lesions, epidermal detachment involving approximately 70% of the body surface area, and a positive Nikolsky sign prompted revision of the diagnosis to TEN. Extensive infectious investigations, including testing for *Mycoplasma pneumoniae*, were negative, and no definite trigger was identified. Following treatment with intravenous methylprednisolone, oral cyclosporine, intensive supportive care, wound management, nutritional and fluid support, pain control, and ophthalmological monitoring, disease progression stabilised and gradual re-epithelialisation occurred. This case demonstrates that painful skin lesions, severe multisite mucositis, purpuric changes, blistering, and epidermal detachment are important warning signs that distinguish TEN from Kawasaki disease. Early recognition and multidisciplinary management may reduce diagnostic delay, complications, and long-term sequelae in children with febrile mucocutaneous syndromes.

Keywords: Kawasaki disease; mucositis; paediatric; Stevens-Johnson syndrome; toxic epidermal necrolysis

TAK1 Inhibition Attenuates TGF- β 1-Induced Activation of the NF- κ B Signalling Pathway in Human Bronchial Epithelial Cells

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Abstract

Chronic airway diseases are characterised by persistent inflammation and progressive airway remodelling, processes driven in part by dysregulated signalling within airway epithelial cells. Transforming growth factor- β 1 (TGF- β 1), a key profibrotic cytokine, activates both canonical Smad-dependent and non-canonical signalling pathways, including nuclear factor-kappa B (NF- κ B), a key regulator of inflammatory gene expression and epithelial responses. Although transforming growth factor- β -activated kinase 1 (TAK1) has been implicated in TGF- β 1 signalling, its role in linking TGF- β 1 stimulation to NF- κ B activation in bronchial epithelial cells remains incompletely understood, limiting the development of targeted therapeutic strategies. This study investigated whether pharmacological inhibition of TAK1 suppresses TGF- β 1-induced NF- κ B signalling in BEAS-2B human bronchial epithelial cells. Cells were pre-treated with the selective TAK1 inhibitor Takinib prior to stimulation with TGF- β 1 (10 ng/mL). Activation of the TAK1–NF- κ B signalling axis was evaluated by Western blot analysis of phosphorylated TAK1, phosphorylated I κ B α and phosphorylated p65, as representative upstream and downstream signalling molecules, followed by densitometric quantification. TGF- β 1 significantly increased phosphorylation of TAK1 (1.5-fold; $p < 0.01$), I κ B α (2.9-fold; $p < 0.0001$) and p65 (3.4-fold; $p < 0.001$) compared with untreated controls, confirming activation of the TAK1–NF- κ B signalling pathway. Pre-treatment with Takinib significantly reduced phosphorylation of TAK1 (22%), I κ B α (48%) and p65 (66%), demonstrating effective suppression of NF- κ B signalling. Collectively, these findings establish TAK1 as a critical signalling node mediating TGF- β 1-induced NF- κ B activation in bronchial epithelial cells and provide mechanistic evidence supporting the pharmacological targeting of TAK1 as a potential therapeutic strategy to limit airway inflammation and remodelling in chronic respiratory diseases.

Keywords: BEAS-2B; NF- κ B signalling; TAK1; TAKinib; TGF- β 1

Resolving Pre-Analytical Interference in Cold Autoimmune Haemolytic Anaemia Through Patient Pre-Warming: A Case Report

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Abstract

Cold autoimmune haemolytic anaemia (cold AIHA) is characterised by cold-reactive autoantibodies that induce red blood cell agglutination at low temperature, resulting in haemolysis and a significant pre-analytical interference. We report a case of repeatedly rejected grossly haemolysed serum specimens that were successfully analysed following patient pre-warming. An 89-year-old gentleman with established cold AIHA was admitted for the management of pulmonary embolism. Multiple serum samples sent for routine biochemical analysis were repeatedly rejected due to gross haemolysis (haemolysis index of 4+), rendering the results unreliable. Following discussion between the attending clinician and pathologist, and considering his underlying cold AIHA, the patient was placed under a warming blanket for two hours before blood collection to minimise cold autoantibody-mediated erythrocyte agglutination and ongoing haemolysis. The blood specimen was then collected and transported immediately to the laboratory. Following patient pre-warming, the subsequently collected serum specimen was visibly less haemolysed (haemolysis index of 0 to 1+), allowing successful laboratory analysis. Results demonstrated hyperbilirubinaemia and elevated aspartate aminotransferase, supportive of ongoing *in vivo* haemolysis, while renal function and electrolyte parameters were interpretable and clinically useful. Resolution of the pre-analytical interference also enabled further laboratory investigations to elucidate the underlying cause of his cold AIHA. This case illustrates that grossly haemolysed serum specimens in patients with cold AIHA can be successfully overcome through patient pre-warming procedure before blood collection. Recognition of this reversible pre-analytical interference allows successful laboratory blood analysis, reduces patient discomfort due to repeated venepunctures, minimises delays in patient management, and ultimately improves patient care.

Keywords: biochemical analysis; cold agglutinins; cold autoimmune haemolytic anaemia; pre-analytical interference; pre-warming

Mind the Gap: Perceived Barriers to E-Waste Recycling among Adults in Putrajaya

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Abstract

Rapid technological growth has made electronic waste (e-waste) the world's fastest-growing waste stream, threatening public health and urban sustainability. Understanding barriers to e-waste recycling is vital for green cities like Putrajaya. This study aimed to identify the barriers to proper e-waste management among adults in Putrajaya. A cross-sectional study was conducted from July to August 2025. A total of 192 respondents were recruited via convenience sampling to answer an online self-administered questionnaire. The study tools were adopted from a previous validated study. Despite Putrajaya's highly developed infrastructure, the public faces significant informational and logistical barriers in managing e-waste. The top barriers to proper recycling were a lack of proper disposal procedures (25%), a perceived shortage of local collection centres (23%), poor publicity regarding existing e-waste disposal (21%), perceived time constraints to manage e-waste (17%), and self-reluctance to recycle the e-waste (14%). The findings suggest that urban development alone may not be sufficient to promote sustainable e-waste recycling practices, as accessibility and information gaps remain important barriers. To transition toward a circular economy, policymakers must prioritize high-visibility collection facilities and aggressive public awareness campaigns, turning environmental knowledge into active community habits.

Keywords: electronic waste (e-waste); environmental health; perception barriers; Putrajaya, Malaysia; sustainable urban management

Association between Chrononutrition and Glycaemic Status in Women with Gestational Diabetes Mellitus: A Preliminary Case-Control Study

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Abstract

Gestational diabetes mellitus (GDM) continues to rise in prevalence despite existing medical nutrition therapy, suggesting current preventive strategies may overlook modifiable behavioural factors such as eating and sleep timing. This preliminary case-control study examined differences in chrononutrition profiles between pregnant women with and without GDM, and their correlation with oral glucose tolerance test (OGTT) results. Five women newly diagnosed with GDM and five healthy pregnant women ($N = 10$), matched for gestational age (20–26 weeks), were recruited via convenience sampling. Sociodemographic data and obstetric history were collected, chrononutrition was assessed using the validated Malay-version Chrononutrition Profile Questionnaire (CPQ), and glycaemic status was determined from OGTT values, with associations analysed using Pearson's correlation. The GDM and non-GDM groups were comparable in age, parity, gestational age and family history of diabetes, but women with GDM had a higher booking BMI (33.6 vs 26.4 kg/m², $p = 0.056$) and higher fasting and 2-hour post-OGTT glucose (both $p = 0.008$). Less frequent breakfast intake correlated with higher fasting glucose ($r = -0.69$, $p = 0.026$), while more frequent night-time waking to eat correlated with higher fasting and 2-hour post-OGTT glucose ($r = 0.74$, $p = 0.014$; $r = 0.63$, $p = 0.050$). These findings suggest circadian-related eating disturbances may be associated with impaired glucose tolerance in pregnancy. Despite the small sample, this study supports further investigation into chrononutrition and sleep as modifiable targets for GDM risk reduction, informing personalised chronobiological interventions in antenatal care.

Keywords: chrononutrition; gestational diabetes mellitus; oral glucose tolerance test; sleep quality

Estimation of Low-Density Lipoprotein Cholesterol (LDL-C) and LDL-C Treatment-Target Classification: A Comparison of Friedewald and Sampson Equations

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Abstract

Low-density lipoprotein cholesterol (LDL-C) is a key therapeutic target in dyslipidaemia management across cardiovascular disease (CVD) risk categories. The Sampson equation has been proposed as an alternative to the traditional Friedewald equation, particularly due to limitations in LDL-C estimation at higher triglyceride (TG) concentrations. This study compared LDL-C values estimated using the Friedewald and Sampson equations and evaluated concordance in LDL-C treatment-target classification. In this retrospective cross-sectional study, 3,847 lipid profiles with TG < 400 mg/dl (4.52 mmol/L) were analysed. LDL-C was calculated using the Friedewald (LDL-F) and Sampson (LDL-S) equations. LDL-C values were stratified according to LDL-C treatment-target thresholds corresponding to ESC/EAS risk categories: < 55, < 70, < 100, and < 116 mg/dL. Pearson correlation and Bland-Altman analysis assessed the relationship and agreement between methods. Concordance of LDL treatment-target classification was assessed by cross-tabulation. A strong correlation was observed between LDL-F and LDL-S (Pearson's $r = 0.9984$, $p < 0.001$). Mean LDL-S was 121.86 ± 41.35 mg/dL compared to 119.82 ± 41.38 mg/dL for LDL-F, with a mean bias of 2.04 mg/dL. LDL Treatment-target classification showed high concordance, with agreement rates of 99.1%, 98.7%, 97.7%, and 98.1% at the < 55, < 70, < 100, and < 116 mg/dL thresholds, respectively. A small positive bias was observed for LDL-S. The Friedewald and Sampson equations demonstrated excellent correlation and high concordance in LDL-C treatment-target classification. The slightly higher LDL-C estimates obtained with Sampson may influence classification around therapeutic thresholds and potentially affect treatment decisions. Further studies using patient-specific CVD risk categories are warranted.

Keywords: cardiovascular risk classification; Friedewald equation; LDL-C treatment targets; low-density lipoprotein cholesterol; Sampson equation

Partial Visual Recovery Following Hyperbaric Oxygen Therapy in Delayed-Presentation Central Retinal Artery Occlusion in Military Personnel: A Case Report

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Abstract

Central retinal artery occlusion (CRAO) is an ocular vascular emergency that results in sudden, profound, and often irreversible severe visual loss. Hyperbaric oxygen therapy (HBOT), a specialized environmental physiological intervention, improves tissue oxygenation to salvage ischemic retina when primary perfusion is lost. A 53-year-old serviceman with cardiovascular risk factors (diabetes, hypertension, ischemic heart disease) experienced acute, painless visual loss in the left eye, preceded by transient amaurosis fugax. He presented four days post-onset. Examination revealed counting fingers vision at one foot, a positive relative afferent pupillary defect (RAPD), abnormal red desaturation, and reduced light brightness. Fundus examination demonstrated a pale macular region with retinal artery attenuation and silver wiring changes; optical coherence tomography (OCT) of the macula showed significant localized macular thinning. Diagnosed clinically with CRAO, the patient underwent two cycles of HBOT despite the extended presentation delay. Following treatment, the patient demonstrated partial visual recovery, with improvement of visual acuity to 6/60 in the affected eye. Hyperbaric oxygen therapy serves as a vital physiological intervention capable of salvaging ischemic retinal tissue and restoring visual acuity even in delayed-presentation CRAO. Incorporating hyperbaric medicine into military health services offers a crucial therapeutic pathway to preserve visual function and maintain long-term duty capability.

Keywords: amaurosis fugax, central retinal artery occlusion, hyperbaric oxygen therapy, ocular emergency, retinal ischaemia

Factors Associated with Knowledge, Attitudes, and Contraceptive Practice Among Malaysian Married Men in Urban Primary Care: A Cross-Sectional Study

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Abstract

Male involvement is pivotal for successful family planning programs, yet male contraceptive practices remain understudied. A cross-sectional study was conducted from February–May 2023, evaluating knowledge, attitude, and practice (KAP) regarding contraception and identifying factors associated with contraceptive use among 477 married men attending Putrajaya Health Clinic in Malaysia. Participants were selected via systematic random sampling and completed a validated, self-administered questionnaire (Cronbach's alpha = 0.71). Expert consensus established categorical thresholds for knowledge (poor: < 75%, average: 75–80%, good: > 80%) and attitude (unsatisfactory: < 85%, satisfactory: ≥ 85%). Contraceptive practice was evaluated through four items capturing lifetime use and specific methods among participants (condoms, calendar method, coitus interruptus, abstinence, and male sterilization) and their partners (female condoms, oral contraceptive pills, and implants). The respondents' mean age was 38.5 ± 7.4 years, with most respondents being Malay (93.1%), tertiary-educated (79.2%), and employed (97.9%). Overall, 39.6% demonstrated good knowledge, 61.0% held a satisfactory attitude, 72.2% reported lifetime contraceptive practice, and 63.3% engaged in active contraceptive practice. Multivariate analysis revealed that having more than two children (adjusted odds ratio, aOR = 12.30, 95% CI: 7.03–21.49, $p < 0.001$), good knowledge (aOR = 2.22, 95% CI: 0.46–10.74, $p = 0.017$), and a satisfactory attitude (aOR = 1.86, 95% CI: 1.18–2.94, $p = 0.008$) were significantly associated with active contraceptive practice. These findings highlight a critical knowledge gap despite moderate practice rates, underscoring the need for targeted educational and attitude-building interventions to improve male contraceptive uptake in primary healthcare.

Keywords: contraception attitude; contraception knowledge; contraception practice; health clinic; married men

Asymptomatic Hypoglycaemia Despite Elevated HbA_{1c} in an Older Adult: A Case Report

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Abstract

Hypoglycaemia is an important concern in older adults with type 2 diabetes mellitus (T2DM), particularly among those receiving sulfonylureas. However, high glycated haemoglobin (HbA_{1c}) may mask hypoglycaemia because it measures average glycaemia rather than glucose variability. This case highlights the discordance between elevated HbA_{1c} and asymptomatic hypoglycaemia. Nocturnal hunger prompts further assessment and help prevents inappropriate treatment intensification. A 69-year-old woman with T2DM, hypertension and dyslipidaemia attended clinic follow-up. She was on metformin 1 g twice daily and modified-release gliclazide 120 mg once daily. She denied hypoglycaemic symptoms, including sweating, tremors, palpitations, and dizziness. However, home glucose monitoring recorded two asymptomatic readings of 3.1 mmol/L. She reported having nocturnal hunger twice weekly, which was relieved by milk and biscuits. Upon review, her HbA_{1c} level was 8.7%. Gliclazide was discontinued and replaced with vildagliptin 50 mg twice daily. She was counselled on regular meals, blood glucose monitoring, and the recognition and management of hypoglycaemia. At the three-month follow-up, nocturnal hunger improved, fasting blood glucose was 7.4 mmol/L, and HbA_{1c} had decreased to 7.9%. This case illustrates that an elevated HbA_{1c} does not exclude asymptomatic hypoglycaemia. Documented low glucose readings and nocturnal hunger prompted medication review and help prevent inappropriate treatment intensification. Without reviewing the home glucose profile, the elevated HbA_{1c} could have led to treatment escalation and increased hypoglycaemia risk. Although nocturnal hypoglycaemia was not documented, nocturnal hunger may be a subtle sign requiring careful assessment. Treatment should therefore consider glucose variability, medication-related risk and atypical symptoms instead of relying on HbA_{1c} alone.

Keywords: glucose self-monitoring; hypoglycaemia; older adult; sulfonylurea; Type 2 diabetes mellitus

Enhancing the Reliability of HbA1c Measurement in Patients with Chronic Kidney Disease: A Clinical Evaluation of an Enzymatic Assay

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Abstract

HbA1c is an established biomarker with recognised diagnostic values for diabetes mellitus (DM) and is widely used to assess long-term glycaemic control. However, in patients with chronic kidney disease (CKD), shortened erythrocyte survival and carbamylated haemoglobin may interfere with HbA1c measurement, potentially affecting glycaemic assessment and clinical decision-making. This study evaluates the clinical performance of an enzymatic HbA1c assay in patients with CKD using high-performance liquid chromatography (HPLC) as the comparator method. A prospective cross-sectional study was conducted involving 48 adults with CKD stages III–V. HbA1c concentrations were measured using the Abbott Architect c Enzymatic assay and the ADAMS A1c HA-8180V HPLC analyser. Linear regression and Bland–Altman analysis were used to assess the relationship and agreement between methods. Linear regression demonstrated an excellent linear relationship between the enzymatic assay and HPLC ($R^2 = 0.9889$), while Bland–Altman analysis demonstrated good agreement with a mean bias of -0.1% . Despite this overall agreement, clinically meaningful differences were observed across the HbA1c measurement range, particularly at lower and higher HbA1c concentrations, which may influence glycaemic assessment and clinical decision-making. Compared with HPLC, the enzymatic assay yielded lower HbA1c values when HbA1c was below 6.1% (bias: -0.5% to -0.6%) and higher values when HbA1c exceeded 11% (bias: $+0.1\%$ to $+1.4\%$). The enzymatic HbA1c assay demonstrated excellent analytical agreement with HPLC. These findings highlight the importance of selecting appropriate HbA1c methodologies for patients with CKD and support the use of the enzymatic assay for reliable HbA1c measurement in this high-risk population.

Keywords: chronic kidney disease; diabetes mellitus; enzymatic assay; HbA1c; high-performance liquid chromatography

Bridging the Conceptual–Implementation Gap in Disaster Health Needs Assessment: An Institutional Case Study of Fire and Rescue Command Leadership in Malaysia

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Abstract

Health Needs Assessment (HNA) is essential for guiding casualty care, optimizing resource allocation, and protecting first-responder health during urban health emergencies. This case study evaluated top-management leadership within the Malaysian Fire and Rescue Department (JBPM) as a single critical institutional case ($n = 1$ command structure) in Kuala Lumpur. To achieve data triangulation, primary key-informant in-depth interview data with executive command leadership were synthesized alongside national disaster directives, operational standard operating procedures (SOPs), and departmental reports. Using the reflexive thematic analysis, four main themes emerged regarding the institutional "conceptual-implementation gap": (1) top management views HNA as an ideal, continuous responsibility spanning pre- and post-disaster phases; (2) current practice relies on pragmatic routines, specifically pre-deployment responder fitness checks and on-scene triage; (3) execution is constrained by a lack of department-specific assessment tools, conceptual ambiguity between "HNA" and operational "risk assessment", and extreme time compression during urban incidents; and (4) there is an urgent need for institutionalized inter-agency guidelines. This single-case analysis demonstrates that field-level prehospita informalities are rooted in macro-level policy gaps. Establishing concise HNA toolkits and formalizing inter-agency handovers with healthcare authorities are critical to aligning top-level command policy with ground-level disaster health outcomes.

Keywords: disaster medicine; fire and rescue services; health needs assessment; institutional case study; urban health

The Effect of Sciatic Nerve Transection on Calretinin-Expressing Inhibitory Islet Interneurons in the Mouse Spinal Dorsal Horn

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Abstract

Nerve injury (PNI) causes neuropathic pain and reduced synaptic inhibition (disinhibition) in the spinal superficial dorsal horn (SDH). Calretinin-expressing (CR+) inhibitory interneurons in lamina II form axoaxonic synapses on non-peptidergic CMrgD primary afferents. We hypothesized that CR+ islet cells may undergo cell death or dendritic atrophy following nerve injury. Unilateral sciatic nerve transection (SNT) was performed in tamoxifen-treated $Ror\beta^{CreERT2}; Ai9$ mice. After four weeks, denervated territory was identified by prostatic acid phosphatase (PAP) depletion. Cell survival was assessed stereologically by counting tdTomato+/CR+/Pax2+ cells. Reconstructions analysed rostrocaudal (RC) and dorsoventral (DV) dendritic extents. SNT did not significantly reduce CR+ interneuron numbers. Mean tdTomato+ cells per section were comparable between injured and intact sides (7.48 vs 7.97; $p = 0.8064$). CR+/Pax2+ cells remained 5.6% of SDH neurons on both sides ($p = 0.9852$). Injured islet cells retained architecture, with no significant differences in RC ($p = 0.4559$) or DV ($p = 0.5953$) dendritic extents. PNI-associated neuropathic pain is more likely related to functional alterations in inhibitory circuitry than structural loss or dendritic remodelling of CR+ islet interneurons.

Keywords: calretinin; inhibitory interneurons; peripheral nerve injury; SNT

Modelling Shift-Dependent Meal-Timing Consistency and Meal-Latency Among Healthcare Shift Workers

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Abstract

This study investigated within-person variations in main-meal timing consistency and meal latency across shift conditions among healthcare workers. A nationwide prospective repeated-measures observational study involved 340 Malaysian healthcare shift workers, yielding 1,360 observations across shifts (morning, evening, night) and off-day. Chrononutrition behaviours were assessed using the validated Chrononutrition Questionnaire for Shift Workers. Generalised estimating equations accounted for repeated observations within participants. Meal-timing consistency was classified as low, partial, or complete, representing 53.2%, 40.8%, and 6.0% of observations, respectively. Ordinal logistic GEE showed a significant association between shift condition and meal-timing consistency (Wald $\chi^2(3) = 53.443$, $p < 0.001$). Compared with off days, the odds of higher consistency were significantly lower during morning (OR = 0.576, 95% CI 0.451–0.735), evening (OR = 0.513, 95% CI 0.415–0.634), and night shifts (OR = 0.532, 95% CI 0.439–0.644). Shift condition was also significantly associated with morning latency (Wald $\chi^2(2) = 335.544$, $p < 0.001$) and evening latency (Wald $\chi^2(2) = 27.413$, $p < 0.001$). Morning latency was longest during morning shifts (4 hours 15 minutes), followed by evening shifts (2 hours 14 minutes) and off days (1 hour 49 minutes). Evening latency was shorter during morning shifts (3 hours 8 minutes), while evening shifts (3 hours 32 minutes) did not differ significantly from off days. These findings demonstrate that shift schedules disrupt meal regularity and latency, with morning shifts producing the greatest latency disturbance. Shift-specific chrononutrition interventions may help strengthen dietary rhythms and support circadian alignment among healthcare workers.

Keywords: chrononutrition; meal-latency; meal-timing; shift worker; sleep timing

Apparently Healthy, Yet High Risk: Hidden Cardiometabolic Burden and Early Outcomes in Young-Onset ST-Elevation Myocardial Infarction

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Abstract

ST-elevation myocardial infarction (STEMI) in young adults may reflect cardiovascular risks that remain overlooked until an acute event. This study aimed to compare cardiometabolic characteristics and early clinical outcomes according to Killip class among young-onset STEMI. This retrospective cross-sectional study included patients aged 18–45 years presenting with STEMI to the Emergency and Trauma Department (ETD), Hospital Tuanku Fauziah, Perlis between 2024 and 2025. Demographic, clinical, laboratory, and early outcome data were extracted from ETD records. Comparisons were performed between patients with Killip I and Killip II–IV. A total of 44 patients (mean age: 39.8 ± 4.18 years; 95.5% men) were included. Overall, high total cholesterol was detected in 70.3%, low high-density lipoprotein cholesterol in 36.8%, and elevated fasting blood glucose in 68.4%. Over half (59.0%) had no known hypertension, diabetes, or dyslipidaemia. Killip II–IV was present in 20.9% of patients. Cardiometabolic abnormalities were comparable between Killip I and Killip II–IV, including high total cholesterol (67.9% vs 77.8%; $p = 0.695$), low high-density lipoprotein cholesterol (37.9% vs 33.3%; $p = 1.000$), and elevated fasting blood glucose (64.3% vs 77.8%; $p = 0.687$). However, cardiac arrest was more frequent in Killip II–IV than Killip I (33.3% vs 0%; $p = 0.007$). A substantial cardiometabolic burden was evident among young adults with STEMI but did not differ significantly across Killip classes. Nevertheless, cardiac arrest was more frequent among patients with greater clinical severity. These findings support early cardiovascular risk recognition and prompt, intensive, evidence-based preventive interventions among young adults with cardiometabolic abnormalities.

Keywords: cardiovascular diseases; dyslipidaemia; male; ST-elevation myocardial infarction; young adults

Severe Paediatric Leptospirosis with Common Neurological Manifestations: A Case Series from Northern Malaysia

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Abstract

Leptospirosis is a neglected tropical disease (NTD) of public health concern in Malaysia. Diverse clinical manifestations, including rare neurological manifestations in children, may mimic other central nervous system infections, causing delayed diagnosis. This study describes the clinical presentation, investigations, and outcomes of paediatric leptospirosis. A retrospective review was conducted on eight children (ages 1–7 years) with laboratory-confirmed leptospirosis admitted to a Malaysian tertiary referral centre in Kedah. Diagnosis was confirmed by Polymerase Chain Reaction (PCR) (75.0%) alone, PCR and Microscopic Agglutination Test (MAT) (25.0%) or MAT alone (0.0%). The clinical presentation, laboratory findings, neuroimaging, management, and outcomes were reviewed. Six of eight patients (75.0%) were male, and all presented with fever. Neurological manifestations occurred in 7/8 (87.5%) patients, including seizures or status epilepticus (62.5%), altered mental status (50.0%), focal neurological deficits (25.0%), and meningism (62.5%). Concurrent respiratory infections were documented in 6/8 (75.0%) patients. Among three (3) patients who underwent neuroimaging, two-thirds exhibited leptomeningeal enhancement, and one-third showed subdural effusion on magnetic resonance imaging. Six children (75.0%) required PICU admission for intubation and intensive management. All received intravenous antibiotic therapy with supportive care. Paediatric leptospirosis may present with severe neurological manifestations that resemble viral encephalitis or bacterial meningitis. In endemic regions, leptospirosis should be considered in the differential diagnosis in children presenting with acute febrile illness presenting with seizure or altered mentation. Early laboratory confirmation, particularly by PCR, may facilitate timely diagnosis and appropriate management.

Keywords: case reports; child; leptospirosis; neurologic manifestations

Blood Gas Profiles Across Escalating Respiratory Support in Malaysian Patients with Severe Leptospirosis

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Abstract

Leptospirosis is a zoonotic febrile tropical disease that poses a notable public health threat in Malaysia. Its actual burden remains unknown owing to underdiagnosis and misdiagnosis, which stem from diagnostic limitations and the undifferentiated, biphasic nature of this disease with its wide clinical spectrum. Blood gas analysis provides information on oxygenation, ventilation, and acid-base status and carries potential prognostic value in the management of severe leptospirosis. This study aimed to determine the association between blood gas profiles and respiratory support modalities among patients with severe leptospirosis. 26 patients with severe leptospirosis and complete arterial and/or venous blood gas readings were recruited from selected hospitals across Peninsular Malaysia between July 2025 and July 2026. The Kruskal-Wallis H test was used to analyse blood gas parameters across three respiratory support modalities: low-flow, non-invasive ventilation, and invasive mechanical ventilation. Continuous variables were summarised as median (interquartile range). Significant differences were observed in arterial pH and arterial PCO₂ across respiratory support modalities ($p < 0.05$), indicating progressive metabolic acidosis, as evidenced by the acid-base imbalance accompanying increasing respiratory support requirements. Patients receiving invasive mechanical ventilation had a higher mortality rate, suggesting that advanced respiratory support was associated with greater disease severity and poorer clinical outcomes. These findings demonstrate that blood gas profiles reflect the severity of respiratory involvement in severe leptospirosis, which was predominantly metabolic in origin. Early baseline blood gas data may assist clinicians in stratifying patients at risk of impending respiratory collapse. However, blood gas profiles are available only for severe cases, thereby limiting the study's conclusions.

Keywords: acid-base balance; blood gas profile; mechanical ventilation; respiratory support; severe leptospirosis

Case Series of Severe Leptospirosis with Multiorgan Involvement in Two Orang Asli Patients

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Abstract

Leptospirosis remains an underrecognized cause of severe febrile illness in rural and indigenous communities in Malaysia, where water exposure is common, and overlapping serology with other endemic illnesses like dengue complicates timely diagnosis. This report describes the clinical spectrum, diagnostic challenges, and outcomes of severe leptospirosis through two laboratory-confirmed cases requiring intensive care at tertiary hospitals in northern and northeastern Peninsular Malaysia between May and June 2026. Clinical, laboratory, and management data were reviewed for both patients. The first, a 50-year-old woman with untreated water consumption, presented with septic shock and severe acute kidney injury (creatinine: 931 $\mu\text{mol/L}$) managed conservatively, with mild bilirubin elevation and thrombocytopenia; leptospirosis rapid test and ELISA were positive despite inconclusive MAT, while dengue IgM positivity without NS1 suggested cross-reactivity rather than co-infection. The second, a 31-year-old woman exposed to well water, developed pulmonary-renal involvement with respiratory failure requiring non-invasive ventilation, severe acute kidney injury (creatinine: 712 $\mu\text{mol/L}$), marked leukocytosis, and mild bilirubin elevation, confirmed by rapid test, ELISA, and MAT (1:3200). Both received intravenous ceftriaxone and doxycycline, one with hydrocortisone for shock, and both recovered fully after 8 and 5 days of admission, respectively. These cases show severe leptospirosis can range from septic shock with renal failure to combined pulmonary-renal syndrome, even in young, previously healthy women, with inconclusive or cross-reactive serology complicating diagnosis in dengue-endemic settings. Findings reinforce the need for early clinical suspicion and prompt empirical antibiotic therapy before confirmatory results are available in resource-limited, endemic areas.

Keywords: dengue cross-reactivity; indigenous rural health; leptospirosis; pulmonary-renal syndrome; severe acute kidney injury