

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P200

Characterising Remote Inflammatory Areas Within the Brain Following Acute Photothrombotic Stroke

Miss Charlotte Barker

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Charlotte is a second year PhD candidate in the Department of Pharmacology (Faculty of Medicine, Nursing and Health Sciences) at Monash University. She works under the supervision of A/Prof Brad Broughton, Prof/ Francine Marques and A/Prof Barbara Kemp-Harper. Her research investigates acute inflammatory responses in brain regions distal to the ischaemic core following ischaemic stroke.

Characterising Remote Inflammatory Areas Within the Brain Following Acute Photothrombotic Stroke

Charlotte MO Barker¹, Samoda Rupasinghe¹, Barbara K Kemp-Harper¹ & Brad RS Broughton¹. Dept of Pharmacol, Monash Univ¹, Clayton, VIC, Australia

Introduction. Post-stroke inflammation results in a high degree of cell death in the brain and thus may be a therapeutic target. Immune cell entry into the brain following ischaemic stroke is documented to occur either through the damaged blood brain barrier and/or the choroid plexus, which is typically proximal to the infarct region in most animal models of stroke. However, stroke patients have been found to exhibit inflammatory responses in the ischaemic hemisphere at sites that are distal to the main site of brain injury, such as the thalamus and pons, as well as the contralateral hemisphere. Whether there is an increase in brain inflammation in the ischaemic and contralateral hemisphere distal to the infarct core in an animal model of stroke remains to be determined.

Aims. To investigate inflammatory responses throughout the entire brain following photothrombotic (PT) stroke.

Methods. Male C57Bl6 mice (8-10-weeks-old) received either sham (n=6-8/group) or PT stroke (n=8-10/group) surgery. Mice were assessed for motor function impairments pre-stroke and at 6 or 24h post-stroke. Brains were collected for infarct volume analysis and immunofluorescent labelling of macrophages/microglia. Brains from additional cohorts of mice were also collected for RT-qPCR analysis of inflammatory markers.

Results. While there was a 2-3-fold stroke-induced increase in the number of F4/80⁺ macrophages/microglia in and around the cortical infarct region, there was also a similar increase in these innate immune cells within the hypothalamic region (p<0.05 vs sham), which is distal to the cortical infarct, at 6 and 24h post-stroke. Unlike the macrophages/microglia within the infarct area, the majority (60-70%) of these immune cells were co-localised with the M2 phenotype marker, CD206. Furthermore, gene expression of IL-1 β , TNF- α , CCL2, P-selectin and ICAM-1 were significantly elevated within the hypothalamic region by 2-40-fold at 24h post-stroke compared to sham (p<0.05). Notably, there appeared to be a gradient of increased pro-inflammatory marker expression and reduced proportion of CD206⁺ cells with proximity to the infarct.

Discussion. The upregulation of key inflammatory chemoattracting molecules post PT-stroke is not only restricted to the infarct but can extend towards distal regions of the brain, including the hypothalamic region, which may represent a point of entry for macrophages/microglia and may be implicated in the post-stroke inflammatory response.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P201

The small-molecule AdipoRon improves cardiac function in a type-2 diabetes mouse model

Dr Miles De Blasio

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Dr Miles De Blasio leads the Cardio-Metabolic Physiology (CMP) laboratory at Monash University and is focussed on learning more about the metabolic alterations that occur in the heart, and the influence of the surrounding pericardial fat in the setting of diabetes and obesity. He is an expert in the endocrine and metabolic basis of diabetes and obesity and the impact that these have on cardiac metabolism and function. He is also interested in understanding how diabetes and obesity impair cardioprotective adiponectin signalling which leads to lipotoxic cardiomyopathy.

The small-molecule AdipoRon improves cardiac function in a type-2 diabetes mouse model.

Miles J De Blasio^{1,2}, Anida Velagic¹, Abhipree Sharma^{1,2}, Minh Deo¹, Cristina F Triffon^{1,2}, Mamun Al Abdullah^{1,2}, Rebecca H Ritchie¹. Cardio-Metabolic Physiology¹; Heart Failure Pharmacology²; Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Monash University, VIC Australia.

Introduction. Diabetes is known to increase the risk of diabetic cardiomyopathy, which is characterised by left ventricular (LV) diastolic dysfunction and cardiac remodelling. The hormone adiponectin is an adipokine which is downregulated in type-2 diabetes (T2D), signals via adiponectin receptors, and is proposed to be involved in cardiac pathology. AdipoRon is a small-molecule, non-selective adiponectin-receptor agonist that has been shown to protect against other diabetic pathologies such as nephropathy however little is known of its effect in the diabetic heart.

Aims. We sought to determine the cardioprotective influence of AdipoRon in T2D-induced cardiomyopathy.

Methods. T2D was induced in 6-week-old male FVB/N mice via streptozotocin (55mg/kg/day, 3 consecutive days, i.p.) and a high-fat diet (42% calories by lipids); controls received citrate vehicle and chow diet (n=10-15 per group). LV function was assessed via echocardiography under isoflurane inhalation anaesthesia (induction 4%, maintenance 1-4%) after 18 weeks of untreated diabetes. AdipoRon (or vehicle) was administered for 8 weeks (50mg/kg, 3 days/week i.p.) before endpoint echocardiography and tissue collection. Data was analysed by one-way ANOVA with Dunnett's *post hoc* test with P<0.05 considered significantly different.

Results. AdipoRon administration blunted hyperglycaemia in T2D mice compared to vehicle-treated T2D mice throughout treatment (P<0.05), although neither T2D nor AdipoRon affected body weight. Significant diabetes-induced impairments in both LV diastolic function (e' , a' , e'/a' , E/e') and systolic function (LV ejection fraction, stroke volume, cardiac output, global longitudinal strain [GLS], and end-diastolic and end-systolic LV mass) in T2D mice were all ameliorated by AdipoRon treatment (P<0.05 for all, ANOVA). The T2D-induced reductions in heart weight and individual chamber weights were however not ameliorated by AdipoRon. Kidney weight was reduced, and gonadal and inguinal fat depot weights were increased, by T2D, all of which tended to be attenuated by AdipoRon (all P<0.05).

Discussion. The therapeutic potential of targeting diabetes-induced downregulated cardiac adiponectin-receptor signalling in T2D with the effective small-molecule AdipoRon may offer new means to improve LV function in the context of T2D-induced cardiomyopathy.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P203

Single-cell transcriptome analyses reveal the roles of B cells in fructose-induced hypertension

Prof Inkyeom Kim

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Kim received his Ph.D. from Kyungpook National University in 1992. He is a Professor, Department of Pharmacology and was a Director, Cardiovascular Research Institute at Kyungpook National University. As a president of the Korean Association of Basic Medical Scientists, he is an established scientist with an international recognition in the area of cardiovascular pharmacology. He is also a fellow of The National Academy of Medicine in Korea. He received numerous awards including the Pfizer Medical Award from the Korean Academy of Medicine in 2013. He is the author or co-author of over 150 peer-reviewed journal papers. He was an Associate Editor of the Korean Journal of Physiology and Pharmacology. He has been serving as the conference chair, the technical program chair, and symposium chair for various conferences including World Congress of Pharmacology. His research is concerned with elucidating the mechanisms of development of essential hypertension and cardiometabolic syndrome. Although hypertension is one of the most common diseases and is a predisposing factor of other diseases such as stroke, heart failure, and chronic renal failure, the mechanism by which essential hypertension develops still remains elusive. He has hypothesized that vascular stresses from excessive alcohol intake, cigarette smoke, hyperlipidemia, hyperglycemia, high salt diet, oxygen free radical, metabolites of gut microbiota, aging and so on, predispose to hypertension through immunity and inflammation. Verification of the hypothesis necessitates utilizing an integrated experimental approach encompassing physiological, biochemical and molecular biological techniques. Examples of these include measurements of vascular contractility, assessment of contraction in permeabilized smooth muscle, FACS, chromatin immunoprecipitation followed by qPCR, and transcriptome or proteomic approaches.

Single-cell transcriptome analyses reveal the roles of B cells in fructose-induced hypertension

Cheong-Wun Kim¹, Sungmin Jang¹, Shiang-Jong Tzeng², and Inkyeom Kim¹.

Department of Pharmacology, BK21 Plus KNU Biomedical Convergence Program, Cardiovascular Research Institute, School of Medicine, Kyungpook National University¹, Daegu 41944, Republic of Korea; Graduate Institute of Pharmacology, College of Medicine, National Taiwan University², Taipei 10051, Taiwan

Introduction. While the immune system plays a crucial role in the development of hypertension, the specific contributions of distinct immune cell populations remain incompletely understood. The emergence of single-cell RNA-sequencing (scRNA-seq) technology enables us to analyze the transcriptomes of individual immune cells and to assess the significance of each immune cell type in hypertension development.

Aims. We aimed to investigate the hypothesis that B cells play a crucial role in the development of fructose-induced hypertension.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Methods and Results. Eight-week-old Dahl salt-sensitive (SS) male rats were divided into two groups and given either tap water (TW) or a 20% fructose solution (HFS) for 4 weeks. Systolic blood pressure was measured using the tail-cuff method. ScRNA-seq analysis was performed on lamina propria cells (LPs) and peripheral blood mononuclear cells (PBMCs) obtained from SS rats subjected to either TW or HFS. The HFS treatment induced hypertension in the SS rats. The analysis revealed 27 clusters in LPs and 28 clusters in PBMCs, allowing for the identification and characterization of various immune cell types within each cluster. Specifically, B cells and follicular helper T (Tfh) cells were prominent in LPs, while B cells and M1 macrophages dominated PBMCs in the HFS group. Moreover, the HFS treatment triggered an increase in the number of B cells in both LPs and PBMCs, accompanied by activation of the interferon pathway.

Conclusions. The significant involvement of B cells in intestinal and PBMC responses indicates their pivotal contribution to the development of hypertension. This finding suggests that targeting B cells could be a potential strategy to mitigate high blood pressure in fructose-induced hypertension. Moreover, the simultaneous increase in follicular B cells and Tfh cells in LPs, along with the upregulation of interferon pathway genes in B cells, underscores a potential autoimmune factor contributing to the pathogenesis of fructose-induced hypertension in the intestine.

P204

Doxorubicin-Induced Cardiotoxicity: Strategies for Cardioprotection

Ms Amanda Croft

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Doxorubicin-Induced Cardiotoxicity: Strategies for Cardioprotection

Lohis Balachandran¹, Kelly Chen¹, Tatt Jhong Haw¹, Amanda Croft¹, Conagh Kelly¹, Aaron Sverdlov¹, Doan Ngo¹. ¹Newcastle Centre of Excellence in Cardio-Oncology, Hunter Medical Research Institute, Hunter New England Local Health District, University of Newcastle and Calvary Mater Newcastle, Newcastle, NSW, Australia

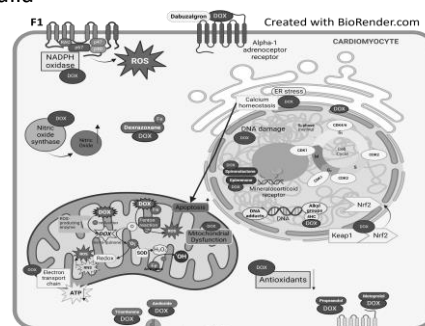
Introduction. Doxorubicin is an anthracycline chemotherapeutic agent used to treat a large number of cancers. However, it has been reported to cause cardiotoxicity including heart failure. Other than dexrazoxane, which is of limited use, there is no approved agent for cardioprotection against doxorubicin-induced cardiotoxicity. Therefore, this study examined human cardiomyocyte viability with various combinations of cardioprotective agents with doxorubicin.

Aims. To identify potential cardioprotective agents to prevent doxorubicin-induced cardiotoxicity.

Methods. Primary human cardiomyocytes (HCM) (PromoCell) were treated for 72 hours with doxorubicin (1 μ M) and a combination of different pharmacological agents targeting distinct cellular components (1 μ M) (Figure 1); (a) mineralocorticoid receptor, (b) adrenergic receptor, (c) sodium channel blockers and (d) alkylating agent. HCM viability with combination treatments was determined using CellTitre-Glo (Promega).

Results. Doxorubicin [22.4 \pm 12.2%], alone at 1 μ M, significantly reduced HCM viability versus vehicle. Combination of doxorubicin with various agents did not result in significant improvement in HCM viability: a) mineralocorticoid receptor (eplerenone [23.0 \pm 2.9%]; spironolactone [21.70 \pm 8.0%]), (b) adrenergic receptor (dabuzalgron [23.8 \pm 3.8%]; propranolol [21.8 \pm 9.7%]; metoprolol [25.1 \pm 7.6%]), (c) sodium channels (amiloride [19.7 \pm 1.7%]; triamterene [18.6 \pm 1.9%]; ivabradine [26.3 \pm 4.9%]) and (d) alkylating agent (4-hydroperoxycyclophosphamide [23.1 \pm 7.7%]) and cardioprotective agent, dexrazoxane [18.7 \pm 6.4%].

Discussion. These cardioprotective agents did not result in improvement in HCM viability when used in combination with doxorubicin. It is possible that these potential cardioprotective agents may not have direct effects on human cardiomyocytes and may affect other components of the cardiovascular system.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P205

Febuxostat ameliorates endothelial dysfunction in indoxyl sulfate-induced human aortic endothelial cells

Ms Hsin Jou Lee

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

My name is Zoe (Hsin-Jou, Lee). I am a PhD candidate in the Institute of Pharmacology at National Yang Ming Chiao Tung University. During my PhD, I focus on investigating the comorbidity between chronic kidney disease (CKD) and cardiovascular diseases (CVD), particularly exploring shared pathophysiological mechanisms like inflammation, endothelial dysfunction, and metabolic disturbances. My research aims to identify therapeutic targets within this framework to develop more effective treatments. By uncovering novel biomarkers and treatment options, I hope to contribute to integrated, personalized approaches for managing these overlapping conditions, ultimately improving patient outcomes and reducing disease burden.

Febuxostat ameliorates endothelial dysfunction in indoxyl sulfate-induced human aortic endothelial cells

Hsin-Jou Lee^{1,2} and Ting-Ting Chang^{1,2,3,4}. Dept of Pharmacol, National Yang Ming Chiao Tung Univ¹, Taipei, Taiwan. Sch of Med, National Yang Ming Chiao Tung Univ², Taipei, Taiwan. Cardiovascular Research Center, Taipei Med Univ Hosp³, Taipei, Taiwan. Biomed Ind Ph.D. Program, National Yang Ming Chiao Tung Univ⁴, Taipei, Taiwan.

Introduction. The prevalence of chronic kidney disease (CKD) is increasing globally. CKD patients have a high risk of cardiovascular disease (CVD). Indoxyl sulfate (IS), a uremic toxin, promotes CVD by increasing reactive oxygen species (ROS) production and impairing neovascularization (Szu Chun Hung et al, 2017). Febuxostat, a selective xanthine oxidase (XO) inhibitor, is reported to have antioxidant and anti-inflammatory effects (Nomura et al, 2013).

Aims. This study aimed to investigate the pharmacological mechanism of febuxostat on IS-induced endothelial dysfunction.

Methods. Human aortic endothelial cells (HAECs) were used for in vitro experiments. IS was used as the stimulator to mimic the CKD conditions in vitro. ROS production was measured using the Amplex Red Hydrogen Peroxide/Peroxidase assay. In addition, the endothelial function was evaluated using migration and tube formation assays. Furthermore, the protein levels were analyzed by Western blotting.

Results. In IS-stimulated HAECs, febuxostat reduced ROS production and the protein level of XO, as well as improved migration and tube formation ability. Additionally, febuxostat reversed the expression of angiogenic proteins such as vascular endothelial growth factor and stromal cell-derived factor 1, which were down-regulated by the stimulation of IS. Furthermore, febuxostat decreased the levels of IS-stimulated pro-inflammatory cytokines, including interleukin (IL)-6, IL-1 β , and tumor necrosis factor- α .

Discussion. Febuxostat could not only inhibit the expression of XO but also reduce ROS production and decrease cellular inflammation in IS-stimulated HAECs. Importantly, febuxostat improves endothelial cell dysfunction from the insults of IS in vitro, which might have therapeutic potential to improve CKD-induced angiogenesis. However, the findings need to be further confirmed by in vivo studies. Collectively, febuxostat may be a new treatment option for CKD-induced vascular disease.

Nomura, et al. (2013) PLoS One 8(9): e75527.

Szu-Chun Hung et al. (2017) J Am Heart Assoc 6(2): e005022.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P206

Post-stroke cognitive impairment and brain hemorrhage are augmented in hypertensive mice

Mr David Wong Zhang

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Post-stroke cognitive impairment and brain hemorrhage are augmented in hypertensive mice

David E. Wong Zhang¹, Tayla A. Gibson Hughes¹, Andrew N. Clarkson¹, Thiruma V. Arumugam¹, Grant Drummond¹, Christopher G. Sobey¹ and T. Michael De Silva¹. ¹Centre for Cardiovascular Biology and Disease Research and Department of Microbiology, Anatomy, Physiology and Pharmacology, La Trobe University, Bundoora, Victoria 3086, Australia.

Introduction. Hypertension is a major cause of morbidity and mortality worldwide. While hypertension is known to be a major risk factor for both stroke and cognitive impairment, the impact of hypertension on stroke-induced cognitive impairment remains unclear.

Aims. To assess the effect of hypertension and/or stroke on brain injury, cognitive outcomes, and the brain transcriptomic profile.

Methods. C57BL/6 mice (n=117; 3-5 mo.) received s.c. infusion of either saline or angiotensin II followed by sham surgery or photothrombotic stroke targeting the prefrontal cortex 7 days later. Cognitive function was assessed at either 7- or 21-days post-stroke with the spontaneous alternation test or the Barnes maze, respectively. Mice were humanely euthanised and brains collected following behavioural testing. For post-mortem analysis, we measured markers of brain injury and neuroinflammation. RNA sequencing was used to quantify transcriptomic changes in the brain.

Results. Angiotensin II infusion increased systolic blood pressure and produced spontaneous hemorrhaging after stroke. In the spontaneous alternation test, the combination of hypertension and stroke reduced alternation rate compared to the normotensive mice that had sham surgery (55.5±3.1% vs. 67.5±2.4%; n=9-11, $P<0.05$). In the Barnes maze, hypertensive mice that received stroke surgery had an increased escape latency compared to other groups (day 3: hypertensive + stroke=166.6±6.0 s vs. hypertensive + sham=122.8±13.8 s vs. normotensive + stroke=139.9±10.1 s vs. normotensive + sham=101.9±16.7 s; n=12-13, $P<0.05$), consistent with impaired learning. Hypertension did not increase markers of blood-brain barrier injury or neuroinflammation. RNA sequencing revealed >1500 differentially expressed genes related to neuroinflammation in hypertensive + stroke vs. normotensive + stroke, which included genes associated with apoptosis, microRNAs, autophagy, anti-cognitive biomarkers and Wnt signaling.

Discussion. These findings indicate that the combination of hypertension and stroke resulted in greater learning impairment and brain injury.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P207

Vericiguat and Verapamil reduce phenylephrine responses in endothelial impaired IMA segments

Mr Alex Minopoulos

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Alex Minopoulos is a fourth-year PhD candidate at the University of Adelaide in the Faculty of Health and Medical Sciences. Under the primary supervision of Professor John Beltrame, Alex's research focuses on cardiovascular disease, specifically coronary vasomotor disorders such as vasospastic angina. His work combines techniques in vascular myography to investigate novel therapeutics and compare them to existing treatments. Alex also utilises a Western Blot assay to examine biomarkers and their activation states, aiming to uncover potential disease mechanisms and potential diagnostic targets.

Vericiguat and Verapamil reduce phenylephrine responses in endothelial impaired IMA segments

Alex Minopoulos^{1,2}, Irene Stafford^{1,2}, Rosanna Tavella^{1,2}, Benedetta Sallustio^{1,2}, David P Wilson⁴, John F Beltrame^{1,2} Adelaide Medical School¹, University of Adelaide, Adelaide, SA, Australia; Basil Hetzel Institute, Central Adelaide Local Health Network², Adelaide, SA, Australia; School of Biomedicine⁴, University of Adelaide, Adelaide, SA, Australia.

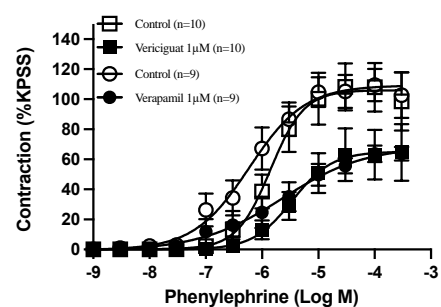
Introduction. Calcium channel blockers (e.g. verapamil) are the benchmark therapy for coronary artery spasm. Vericiguat is a novel, soluble guanylate cyclase (sGC) stimulator that produces vasodilation independent of nitric oxide (NO) synthesis.

Aim. To compare vericiguat vs verapamil pre-treatment on phenylephrine (PE) constrictor responses in isolated human internal mammary artery (IMA) segments with impaired endothelial relaxation responses.

Methods. Remnant IMA segments from coronary artery bypass grafting surgery patients were suspended in a vascular myograph and subjected PE concentration-response curves (0-300 μ M), control. Endothelial function was assessed using bradykinin (0-30 μ M), with impaired endothelial function defined as <50% vasorelaxation. The segments were then pre-treated with vericiguat 1 μ M or verapamil 1 μ M and the PE concentration-response curves repeated. Treatment responses were compared to control PE constrictor responses (Emax, LogEC50) using two-way ANOVA with repeated measures (Sidak).

Results. Compared to controls, vericiguat and verapamil inhibited both PE maximal constrictor responses (Emax: 107.9 \pm 15.7 vs 66.18 \pm 18.1, P<0.05 and 107.3 \pm 10.5 vs 66.99 \pm 4.8, P<0.05, respectively) and the half maximal effective concentration (LogEC50: -5.929 \pm 0.2107 vs -5.361 \pm 0.16 P<0.05 and LogEC50: -6.272 \pm 0.20 vs -5.645 \pm 0.29, P<0.05, respectively; see Figure).

Discussion. In IMA segments with impaired endothelial responses, pre-treatment with vericiguat was as effective as verapamil in inhibiting PE maximal constrictor responses and reducing the sensitivity to PE. Thus vericiguat may be useful in the treatment of coronary vasomotor disorders with endothelial dysfunction.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P208

A novel Drp1 inhibitor to protect against anthracycline-induced cardiotoxicity.

Miss Yali Deng

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Yali Deng has completed her Bachelor of Biomedicine (Honours) at The University of Melbourne in 2021 and is currently a third-year PhD candidate at St Vincent's Institute of Medical Research, specialising in cardio-oncology. Her research focuses on the role of dynamin-related protein 1 (Drp1) in protecting against anthracycline-induced cardiomyopathy, utilising advanced research models such as human induced pluripotent stem cells, cardiac tissue engineering, microfluidics, and murine models. Passionate about translational research, Yali aims to bridge the gap between basic and clinical science to accelerate drug development. She has previously worked as a business development intern under Research Innovation and Commercialisation stream at The University of Melbourne, helping researchers to translate their discoveries into practical applications.

A novel Drp1 inhibitor to protect against anthracycline-induced cardiotoxicity.

Yali Deng¹, Jessica Holien², Doan Ngo³, Anne Kong¹, Jarmon G. Lees¹, Shiang Y. Lim¹. St Vincent's Institute¹; RMIT University², Melbourne, VIC, Australia; University of Newcastle, NSW, Australia³.

Introduction. Doxorubicin is an effective chemotherapy drug but may cause doxorubicin-induced cardiotoxicity through mitochondrial dysfunction. Increased dynamin-related protein 1 (Drp1)-mediated mitochondrial fission has been observed in both doxorubicin-induced cardiotoxicity and cancer cells, giving them a survival advantage. Our lab has discovered a small molecule called OB37, a novel Drp1 inhibitor that inhibits the GTPase activity of human Drp1.

Aims. To investigate whether OB37 has the potential to induce cancer cell death and protect the heart from doxorubicin-induced cardiotoxicity.

Methods. The anti-cancer effects of doxorubicin (0.05 μM) +/- OB37 (50 μM) for 2 days were assessed in 2D and 3D culture of MG63 osteosarcoma cells by CellTiter-Glo (cell viability). Mechanistic studies include MitoSOX (mitochondrial superoxide), TMRM (mitochondrial membrane potential), H2A.X (DNA damage) assays. The cardioprotective effects of OB37 (5-50 μM) against doxorubicin-induced toxicity (0.5 μM for 2 days) was assessed in 3D cardiomyocyte spheroids derived from human induced pluripotent stem cells using lactate dehydrogenase (cell death) assay.

Results. In the 2D MG63 cells, OB37 significantly increased cell death and synergised with doxorubicin to enhance cell death ($n=9$, $P<0.01$). Mechanistically, doxorubicin, but not OB37, significantly increased mitochondrial superoxide production, mitochondrial hyperpolarisation and DNA damage. In 3D MG63 spheroids, OB37 significantly reduced MG63 cancer spheroid cell viability ($n=9$, $P<0.0001$), but did not show a synergistic effect with doxorubicin. This decrease in cancer cell viability was accompanied by increased mitochondrial superoxide production ($n=6$, $P<0.01$) and mitochondrial depolarisation ($n=2$, $P<0.001$). In 3D cardiomyocyte spheroid, OB37 significantly protected against doxorubicin-induced cardiotoxicity in a dose-dependent manner by reducing the release of lactate dehydrogenase ($n=3$, $P<0.001$).

Discussion. OB37 demonstrated cardioprotective effects against doxorubicin-induced toxicity and exhibited anticancer effects in MG63 osteosarcoma cancer cells. By inhibiting Drp1, OB37 holds potential to advance cancer treatment by enhancing the therapeutic efficacy of doxorubicin while minimising cardiovascular damage.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P209

Mitochondrial-targeted therapies exhibit cardioprotection in diabetes-induced human cardiac organoids

Mr Alex Parker

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Alex has completed a Bachelor of Science (human physiology) at Edith Cowan University and a Master of Biomedical Science at the University of Melbourne. He is currently a PhD candidate at the Monash Institute of Pharmaceutical Sciences and is investigating mitochondrial-targeted therapies to limit the structural and functional changes in diabetic cardiomyopathy.

Mitochondrial-targeted therapies exhibit cardioprotection in diabetes-induced human cardiac organoids

Alex M. Parker^{1,2}, Jarmon Lees^{1,2}, Ren J. Phang², Sonya Song¹, Shiang Y Lim^{1,2}, Miles J. De Blasio¹, Rebecca H. Ritchie¹. Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Melbourne, VIC, Australia¹; St. Vincent's Institute of Medical Research, Melbourne, VIC, Australia².

Introduction. Mitochondrial dysregulation is implicated in many complications of type 2 diabetes (T2D), including the heart. Mitochondrial-targeted therapies 10-(6'-plastoquinonyl)-decyl-triphenylphosphonium (SkQ1), [10-oxo-10-[4-(3-thioxo-3H-1,2-dithiol-5-yl)-phenoxy]-decyl-triphenylphosphonium (AP39) and Elamipretide (SS31) limit renal T2D complications, but their cardioprotective potential in diabetes has not been fully resolved.

Aims. We sought to obtain the first evidence of the cardioprotective potential of SkQ1, AP39 and SS31 in T2D, using a human induced pluripotent stem cell (iPSC)-derived 3D multicellular cardiac organoid model of diabetic cardiomyopathy.

Methods. Human cardiac organoids (foreskin-2 cell-line) were generated from human iPSC-derived cardiomyocytes, cardiac fibroblasts and endothelial cells, and subjected to T2D-like milieu (20 mM glucose, 0.25 mM palmitate, 0.1 mM linoleic acid, 0.1 mM oleic acid, 5 nM endothelin-1 and 0.5 μ M cortisol) for 4 days (controls subjected to 5.55mM glucose/14.45 mM mannitol). On day 2, cardiac organoids were treated with SkQ1 (50nM), AP39 (50nM), TPP (50 nM; the mitochondrial-targeting moiety of SkQ1 and AP39), SS31 (1 μ M) or vehicle. On day 4, cardiac organoids contractile function (captured via Olympus IX71), mitochondrial superoxide (MitoSOX assay), mitochondrial membrane potential (Tetramethylrhodamine-methyl-ester assay), and cellular injury (lactate dehydrogenase) were evaluated.

Results. After 4 days, T2D milieu increased mitochondrial superoxide levels and cellular injury, which were blunted by all 3 interventions. T2D milieu also prolonged total contraction duration, time-to-peak (indicative of systolic dysfunction) and relaxation duration (indicative of diastolic dysfunction) in cardiac organoids. Interestingly, all 3 functional parameters were attenuated by AP39 and SS31, but not by SkQ1.

Discussion. These findings highlight the cardioprotective potential of selected mitochondrial-targeted therapies to limit T2D-induced cardiac dysfunction, mitochondrial dysregulation and cellular injury at least *in vitro*. These findings suggest the progression of candidates such as AP39 and SS31 into preclinical models of T2D-induced cardiomyopathy *in vivo*.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P210

Analysis of 15,339 NSTEMI admissions for 12-month medication use according to revascularisation

Mr Adam Livori

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Analysis of 15,339 NSTEMI admissions for 12-month medication use according to revascularisation

Adam C Livori^{1,2}, Zanfina Ademi^{1,3}, Jenni Iilomäki^{1,3}, Adam J Nelson^{4,5}, J.Simon Bell^{1,3}, Jedidiah I Morton^{1,6} 1. Centre for Medicine Use and Safety, Monash University, Parkville, VIC, Australia; 2. Pharmacy department, Grampians Health, Ballarat, VIC, Australia; 3. School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia; 4. Victorian Heart Institute, Melbourne, Victoria, Australia; 5. Duke Clinical Research Institute, Duke University, Durham, North Carolina, USA; 6. Baker Heart and Diabetes Institute, Melbourne, VIC, Australia

Introduction. Clinical guidelines recommend secondary prevention medications following myocardial infarction (MI) regardless of percutaneous coronary intervention (PCI) or coronary artery bypass grafts (CABG).

Aims. To investigate 12-month patterns of medication use according to revascularisation strategy following non-ST elevation myocardial infarction (NSTEMI).

Methods. All hospital admissions for NSTEMI among patients aged 30 years and older in Victoria, Australia, were identified between July-2012 and June-2017. Our linked dataset included the Victorian Admission Episodes Dataset, Pharmaceutical Benefit Scheme, Medicare Benefits Schedule, and National Death Index. We investigated medication use via proportion of days covered (PDC) over a 12-month period from the date of hospital discharge for P2Y12 inhibitors (P2Y12i), statins (total and high-intensity), ACE inhibitors/angiotensin receptor blockers (ACEi/ARBs), and beta-blockers. Analyses were performed using adjusted regression models, stratified by revascularisation strategy.

Results. Of 38,284 NSTEMI admissions, there were 15,399 admissions with revascularisation within index the admission or 30 days post discharge (11,754 with PCI and 3,645 with CABG). Following statistical adjustments, predicted 12-month PDC for P2Y12i was 0.82(0.80-0.83) vs. 0.12(0.09-0.15); ACEi/ARB were 0.62(0.60-0.65) vs. 0.43(0.39-0.48); beta-blockers were 0.53(0.51-0.55) vs. 0.63(0.58-0.66); statins were 0.79(0.78-0.81) vs. 0.78(0.74-0.81); and high intensity statins were 0.49(0.47-0.51) vs. 0.55(0.50-0.59), for PCI and CABG, respectively.

Discussion. Post-discharge dispensing of secondary prevention medications differed with respect to revascularisation strategy from 2012-2017, despite clear evidence of benefit in both strategies. Interventions are needed to address possible clinician and patient uncertainty regarding the benefits of secondary prevention medications, regardless of revascularisation strategy.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P211

Sex-selective exaggerated obesity-induced cardiometabolic phenotype in gastric inhibitory polypeptide receptor-deficient mice.

Results	Male				Female			
	WT		GIPRKO		WT		GIPRKO	
Genotype	Chow	HFD	Chow	HFD	Chow	HFD	Chow	HFD
BW	37.6±1.3	45.6±1.9	33.9±0.8	39.1±1.1 ^{^^}	29.5±1.0	40.4±1.4	26.9±0.9	35.4±0.9 ^{^^}
LV EF (%)	44.7±1.9	45.6±2.2	35.8±2.6	32.9±4.6	42.4±2.7	40.6±3.4	33.9±6.3	26.9±5.9
GLS (%)	-14.8±1.0	-11.4±0.8	-10.4±1.8	-12.0±1.5	-11.6±0.6	-12.3±1.8	-12.5±3.5	-6.3±2.0
FS (%)	18.9±2.0	21.8±1.5	15.9±1.8	14.6±1.2 [^]	17.4±1.8	18.9±1.7	13.2±2.4	12.7±1.5
TNF α	1.0±0.2	0.8±0.1	1.7±0.2 [*]	1.4±0.1	1.0±0.1	0.9±0.1	1.0±0.2	0.9±0.2
SOD2	1.0±0.1	1.3±0.1	2.7±0.6 ^{**}	2.6±0.4 [^]	1.0±0.1	1.1±0.1	2.3±0.4 ^{***}	3.0±1.4 ^{^^^}
B-MHC	1.0±0.1	1.2±0.2	2.7±0.5 [*]	2.5±0.5 [^]	1.0±0.2	0.8±0.1	2.3±0.4 [*]	2.5±0.5 ^{^^}

2-way ANOVA, Tukey's *post hoc*; *P<0.05 vs sex-matched WT chow; **P<0.01 vs sex-matched WT chow; ***P<0.001 vs sex-matched WT chow; ^P<0.05 vs sex-matched WT HFD; ^^P<0.01 vs sex-matched WT HFD; ^^P<0.001 vs sex-matched WT HFD

Mr Timothy Roberts

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Sex-selective exaggerated obesity-induced cardiometabolic phenotype in gastric inhibitory polypeptide receptor-deficient mice.

Timothy Roberts, Md Abdullah Al Mamun, Laura Cookson, Shelby Cree, Dana Hutchinson, Denise Wootten, Miles J De Blasio, Rebecca H Ritchie, Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Parkville, VIC, Australia.

Introduction. The gastric inhibitory polypeptide receptor (GIPR) has been implicated as a target in the treatment of type-2 diabetes and obesity and has been suggested to play a protective role in cardiometabolic homeostasis.

Aims. To investigate the contribution of the GIPR on cardiometabolic function in male and female mice.

Methods. Male and female C57Bl6/N (wild-type; WT) and global GIPRKO mice were placed on a high-fat diet (HFD; 60%kJ lipids) or standard rodent chow from 8 to 28 weeks of age. One week before endpoint, assessment of left-ventricular (LV) systolic and diastolic function via echocardiography (Vevo3100) in anaesthetised mice (isoflurane). Bodyweights were monitored weekly, with RTqPCR performed at endpoint for markers of LV pro-inflammatory/pro-fibrotic and mitochondrial gene expression.

Results. GIPRKO imparts impairment in cardiac phenotype in HFD-fed female mice in global longitudinal strain (GLS) and LV ejection fraction (EF), but not in males. Conversely, receptor deficiency imparts impairment in cardiac phenotype in HFD-fed male mice in fractional shortening (FS), but not in females. Differences in pro-inflammatory TNF α gene expression were evident in chow-fed male GIPRKO mice and not females. GIPRKO imparts increased pro-fibrotic β -myosin heavy chain (B-MHC) and mitochondrial superoxide dismutase 2 (SOD2) gene expression, irrespective of sex and diet.

Discussion. Obesity selectively impairs LV function and induces LV remodelling differentially in male and female mice, which is exaggerated by global GIPR deficiency. These results suggest that the GIPR may play a protective role in the heart. These sex-specific differences may have implications for the relative efficacy of dual incretin agonists (targeting both the glucagon-like peptide-1 receptor and GIPR) in females versus males.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P212

Diclofenac sodium attenuates APOC3-rich LDL-induced endothelial dysfunction and atherosclerosis in diabetic model

Dr Bo-yi Pan

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Bo-Yi PAN (Lulji Taraqaz) is an indigenous Paiwan scholar from Taiwan, currently pursuing a Ph.D. in China Medical University. His research focuses on the mechanisms by which lipoproteins contribute to cardiovascular diseases related to diabetes, emphasizing both clinical pharmacology and natural products. Passionate about bridging traditional medicine with modern science, Bo-Yi aims to develop innovative therapeutic approaches that enhance health outcomes for patients.

Diclofenac sodium attenuates APOC3-rich LDL-induced endothelial dysfunction and atherosclerosis in diabetic model

Bo-Yi Pan¹, Chen-Sheng Chen,² Fang-Yu Chen¹, Ming-Yi Shen^{1,3}. Graduate Institute of Biomedical Sciences, China Medical University¹; The Ph.D. Program for Cancer Biology and Drug Discovery, China Medical University and Academia Sinica²; Department of Medical Research, China Medical University Hospital³, Taichung Taiwan.

Introduction. Cardiovascular disease is a leading cause of death in diabetes mellitus patients. Recent studies suggest that APOC3-rich low-density lipoprotein (AC3RL) promotes atherosclerosis progression by inducing endothelial dysfunction. Diclofenac sodium inhibits COX2, a key factor in atherosclerosis development.

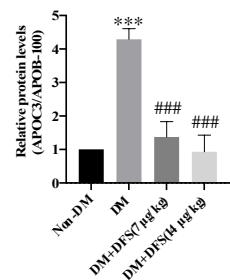
Aims. To investigate the mechanisms by which low-dose DFS attenuates AC3RL-induced endothelial cell apoptosis and its potential to mitigate atherosclerosis progression in diabetic models with hyperlipidemia and hyperglycemia.

Methods. We evaluated low-dose DFS's effects on AC3RL-induced apoptosis in human aortic endothelial cells (HAECs) using Hoechst-33342 staining, DCFH-DA analysis, and Western blot.

Atherosclerosis in streptozotocin (STZ)-treated mice was assessed with Oil Red O staining and immunohistochemistry (IHC).

Results. We isolated AC3RL from diabetic patients with cardiovascular diseases, finding elevated levels compared to non-diabetic controls (n=10). In HAECs, DFS (0.3-1 μ M) reduced AC3RL-induced apoptosis and ROS, inhibiting the upregulation of apoptosis-related proteins (BAX/BCL2, cleaved caspase-3) and the inflammatory factor COX-2. In diabetic animal models with hyperlipidemia, the severity of arterial atherosclerosis, endothelial cell COX-2 protein expression, and apoptosis increased. DFS treatment mitigated lesion severity. In plasma LDL, apoC3 protein expression were higher in diabetic mice than in non-diabetic mice; however, DFS-treated mice showed lower levels than untreated diabetic mice.

Discussion. DFS can impeded atherosclerosis development by suppressing AC3RL-induced endothelial cell apoptosis and abnormal lipid accumulation.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P213

The mPGES-1/PGE₂/EP4 axis induces recovery from ischemia condition via recruitment of Tregs

Prof Hideki Amano

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

The mPGES-1/PGE₂/EP4 axis induces recovery from ischemia condition via recruitment of Tregs

Hideki Amano¹, Koji Eshima², Yoshiya Ito¹, Kanako Hosono¹, Shizuo Akira³, Shuh Narumiya⁴,
Department of Pharmacology, Kitasato University School of Medicine¹, Kanagawa, Japan.

Department of Immunology, Kitasato University School of Science², Kanagawa, Japan. Laboratory of Host Defense, WPI Immunology Frontier Research Center, Osaka University³, Osaka, Japan. Department of Drug Discovery Medicine, Kyoto University Graduate School of Medicine⁴, Kyoto, Japan.

Introduction. Microsomal prostaglandin E synthase-1 (mPGES-1)/prostaglandin E₂ (PGE₂) induces angiogenesis through the prostaglandin E₂ receptor (EP1–4). Regulatory T cells (Tregs) inhibit immune responses, have been implicated in angiogenesis.

Aims. This research was investigated that mPGES-1/PGE₂-EP signaling could contribute to recovery from ischemic conditions by promoting accumulation of Tregs.

Methods. Wild-type (WT), mPGES-1-deficient (*mPges-1*^{-/-}), and EP4 receptor-deficient (*Ep4*^{-/-}) male mice 6–8 weeks old were used. Hindlimb ischemia was induced by femoral artery ligation. Recovery from ischemia was estimated by using laser doppler.

Results. Recovery from ischemia was suppressed in *mPges-1*^{-/-} mice and compared with WT mice. The number of FoxP3⁺ cells in ischemic muscle tissue was decreased in *mPges-1*^{-/-} mice compared with that in WT mice. Expression levels of transforming growth factor-β (TGF-β) and stromal cell derived factor-1 (SDF-1) in ischemic tissue were also suppressed in *mPges-1*^{-/-} mice. The number of accumulated FoxP3⁺ cells and blood flow recovery were suppressed when Tregs were depleted by injecting antibody against folate receptor 4 (FR4) in WT mice but not in *mPges-1*^{-/-} mice. Recovery from ischemia was significantly suppressed in *Ep4*^{-/-} mice compared with WT mice. Furthermore, mRNA levels of *Foxp3* and *Tgf-β* were suppressed in *Ep4*^{-/-} mice. Moreover, the numbers of accumulated FoxP3⁺ cells in ischemic tissue were diminished in *Ep4*^{-/-} mice compared with *Ep4*^{+/+} mice.

Discussion. These findings suggested that mPGES-1/PGE₂ induced neovascularization from ischemia via EP4 by promoting accumulation of Tregs. Highly selective EP4 agonists could be useful for treatment of peripheral artery disease.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P214

Pharmacological inhibition of interleukin-18 attenuates deoxycorticosterone/salt-induced hypertension, renal inflammation and capillary rarefaction

Miss Buddhila Wickramasinghe

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Buddhila Wickramasinghe is a third-year PhD candidate in the Hypertension and Diabetes division at the Centre for Cardiovascular Biology and Disease Research, La Trobe University, Melbourne, Australia. Her research focuses on understanding the role of the immune system in hypertension and chronic kidney disease by utilizing various animal models and in vitro techniques. As she continues to develop her research profile, she has presented her work at both national and international conferences, including the High Blood Pressure Research Council of Australia ASM and International Society of Hypertension Scientific Sessions. In addition to her research, Buddhila advocates for HDR students as the student representative for the Cardiovascular SIG of ASCEPT. She is also dedicated to promoting STEM education and inspiring the next generation of scientists by engaging with primary and high school students.

Pharmacological inhibition of interleukin-18 attenuates deoxycorticosterone/salt-induced hypertension, renal inflammation and capillary rarefaction

Buddhila Wickramasinghe¹, Narbada Saini¹, Jordyn Thomas^{1,2}, Brooke Huuskens¹, Henry Diep^{1,2}, Christopher G Sobey¹, Maria Jelinic¹, Grant R Drummond¹, Antony Vinh¹. Centre for Cardiovascular Biology and Disease Research, La Trobe Institute for Molecular Science, La Trobe University, Bundoora, VIC, Australia¹; Victorian Heart Institute, Monash University, Clayton, VIC, Australia².

Introduction. Circulating levels of the pro-inflammatory cytokine, interleukin-18 (IL-18), are elevated in patients with hypertension and chronic kidney disease (CKD). Moreover, genetic IL-18 deletion prevents the development of hypertension and renal injury in uninephrectomised mice treated with deoxycorticosterone acetate and high salt (1K/DOCA/salt, a model of CKD). Thus, IL-18 represents a novel drug target to treat hypertension and CKD.

Aims. Determine if pharmacological inhibition of IL-18 protects against 1K/DOCA/salt-induced hypertension and CKD.

Methods. Male C57BL/6 mice (n=11-12/group, 12 weeks old) were randomly assigned to receive a control IgG or anti-IL-18 neutralising monoclonal antibody (30 mg/kg, *i.p.*) 3 days prior to induction of hypertension, and every 3 days thereafter. Isoflurane anaesthetised mice (induction: 2 L/min, 5% in O₂; maintenance: 0.4 L/min, 2.5% in O₂) received uninephrectomy and implantation of a DOCA pellet (2.4 mg/d, *s.c.*) with saline drinking water (0.9% NaCl). Normotensive controls received a placebo pellet (*s.c.*) with normal drinking water. Blood pressure (BP) was measured weekly (tail-cuff). After 21 days, mice were humanely killed and kidneys were collected to assess fibrosis (picrosirius red staining), immune cell infiltration (flow cytometry) and renal capillary density (immunofluorescence).

Results. Anti-IL-18 treatment did not affect systolic BP in placebo mice (118±2 mmHg Vs 122±3 mmHg in control IgG), but significantly blunted hypertension in 1K/DOCA salt mice (139±6 mmHg Vs 159±6 mmHg in control IgG; *P*<0.05). 1K/DOCA/salt-induced leukocyte (CD45⁺) accumulation in the kidneys was reduced in anti-IL-18-treated mice (0.9±0.1 ×10⁵ cells/kidney) compared to control IgG treatment (1.6±0.3 ×10⁵ cells/kidney; *P*<0.05). Further analysis revealed reductions

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



in myeloid cells (CD11b⁺; $P < 0.05$), specifically macrophages (F4/80⁺; $P < 0.05$). 1K/DOCA/salt-induced renal capillary rarefaction but not fibrosis was significantly prevented in anti-IL-18-treated mice ($P < 0.05$).

Discussion. Neutralisation of IL-18 prevents experimental hypertension possibly via a reduction in renal inflammation and renal capillary rarefaction. IL-18 may represent a novel drug target to treat hypertension and kidney disease.

P215

Adipose overexpression of mitochondrial catalase alters cardiac proteome during cancer-induced cardiac cachexia.

Ms Amanda Croft

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Adipose overexpression of mitochondrial catalase alters cardiac proteome during cancer-induced cardiac cachexia.

Amanda J Croft^{1,3}, Conagh Kelly^{2,3}, Dongqing Chen^{2,3}, Tatt Jhong Haw^{1,3}, Lohis Balachandran^{1,3}, Aaron L Sverdlow^{1,3,4}, Doan TM Ngo^{2,3}. 1. School of Medicine and Public Health, University of Newcastle, NSW, Australia; 2. School of Biomedical Sciences and Pharmacy, University of Newcastle, NSW, Australia; 3. Hunter Medical Research Institute, Newcastle, NSW, Australia; 4. Hunter New England Health, Newcastle, NSW, Australia.

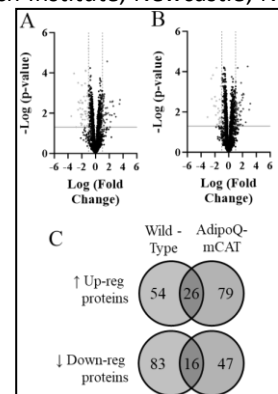
Introduction. A debilitating result of colorectal cancer (CRC) is cachexia: fat/muscle wasting that leads to cardiac atrophy and heart failure. Adipose tissue undergoes extensive remodelling during CRC, including inflammation, oxidative stress and lipolysis that promote cardiac cachexia and predict survival in patients. Here, we hypothesised that improving adipose tissue health by adipose-targeted overexpression of the antioxidant mitochondrial catalase (mCAT) can alter the cardiac proteome and thereby improve cardiac cachexia.

Aims. To determine cardiac proteome changes conferred by adipose-overexpression of mCAT during AOM-DSS model of colitis-associated CRC.

Methods. AdipoQ-mCAT transgenic (TG) mice were generated by crossing AdipoQ-Cre with floxed mCAT mice. Colitis-associated CRC was induced using AOM/DSS protocol in TG and wild-type (WT) mice. Cardiac tissue from WT and TG mice with CRC were compared to healthy tissues via bottom-up proteomic analysis. DAVID/STRING databases were used for functional enrichment analyses.

Results. Proteomic analysis showed 80 up- and 99 down-regulated proteins in WT mice treated with AOM-DSS (Figure A), and 105 up- and 63 down-regulated proteins in TG hearts (Figure B), but only 26 up- and 16 down-regulated proteins were found in both genotypes (Figure C). Functional enrichment analysis indicated extracellular matrix, cell cycle, redox response and lipid metabolism are altered in WT hearts by AOM-DSS treatment, whereas mitochondrial organisation and metabolic pathways were altered in TG hearts with AOM-DSS treatment.

Discussion. We have demonstrated cardiac tissues undergo significant molecular changes during CRC induction, however it is unknown whether this directly contributes to cardiac cachexia development. Adipose-overexpression of mCAT significantly changes the cardiac proteomic response to CRC induction, suggesting targeting antioxidants to adipose tissue may be developed into a promising treatment strategy for cardiac cachexia in CRC patients.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P326

Tilianin suppresses NLRP3 inflammasome to mitigate myocardial ischemia/reperfusion injury

Prof Shoubao Wang

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

PI of the National Center for Pharmaceutical Screening, Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College. He obtained his Ph.D. in Pharmacology from Peking Union Medical College in 2009. From 2013 to 2015, he completed a postdoctoral fellowship program at the University of Manchester in the UK. In 2015, he returned to China and served as editorial board member of such journals as *Pharmaceutical Research*, *Modern Chinese Medicine*, *International Journal of Drug Discovery and Pharmacy (IJDDP)*, *Allergy Medicine*, *Chinese Journal of Arteriosclerosis*, *Herald of Medicine*, *Chinese Pharmaceutical Journal*, *Pharmacology and Clinics of Chinese Materia Medica*, etc.

His research interests are cardio-cerebrovascular pharmacology and new drug discovery. He has published more than 60 research papers in *Nature Communications*, *British Journal of Pharmacology*, *Acta Pharmaceutica Sinica B* and other well-known journals. He has applied for 10 national invention patents and 6 grants. He participated in the compilation (translation) of 22 books, and the research and development and application of new drugs such as new Nirendipine tablets, Baikeli chewable tablets and Salvianolic acid A. He has won Natural Science Award of the Ministry of Education, Beijing Science and Technology Progress Award, and China Medical Science and Technology Award.

Tilianin suppresses NLRP3 inflammasome to mitigate myocardial ischemia/reperfusion injury

Shoubao Wang, Di Wu, Tianyi Yuan, Lianhua Fang, Guanhua Du.

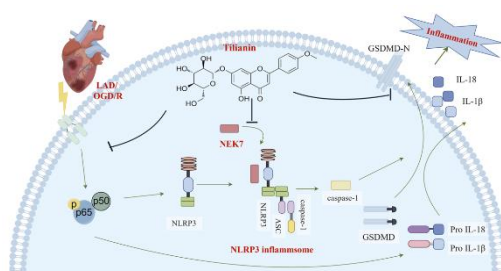
Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Introduction. Tilianin, a flavonoid compound derived from *Dracocephalum moldavica* L., is recognized for its diverse biological functionalities, in particular alleviating myocardial ischemia-reperfusion injury (MIRI).

Aims. This is aimed to investigate the effects of tilianin on NLRP3 inflammasome and explore its anti-MIRI mechanisms.

Methods. In this study, rats undergoing the ligation and subsequent release of the left anterior descending (LAD) coronary artery and H9c2 cardiomyocytes subjected to oxygen-glucose deprivation/reoxygenation (OGD/R) were used.

Results. Echocardiography, TTC staining and TUNEL staining demonstrated that tilianin remarkably improved cardiac function and mitigated myocardial damage in MIRI rats. Tilianin decreased the levels of TLR4, p-NF- κ B, NLRP3, and ASC in MIRI rats and H9c2 cells exposed to OGD/R, alongside a significant reduction in cleaved gasdermin D (GSDMD), mature IL-1 β and IL-18. Tilianin protects cardiomyocytes from MIRI by suppressing NLRP3 inflammasome via inhibition of TLR4/NF- κ B and disruption of the NEK7/NLRP3 interface.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion. The present study elucidated the anti-inflammatory role of tilianin against MIRI and explored its underlying mechanisms. Tilianin exerted its anti-inflammatory effects by inhibiting the expression of NLRP3 and pro-inflammatory cytokines through the suppression of TLR4/NF- κ B signaling pathway. Additionally, the interaction between NEK7 and NLRP3 also mediated the anti-inflammatory activities of tilianin in the context of MIRI. These findings underscored the potential of tilianin as a promising therapeutic candidate for MIRI.

P216

Development and evaluation of online medication support tools for older people

Ms Temitope Esther Afolabi

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

With a keen interest in geriatric medicine, research and education, Esther is currently undertaking her Doctor of Philosophy at The University of Sydney under main supervisor Professor Sarah Hilmer. Her research centres round codesigning digital solutions for older people, that optimises medication management and promotes collaboration with health care practitioners.

Development and evaluation of online medication support tools for older people: a systematic review protocol

Temitope E Afolabi^{1,2}, Sarah Hilmer^{1,2}, Lisa Kouladjian O'Donnell^{1,2}, Christopher Etherton-Beer³. Faculty of Medicine and Health, The University of Sydney¹, Sydney, NSW, Australia; Laboratory of Ageing and Pharmacology, Kolling Institute of Research², Sydney, NSW, Australia; School of Medicine, University of Western Australia³, Crawley, WA, Australia.

Introduction. The explosion of Health Information Technologies (HIT) has ushered in new paradigms in healthcare with a shift towards consumer-led care models via the development of online consumer-facing healthcare applications including online medication support tools. Emerging evidence indicates that use of online HIT by patients and caregivers is high, even among older people (Mace et al. 2022). However, little is known about the development and evaluation of online health and medication applications for older people (Gleason et al. 2023).

Aim. To systematically evaluate the literature on the development and evaluation of online medication support tools for older people.

Methods. A systematic search from inception to June 2024 will be conducted in OVID, PubMed, and Embase to identify relevant studies on the development and evaluation of online medication support tools for individuals. The protocol will be registered in PROSPERO, following PRISMA guidelines. Two authors will independently screen the titles and abstracts of identified studies, review the full texts of short-listed articles, and assess study quality using the Joanna Briggs Institute Risk of Bias assessment tool. Covidence will be used for data extraction and results will be synthesized systematically. The plausibility of a meta-analysis will also be assessed.

Discussion. The rapid pace of innovation in health systems' use of online patient platforms and rising global prevalence of older people and medication use, warrants a systematic review of the evidence surrounding online medication support tools for older people. This systematic review will inform the development of a similar intervention to be developed during my PhD candidature.

Gleason, K. T., et al. (2023). "Patient portal interventions: a scoping review of functionality, automation used, and therapeutic elements of patient portal interventions." *JAMIA Open* 6(3): ooad077.

Mace, R. A., et al. (2022). "Older adults can use technology: why healthcare professionals must overcome ageism in digital health." *Transl Behav Med* 12(12): 1102-1105.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P217

Comparison of methods to estimate busulfan exposure in paediatric bone marrow transplantation

Miss Nishat Siddique

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Nishat Siddique is due to complete her Bachelor of Pharmacy (Honours) with a Major in Clinical and Experimental Therapeutics in November 2024. In addition to her studies, Nishat currently works as a pharmacy assistant and has gained valuable experience across community, rural, and hospital pharmacy settings. She is passionate about integrating research and clinical practice, with her current project focusing on methods to estimate busulfan exposure in paediatric hematopoietic stem cell transplantation, aiming to influence clinical practice at Queensland Children's Hospital. Next year, Nishat will be undertaking an internship at Prince Charles Hospital where she hopes to continue to contribute towards advancing patient care and quality improvement in pharmacy practice."

Comparison of methods to estimate busulfan exposure in paediatric bone marrow transplantation

Nishat Siddique¹, Christine E. Staatz¹, Rachael Lawson². School of Pharmacy, Uni of Qld¹, Brisbane, QLD, Australia; Dept of Pharmacy, Queensland Children's Hosp², Brisbane, QLD, Australia.

Introduction. Busulfan is a drug used in paediatric bone marrow transplantation. It has a narrow therapeutic index and displays non-linear pharmacokinetics. Changing from non-compartmental analysis (NCA) to Bayesian model-based methods (MBM) for estimating exposure requires an understanding of the relative difference between the two.

Aims. (i) to compare busulfan exposure (AUC_{cum}) estimated by NCA to that estimated by MBM based on full sampling across all four days of busulfan therapy (ii) to compare busulfan exposure (AUC_{cum}) estimated by MBM based on full sampling across all four days of therapy to that based on full sampling from dose 1 only of therapy; and to that based on full sampling from dose 1 and day 3 only of therapy.

Methods. Retrospective pharmacokinetic data characterising intravenous busulfan usage in paediatric bone marrow transplant recipients was obtained from hospitals across Australia and New Zealand. Patient specific characteristics, busulfan dose and concentration-time measurements were entered into NCA and MBM software to give predictions of busulfan AUC_{cum} . The distribution of AUC_{cum} values generated from the different analysis methods and sampling techniques were compared statistically using a Wilcoxon rank sum test.

Results. Pilot data from 50 subjects with a total of 1299 busulfan concentration-time measurements were included in the analysis. The median patient age was 4.5 years [range: 1.6-18.1]. The median AUC_{cum} estimated based on full sampling across all four days of therapy using NCA was 76.9 mg·h/L [range: 61.3-94.1]. The median AUC_{cum} estimated based on full sampling using MBM was 80.0 mg·h/L [range: 65.0-97.9]. There was a significant difference in AUC_{cum} values when applying NCA and MBM techniques on the same dataset ($n=50$, $P=0.03$). The median AUC_{cum} estimated based on full sampling

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



from day 1 only of therapy was 81.1 mg·h/L [range: 66.9-99.8], while median AUC_{cum} estimated based on full sampling from day 1 and 3 only of therapy was 79.5 mg·h/L [range: 63.8-116.6]. There was no significant difference in AUC_{cum} values when applying MBM and comparing full sampling across all four days of therapy to full sampling from day 1 only of therapy ($n=50$, $P=0.81$); or to full sampling from day 1 and 3 only ($n=50$, $P=0.17$).

Discussion. Both NCA and MBM techniques are used clinically. It is important to consider the method of estimating busulfan exposure in paediatric bone marrow transplantation and make adjustments if switching between methods.

P218

Efficacy Quantitative Evaluation of Targeted Pulmonary Hypertension Drugs based on MBMA

Prof Shi Aixin

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Female, Professor, Ph D, Chief Pharmacists, Clinical Trial Center, Beijing Hospital, National Center of Gerontology; Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, P R. China. Master's Supervisor of Peking Union Medical College, Institute of Geriatrics, Beijing Hospital and Shenyang Pharmaceutical University.

Main research directions include Clinical Pharmacology, Pharmacometrics and Clinical Research of new drugs & Analysis Techniques.

More than 20 years engaged in clinical pharmacology research. Completed more than 150 phase I clinical studies of new drugs as the Principal Investigator or co-investigator. Published more than 130 papers in SCI and domestic core journals.

Efficacy Quantitative Evaluation of Targeted Pulmonary Hypertension Drugs based on MBMA

Aixin SHI, Zhixing CHEN, Panpan XIE, Clinical Trial Center, Beijing Hospital, National Center of Gerontology; Institute of Geriatric Medicine, Chinese Academy of Medical Science, Beijing, PRC

Introduction. The Model-based meta-analysis (MBMA) method has many advantages and can be used for quantitative evaluation of drug efficacy and provide basis for clinical drug use.

Aims. In this study, we will utilize the MBMA method to establish a pharmacodynamic model for the targeted Pulmonary Hypertension (PH) drugs, and evaluate the efficacy of drugs quantitatively and obtain the time-effect relationship for providing guidance for clinical drug use.

Methods. The change in 6-minute walk distance (6MWD) from baseline was utilized as the efficacy index. Based on the nonlinear mixed-effect model, a pharmacodynamic model was developed to describe the time-effect relationship of drugs in PH patients, respectively. The stepwise covariate model was utilized to screen covariates and determine influencing factors on drug efficacy.

Tab1. Pharmacodynamic parameters and correction values of drugs predicted by the model^{a,c}

Treatment ^a	Arms ^a (Sample size) ^{a,c}	E_{max} ^a (95% CI) ^{a,c}	$E_{max,corrected}$ ^a (95% CI) ^{a,c}	ET_{50} ^a (95% CI) ^{a,c}
ERA ^a	34 ^a (1727) ^{a,c}	54.57 ^a (47.86, 61.29) ^{a,c}	57.58 ^a (49.65, 65.51) ^{a,c}	7.71 ^a (5.32, 10.11) ^{a,c}
PDES ^a	28 ^a (1491) ^{a,c}	64.46 ^a (53.59, 75.33) ^{a,c}	63.13 ^a (54.66, 71.60) ^{a,c}	6.34 ^a (4.79, 7.90) ^{a,c}
sGC ^a	6 ^a (675) ^{a,c}	47.86 ^a (37.08, 58.64) ^{a,c}	60.47 ^a (46.87, 74.08) ^{a,c}	10.02 ^a (3.32, 16.72) ^{a,c}
Pro A ^a	18 ^a (1807) ^{a,c}	83.17 ^a (56.11, 110.24) ^{a,c}	76.79 ^a (55.53, 98.05) ^{a,c}	8.86 ^a (4.77, 12.95) ^{a,c}
PRA ^a	5 ^a (708) ^{a,c}	96.29 ^a (39.76, 152.83) ^{a,c}	101.41 ^a (53.11, 149.71) ^{a,c}	30.13 ^a (4.64, 55.62) ^{a,c}
Combination ^a	17 ^a (1530) ^{a,c}	70.53 ^a (56.38, 84.68) ^{a,c}	71.34 ^a (56.95, 85.73) ^{a,c}	14.07 ^a (5.79, 22.36) ^{a,c}
Placebo ^a	57 ^a (4584) ^{a,c}	3.60 ^a (2.72, 4.49) ^{a,c}	- ^a	0.027 ^a (0.026, 0.027) ^{a,c}

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Results. A total of 108 trials comprising 7938 participants were included in the analysis. Five classes of targeted drugs were evaluated including endothelin receptor agonists(ERA), phosphodiesterase type V inhibitors(PDE5i), soluble guanylate cyclase stimulators(sGC), prostacyclin analogues(Pro A) and prostacyclin receptor agonists(PRA). The findings revealed that the drug efficacy was Pro A > PRA > PDE5i > drug combination > ERA > sGC. E_{max} (Maximum drug effect) value of Pro A was 101.41 meters (95% CI: 53.11, 149.71), higher than other drugs significantly. PDE5i had the shortest onset time with 6.34 weeks compared to other drugs.

Discussion. This study utilized MBMA method to evaluate the efficacy and influencing factors of targeted PH drugs quantitatively. The results of this study show the difference in the efficacy of these 6 types of targeted drug therapy for PH, and provide important quantitative information for the clinical application of targeted therapy for PH.

P219

Population pharmacokinetics of benzathine penicillin G in pregnant women with syphilis

Mr Eshetie Melese Birru

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Mr. Eshetie Melese Birru is a PhD candidate in Pharmacy at Curtin University, with extensive experience in research, academia, and community service. He was previously a senior lecturer and head of the Department of Pharmacology at the University of Gondar, Ethiopia. Specializing in pharmacology, Mr. Birru has a solid foundation in pharmacy and a deep commitment to advancing the field. He has published over 35 research articles in the areas of experimental and clinical pharmacology, pharmacy, and public health.

Population pharmacokinetics of benzathine penicillin G in pregnant women with syphilis

Eshetie Melese Birru^{1,2}, Brioni R. Moore^{1,3,4,5}, Laurens Manning^{4,5}, Sam Salman⁵, Madhu Page-Sharp¹, Chernet Baye², Kevin T. Batty^{1,3}

¹Medical School, Curtin Univ, Bentley, WA, Australia, ²College of medicine and Health Sciences, University of Gondar, Gondar, Ethiopia, ³CHIRI, Curtin Univ, Bentley, WA, Australia, ⁴Medical School, UWA, Australia, Crawley, WA, ⁵Wesfarmers Centre of Vaccines and Infectious Diseases, TKI, Nedlands, WA, Australia

Introduction: Benzathine (benzyl)penicillin G (BPG) is the recommended first line treatment for syphilis amongst pregnant women. After injection, BPG slowly dissolves and dissociates to benzylpenicillin, which distributes into the bloodstream. However, there is paucity of pharmacokinetic data of benzylpenicillin among pregnant women and there are quality, adherence, and treatment failure concerns on BPG deployment for treatment of infectious diseases, especially in poor socio-economic settings.

Aims. to investigate the population Pharmacokinetics of benzylpenicillin after intramuscular BPG administration in pregnant women with syphilis

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Methods: We conducted a longitudinal pharmacokinetic study of BPG in pregnant women in University of Gondar Hospital, Ethiopia, from Jan 2023- Dec 2023. Pregnant women >18 years of age and >14 weeks gestation who were receiving BPG for treatment of syphilis (2.4MIU/week for 3 consecutive weeks) were recruited. Dried blood spots (DBS) were collected at 0-, 1-, 3-, 7-, 14-, 15-, 16-, 21-, 28-, 35-, 42-, and 56-days post first BPG dose administration. Plasma samples, for internal validation, were also collected at Day 0, 7, and 14. Samples were stored at -80°C until shipment to Perth, Australia for analysis. Benzylpenicillin concentrations were determined using a validated LC-MS/MS assay. Concentration-time data sets to be analysed using non-linear mixed effects modelling (NONMEM) with consideration of covariate such as stage of pregnancy and renal function.

Parameters	Mean ± SD
Age (years)	28.3±5.6
Weight (kg)	54.3±6.8
Body mass index	21.8±2.6
Gravida	2.9±1.8
Para	1.8±1.8
Gestational age (weeks)	24±7.4
HCT (% volume)	37.9±2.4

The study has been ethically approved by

University of Gondar IRB: Rfe: VP/RTT/05/301/2022,

Curtin University HREC: HRE2023-0085, and

Federal Ministry of Education (Ethiopia): NRERC Ref: 17/152/156/23.

Results: Pharmacokinetic data will be available on end of August 2024.

Discussion: Pending

P220

Acceptability and implementation challenges of rheumatic heart disease prophylaxis: a qualitative study

Mr Eshetie Melese Birru

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Mr. Eshetie Melese Birru is a PhD candidate in Pharmacy at Curtin University, with extensive experience in research, academia, and community service. He was previously a senior lecturer and head of the Department of Pharmacology at the University of Gondar, Ethiopia. Specializing in pharmacology, Mr. Birru has a solid foundation in pharmacy and a deep commitment to advancing the field. He has published over 35 research articles in the areas of experimental and clinical pharmacology, pharmacy, and public health.

Acceptability and implementation challenges of rheumatic heart disease prophylaxis: a qualitative study

Eshetie Melese Birru¹, Kevin T. Batty^{1,2}, Laurens Manning^{3,4}, Stephanie L. Enkel⁵, Brioni R. Moore^{1,2,3,4}

¹Medical School, Curtin Univ, Bentley, WA, Australia, ²CHIRI, Curtin Univ, Bentley, WA, Australia, ³Medical School, UWA, Australia, Crawley, WA, ⁴Wesfarmers Centre of Vaccines and Infectious Diseases, TKI, Nedlands, WA, Australia

Introduction: Rheumatic heart disease (RHD), a chronic cardiac sequela of untreated acute rheumatic fever, remains a major public health issue due to its continuing burden in low-income areas and disadvantaged populations. Benzathine penicillin G (BPG) is a well-established secondary prophylactic agent for RHD. However, implementation of successful BPG prophylactic strategies is often hampered by factors such as logistics and perceived safety concerns.

Aims. The principal objective of the present study was to explore perceived acceptability and implementation challenges of BPG treatment for RHD in Ethiopia, from the perspective of health care providers (HCPs).

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Methods: A descriptive qualitative study using semi-structured interview guides with service providers working in four public hospitals of Ethiopia was conducted, from April to June 2022. Health care providers (physicians and nurses) who had at least one year experience in delivering RHD secondary prophylactic care service and were willing to participate in the study and provide informed consent, were selected using purposive sampling methods. The in-depth interviews were audio recorded, transcribed verbatim, and then translated into English for analysis. The analysis was done using framework method thematic analysis (NVivo v12). The identified behavioural factors were mapped onto a theoretical framework of acceptability (TFA), & Capability, Opportunity, Motivation-Behaviour (COM-B) model. The study was Conducted and reported as per consolidated criteria for reporting qualitative research (COREQ) recommendation.

Results: Twenty-two interviews were conducted with HCPs (mean age 39±10 years), of which 55% were nurses. Insight into BPG use and acceptability in Ethiopian public hospitals was categorised in four major themes related to: (i) HCPs (e.g., fear of anaphylactic reaction), (ii) health system barriers (e.g., BPG shortage), (iii) patient/caregiver perceptions (e.g., over expectation of treatment outcomes), and (iv) product (e.g., anaphylactic reaction, needle blockage).

Discussion: HCPs acknowledged numerous barriers which demonstrate the complicated nature of BPG based secondary prophylaxis of RHD in Ethiopia. This necessitates multidimensional interventions including behavioural (e.g., HCPs training, patient education) and pharmaceutical reformulation strategies to improve BPG uptake for secondary prophylaxis of RHD.

P221

How aged care home workers understand the PRACTICE tool? cognitive interview study

Mr Boyi (Douglas) Chen

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

How do aged care home staff and health care professionals understand the Psychotropic medicines use in Residents And Culture: Influencing Clinical Excellence (PRACTICE) tool? A cognitive interview study

Boyi Chen¹, Yun-Hee Jeon², Timothy Chen¹, Danijela Gnjidic¹, Jane Thompson³, Mouna Sawan¹. Sydney Pharmacy School, Faculty of Medicine and Health, Univ. of Sydney, Camperdown, NSW, Australia¹, Sydney Nursing School, Faculty of Medicine and Health, The Univ. of Sydney, Camperdown, NSW, Australia², Public contributor³

Introduction. The alarmingly high use of psychotropic medications continues to be common in residential aged care homes despite the risk of harm and limited efficacy in people living with dementia. Research has shown that the organisational culture of aged care homes influences psychotropic medication use in residents with dementia. The PRACTICE (Psychotropic medicines use in Residents And Culture: Influencing Clinical Excellence) tool was developed to comprehensively evaluate the organisational culture of aged care homes specific to the use of psychotropic medications.

Aims. To evaluate the comprehensibility, relevance, and comprehensiveness of the PRACTICE tool among end-users.

Methods. Cognitive interviews were conducted with participants representing a broad range of health disciplines across Australia. Interviews were performed using the combination of think aloud technique and verbal probing. Interviews were transcribed and content coded for participants' perceptions of the PRACTICE tool. Items were modified based on findings from the cognitive interviews, participants' suggestions for rewording of the items to improve clarity and discussions with the research team.

Results. A total of 20 cognitive interviews were conducted. Based on the cognitive interviews, 48 out of 63 items were modified. Reasons for modification were categorised into three themes: 1) Items changed to align with the aged care home staff's scope of practice; 2) Items adjusted to prevent un-intended blame from reading the items; and 3) Items modified to prevent potential misinterpretation of their intended meaning. Three items were added to improve the comprehensiveness of the tool. Most participants reported that they understood items in the PRACTICE tool, and they considered items as relevant and acceptable for the evaluation of organisational culture related to psychotropic medication use in residential aged care homes.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion. Our study confirms that the PRACTICE tool is relevant and comprehensive in assessing organizational culture specific to psychotropic medication use in aged care homes. The updated PRACTICE tool can be used to inform tailored strategies to support appropriate use of psychotropic medications.

P222

Machine learning models for personalised dosing of oral anticoagulants: a systematic review

Prof Michael Barras

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Prof Michael Barras is the Director of Pharmacy at the Princess Alexandra Hospital, Brisbane, and a Research Conjoint with the School of Pharmacy, The University of QLD (Hospital 0.8 FTE / UQ 0.2 FTE). He currently supervises 8 HDR students who are conducting research related to medication safety, health informatics and advanced scope clinical pharmacy.

Machine learning models for personalised dosing of oral anticoagulants: a systematic review

Authors: Michael Barras^{1,2}, Leila Shafiee Hanjani¹, Nazanin Falconer^{1,2}, Ahmad Abdel-Hafez³, Stephen Canaris³, Ian Scott⁴. School of Pharmacy, The University of Queensland, Brisbane, QLD¹; Pharmacy Dept, Princess Alexandra Hospital, Brisbane, QLD²; Digital Health & Informatics, Metro South Health, QLD³, School of Medicine, The University of Queensland, Brisbane, QLD⁴.

Aim: To identify and critically appraise studies of machine learning (ML) derived prediction models for determining the optimal dose of oral anticoagulants (OACs).

Methods: Five databases were searched from inception to April 2024 using key search terms synonymous with artificial intelligence or ML, 'prediction', 'dose', and 'oral anticoagulants'. OACs included vitamin K antagonists (VKAs) - warfarin, acenocoumarol, phenprocoumon, and direct acting oral anticoagulants (DOACs) - apixaban, rivaroxaban, dabigatran. Studies must have used ML methods to develop models that predicted an optimal dose of an OAC. The PROBAST checklist was used to assess quality and risk of bias. Two researchers independently extracted data and reviewed each study.

Results: Of the 7791 retrieved abstracts, 164 underwent full text review and 54 studies met the inclusion criteria. Studies all used supervised learning approach with those using ANN, neurofuzzy methods and ANFIS reporting the best predictive performance. All but 1 study of DOACs evaluated VKAs. The target outcome for the majority (n = 37) was a "stable therapeutic dose. The remaining either measured a fixed dose, predicted a dose range, classified the dose as 'adequate' or 'inadequate', or predicted a safety metric. Two studies used a prospective design, however both had small cohorts (n=240 and 115) and only 1 externally validated the model. A multicentre study recruited 15,108 participants and the model was externally validated. However, this study, like 22 others, did not test genetic features that influence drug metabolism and clearance which are important for VKA models. Studies varied widely in reporting of study participants, feature characterisation and selection, handling of missing data, sample size, and the intended clinical application of the model. All studies had high risk of bias, influenced by insufficient reporting of methods and lack of external validation of the models.

Discussion: ML models for OAC dosing focus on warfarin, with only one study evaluating DOACs. Existing studies are limited by low methodological quality, inadequate reporting of findings, and absence of external and impact evaluation.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P223

Barriers of rheumatic heart disease secondary prophylaxis: Exploring patients' experience

Mr Eshetie Melese Birru

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Mr. Eshetie Melese Birru is a PhD candidate in Pharmacy at Curtin University, with extensive experience in research, academia, and community service. He was previously a senior lecturer and head of the Department of Pharmacology at the University of Gondar, Ethiopia. Specializing in pharmacology, Mr. Birru has a solid foundation in pharmacy and a deep commitment to advancing the field. He has published over 35 research articles in the areas of experimental and clinical pharmacology, pharmacy, and public health.

Barriers of rheumatic heart disease secondary prophylaxis: Exploring patients' experience

Eshetie Melese Birru¹, Kevin T. Batty^{1,2}, Laurens Manning^{3,4}, Stephanie L. Enkel⁵, Brioni R. Moore^{1,2,3,4}

¹Medical School, Curtin Univ, Bentley, WA, Australia, ²CHIRI, Curtin Univ, Bentley, WA, Australia, ³Medical School, UWA, Australia, Crawley, WA, ⁴Wesfarmers Centre of Vaccines and Infectious Diseases, TKI, Nedlands, WA, Australia

Introduction: Acute rheumatic fever (ARF) is an auto-immune condition caused by a bacterium, namely, group-A streptococcus. If left untreated it causes rheumatic heart disease (RHD), and then permanent heart valve damage. Benzathine penicillin G (BPG) is the main stay of ARF and RHD secondary prophylaxis. However, BPG delivery to RHD patients is suboptimal and potential barriers, from the perspective of participants, are not well explored.

Aims. To explore barriers that impact on RHD secondary prophylactic treatment from the patient perspective.

Methods: A descriptive qualitative study, in adherence with consolidated criteria for reporting qualitative research (COREQ), was conducted in Ethiopia in 2022. RHD patients (aged 7-17 years, and their care givers (as appropriate)) who have been receiving secondary prophylactic medication and follow up for at least 6 months were purposively recruited with different experience, demographic characteristics, and cultural settings. Investigator led focus group discussions using topic guides were conducted to ascertain factors affecting patients' experience of BPG secondary prophylaxis for treatment of ARF/RHD. Data were transcribed and translated for thematic framework analysis (NVivo v12).

Results: Participants (n=30) described several perceived barriers in the implementation of BPG, principally: shortage of BPG, injection pain, lack of cooperative health care provider to deliver BPG injection, poor follow up services and service inaccessibility. As a result of these barriers, participants were more likely to have poor treatment adherence and cease regular treatment with BPG. Although participants had concerns with the required duration of treatment, majority of them were satisfied by the treatment outcomes. Overall, participants recommended the need to have improved BPG supply, provider-patient interaction, and accessibility of health care services.

Discussion: Our study reveals that RHD secondary prophylaxis has multiple barriers, not only drug related but also at provider, individual and system levels. Thus, strategic approaches that involves all stakeholders and contextualize chronic care model could minimize and/or combat multiple obstacles for improved outcomes on RHD secondary prophylaxis.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P224

Optimising the language and format of deprescribing recommendations to support implementability

Dr Aili Langford

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr Aili Langford is a registered pharmacist, Lecturer and NHMRC Emerging Leader Research Fellow at the University of Sydney Pharmacy School. Dr Langford's research focuses on enhancing medication safety and effectiveness through deprescribing, and the implementation of clinical practice guidelines to improve health outcomes.

Optimising the language and format of deprescribing recommendations to support implementability

Aili V Langford^{1,2}, Shin Liao², Sheryn Loh², Frank Moriarty³, Danijela Gnjidic¹, Wade Thompson⁴, Barbara Farrell⁵, Danielle Pollock⁶, Naghham Ailabouni⁷, Emily Reeve². ¹Sydney Pharmacy School, The University of Sydney, NSW, Australia. ²Centre for Medicine Use and Safety, Monash University, VIC, Australia. ³School of Pharmacy and Biomolecular Sciences, RCSI University of Medicine and Health Sciences, Dublin, Ireland. ⁴Department of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia, Canada. ⁵Bruyère Research Institute, Ottawa, Canada. ⁶Health Evidence Synthesis Recommendations and Impact, The University of Adelaide, ADL, Australia. ⁷School of Pharmacy, The University of Queensland, QLD, Australia.

Background: Deprescribing guidelines exist for a limited number of medication classes. Integration of deprescribing recommendations into clinical practice guidelines may enhance their reach and adoption.

Objectives: To elicit the perspectives of healthcare professionals on the preferred content, format and language of deprescribing recommendations for inclusion in clinical practice guidelines.

Methods: Australian medical doctors, pharmacists, registered nurses and nurse practitioners were recruited. Individual semi-structured interviews were conducted. A qualitative framework analysis was performed, mapping findings to the domains of the Guideline Language and Format Instrument (GLAFI).

Results: Participants (n=24) recognised a need for greater deprescribing guidance, through recommendations that address *when, why* and *how* to deprescribe. A tension was revealed between participants' desire for succinct and uncomplicated language, and a want for detailed and comprehensive deprescribing instruction. There was inconsistency in opinions of where deprescribing recommendations should be located, with some suggesting co-location with respective prescribing recommendations and others supporting a deprescribing-specific guideline section. Inclusion of information about the strength and certainty of evidence informing recommendations was considered important but was viewed as a deterrent to implementation if a 'weak/conditional' or low certainty recommendation was presented.

Conclusions: Healthcare professionals consider content, format and language of deprescribing recommendations to be intrinsic to implementability. These findings will inform the development of a template to support guideline developers in crafting clear, concise and actionable deprescribing recommendations.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P225

Factors contributing to variability in response to follitropins: a systematic review

Ms Toni Michael

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Toni is a PhD student at the University of Sydney, School of Pharmacy. Her research is focused on understanding factors which contribute to the variability in urate response to gout medications and ovarian response to IVF medications (supervised by Dr. Sophie Stocker). She has received two awards for oral conference presentations.

Factors contributing to variability in response to follitropins: a systematic review

Toni Michael¹, Ranita Kirubakaran², Tanay Parab¹, Mark Grosser³, Beverley Vollenhoven⁴, Vinayak Smith^{3,4,5}, Sophie Stocker¹. Sch of Pharm, Univ of Sydney¹, NSW; Dept of Pharm, Ministry of Health², Malaysia; 23Strands Pte Ltd³, NSW; Dept of Obst and Gynaecol, Monash Univ⁴, VIC. Virtus Health Pte Ltd⁵, NSW.

Introduction. Controlled ovarian hyperstimulation (COH) for in vitro fertilisation (IVF) involves the administration of follicle-stimulating hormones, such as follitropin alfa, beta, or delta (follitropins). Oocyte response to COH is uncertain and variable, with many women requiring multiple IVF cycles to become pregnant. Understanding the factors contributing to the variability in response to follitropins is a strategy to improve individual response to COH therapies.

Aims. To identify factors contributing to variability in response to follitropins in women undergoing COH.

Methods. The EMBASE, PubMed and SCOPUS databases, and the references of included articles were systematically searched from database inception up to 14 January 2024. The search strategy included follicle-stimulating hormones, pharmacokinetics, dose, and IVF terminology. Studies conducted in women undergoing IVF with data on the duration of COH therapy, the total dose of follitropin administered, and the number of oocytes retrieved, were included. Descriptive (median [range]) and linear regression analysis ($P < 0.05$) were performed on summary statistics.

Results. From the 3,849 studies identified, 329 were eligible. Of these, 126 studies reported on follitropin alfa, beta, and/or delta. The age and BMI of the women undergoing IVF were 32 years [20–42] and 22.8 kg/m² [20.2–61.3]. The average total dose of follitropin alfa, beta and delta was 2000 IU [1008–4538], 1800 IU [700–4040], and 84 µg [50–124], respectively, with COH lasting for 10 days [6–18]. On average, 11 [2–21] oocytes were retrieved. For follitropin alfa, a longer duration of COH ($P = 0.03$), and older age ($P < 0.0001$) decreased the number of oocytes retrieved ($R^2 = 0.28$, $P < 0.0001$). Similarly, for follitropin beta, a longer duration of COH ($P = 0.02$) and older age ($P = 0.01$) reduced the number of oocytes retrieved ($R^2 = 0.15$, $P = 0.002$). For follitropin delta, a lower total dose administered ($P < 0.0001$) and older age ($P = 0.02$) reduced the number of oocytes retrieved ($R^2 = 0.72$, $P < 0.0001$).

Discussion. In addition to the age of a woman undergoing COH for IVF, the total dose of follitropin administered and the duration of COH impact the success of oocyte retrieval. These factors should be considered when individualising follitropin dosing to improve COH treatment response. The impact of other factors on oocyte retrieval, such as previous cycle number, should be explored further to additionally inform follitropin dosing.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P226

Concomitant Green Tea Consumption Can Significantly Influence the Pharmacokinetics of Medications

Ms Nicki Kyriacou

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Nicki Kyriacou is a PhD candidate within the Sydney Pharmacy School (Bachelor Adv Sci (Hons)). She has previously supported the Ethnopharmacology Team in the Clinical Pharmacology Modelling & Simulation group to profile ethnic sensitivity for GSK R&D. Her current research aims to investigate the impact of geographic ancestry on inter-individual variability in the pharmacokinetics of tyrosine kinase inhibitors."

Concomitant Green Tea Consumption Can Significantly Influence the Pharmacokinetics of Medications

Nicki M Kyriacou, Annette S Gross, Andrew J McLachlan. Sydney Pharmacy School, Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia.

Introduction. Individuals consuming green tea with their medications may be at risk of clinically important green tea-drug interactions, which result in altered systemic drug exposure and can influence the safety and efficacy of a medicine. *In vitro* analyses and *in vivo* animal studies indicate that green tea catechins (e.g., epigallocatechin-3-gallate, EGCG) can influence important determinants of drug pharmacokinetics (PK).

Aims. To investigate the effect of concomitant green tea administration on drug PK through a literature review.

Methods. A systematic search strategy was employed (MEDLINE, Embase) to identify clinical green tea PK interaction studies. The effect of green tea on drug PK parameters, the proposed mechanism of interaction and details of green tea administration were collected to explore trends in green tea exposure and the magnitude of PK interaction.

Results. Of the 18 clinical studies identified, 16 were conducted in healthy participants and 2 were in participants with breast cancer or pulmonary fibrosis. The majority (n = 13, 72%) of these studies reported a statistically significant decrease (20-99%) in drug systemic exposure (e.g., nadolol, lisinopril, raloxifene), 1 study (6%) showed a 50% increase in drug exposure and 4 studies (22%) reported no change in drug PK (e.g., fluvastatin, tamoxifen) with concomitant consumption of green tea. There was no difference in the magnitude of the green tea-interaction between acute and chronic (3-13 days) green tea dosing, highlighting a lack of time-dependence in the degree of green tea-interaction. Green tea was proposed to have the largest effect in the gastrointestinal tract where catechins altered the intestinal absorption of orally administered drugs by reducing drug solubility and/or inhibiting drug transporter activity (e.g., organic anion transporter peptides). The administration of green tea differed considerably between studies, in terms of the form (e.g., freshly brewed tea, commercial beverage, concentrated extract), catechin dose (50-860 mg) and schedule of administration, making it difficult to observe a dose-dependent effect of green tea on drug PK.

Discussion. Concomitant administration of green tea can significantly alter drug PK leading to the potential for clinically significant changes in efficacy and safety. These green tea interactions were mostly reported for cardiovascular drugs. Therefore, further research investigating additional drugs (e.g., anti-cancer agents) is warranted to understand the influence of green tea on drug PK and the role of specific PK determinants.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P227

Safety of a computerised physician order entry system assessed using simulation scenarios

Mr Milan Sundermann

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Milan is a PhD student in his last year of study at the University of Otago – Christchurch. His PhD project is focused on evaluating and optimising digital clinical decision support tools in hospital to promote medication safety. Milan is interested in harnessing the large volumes of routinely collected healthcare data in hospitals to inform and improve medicine use. As a current student, Milan is part of the ASCEPT student forum committee and the organising committee for the ASCEPT New Zealand forum

Safety of a computerised physician order entry system assessed using simulation scenarios

Milan Sundermann¹, Lorna Pairman¹, Matthew Doogue^{1,2}, Paul Chin^{1,2}. Department of Medicine, University of Otago¹, Christchurch, New Zealand; Department of Clinical Pharmacology, Health New Zealand², Christchurch, New Zealand.

Introduction. Inpatient prescribing errors are common, costly, and result in preventable patient harm. Computerised physician order entry (CPOE) systems have been introduced to facilitate safer prescribing, yet often fail to protect against prescribing errors. In various countries including New Zealand, Australia, and the United Kingdom, the CPOE system MedChart™ is used for hospital-based prescribing. At our tertiary institution a mixture of standard configuration and local configuration of alerts and warnings are implemented.

Aims. This study aimed to assess the vulnerability of MedChart™ to prescribing errors.

Methods. Ten prescribers were recruited to each attempt a set of 16 erroneous test scenarios in MedChart™. The ease with which prescribers completed the test cases was recorded using a five-point Likert scale (1 = easily, 5 = impossible). For scenarios involving two prescriptions, five prescribers were instructed to sign-off prescriptions sequentially, whilst five prescribers were instructed to sign-off simultaneously. Likert scores were summarised using medians (range). Differences in median and minimum scores ≥ 1 were defined as showing clinically significant inter-prescriber variability. Likert scores were compared using Mann-Whitney U tests.

Results. The median (range) ease of completing test scenarios overall was 3.0 (1-5). The best protection (Likert 5) was against erroneously omitting a dose and erroneously specifying 'as required' dose frequency for a regularly prescribed medicine. The worst protection (Likert 1) was for six scenarios, three of which involved drug-drug interactions. Sequential prescribing was associated with greater protection than simultaneous prescribing for only one scenario involving duplicate enoxaparin prescribing (median 3.0 vs 1.0, $p = 0.012$). Inter-prescriber variability was clinically significant for two scenarios: prescribing insulin aspart with inappropriate units (median 4.5, minimum 2), and prescribing phenytoin chewable tablets as 'applicatorsful' (median 3, minimum 2).

Discussion. Vulnerability testing of MedChart™ identified opportunities to improve protection against common prescribing errors. System protections were bypassed due to varying prescriber workflows. These factors need to be carefully considered when designing and configuring CPOE system protections.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P228

Embedding deprescribing recommendations in clinical practice guidelines: insights from guideline developers

Ms Shin Liau

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Shin is a pharmacist and research fellow at the Centre for Medicine Use and Safety (CMUS) at Monash University. Her research focuses on optimising medication management for frail older populations, including community-dwelling individuals with dementia and aged care residents. Driven by a passion for enhancing the quality use of medicines, she aims to advance ageing research by reducing unnecessary and potentially inappropriate medication use, thereby mitigating medication-related harms in older Australians. In addition to her research, Shin serves as Chair of the Australian Association of Gerontology (AAG) Victorian Student and Early Career Group and as a member of the Australian Deprescribing Network (ADeN) committee.

Embedding deprescribing recommendations in clinical practice guidelines: insights from guideline developers

Emily Reeve^{1,2}, Deanna Mill², Shin Liau¹, Selina Leung¹, Danijela Gnjidic³, Danielle Pollock⁴, Nagham Ailabouni^{2,5}, Wade Thompson⁶, Frank Moriarty⁷, Dorsa Maher², Barbara Farrell⁸. Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Melbourne, VIC, Australia; Clinical and Health Sciences, University of South Australia², Adelaide, SA, Australia; Faculty of Medicine and Health, University of Sydney³, NSW, Australia; Health Evidence Synthesis Recommendations and Impact, University of Adelaide⁴, SA, Australia; Faculty of Health and Behavioural Sciences, University of Queensland⁵, QLD, Australia; Faculty of Medicine, University of British Columbia⁶, Vancouver, BC, Canada; Royal College of Surgeons in Ireland⁷, Dublin, Ireland; Bruyère Research Institute⁸, Ottawa, ON, Canada.

Introduction. Healthcare professionals use clinical practice guidelines for evidence-based recommendations in conjunction with clinical expertise and patient preferences to inform treatment decisions. Clinicians often face challenges on when and how to discontinue medications due to the lack of guidance in clinical practice guidelines.

Aims. To explore the barriers and enablers to integrating evidence-based deprescribing recommendations into clinical practice guidelines.

Methods. Semi-structured interviews were conducted with guideline developers – including chairs, methodologists, clinicians, and consumer representatives – in addition to key stakeholders from organisations that play a role in informing guideline development. The interviews were qualitatively analysed using conventional content analysis.

Results. Overall, 25 participants were interviewed (n=17 guideline developers; n=8 stakeholders that inform guideline development). Participants were from Australasia, North America, and Europe, with varied experience ranging from involvement in 1 to more than 20 guidelines. Barriers and enablers identified included the alignment of deprescribing with goals of guidelines, attitudes towards or knowledge of deprescribing, availability of evidence to inform recommendations, internal and external influences on the scope of guidelines, logistical aspects, considerations for implementation, possible negative consequences, and complementary movements or clinical areas.

Discussion. While enablers for including deprescribing recommendations exist, the involvement of a champion within the guideline development group or endorsement from respected organisations is likely necessary to ensure their incorporation within the scope of guidelines. Pharmacists and geriatricians can act as champions for deprescribing within guideline development groups.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P229

Physiologically Based Pharmacokinetic Model Development, Validation, and Application of KY0467 in Pediatric

Mrs Panpan Xie

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Panpan XIE, Master of Shenyang Pharmaceutical University, Associate chief pharmacist, Clinical Trial Research Center, Beijing hospital, China.

Mainly focuses on Phase I clinical research of new drugs and the application of PBPK model simulation in clinical research and the PK/PD characteristics prediction of special population (elderly, children, etc.), participated in more than 40 phase I clinical studies, including more than 10 studies on first in human clinical research of new drugs, participated in the National Key research and development program plan, Capital's Funds for Health Improvement and Research and National High Level Hospital Clinical Research Funding. In the past 5 years, published more than 10 articles, including 5 SCI articles. E-mail address: xpp19881006@163.com.

Physiologically Based Pharmacokinetic Model Development, Validation, and Application of KY0467 in Pediatric

Pan-pan Xie, Ai-xin Shi. Clinical Trial Center, Beijing Hospital, National Center of Gerontology; Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, P.R.C.

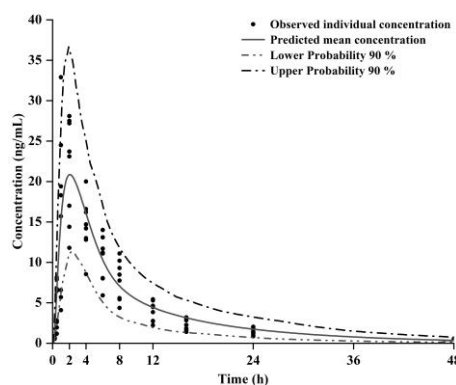
Introduction. KY0467 granules is a novel developed anti-EV71 drug in clinical research for the treatment of hand, foot and mouth disease. Physiologically-Based Pharmacokinetic (PBPK) models have been widely applied to predict the drug exposure in pediatric, which can provide quantitative data support for dose selection in clinical trial design.

Aims. 1) Established PBPK model of KY0467 granules in rats and dogs; 2) Developed the adults PBPK model extrapolated from preclinical model verified by observed data; 3) Extrapolated the adults PBPK model to infants (28 days-23 months) and children (24 months-5 years) to predict the drug exposures of KY0467 granules in the infants and children.

Methods. The PBPK model was developed by integrating physiologic and drug-specific parameters and then optimized and validated using the observed data. Comparing the different prediction methods of human clearance to predict the first human pharmacokinetic of KY0467 granules in Chinese healthy adult. The validated adult PBPK model was extrapolated to predict the exposure in infants and children and compared with that of adults to obtain possible effective doses.

Results. The PK profiles of predicted were similar to observed and the predicted T_{max} , C_{max} and AUC values were within 2-fold of the observed values for the animals and adults PBPK model, the population simulation in adults showed that the individual data can be in the 90% probability prediction range at the dosing of 30 mg. The predicted effective dose for the infants and children were 9 mg and 0.5mg/kg in the 90% probability prediction range, respectively.

Discussion. The mechanistic PBPK model of KY0467 granules was successfully developed and validated by the observed data, applied to predict the effective dose in infants and children, which provided dose reference for the clinical trial design.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P230

Epicatechin suppresses C-C motif chemokine ligand 19 expression and ameliorates periodontitis

Dr Tomomi Sano

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Tomomi Sano was earned Ph.D. (Dental Science) from Hiroshima University. I became an Assistant Professor in Department of Periodontology, Faculty of Dental Science, Kyushu University in 2016. Current Position is an Assistant Professor in Department of Cell Biology, Aging Science, and Pharmacology, Faculty of Dental Science, Kyushu University from 2020.

The worsening of periodontal disease has a negative impact on the health of the entire body I believe that by treating periodontal disease appropriately, it is possible to maintain oral health and promote the health of the entire body. Therefore, I am conducting research to clarify the mechanism by which local inflammation amplified by the progression and chronicity of periodontal disease affects organs throughout the body. I am also interested in research aimed at discovering substances with anti-inflammatory effects and applying them to periodontal disease.

Epicatechin suppresses C-C motif chemokine ligand 19 expression and ameliorates periodontitis

Tomomi Sano¹, Meiqun Yuan¹, Akiko Mizokami², Takashi Kanematsu¹. Department of Cell Biology, Aging Science and Pharmacology¹, and OBT Research Center², Faculty of Dental Science, Kyushu University, Fukuoka, Japan

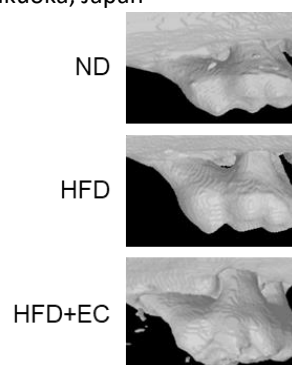
Introduction. Periodontitis is a prevalent chronic inflammatory disease requiring the development of drug-based therapies. Epicatechin (EC) is a major polyphenol in cocoa extract and possesses numerous pharmacological properties.

Aims. This study aimed to investigate the suppressive effect of epicatechin on C-C motif chemokine ligand 19 (CCL19)-mediated periodontitis using a mouse model.

Methods. Experimental periodontitis was induced by ligating 5-0 silk around the maxillary molar for 7 days. Immunohistochemical staining of gingival tissues was performed on paraffin sections using an anti-CCL19 antibody. Expression of CCL19 in gingival tissues assessed. Murine gingival fibroblasts ESK-1 cells were stimulated with LPS, and CCL19 expression was quantified. Mouse macrophage-like RAW264.7 cells were pretreated with EC and then stimulated with CCL19 to quantify the expression of inflammatory cytokines. Male mice were fed with a normal diet (ND), high-fat diet (HFD), or HFD containing EC (HFD + EC), and subjected to ligature-induced experimental periodontitis. 3D micro-CT images of the maxillary molar and alveolar bone loss areas were analysed.

Results. CCL19 expression was high in mouse gingiva with ligature-induced periodontitis. CCL19 expression was increased by LPS stimulation in ESK-1 cells, and CCL19 induced the production of TNF- α and IL-1 β in RAW264.7 cells. Importantly, LPS-enhanced CCL19 expression in ESK-1 cells was significantly suppressed by pretreatment with EC. Consistently, EC administration significantly reduced alveolar bone resorption, and expression of CCL19 and proinflammatory cytokines in the inflamed gingiva in HFD-fed mice.

Discussion. We demonstrated that sustained systemic administration of EC significantly attenuates alveolar bone resorption during periodontitis. Moreover, EC intake suppressed the expression of proinflammatory cytokines in macrophages and ameliorated inflammation of gingival tissues by suppressing CCL19 expression in gingival fibroblasts. Therefore, consistent intake of EC may be a potential therapeutic strategy for treating periodontitis.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P231

Systematic Review: Impact of Anti-TNF and Small Molecules on Depression/Anxiety in IBD

Mr Irwin Kashani

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Irwin Kashani is an Advanced Trainee in Clinical Pharmacology at Flinders Hospital, where he plays a pivotal role in both clinical practice and research. Under the mentorship of Professor Arduino Mangoni and Dr Tilenka Thynne, Dr. Kashani actively contributes to the Southern Oncology Clinical Research Unit (SOCRU) and is a co-investigator in multiple oncology clinical trials. His work spans oncology, complex hypertension, endocrinology, and gastroenterology clinics, reflecting his comprehensive expertise in multidisciplinary patient care.

Dr. Kashani's research focus includes evaluating the impact of biologics and small molecule therapies on mental health outcomes in autoimmune conditions. He is currently developing a systematic review and meta-analysis on this topic, employing rigorous methodologies such as the JBI framework. His clinical trials experience also extends to large IBD studies conducted at the Royal Brisbane and Women's Hospital, where he completed advanced GCP training.

A committed educator, Dr. Kashani regularly presents at journal clubs, teaches junior staff, and participates in quality improvement initiatives. His leadership and adaptability have been honed through roles in high-pressure medical and surgical settings, and he brings a patient-centered approach to his practice.

Dr. Kashani is passionate about the intersection of molecular therapies and clinical pharmacology, combining his interest in acute medicine with chronic disease management. With several international publications and oral presentations to his name, he strives to advance evidence-based practice while fostering therapeutic relationships with patients.

Systematic Review and Meta-Analysis: Impact of Anti-Tumor Necrosis Factor and Small Molecule Therapy on Depression and Anxiety in Inflammatory Bowel Disease Patients

Irwin Kashani, Reme Mountifield, Alex Barnes, Arduino Mangoni and Tilenka Thynne. Department of Clinical Pharmacology, Flinders Hospital and Flinders University, Adelaide, SA, Australia

Introduction. Depression and anxiety are common comorbidities in patients with inflammatory bowel disease (IBD). Anti-tumor necrosis factor (TNF) biologics and small molecule therapies have been used to manage IBD, but their impact on depression and anxiety remains unclear.

Aims. This systematic review and meta-analysis aim to evaluate the impact of anti-TNF biologics and small molecule therapies on depression and anxiety in patients with IBD.

Methods. A comprehensive literature search will be conducted in PubMed, EMBASE, and Cochrane Library to identify relevant studies using JBI system. Studies reporting on the impact of anti-TNF biologics and small molecule therapies on depression and anxiety in IBD patients will be included. Data will be extracted, and a meta-analysis will be performed using random-effects models to estimate pooled effect sizes.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Results. Preliminary results will be presented, including the number of studies identified, study characteristics, and summary estimates of the impact of anti-TNF biologics and small molecule therapies on depression and anxiety in IBD patients. Subgroup analyses will be conducted based on type of therapy, IBD subtype, and other relevant factors.

Conclusion. This systematic review and meta-analysis will provide a comprehensive evaluation of the impact of anti-TNF biologics and small molecule therapies on depression and anxiety in patients with IBD. The findings will help guide clinical practice and future research in this area.

P232

Developing a quality assessment tool for comprehensive medication reviews in primary care.

Mrs Aneesa Abdu

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Aneesa is a final year student completing the Bachelor of Pharmacy with Honours at The University of Sydney. Her research focusses on improving the interdisciplinary communication skills of practising pharmacists and pharmacy students. She is interested in education development to improve the interpersonal skills of emerging health professionals to advocate for greater emphasis on collaborative patient-centred care. Aneesa has previously presented her research at the 2024 AdPha Medications Management Conference and to her academic peers at The University of Sydney.

Developing a quality assessment tool for comprehensive medication reviews in primary care.

Aneesa Abdu¹, Rebekah Moles¹, Beatrice Wigmore¹, Timothy Yeo¹, Stephen Carter¹. Sydney Pharmacy School, Univ of Sydney¹, Sydney, NSW, Australia

Introduction. To effectively communicate clinical recommendations to general practitioners in medication reviews, pharmacists are expected to masterfully compose comprehensive written reports. Previous reviews suggest that a quality assessment tool should be developed for reviewing pharmacists' written communication skills. The first iteration of a tool has been developed by aggregating existing reporting tools including: The 'Basger-C' and modified DOCUMENT classification systems to identify how drug related problems and recommendations were articulated; the 'Subjective, Objective, Assessment, Plan Note' for assessing completeness of relevant content; the 'Situation, Background, Assessment, Recommendation' tool for evaluating the cohesiveness of the communication of each issue description; and the 'Written Communication VALUE Rubric' for assessing the use of linguistic conventions including vocabulary and syntactical mechanics. This study adopts a systematic framework for developing quality assessment tools, which requires that the tool be refined via expert panel after pilot testing.

Aims. To pilot test a quality assessment tool for comprehensive medication reviews in primary care.

Methods. Pilot testing involved quality assessment of (n=5) Home Medicine Reviews sampled from the #STOP Study by an expert panel of 3. Differences in rating were resolved through discussion. Percentile ratings of the completeness of relevant content, mastery of linguistic conventions and cohesiveness of writing quality of each report were descriptively reported. The utility of the tool was qualitatively assessed for usefulness and ease of use.

Results. Preliminary results demonstrate that pharmacists documented a mean of 63.2% (range 48.6% to 75.5%) of relevant content required to ensure findings and recommendations were completely interpretable. Pharmacists mastered a mean of 90.0% (range 84.6% to 97.5%) of the linguistic conventions and applied a mean of 76.9% (range 63.5% to 95.8%) of the cohesive characteristics needed for ideal written interprofessional communication. Expert panel consensus found the first revision of the quality assessment tool to be useful but tedious.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion. In this preliminary analysis, several amendments have been suggested to improve the overall usability of the tool including the aggregation of some categories to reduce its overall tedium. The tool was found to be useful as it exposed a high proportion of incomplete relevant content and highlighted variability in the cohesiveness of written reports. A revised quality reporting tool may be useful for teaching, assessment, and professional development.

P233

Implementation of a "Blocked Curriculum" Teaching Model in a Second-Year Pharmaceutics Course

Dr Tim Barnes

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Tim is the Pharmaceutical Science Program Director in the Clinical and Health Sciences Unit at the University of South Australia. He is a material scientist, with experience in the formulation and development of nanomedicines, including lipid-based systems (e.g. emulsions, liposomes, cubosomes), porous inorganic micro/nano-particles (e.g. silica/silicon) and polymers (e.g. PLGA, dendrimers). Tim has authored over 50 international journal articles, 30 international conference papers and 40 major project reports to industry.

Tim has been teaching into the Pharmacy and Pharmaceutical Science Programs at UniSA for more than 14 years, particularly focussed on teaching second and third-year students formulation science. He has undertaken SoTL research to improve the learning experience of students, including around the scaffolding of compounding skills development across multiple courses, the impact of teaching and learning activities on student engagement and learning as well as the influence of AI on assessment and student learning in higher education.

Implementation of a "Blocked Curriculum" Teaching Model in a Second-Year Pharmaceutics Course

Sarah Davey¹, Josephine Crockett^{1,2}, Timothy J Barnes¹. Clinical and Health Sciences, University of South Australia¹, Adelaide, SA, Australia; Pharmacy Regulation Authority SA², Adelaide, SA, Australia.

Introduction. A question that is regularly asked in the teaching of chemistry is "just how important are practicals?", and, more importantly, how do they impact on student learning.

Aims. To evaluate the impact of different teaching modalities on student engagement with course content. We then explore the influence of delivering content and practical activities in discrete teaching "blocks", to determine the impact of teaching activity proximity on student learning.

Methods. This study involved undergraduate second-year students in the Bachelor of Pharmacy and Bachelor of Pharmaceutical Science programs, enrolled in the courses Dosage Form Design 1 (DFD1, 1st semester) and Dosage Forms Design 2 (DFD2, 2nd semester). The data was obtained using mixed methods for qualitative data using anonymous Likert-scale and short answer surveys completed early in DFD1, early in DFD2 and at the end of DFD2. In addition, de-identified focus groups were run to provide additional insight into themes emerging from student survey responses.

Results. Student responses demonstrate that in-person activities such as tutorials/workshops and practicals, engaged them with the content. Interestingly, although students in general do not mind lectures, they were perceived as being "not engaging". From thematic analysis of student responses about the "blocking" of tutorial/workshop and practical activities in DFD1, the two top emerging themes were 1) Reinforcement of Learning, e.g. "Allowed for topics to be reinforced soon

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



after learning them, helped to consolidate info" and 2) Retention of Content Due to Proximity, e.g. "Learning about the material in the same practical block was VERY VERY helpful as I could remember the material for the prac/vice versa".

Discussion. This project speaks to the affordances of online content delivery and creative timetabling to deliver an enhance student learning experience. This work also evaluates to the broader question of student engagement with learning activities, and the potential impact of timetabling on student learning. Finally, it provides additional insight into the question: how integral are practical activities to student learning of chemistry?

P234

Australian pharmacists' perspectives on the place of pharmacology in their professional practice

Dr Anna-Marie Babey

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr Anna-Marie Babey received her PhD from McGill University in Montreal, undertook post-doctoral work on opioid tolerance with Prof Gavril Pasternak at the Memorial Sloan-Kettering Cancer Center in New York, and with Prof Ping-Yee Law in the Department of Pharmacology at the University of Minnesota. She is currently a member of the School of Science & Technology at the University of New England, and has an extensive history of teaching and curriculum development across 9 different degree programs at 2 Australian universities. She is particularly interested in developing learning activities that enhance students' creativity, adaptability, and critical-thinking skills as part of her commitment to education quality. She is an active member of the ASCEPT Education Forum, having previously served as Secretary, a Councillor of the IUPHAR-Education Section, a member of the Australasian core concepts of pharmacology project, and a member of the IUPHAR-Education core concepts of pharmacology research team.

Australian pharmacists' perspectives on the place of pharmacology in their professional practice

Madeleine De Grandi¹, Anna-Marie Babey². Aged Care Department, Ramsay Pharmacy, Glen Huntly, VIC, Australia; Biomedical Sciences, University of New England², Armidale, NSW, Australia

Introduction. Pharmacology has been cited as an important component of clinical decision-making in pharmacy, leading to improved patient outcomes. The changing scope of pharmacists' practice and the explosion of new drug knowledge, calls for a re-evaluation of pharmacology education and its place in contemporary pharmacy.

Aims. To determine how Australian pharmacists perceive pharmacology knowledge, including its definition, role in pharmacy practice, impact on scope of practice, and place in pharmacy education.

Methods. Registered pharmacists in Victoria, Australia were recruited at their places of work and interviewed about their perspectives on pharmacology, particularly its place in contemporary pharmacy education (UNE HREC Approval HE23-018). Responses to open-ended questions were deidentified and transcribed, then answers coded and evaluated using inductive thematic analysis to assess attitudes and perceptions.

Results. Of the 17 pharmacists interviewed, 13 practice in community pharmacies, 3 in hospitals, and 1 in both settings. Participants consistently included pharmacodynamics as part of their pharmacology definition, however, only half included pharmacokinetics and drug structure. Unanimously, pharmacology was perceived to be essential foundational knowledge for pharmacy practice and interviewees advised against its dilution within pharmacy education. Three themes arose

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



regarding the impact of pharmacology on patient outcomes: improving patients' understanding of their medications; assisting in clinical decision-making; and improving medication safety. Additionally, participants believed that pharmacology is critical to a pharmacist's identity and role within multidisciplinary teams. Similarly, pharmacists felt that pharmacology underpins additional competencies, such as diagnostics, that are required for the expansion of their scope of practice.

Discussion. Though complexities exist within pharmacists' perceptions of pharmacology, the responses of participants in this study shared the attitude that it plays an important role in current and future practice, solidifying its place in pharmacy education. As pharmacists' responsibilities evolve, understanding the influence pharmacology knowledge has on patient outcomes and pharmacist identity will be invaluable.

P235

What does Community Want? How pharmacy should walk with First Nations Australians

Mr Alexander Burke

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

What does Community Want? - A Qualitative Study of how the pharmacy profession should walk with First Nations Australians

Alexander W Burke¹, Bandana Saini¹, Faye McMillan², Rebekah Moles¹ School of Pharmacy, University of Sydney¹, Sydney, NSW, Australia; School of Public Health, University of Technology Sydney², Sydney, NSW, Australia

Introduction. First Nations people have a rich culture and connection to land. However, post colonisation, health disparities have arisen because of dispossession and discriminating policies that have impacted their social determinants of health. Little is known about how First Nations people view the pharmacy profession and the way it impacts their wellbeing and regards their cultural needs.

Aims. This qualitative study aimed to explore First Nations people's concerns with the pharmacy profession and how they perceived they could be included in developing improvements across the sector.

Methods. Semi-structured interviews (n=30) were conducted with Aboriginal and/or Torres Strait Islander Australians from multiple communities. Interviews were audio-recorded and transcribed verbatim by a third-party transcription service. Transcripts were then thematically coded through an inductive approach.

Results. Multiple themes were identified about community issues with pharmacies, pharmacists, and pharmacy institutions such as issues with communication to patients, and systemic failings of racism and discrimination. Despite these failings, community members openly expressed their thoughts to how pharmacy can begin to mend these lacking areas. For example, pharmacy schools could send students out on placements within First Nations communities, First Nations people could be invited into classrooms to share their stories and pharmacies could reach out to communities and make themselves known. These types of engagement were perceived to be a start to making pharmacy more inviting to First Nations people.

Discussion. The Pharmacy profession and teaching institutions need to spend more time and effort consulting with First Nation communities to receive their input about what affects them and take these considerations to heart to start implementing change.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P236

Comparative Resilience: Are mature aged students more resilient than school leavers?

Mr Amith Bombuwelage Don

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

My name is Angelo Don and I am a PhD Candidate at Monash University in Pharmacy Education. My topic revolves around the implementation of resilience education in pharmacy interns to ensure they have a smoother transition into sole practise. I have completed my pharmacy internship in 2022 through Monash University and have worked as a clinical pharmacist at Epworth Richmond Hospital throughout 2023; recently started working at the Alfred Hospital alongside teaching at Monash University. Education is my passion and shaping the future generation is what keeps me eager to continue practicing and educating.

Comparative Resilience: Are mature aged students more resilient than school leavers?

Alexandra Steel¹, Nilushi Karunaratne¹, Betty Exintaris¹, Simon James², Abdullah Jaafar¹, Angelo Don¹, David Wei Dai³, Angelina Lim^{1,4}. ¹Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Melbourne, VIC, AUS ²School of Information Technology, Deakin University, Geelong, VIC, AUS ³UCL Institute of Education, University College London, UK ⁴Murdoch Childrens Research Institute, Royal Children's Hospital, Melbourne, VIC, AUS

Introduction. Our pharmacy workforce requires resilient lifelong learners. Pharmacy students' cohorts consist of diverse learners including Mature age learners who face unique challenges. Understanding the nuances of a diverse group of learners can help improve teaching and preparation for the workforce.

Aims. To compare the difference in resilience between mature age graduate entry (GE) learners and school leaver undergraduate (UG) learners and how it impacts their academic outcomes.

Methods. We employed a sequential explanatory mixed methods design using surveys, assessment data and semi-structured interviews. Assessment data were primarily obtained from four assessments completed by both UG and GE cohorts (Multiple Choice Questions, MyDispense exam, Objective Structured Clinical Exam and the Final Written Examination). A self-reported resilience survey was given to all GE and UG students at the end of their first semester. Semi-structured interviews were then conducted online with students who opted into the interviews. We used Cognitive behavioural model of resilience to unpack the findings.

Results. All of the 64 GE students and 208 UG students (74%) completed the self-reported survey with 36 GE students (56.3%) and 118 UG students (56.7%) reporting having experienced burnout. Those within the UG cohort who indicated support from partner, friends and family did slightly better on the MyDispense exam, median of 95.95 vs 92.5 ($p = 0.0452$) whereas those who indicated no coping methods (but not "-"), tended to do slightly worse in the MyDispense test 89.15 vs 93.875 ($p = 0.01369$). Those within the GE cohort who indicated rest and recuperate (15) scored worse on the MCQ, median of 76 vs 90.78125, $p = 0.006351$ whereas those who noted natural stress performed better in the final exam, 92 vs 73 ($p = 0.02022$). The three key environmental factors that contributed to both cohorts were workload, receiving feedback and psychosocial support.

Discussion. Overall, this study highlights the prevalence of burnout amongst both cohorts. Both cohorts demonstrated similar factors contributing to resilience, with GE students accepting the importance of natural stress in managing their workload. Data from this study enables educators to tailor workload, feedback and psychosocial support catered to the individuals given their resilience.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P237

Leveraging Generative AI for Core Concept Identification in Pharmacology: A Proof-of-concept Study

Mrs Alison Etukakpan

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Alison Etukakpan is a Pharmacist and PhD candidate in Pharmacy and Pharmaceutical Science Education at Monash University, where she also serves as a Casual Teaching Associate. Her PhD research aims to generate a comprehensive list of core concepts in pharmacotherapy education by systematically obtaining concepts from pharmacotherapy texts and experts, evaluating them against established core concepts criteria, and undertaking a consensus process with international experts. Her research incorporates innovative approaches including text mining and generative artificial intelligence. Prior to her doctoral studies, she served as the Educational Partnerships and Projects Manager at the International Pharmaceutical Federation (FIP), where she led initiatives for pharmaceutical education transformation across WHO regions.

Leveraging Generative AI for Core Concept Identification in Pharmacology: A Proof-of-concept Study

Alison U. Etukakpan¹, Jae Y. Han¹, Paul J. White¹. Pharmacy and Pharmaceutical Science Education Theme, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Parkville, VIC, Australia

Introduction: Identifying the core concepts of a discipline is crucial for effective educational practices. Traditional methods like textbook analysis and expert panels are labour-intensive and time-consuming. This study explores generative AI (GAI) as a complementary tool for identifying core concepts using pharmacology as a case study.

Aims: To investigate the extent to which GAI can accurately identify core concepts of pharmacology when given the same context and prompts as domain experts.

Methods: N-grams, contiguous sequences of n terms from introductory chapters of pharmacology textbooks, previously consolidated with expert opinions and interpreted into core concepts by pharmacology experts¹ were used. The top 500 N-grams by Term Frequency-Inverse Document Frequency scores were interpreted by the GAI model Claude.AI, prompted with similar context and questions provided to pharmacology experts; to identify core concepts based on five criteria: fundamental, useful, enduring, challenging, and complex.

Results: The GAI accurately generated 18 exact matches out of the 25 core concepts of pharmacology education established by pharmacology experts, including absorption, drug-receptor interaction, adverse drug reaction, drug interaction, and mechanism of drug action.

Discussion: Findings suggest GAI can complement human expertise in identifying core concepts being the big, important and fundamental ideas of a discipline; by leveraging succinct prompt engineering with alignment of expert rating criteria and N-gram distinctiveness. GAI offers a faster turnaround, not replacing expertise, but highlighting AI-human integration potential. This proof-of-concept study paves the way for a novel methodology that could be applied across various academic domains to facilitate rapid concept identification and mapping. It also demonstrates the need for further exploration of GAI in educational applications and domain ideation processes.

¹White, et al., (2022). Identifying the core concepts of pharmacology education: A global initiative. *British Journal of Pharmacology*, 180(9), 1197-1209. <https://doi.org/10.1111/bph.16000>

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P238

Causes and outcomes of underperforming pharmacy students: implications for policy and practice

Mrs Alice Campbell

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Alice is a dedicated professional in the field of pharmacy with a diverse background spanning both clinical practice and academic research. Graduating with a Bachelor of Pharmacy from the University of Sydney in 2015, Alice pursued a Master of Philosophy in research, completing it in 2021. She has since accumulated extensive experience as a community pharmacist and contributed to academia as a tutor and guest lecturer at the University of Sydney. Currently, Alice is advancing her expertise through a PhD in Pharmacy Education while also serving as the Training Manager at Aspen Pharmacare. Her work integrates clinical practice with innovative educational strategies, reflecting a commitment to enhancing pharmaceutical education and training.

Causes and outcomes of underperforming pharmacy students: implications for policy and practice

Alice Campbell¹, Tina Hinton^{1,2}, Narelle C da Costa¹, Sian E O'Brian¹, Danielle R Liang¹, and Nial J Wheate¹. Sydney Pharmacy School, Faculty of Medicine and Health The University of Sydney, NSW; Australia¹; Charles Perkin Centre², Faculty of Medicine and Health, The University of Sydney, NSW, Australia.

Introduction. Understanding the key determinants of student success and failure has become increasingly important for higher education institutions and governments due to the cost of attrition. It is important to investigate reasons for attrition and potential opportunities for improvement in student teaching and engagement in pharmacy degrees as studies are limited.

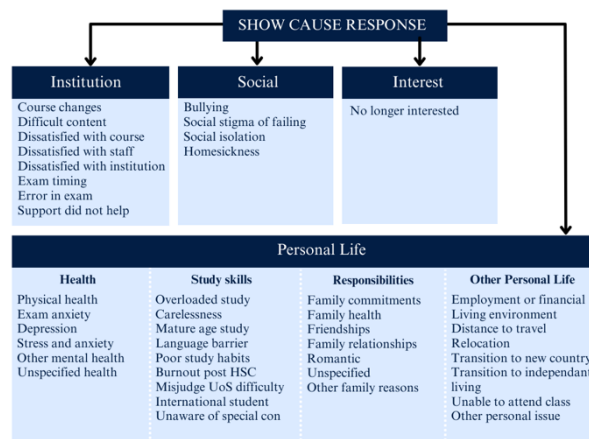
Aims. This study aimed to understand the key determinants for poor academic performance of students completing a Bachelor of Pharmacy (BPharm), Bachelor of Pharmacy and Management (BPharmMgmt), or Master of Pharmacy (MPharm).

Methods. Data were collected on pharmacy students who had not met academic progression requirements between 2008 and 2018 at The University of Sydney, Australia. Descriptive studies

were used to analyse student characteristics using SPSS software, and student self-reported reasons for poor performance were analysed reflexively using thematic analysis procedures using NVivo.

Results. This study included 164 pharmacy students. Show cause students were less likely to graduate if they transferred from another degree program ($P=0.0002$) or failed more than three units of study (UoS; $P<0.0001$). The most commonly failed UoS were related to organic or pharmaceutical chemistry, and the top student self-reported reasons for poor performance was stress/anxiety, physical health, and depression.

Discussion. Pharmacy schools should aim to address student foundational knowledge in chemistry, identify at-risk students early using pre-subject testing, and provide better services to address student mental health.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P239

Fostering study skills, connectedness and belonging in international students: Night Against Procrastination

Dr Betty Exintaris

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Betty Exintaris is an Education-Focused academic, Associate Dean of Learning and Teaching, Associate Dean Equity, Diversity and Inclusion at Monash University's Faculty of Pharmacy and Pharmaceutical Sciences. With over 20 years of experience in teaching physiology and pharmacology, her expertise lies in innovative, inclusive teaching practices that enhance student engagement and learning.

Fostering study skills, connectedness and belonging in international students: Night Against Procrastination

Nilushi Karunaratne¹, Edris Chan¹, Zoe Porter¹, Zi Xing Mun¹, Yijia Ji¹, Jiun Wye Fan¹, Amber Lin¹, Zheng Zhe Mah¹, Gyuwon Kim¹, Nathan Kim², Betty Exintaris¹. Pharmacy and Pharmaceutical Sciences Education, Monash University¹, Melbourne, VIC, Australia. Non-Residential Colleges, Monash University²

Introduction. 'Night Against Procrastination' is an initiative first introduced in Australia by Pozzi and Naish (2022) to support students with procrastination during exam preparation, while also fostering a sense of belonging and connectedness.

Aims. To provide international students with academic study support, as well as multiple opportunities to engage and connect with their peers in the last week of semester, just prior to the exam period.

Methods. The academic led international student engagement program PIES (Parkville International and Exchange Students) teamed with PISA (Parkville International Students Association) and LUPA (Non-residential colleges) to co-design the activities. Using students as partners, relaxation or study 'stations' were co-created. Station 1 was set up as a massage station with a professional masseuse, Station 2 was set up with puzzles, colouring books and a zen garden, Station 3 was run as a micro meditation class, Station 4 was a study and international snack station and the last station was set up for board games as well as dinner. The event was designed to span 4 hours with the stations running simultaneously, in separate rooms across campus.

Results. The intervention attracted 64 international students across both degree programs (Pharmacy and Pharmaceutical Sciences) attended the event. Several domestic students also attended, having been invited by their friends who were international students. The study station was supported by 2 academics and focused on exam preparation which allowed students to engage with the academics or quietly study on their own before interacting with the other stations and also having dinner. Remaining stations were facilitated by PISA or HDR students. >70% of students also engaged with the study station. The feedback was overwhelmingly positive.

Discussion. This initiative will be used in subsequent semesters to foster a sense of belonging among students and staff, while providing academic study advice at a critical time in the semester.

Pozzi P & Naish E (2022) Students, Transitions, Achievement, Retention and Success (STARS) Conference, 2022-07-04 - 2022-07-06.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P240

Assessing growth mindset and metacognitive awareness of teamwork among undergraduate pharmacy students

Ms Mudiyansele Arani Senanya Dasanayake

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Assessing growth mindset and metacognitive awareness of teamwork among undergraduate pharmacy students

Arani S Dasanayake¹, Angelina Lim¹, Simon James¹, Betty Exintaris¹, Nilushi Karunaratne¹. Pharmacy and Pharmaceutical Sciences Education, Monash University¹, Melbourne, Vic, Australia.

Introduction. Teamwork is an essential skill that pharmacy students must develop to be able to work intra-professionally and inter-professionally in the workplace.

Aims. Use the Baseline Teamwork Assessment Tool (TBAT) to evaluate and assess the growth of teamwork skill aptitudes, growth mindsets, and metacognitive awareness of effective teamwork strategies in undergraduate Pharmacy students from 1st to 3rd year of their degree program.

Methods. A sequential explanatory mixed methods study. The TBAT was delivered to first-year pharmacy students in 2022 and then to the same cohort of students in 2024 as third-year pharmacy students. The paired Wilcoxon test was used to compare the differences in scores from 1st to 3rd year. Differences in international vs domestic student responses and graduate entry (GE) vs undergraduate (UG) student responses were also assessed. Semi-structured interviews were then conducted with students to investigate factors that affected the changes in scores.

Results. Statistical analysis revealed a significant improvement in the 'kind of person' mindset among domestic students, while no significant change was observed in intelligence scores, and this increase was not seen among international students. Comparing undergraduate and graduate entry students showed no statistically significant difference in growth mindset scales. Changes in team member attributes from 1st to 3rd year were statistically significant in the 'humble' and 'smart' categories. Domestic students experienced a significant change only in the 'smart' score, while international students saw a significant change in the 'humble' score. However, no significant differences were found when comparing changes between international and domestic students or between UG and GE cohorts.

Discussion. According to the findings, all students perceive intelligence as a more fixed trait compared to personality. The findings emphasize the need to tailor interventions to support students' development of teamwork skills and growth mindsets in pharmacy education.

Karunaratne, N., Lyons, K., Molcik, E., & Exintaris, B. (2024). Teamwork baseline assessment tool: Sparking teamwork dialogues in health professions training. *Medical Teacher*, 1–3. <https://doi.org/10.1080/0142159X.2024.2330566>

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P241

Teaching clinical skills online in pharmacy education: a scoping review

Ms Lailaturrahmi

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Lailaturrahmi is a PhD student at Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Australia. She is a pharmacist and a pharmacy academic at Universitas Andalas, Indonesia. Her research project explores how therapeutic decision-making skills can be developed, implemented, and evaluated in Indonesian undergraduate pharmacy education, supervised by Dr Ian Larson, Dr Suzanne Caliph, and Dr Thao Vu. Her presentation at this conference explores the application of a scoping review method to map the literature on teaching clinical skills online in pharmacy education.

Teaching clinical skills online in pharmacy education: a scoping review

Lailaturrahmi^{1,2}, Suzanne Caliph¹, Thao Vu¹, Ian Larson¹. Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Parkville, VIC, Australia; Faculty of Pharmacy, Universitas Andalas², Padang, Indonesia

Introduction. Clinical skills are commonly taught face-to-face to pharmacy students by educators in a classroom or a skills laboratory. However, this mode of delivery is affected by the increasing number of students, insufficient availability of educators, and time and space constraints. Online learning can address these limitations and enable learning beyond physical and time limitations.

Aims. To explore the design and implementation of online teaching of clinical skills in pharmacy education.

Methods. This scoping review followed the five-stage framework by Arksey and O'Malley (2005). A literature search was conducted in MEDLINE, CINAHL, and ERIC databases, resulting in 396 records. The eligibility criteria for article screening were developed and validated by four reviewers. Disagreement was resolved through discussion. The identified articles were screened using the eligibility criteria. Qualitative data analysis was performed to identify purposes, methods, outcomes, enabling factors, and limiting factors of teaching clinical skills online.

Results. Sixty-five articles that met the eligibility criteria were included in this review. Online synchronous, asynchronous, and blended learning were implemented to teach clinical skills, such as dispensing skills, communication skills, and therapeutic problem-solving skills. Outcomes such as student satisfaction and confidence were often assessed in online learning. Teaching clinical skills online could be enabled by convenience, familiarity, and highly interactive online tools. On the other hand, poor online learning design, the time required for preparation, and technological issues can hinder the implementation of teaching clinical skills online.

Discussion. The findings can be applied to improve online learning design and implementation to help pharmacy students gain the clinical skills they need.

Arksey, H., & O'Malley, L. (2005). Scoping studies: towards a methodological framework. *International Journal of Social Research Methodology*, 8(1), 19-32.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P242

Evaluation of a training program for pharmacist-delivered depression screening for older adults

Miss Duha Gide

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Evaluation of a training program for pharmacist-delivered depression screening for older adults

Duha Gide¹, Sarira El-Den¹, Kevin Ou², Lisa Kouladjian O'Donnell^{1,3}, Natasa Gisev⁴, Claire O'Reilly¹. School of Pharmacy, Univ of Sydney¹, Sydney, NSW, Aus; Pharmaceutical Society of Australia², Sydney, NSW, Aus; Kolling Institute, Univ of Sydney³, St Leonards, NSW, Aus; National Drug and Alcohol Research Centre, UNSW⁴, Sydney, NSW, Aus.

Introduction. Approximately 10-15% of older adults (≥ 65 years) experience late-life depression (LLD). It is imperative that pharmacists receive training to identify patients at risk of LLD and ensure timely and appropriate referral.

Aims. To evaluate the impact of a mental health training program on community pharmacists' and pharmacy staffs' knowledge, attitudes and confidence, as well as community pharmacists' acceptability, regarding LLD screening.

Methods. A training program was developed and delivered to community pharmacists and pharmacy staff participating in the EMPATHISE pilot study, whereby community pharmacists screened older adults for depression. The training program consisted of 'Blended Mental Health First Aid in the Pharmacy', and training on the identification and management of LLD, including the use of the Geriatric Depression Scale-15 (GDS-15). A 68-item survey instrument was developed, containing the Social Distance Scale, Depression Attitudes Questionnaire, Knowledge of Late-life Depression questionnaire, and items exploring acceptability of such services. Participants were invited to complete the survey at baseline (T1), immediately post-training (T2), and 3-months post-training (T3). Data was analysed using descriptive statistics and repeated measures analysis of variance (ANOVA).

Results. Participants ($n=89$) from 53 pharmacies across New South Wales participated in the survey. Most participants were community pharmacists ($n=66$). At T2, participants demonstrated significant improvements in their knowledge regarding depression being a normal phenomenon in older adults ($p<0.019$) and believed LLD screening to be within their scope of practice ($p<0.021$). At T2 and T3, participants demonstrated significant improvements in confidence ($p<0.003$) regarding LLD screening, and increased knowledge regarding how to use the GDS-15 ($p<0.001$) and actions to take if screening identified an older person as being at high risk of depression ($p<0.001$).

Discussion. The training program improved community pharmacists' capability and acceptability regarding LLD screening, as well as their knowledge of LLD, and provided them with the skills and confidence to provide such services. Thus, training prior to LLD screening is vital to ensure community pharmacists are well-equipped to screen and refer older adults at risk of depression.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024
Melbourne Convention &
Exhibition Centre, Australia



P243

Students' experiences, perceptions of hybrid learning in pharmacology education: A case study

Dr Suong Ngo

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Dr Suong Ngo has been a member of ASCEPT since 1999 and actively contributed to ASCEPT Annual Scientific Meetings, AGMs and Education Forum, Symposium. Suong has been working closely with Fellow ASCEPT educators on developing the core concepts of pharmacology education and is part of the Australian and New Zealand Core Concepts Group (CC-PEG) (White et al., 2021; Santiago, Davis et al., 2021, Guilding et al., 2023) and was one of the attendees at the Inaugural Core Concepts of Pharmacology Education Workshop, held at Monash University Prato Centre, Italy in July 2022 as part of the IUPHAR Education project. Her current research focuses on the anti-cancer stem cell effects of cruciferous vegetables' constituents. Overall, she has published over 50 research papers in high quality specialised scientific journals, including in BJP and JPRP. Suong is a Committee Member of the ASCEPT Equity, Diversity and Inclusion Committee.

Students' experiences and perceptions of hybrid learning in pharmacology education: A case study

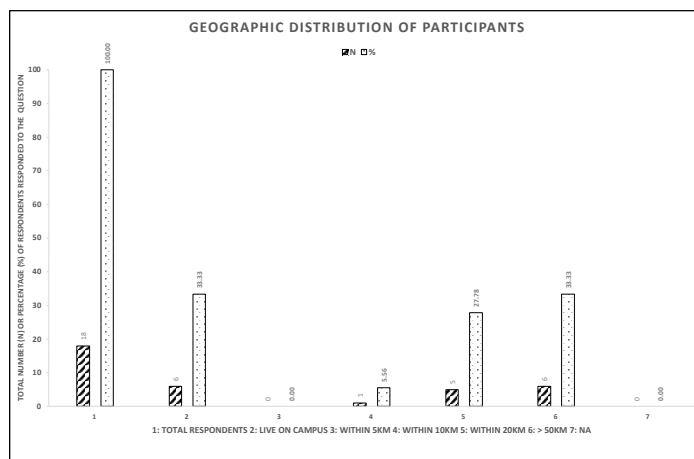
Suong N T Ngo. The University of Adelaide, Roseworthy Campus, Adelaide, SA, Australia.

Introduction. Integration of on-line and hybrid, blended learning was required during the COVID-19 pandemic across university sector to ensure continuing provision of education. However, there is limited data on learners' perception of online learning. The current study aims to evaluate students' experiences and perceptions of hybrid learning in a pharmacology course.

Methods. A total of 28 Doctor of Veterinary Medicine (DVM1) students who enrolled in Veterinary Clinical Pharmacology and Toxicology course in Semester 1 20223 at Adelaide Uni participated in an on-line anonymous survey. The survey questionnaire comprised of approximately 9 key items, in a mixture of question styles which

explored 3 main themes: general demographics (e.g. gender, study level/status, live on campus), student's perception of advantages and disadvantages of hybrid delivery, and challenges experienced by students with online learning).

Results, Discussion. Overall, flexibility in online learning was considered an advantage by majority of participants, in particular allowed learners to study in their own space, time and to better arrange/manage between work and study schedule for some participants, which was as expected. Challenges experienced in online learning from participants who answered the question (N = 13) included self-motivation (30.77%), time management (23.08%), lack of face-to-face interaction (23.08%), mental health (7.69%), prioritise study vs personal/family (15.38%). The findings from this study provide educators useful insights on support needed by students in online learning and inform better approaches for the design of online activity to enhance student active learning/engagement.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P244

Adapting team-based oral presentations for students in online and blended subjects

A/Prof Ross O'Shea

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr Ross O'Shea is a teaching focussed Associate Professor in Pharmacology at La Trobe University. Ross gained his PhD from the University of Melbourne in 1997 in neuropharmacology and worked as a biomedical researcher until 2010 before moving to La Trobe. Ross now teaches pharmacology to students from a variety of science and allied health courses, as well as coordinating the Bachelor of Science degree. He is passionate about student engagement and designing authentic assessments that ensure academic integrity in a world where generative artificial intelligence is improving rapidly.

Adapting team-based oral presentations for students in online and blended subjects

Ross D O'Shea¹ & Elvan Djouma¹, Dept of Microbiol, Anat, Physiol and Pharmacol, La Trobe University¹, Bundoora, VIC, Australia.

Introduction. Team-based presentations are widely used in university subjects to address Intended Learning Outcomes (ILOs) and improve student skills in teamwork. Since we allow students the flexibility to choose on-campus or online workshops in our pharmacology subjects, considerations need to be made around how assessments involving presentations are managed in an equitable way in subjects with different modes of delivery.

Aims. We aimed to modify team-based oral presentations so that teams were required to create a video recording of team presentations, providing equitable opportunities for all students, regardless of whether they were attending on-campus or online classes.

Methods. Team-based oral presentations in our pharmacology subjects were previously delivered synchronously in class, but we considered technological issues associated with students delivering the same standard of work synchronously online to be a significant barrier. Instead of presenting live, teams in either mode of delivery were required to record their presentations and upload the video for assessment. We provided clear instructions to students about technical aspects of creating the recording, using Microsoft PowerPoint or Zoom (students have access to this software via the University's software licence), using similar guidelines for the content of the assessment as were used for live presentations. We compared the marks for these presentations for live presentations (2018-2019) and recorded presentations in on-campus and online cohorts (2020-2023).

Results. Videos recorded by student teams were generally of good quality, and marks were not significantly different between the 3 groups (live/synchronous, recorded/on-campus and recorded/online; one-way ANOVA $F(2, 270) = 1.0209$, $P = 0.362$). A common issue in early implementation was poor audio quality in recordings, so additional support around this issue was included in the instructions to students. Some teams experienced difficulty keeping their recording to the specified time limit, but this was also an issue in live synchronous presentations.

Discussion. Modifying team-based presentations to a recorded format has allowed students to complete these tasks equitably and fulfill the ILOs, regardless of whether they were in on-campus or online workshops. An added advantage of this approach is that assessment of the work does not need to be done live and students can access recordings.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P245

Systematic Review of Generative Artificial Intelligence Applications in Health Profession Education

Mr Thai Duong Pham

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Thai Duong Pham is a PhD candidate and pharmacist, who has a general research interest in advancing education through the integration of Generative AI, focusing on its potential to support self-directed learning by fostering student autonomy and enhancing knowledge acquisition. His studies investigate how Generative AI tools enable students to take control of their learning and achieve academic success, along with impacts on motivation, metacognition, and engagement. Previously a pharmacy student, Thai Duong Pham was recognised as a Monash Dean's Scholar and recipient of a Summer Vacation Research Scholarship. He has contributed through collaborative research, demonstrating a dedication to advancing the fields of pharmacy and education.

Systematic Review of Generative Artificial Intelligence Applications in Health Profession Education

Thai Duong Pham¹, Travis Lay¹, Angelina Lim¹, Betty Exintaris¹, Nilushi Karunaratne¹, Elizabeth Yuriev¹, Danny Liu², Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Melbourne, VIC, Australia; Educational Innovation Team, Office of the Deputy Vice-Chancellor (Education), The University of Sydney², Sydney, NSW, Australia

Introduction. Generative artificial intelligence (GenAI) offers significant potential in health professions education. This systematic review examines the existing literature on GenAI's application and its impact on student learning outcomes.

Aims. This study aims to synthesise evidence on the use of GenAI tools in health professions education.

Methods. A systematic review was conducted. The electronic databases (Education Database, ERIC, Ovid Embase, Ovid Medline, and Scopus) were searched for articles published up until May 2024. Articles were included if they focused on GenAI applications in formal health profession training, peer-reviewed original research, conducted in formal educational settings.

Results. Twenty-one papers met the inclusion criteria (Figure 1). These studies revealed that students primarily used GenAI to enhance theoretical knowledge and clinical skills, with ChatGPT being the most popular tool. Medical education had the highest number of papers, followed by nursing and pharmacy education. Key challenges included concerns about data accuracy and ethical considerations, while the outcomes reported were improved student engagement, personalised feedback, and enhanced learning environments.

Discussion. The findings highlight that GenAI is being used by health profession students mainly for enhancing learning experience and assessment preparation. However, addressing challenges related to data privacy, ethics, and accuracy as been flagged as a common concern. Future research should focus on the long-term benefits of using GenAI by health professional students and its significant impact on their practice, education, and overall development.

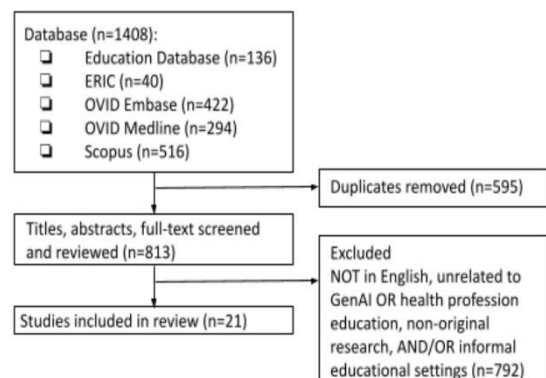


Figure 1: PRISMA flowchart of the literature search and study selection

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P246

Identifying educational needs of pharmacists engaging in professional development: a systematic review

Mr Yalin Ozucelik

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Yalin Ozucelik holds a Bachelor of Arts/Bachelor of Laws from The University of Queensland, a Bachelor of Dramatic Art from the National Institute of Dramatic Art, and is a Bachelor of Pharmacy graduand and Honours candidate at the School of Pharmacy, Faculty of Medicine and Health, University of Sydney. During his Honours candidature, he co-authored a systematic review identifying the educational needs of pharmacists engaging in continuing professional development and conducted research exploring community pharmacists' experiences of regulatory change. He looks forward to entering the profession as an intern next year.

Identifying educational needs of pharmacists engaging in professional development: A systematic review

Yalin Ozucelik¹, Jack C Collins¹, Jessica Pace¹. School of Pharmacy, Faculty of Medicine and Health, University of Sydney¹, Camperdown, NSW, Australia 2006

Introduction. There have been significant changes in pharmacists' scope of practice over the last two decades. Globally, this has precipitated a need for pharmacy governing bodies to update professional development frameworks to meet the challenge of future-proofing the pharmacy workforce. It is essential to determine the educational needs of pharmacists to ensure this challenge is met.

Aims. To review the literature identifying educational needs of pharmacists engaging in professional development.

Methods. A comprehensive search was undertaken in MEDLINE, Embase, IPA and ERIC using a search strategy constructed from the concepts "pharmacists", "continuing professional development" and "priorities, interests and preferences" to identify relevant literature published between January 2004 and March 2024. Results were screened against eligibility criteria and data from the retrieved records were extracted into a table, appraised for quality, and synthesised narratively.

Results. The studies that were identified for inclusion (n = 31) utilised either quantitative (n = 16), qualitative (n = 8) or mixed (n = 7) methods. There were 13 studies that described the needs of pharmacists from the Middle East and a majority of all the studies (n = 19) involved pharmacists across more than one practice setting. Three key domains of need were identified: priority topics for education (including disease management, pharmacotherapy and skills-based topics incorporating clinical, counselling and communication skills); reinforcement of learning (such as through summary documents, assessments, evaluations, feedback and peer-sharing); and support for successful engagement, across all levels of governance from employers and organisations to professional bodies and regulatory authorities.

Discussion. Long sought-after regulatory milestones that permit expanded scope of practice, and involve increased patient care services, are being achieved. However, the needs-based education necessary to accommodate required practice changes is lacking. The identification of needs is, therefore, essential. This review identified commonalities of need despite diversity of location and practice setting. The promotion of skill learning over simple knowledge acquisition, strategies to reinforce this learning, and the implementation of support frameworks were revealed as essential areas of focus for continuing pharmacy education providers and regulators.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P247

Core Concepts in Pharmacology: Impact on Educators (Pilot survey)

A/Prof Alison Shield

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Core Concepts in Pharmacology: Impact on Educators (Pilot survey)

Alison Shield¹, Anna-Marie Babey², Gregg Maynard³, Marina Junqueira Santiago⁴. Faculty of Health, University of Canberra¹, Bruce, ACT, Australia; School of Science & Technology, University of New England², Armidale, NSW, Australia; School of Dentistry & Medical Sciences, Charles Sturt University³, Orange, NSW, Australia; Department of Biomedical Science, Macquarie University⁴, Macquarie Park, NSW, Australia.

Introduction. In 2020 a group of Australian and New Zealand pharmacology educators embarked on a quest to define the pharmacology core concepts. This endeavour provided the basis for the IUPHAR Core Concepts of Pharmacology Education Project collaboration, which seeks to transform pharmacology education internationally. While the intended impact on learners is to improve their conceptual understanding of pharmacology, the impact on educators is less clear.

Aims. This project explores how the core concepts projects have impacted on pharmacology educator teaching practices.

Methods. A cross-sectional survey in Qualtrics was distributed to the Core Concepts in Pharmacology Expert Group, and ASCEPT Education Forum members to collect pilot data prior to broader distribution.

Results. A diverse cross section of educators responded to the survey, varying in their pharmacology training, types of academic appointments and institutional contexts. On average they had taught pharmacology for 15 years and could be found in the classroom more than an hour per week for more than 7 weeks annually. Despite their experience, not all educators felt confident to teach across all aspects of pharmacology. There was unanimous agreement that their awareness of, and/or involvement in core concepts projects had been a useful prompt to reflect on their teaching practice, refine their understanding of core pharmacology concepts and provide insights into how other educators think about pharmacology to better inform their practice.

Discussion. Although derived from a biased convenience sample, these results suggest that projects like the core concepts of pharmacology can inspire educators to revitalise their teaching and help to build a community of practice. Further evaluation is required to determine the broader impact on pharmacology teaching practices.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P248

Alternatives to Animal Models in Teaching Pharmacology Core Concepts— An Educators' perspective

Dr Rahini Ragavan

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Rahini Ragavan is a Lecturer (Teaching Focussed) in the Department of Physiology and Pharmacology, La Trobe University. Her PhD was in the Department of Pharmacology, Monash University and her focus was on investigating the cardiovascular effects of animal venom. She has over 8 years of experience delivering workshops, tutorials and wet practicals to undergraduate science, allied health and biomedical science students. Recently she has been involved in curriculum development for third year pharmacology subjects. Her passion is inspiring the next generation of STEM students to continue their education in research and STEM related careers. She is also interested in collaborating with other academics in education research, more specifically how to retain long term student engagement and involvement in STEM courses.

Alternatives to Animal Models in Teaching Pharmacology Core Concepts— An Educators' perspective

Rahini Ragavan, Antony Vinh, Michael De Silva, Ross D O'Shea and Elvan Djouma. Department of Microbiology, Anatomy, Physiology and Pharmacology, La Trobe University, Bundoora, VIC, Australia

Introduction. Core concepts in pharmacology are traditionally taught with the use of animal models. Increasingly, there has been a growing emphasis on finding alternatives across both drug discovery and development, as well as tertiary education. This is due to many factors including consideration of the "3R's", to replace, reduce and refine the use of animals for teaching and research.

Aims. To design and develop a series of authentic workshops and practicals to introduce and consolidate the core concepts of pharmacology to third year biomedical science students undertaking a new major in physiology and pharmacology at La Trobe University, without the use of animal models.

Methods. We conducted a literature review on the use of non-animal models for teaching pharmacology core concepts and categorised the results according to a collaborative consensus on how effective the teaching tool would be to the student versus the feasibility and cost of resources.

Results. We designed and developed two practicals that used computer simulations and cell-based assays to consolidate student understanding of pharmacodynamics and autonomic nervous system pharmacology. For other core topics (pharmacokinetics, central nervous system pharmacology, drugs of abuse, poisons and toxins and adverse drug reactions), we developed a series of two-hour interactive workshops. This involved the incorporation of individual quizzes, team-based worksheets, group discussions, case studies and industry-based applications.

Discussion. Students engage and learn better when the content and assessments are authentic and contain real world applications. Globally, research and development priorities are moving towards non-animal models in medical product development. Thus, our practicals and workshops are focussed on providing students with authentic experiences to equip them with the skills required for employability in the medical and pharmaceutical industry. Active learning in workshops and practicals has been shown to enhance student knowledge and engagement. Feedback and evaluation from students post-delivery will enable us to implement further changes for subsequent curriculum delivery.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P249

Pharmacists, interns and students' views on preparedness and training for domestic violence

Dr Harjit Kaur Singh

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Pharmacists, interns and students' views on preparedness and training for domestic violence

Harjit Khera¹, Rita Wardan¹, Amy Ong¹, Jasvin Malhotra¹, John Lobaton¹, Marvin Shengola¹, Thuan Vu¹, Suzanne Caliph¹.
Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Melbourne, VIC, Australia.

Introduction. Domestic violence (DV) is a significant global health problem with ill effects on physical and mental health that can often go unnoticed amongst healthcare professionals. Pharmacists as readily accessible primary healthcare providers are ideally positioned to be the first point of contact for individuals affected by DV. Therefore equipping pharmacists and pharmacy students with the necessary knowledge and training to identify and respond to DV is essential for providing timely and effective support.

Aims. The project aims to explore pharmacists', interns', and students' perceptions of their roles, training needs, and confidence in identifying and responding to individuals affected by DV.

Methods A self-administered anonymous survey was designed to examine pharmacists and pharmacy students' knowledge, perceptions, and training needs regarding domestic violence (DV). Both qualitative and quantitative survey responses were analysed in this study.

Results. Our results indicated that pharmacists, interns and pharmacy students did not feel confident in assisting patients affected by DV, attributed to lack of training. Forty-seven percent of student and pharmacist participants expressed uncertainties in referring DV victims due to limited knowledge. Eighty-three percent of participants expressed the need for DV education and training of pharmacists to effectively address and assist DV victims encountered in practice. Participants suggested simulation role-play workshops and videos for DV education in pharmacy.

Discussion. Our study found pharmacists, interns and students felt inadequately prepared to effectively support DV victims, due to inadequate training and resources. Despite being the most accessible primary healthcare professionals, pharmacists may lack the knowledge and skills to assist DV victims they encounter in practice. Mental health challenges in broaching the topic with patients may arise from uncertainty about how to navigate difficult conversations. Our findings highlight the need for DV training and education in the pharmacy curriculum.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P250

Enhancing research skills through seminar analysis: Team-based learning approach in pharmaceutical education

Dr Yassmin Samak

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Yassmin Samak is an Education-Focussed Lecturer in Monash University's Faculty of Pharmacy and Pharmaceutical Sciences with over 15 years of teaching experience. She holds a PhD in Pharmaceutical Sciences from the University of Queensland, with research focused on drug delivery systems. Dr. Samak's teaching emphasises innovative, team-based learning activities that apply knowledge and skills to real-world pharmaceutical science and pharmacy practice. Her excellence in education has earned her prestigious awards, including the Australian Award for University Teaching (2022), Monash's Vice-Chancellor's Award for Excellence (2021), and the Faculty Teaching Award (2020).

Enhancing research skills through seminar analysis: Team-based learning approach in pharmaceutical education

Yassmin Samak¹, Yunyang (Eileen) Zhou¹, Alex Parker¹, Nilushi Karunaratne¹, Betty Exintaris¹. Pharmacy and Pharmaceutical Sciences Education, Monash University¹, Melbourne, VIC, Australia

Introduction. Traditional learning approaches often fail to equip students with the critical analysis skills needed for real-world research. In response, a new workshop featuring an active, team-based learning (TBL) strategy has been introduced in the BPS4001 Advanced Pharmaceutical Science unit.

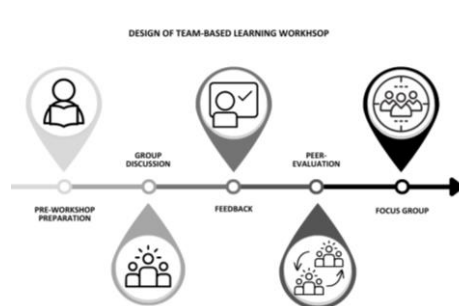
Aims. The design of this workshop aims to develop students' ability to critique seminars through a hands-on, peer-interactive approach.

Methods. In preparation for the workshop, students individually watched an instructional video on seminar critique and reviewed a 50-minute seminar. During the session, they worked in groups of 5-6 using two templates: the first for initial reactions via 5-point Likert scales, and the second for deeper analytical feedback. Academics provided feedback throughout. The workshop concluded with students exchanging critiques for peer evaluation.

A focus group of four students later discussed the workshop's design and implementation.

Results. The workshop setup allowed students to refine their initial individual critique through highly engaged group discussions and academic feedback. The focus group highlighted the value of gaining diverse perspectives and discussed their increased confidence levels in terms of seminar content analysis and presentation style evaluation.

Discussion. Studies show that TBL can be an effective approach to enhance critical thinking in pharmacy education¹. In our workshop, the structured templates and academic feedback provided a clear framework for analysis, while the peer-interactive component encouraged a sense of accountability and fostered a collaborative learning environment. The dynamic workshop's design and iterative process of individual critique, feedback, and peer discussion resulted in effective peer learning and has proven to be a promising method for developing students' seminar critique skills.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P251

Improving pharmacy student confidence in pharmacogenomics: finding the optimal educational combination

Miss Ruby Soueid

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Ruby Soueid is a graduate pharmacist currently completing her internship at The Children's Hospital at Westmead. Her research focuses on enhancing the knowledge and confidence of pharmacy students in pharmacogenomics, with the aim of optimising its clinical application. Ruby is deeply passionate about advancing patient-centred care through the integration of pharmacogenomics, and is dedicated to contributing to the development of innovative educational strategies that will facilitate the clinical adoption of pharmacogenomics.

Improving pharmacy student confidence in pharmacogenomics: finding the optimal educational combination

Ruby Soueid¹, Toni Michael¹, Pete Yeap¹, Fanfan Zhou¹, Stephen Hughes¹, Betty Chaar¹, Rose Cairns¹, Kellie Charles¹, Sophie Stocker¹. School of Pharmacy, Faculty of Medicine & Health, The Univ of Sydney¹, Sydney, NSW

Introduction. The lack of pharmacogenomics (PGx) use in clinical practice is attributed to a lack of confidence of healthcare professionals to interpret and apply PGx data to patient cases. Pharmacists play a key role in PGx service provision, so innovative pedagogical approaches are essential to develop student competence to upskill workforces.

Aims. To compare the impact of three pedagogical approaches (including lectures, workshops, opportunities to undergo PGx testing and role-play assignments) on pharmacy students' perceived confidence to apply PGx knowledge.

Methods. A PGx module was delivered to second year pharmacy students and was adapted across three cohorts (one class in 2023, two classes in 2024). The first cohort (A) (N=252) received PGx lectures only. The second cohort (B) (N=48) received lectures and an opportunity to undergo free PGx testing. The third cohort (C) (N=209) received the same as B, as well as a workshop with a group assignment (video role play between a pharmacist and a prescriber or patient about PGx and test result interpretation). Pre- and post-module Likert-scaled surveys assessed students' perceptions of confidence in PGx application. Descriptive statistics and paired T-tests were used. Improvements in moderate and extreme confidence results are presented.

Results. Confidence in designing a dose regimen based on PGx test results increased in all three cohorts (A: 27%, B: 29%, C: 41%). Confidence also increased in student self-reported ability to communicate recommendations to other healthcare professionals (A: 36%, B: 39%, C: 49%), and in their ability to educate patients about the ethical implications associated with PGx testing (A: not assessed, B: 31%, C: 42%). The pedagogical approach that included lectures, opportunity to undergo PGx testing and a workshop with a video role play assignment, found the greatest improvement in confidence (11%, cohort B vs C and 14%, cohort A v C).

Discussion. Individual teaching methods to deliver PGx education to pharmacy students supported an increase in students perceived confidence in implementing PGx. Optimal outcomes were demonstrated by the combined pedagogical approach that included experiential learning, such as case-based learning and counselling role-plays. These methods may be beneficial in other pharmacy curricula, and other medical disciplines, to instil a confidence in PGx in the next generation of healthcare professionals and thereby steward PGx guided medication management.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P252

Exploring pharmacists' mental health support behaviours via simulated patients: mixed-methods pilot study

Mrs Tina Ung

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Tina Ung, BPharm (Hons I), is a Community Pharmacist, Education-Focussed Academic and PhD Candidate at The University of Sydney School of Pharmacy. Tina is the grateful recipient of the Elizabeth Wunsch Postgraduate Research Scholarship in Mental Health and Pharmacy Services. Tina's thesis explores how we can partner with mental health stakeholders to co-design, deliver and evaluate pharmacy education and continuing professional development activities in mental health via simulated patients. Tina looks forward to presenting her research at the ASCEPT-APFP-APSA Joint Congress 2024.

Exploring pharmacists' mental health support behaviours via simulated patients: mixed-methods pilot study

Tina X Ung¹, Sarira El-Den¹, Rebekah J Moles¹, Jack C Collins¹, Kevin Ou², Jenny Chen¹, Claire L O'Reilly¹.

School of Pharmacy, The University of Sydney¹, Sydney, NSW, Australia;

The Pharmaceutical Society of Australia², Sydney, NSW, Australia.

Introduction. Simulated patient (SP) role-plays provide a safe and relevant learning experience for pharmacy students, improving confidence and attitudes towards providing mental health support (Ung et al, 2023). Little research explores the use of SP role-plays, enacted by trained actors, with pharmacists.

Aims. To pilot the adaptation of SP role-plays from the classroom with university students into a workshop with pharmacists, evaluate their impact on pharmacists' intended mental health support behaviours, and explore pharmacists' experiences of the workshop.

Methods. Pharmacists attended a workshop at an annual national professional conference in July 2023. Trained actors enacted simulated scenarios (previously developed for pharmacy education) with role-playing pharmacist volunteers, while being observed by peers, a workshop facilitator and mental health consumer educator (MHCE). Immediately post-roleplay, role-playing pharmacists engaged in self-assessment, performance feedback and debrief discussions. Pharmacists completed pre- and post-workshop surveys exploring intended mental health support behaviours, and were invited to a follow-up interview. Role-play scores, survey scores, and interview transcripts were analysed.

Results. Thirty-five pharmacists attended the workshop. Sixteen role-plays were conducted with 14 analysed. Pharmacist self-assessment scores were lower than MHCE scores ($p=0.028$). The role-plays increased observing and participating pharmacists' intentions in supporting a person experiencing mental health crises (suicide or psychosis), as well as encouraging other supports ($p<0.05$). Four themes emerged from interviews ($n=4$): realistic context for skills application and practice, benefits of observing, self-assessment and feedback, integrating into clinical practice.

Discussion. SP role-plays may be used to observe and enhance pharmacists' mental health support behaviours. The SP method may be adapted into clinical practice as a workplace-based assessment, to upskill pharmacists in providing mental health support.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P253

VitOOLs VIRTUAL LABORATORY: immersive and integrative undergraduate training in pharmacology

A/Prof Lisa Bg Tee

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Lisa Tee is an Associate Professor and Biomedical Scientist with over 30 years' experience in research and teaching. Lisa commenced research in Clinical Pharmacology while undertaking her PhD in London University and has been actively engaged in teaching and research in Australia since 1986. As chief investigator, she was awarded funding from several resources including NHMRC and Cancer Foundation. Lisa's excellence and innovation in teaching has been recognised with the Australian Excellence and Innovation in Teaching (2011) and the National Teaching Fellowship (2016). Lisa's teaching aims to empower students with the learning skills to understand difficult concepts leveraging on current technology. She is the founder of MyCourseMap (interactive curriculum mapping tool) and co-founder of VitOOLs (immersive virtual learning platform) and recognised with a Curtin Innovation Award (2021). Lisa is presently working collaboratively with colleagues and clinicians in the transformation of 2D medical imaging into 3D visualisation, creating the "3D virtual patient".

VitOOLs VIRTUAL LABORATORY: immersive and integrative undergraduate training in pharmacology

Rima Caccetta¹, James Alex², Xuebin Chen³, Lisa BG Tee¹. Curtin Medical School¹, School of Elec Eng, Comp and Math Sci², Curtin University, Bentley, WA, Australia; School of Biomedical Sciences, Pharmacology & Toxicology³, UWA, Nedlands, WA, Australia.

Introduction. Laboratories are diminishing world-wide and there is increasing strain on hands on training. To fill this growing gap whilst adding a unique integrated perspective, VitOOLs was created. VitOOLs is a virtual platform of clinics, patients and laboratories that take students, clinicians and patients from the signs and symptoms to the cellular level and the mechanism of action.

Aims. To evaluate student perception, engagement and usability of the VitOOLs VR LAB and compare usability of VR LAB with Oculus headset versus on-screen to complete the virtual experiments.

Methods. The VR LAB was embedded in a tutorial of a key challenging 2nd year unit (PHRM2003) in the BHP Pharm course at Curtin in 2023. We further evaluated the usability of the VR LAB for teaching pharmacology specifically to identify benefits and challenges in using the different modes: VR Oculus headset versus on-screen. The evaluation was conducted in two phases: (1) students in a Pharmacy unit at Curtin (PHRM2003) and in a Biomedical Sciences unit at UWA (IMED2002) trialed the prototypes in class followed by voluntarily completing a system usability scale (SUS) questionnaire, and (2) a one-on-one session is being conducted with students and teaching teams.

Results. Tutorial attendance in 2023 increased markedly to 98% (other tutorials: <70%). The survey has been completed by 231 individuals thus far, 66% females, 32% males and 2% others; most students 54% used the VR LAB with Oculus. Current SUS data shows the VR Oculus headset and on-screen prototypes are acceptable for use and indicated high positive sentiment in respect to learning experience, which are further supported by participant comments. Although most (57.4%) students had no issues using the Oculus, 26.6% reported that never previously used a headset was an issue; however, they enjoyed the experience and had lots of fun.

Discussion. Positive user sentiments highlighted the benefits of VitOOLs VR LAB with Oculus or on-screen as a good visual learning tool which is interactive, realistic and useful for distance online learning. However, some students who were less

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



familiar with using a headset felt less confident in using the Oculus and thus the on-screen version is a suitable alternative. Other relevant data will be further discussed in the presentation.

P254

An e-card game to promote student engagement in pharmacology: A 3-year data.

A/Prof Pornpun Vivithanaporn

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

I am an Associate Professor at the Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand. Pornpun graduated from the University of Texas Medical Branch and was a postdoctoral researcher at the University of Alberta, Canada. I developed PharMatch, an online card game to help students learn to memorize drugs and their properties in 2021, and won an Innovative Teaching Award from Mahidol University in 2023.

An e-card game to promote student engagement in pharmacology: A 3-year data.

Vivithanaporn P¹, Temsang P², Jutamaneeroj D², Paichamnan Y¹ Chakri Naruebodindra Medical Institute, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Samut Prakan, TH¹; Innovation and Education Technology Section, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Samut Prakan, TH²

Introduction. As the first topic of pharmacology teaching, learning autonomic nervous system (ANS) pharmacology contains many unfamiliar terminologies to students. Therefore, information overload is a common problem and there is a need to initiate a fun and effective add-on tool to help students memorize these drugs.

Aims. We aimed to create an electronic game called PharMatch to help students match ANS drugs with their mechanism of action, indications, and side effects.

Methods. PharMatch contains 4 types of cards: drug name, mechanism of action, indication, and side effect. The card layout is similar to a solitaire game. Players match each drug name (18 cholinergic and 28 adrenergic drugs) with other properties. Self-drawn cartoon figures are used to illustrate indications and side effects. The time will stop when players collect a full stack of five drugs. PharMatch was launched as a supporting learning tool from the academic year 2022 to 2024. Self-rating scores using a Likert scale of 1 to 5 and comments were collected after the summative examination.

Results. Ramathibodi Medical School has 177 to 206 students during the academic year 2022 to 2024. The participation rate defined as at least one finished game increased from 60.3% in 2022 to 79.6% in 2024. The percentage of students who finished the game more than 50 times was 19.6%, 24.3%, and 27.2%, in 2022, 2023, and 2024, respectively. The self-rating scores of drug name memorization were 4.29, 4.25, and 4.32, respectively.

Students regarded PharMatch as useful and fun. They also liked the graphic and the challenge that one drug was paired with several indications or side effects.

Discussion. The increase of student engagement points out that game-based learning can be a solution for subjects with information overload like pharmacology. Therefore, an e-card game like PharMatch is an effective learning tool.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P255

Decolonising pharmacy curricula: a scoping review

Dr Megan Waldhuber

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Megan is an education-focused lecturer in the faculty of Pharmacy and Pharmaceutical Sciences and a practising pharmacist. Megan has a particular interest in integrative curriculum development to enhance student learning experiences. With a background in microbiology and molecular biology, Megan continues to explore innovative ways to connect conceptual understanding of these fields with discipline-specific and generic skills, as well as seeking to incorporate diverse perspectives such as those of Indigenous Australians.

Decolonising pharmacy curricula: a scoping review

Minh-Hoa Nguyen¹, Behira Tan Wei Tang¹, Vanessa Okorom¹, Yucheng Song¹, Vongcheng Sary¹ and Megan Waldhuber¹. Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Parkville, VIC, Australia.

Introduction. There is a recognised need to decolonise the curriculum of healthcare professional degrees to develop more culturally responsive practitioners, with the ultimate goal of addressing inequities and improving health outcomes for Indigenous peoples.

Aims. This scoping review aims to map the methods that have been used to decolonise pharmacy curricula globally.

Methods. The scoping review was based on the JBI framework for scoping reviews. Three major databases, PubMed, MEDLINE and ERIC were searched for articles published in English, with no date restrictions. Inclusion criteria focused on the authors' definition of decolonisation (relating to race and ethnicity), pharmacy education, and the methodology used to decolonise the curriculum. Articles from grey literature, or those without Monash institutional access were excluded from the search. Data extraction concentrated on the methodologies used for curriculum decolonisation.

Results. A total of 40 articles were included in the review. From these, the methods used for decolonisation of pharmacy curricula were divided into 2 main categories: methods focused on improving cultural competency and methods focused on improving Indigenous knowledges.

Discussion. This study gives an overview of the types of methodologies employed to diversify pharmacy curricula through decolonisation, providing pharmacy educators with potential pathways to build cultural competency and enrich the curriculum with Indigenous knowledges.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P256

Student and supervisor perspectives on undergraduate skill development for research pathways

Dr Megan Waldhuber

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Megan is an education-focused lecturer in the faculty of Pharmacy and Pharmaceutical Sciences and a practising pharmacist. Megan has a particular interest in integrative curriculum development to enhance student learning experiences. With a background in microbiology and molecular biology, Megan continues to explore innovative ways to connect conceptual understanding of these fields with discipline-specific and generic skills, as well as seeking to incorporate diverse perspectives such as those of Indigenous Australians.

Student and supervisor perspectives on undergraduate skill development for research pathways

Megan Waldhuber¹, Nilushi Karunaratne¹ and Betty Exintaris¹. Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Parkville, VIC, Australia.

Introduction. The interest in skill development for graduates entering the workforce has been growing over several years, however, less is known about skill development to prepare students pursuing research pathways beyond their undergraduate degrees.

Aims. To compare student and supervisor perceptions of the skills required, and level of development of these skills, to undertake an Honours year.

Methods. Students were surveyed prior to commencement of the 2023 Honours programme, supervisors were surveyed prior to the 2024 Honours intake. Surveyed skills (adapted from Hanson & Overton, 2010) included a range of discipline-specific skills/knowledge (e.g. chemical terminology and manipulative laboratory skills) and generic skills (e.g. professional, ethical behaviours and report writing skills).

Results. The survey was completed by 28 students and 15 supervisors. Comparisons between the two groups revealed a common theme where perceived importance of all skills was greater than the perceived level of mastery. Both students and supervisors rated manipulative laboratory skills and analytical skills (such as raw data processing) among the top 3 discipline-specific skills and knowledge. Supervisors also rated safe chemical handling among the most important skills, while students favoured their knowledge of fundamental pharmacology principles. Students and supervisors identified report writing and time management/organisational skills among the most important generic skills. Supervisors perceived professional and ethical behaviour to be the most important generic skill.

Discussion. This study provides insight into the types of skills desired by Honours supervisors and compares this with the skills students perceive as most important. We identify a mismatch between perceived importance and level of attainment by both students and supervisors of both discipline-related and generic skills for students embarking on research training.

Hanson S & Overton T (2010) Report, Higher Education Academy and UK Physical Sciences Centre

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P257

The impact of medication swallowing lubricants on drug dissolution

Dr Ayman Allahham

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Ayman has more than 13 years of experience in teaching pharmaceutical Science courses with focus on the quality assurance and accreditation standards of education in tertiary institutions.

Building on his higher education and research in Monash University (from Honours to PhD), his personal skills and previous industrial experience, Ayman has maintained and developed his professional success and achievement through successful collaboration with the pharmaceutical industry through training, student visits and industrial student projects are examples of his achievements.

Ayman has a wide range of research interests in the area pharmaceutical physicochemical properties, formulation, in vitro assessment and stability and their applications for respiratory and gastrointestinal drug delivery. Recently, Ayman is focused on working on pharmaceutical projects that provide evidence for a better health/pharmacy practice

The impact of medication swallowing lubricants on drug dissolution

S. Fatima, V. B. Nooney, Barbora deCourten, T. Thrimawithana, and A. Allahham. RMIT University, Australia

INTRODUCTION. Patients with dysphagia risk aspiration pneumonia when swallowing medications. To prevent aspiration, medications are often crushed and administered with lubricants (1). Lubricants are also used by elderly individuals and those who fear taking tablets, but the impact on medication dissolution profiles is not well studied.

AIMS. This research aims to characterize how lubricants affect the dissolution profiles of gliclazide, a commonly used drug in dysphagia management.

METHODS. Gliclazide, used as the model drug (80 mg tablets). Dissolution was conducted using USP dissolution method II (Distek Model 2500) under three conditions: without a lubricant, with Gloup Forte, and with extremely thickened water, in buffer at pH 6.8 and reverse osmosis water. Samples were collected at 5, 10, 15, 20, 45, and 60 minutes, filtered, diluted, and analyzed using a UV spectrophotometer (Mettler-Toledo) at 225 nm.

RESULTS. The addition of Gloup Forte significantly slowed the dissolution rate of gliclazide compared to no Gloup, while extremely thickened water had no significant impact.

DISCUSSION. The findings indicate that Gloup Forte significantly impedes Gliclazide dissolution, while extremely thickened water does not, emphasizing the need for careful selection of lubricants in dysphagia management to ensure effective medication delivery.

1. Wright DJ, Smithard DG, Griffith R. Optimising Medicines Administration for Patients with Dysphagia in Hospital: Medical or Nursing Responsibility? *Geriatrics (Basel)*. 2020;5(1):9.

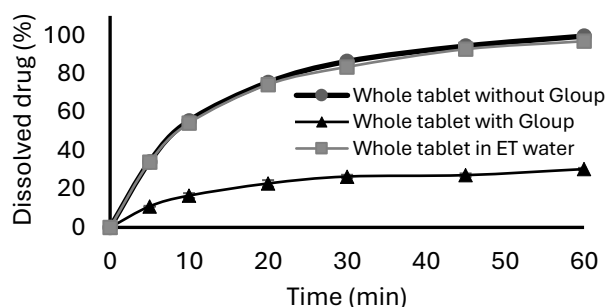


Figure 1: Gliclazide dissolution (%) in buffer pH 6.8 under various condition

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P258

Compatibility of frequently prescribed paediatric IV medications in glucose and saline fluid

Miss Shoohb Alassadi

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Compatibility of frequently prescribed paediatric IV medications in glucose and saline fluid

Shoohb Alassadi¹, Nial Wheate¹, Sophie Brown², Deshina Naidoo². School of Pharmacy, University of Sydney¹, Sydney, NSW, Australia; The Sydney Children's Hospital's Network², Westmead, NSW, Australia

Introduction: Clinicians in practice have raised concern that there is limited published data available to support the safe co-administration of intravenous (IV) medications with commonly prescribed and utilised paediatric IV fluids. A combination of sodium chloride (saline, 0.9% w/v) and glucose (5% w/v) is the most commonly prescribed intravenous fluid for children.

Aims: The aim of this study was to assess the stability and physical compatibility of the 15 most prescribed paediatric IV medications in glucose/saline fluid.

Methods. The study utilised a range of analytical techniques including UV spectrophotometry, nuclear magnetic resonance (NMR), thin-layer chromatography (TLC), high-performance liquid chromatography (HPLC), liquid chromatography-mass spectrometry (LC-MS), and pH analysis. Each medication was prepared in either just saline or glucose/saline solutions and with paired samples kept both at room temperature and at 4 °C and analysed for physical chemical stability overtime intervals of 1 h to 7 days.

Results. The analysis revealed variable stability and compatibility among the medications tested. Of particular concern was the demonstrated physical instability and significant degradation of penicillin-based drugs in glucose/saline when compared with their preparation in saline.

Discussion. The findings of this study underscore the importance of selecting appropriate IV fluids for paediatric IV medications and ensure their timely use after preparation to ensure stability and efficacy.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P259

Targeting Cathepsin S Modulates Tumor Immunity in Head and Neck Cancer

Prof Jang-yang Chang

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Education: National Defense Medical Center, Taipei, Taiwan

Current position:

1. Chair Professor, College of Medicine, Taipei Medical University
2. Director of TMU Research Center of Cancer Translational Medicine, Taipei Medical University

Work Experience:

1. Chair Professor and Superintendent of Taipei Cancer Center, Taipei Medical University
2. Distinguished Investigator and Director of Institute of Biotechnology and Pharmaceutical Research, National Health Research Institutes, Taiwan
3. Executive Vice President, National Cheng Kung University, Taiwan
4. Distinguished Professor and Dean, College of Medicine, National Cheng Kung University, Taiwan
5. Distinguished Professor and Director of National Institute of Cancer Research, NHRI, Taiwan

Certification

1. Board of Internal Medicine, Taiwan.
2. Board of Hematology, Taiwan
3. Board of Medical Oncology, Taiwan

Major Research areas:

1. Anticancer drugs Clinical trial
2. Anticancer drug development and mechanism study

Targeting Cathepsin S Modulates Tumor Immunity in Head and Neck Cancer.

Jang-Yang Chang^{1,2*}, Yung-Chieh Chang^{1,2}, Shan-Hung Chen², Kwang-Yu Chang^{2*}

¹ TMU Research Center of Cancer Translational Medicine, Taipei Medical University, Taipei, Taiwan. ² National Institute of Cancer Research, National Health Research Institutes, Tainan, Taiwan.

Introduction: Overexpression of cathepsin S (CTSS), a lysosomal cysteine protease, was found in most types of tumor tissues comparing with the normal tissues. The expression level of CTSS is associated with tumor progression. Knowing that CTSS regulates angiogenesis, metastasis and antigen presenting in cancer cells. Therefore, CTSS was suggested as a therapeutic target for cancer treatment. We developed a novel specific CTSS activity inhibitor, RJW-58, and demonstrated its metastatic inhibitory effect in head and neck cancer (HNC) and triple negative breast cancer. However, the tumor immunity modulation effect of targeting CTSS is still not well understood.

Aims: We aim to explore the tumor immunity modulation effect of CTSS in HNC *in vitro* and *in vivo*.

Methods: HNC patients' samples were used to investigate the correlation among CTSS and CD8⁺ T cell infiltration level. Syngeneic HNC mice model was utilized to investigate the anti-cancer effects and the tumor immunity modulation effects of RJW-58 and the combination with immunotherapy. For investigating the molecular mechanism in HNC cell lines, we utilized various cell experiments to support the effect of RJW-58.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Results: Inverse correlation between CTSS and IL-7 were found in our HNC patients' samples. In addition, we also found more CD8⁺ T cell infiltration in the CTSS low-expressing HNC patients. We demonstrated that RJW-58 suppressed tumor growth and increased the secretion level of IL-7 *in vitro* and *in vivo*. Then, we cotreated HNC syngeneic mice with RJW-58 and anti-IL-7 antibodies and proved that the anti-cancer effect of RJW-58 was through upregulating the secretion level of IL-7 resulting in promoting CD8⁺ T cell infiltration. Furthermore, results of combination therapy of RJW-58 and anti-PD-1 antibodies in HNC syngeneic mice model showed that a persistent inhibitory effect against tumor regrowth after completion of the drug administration schedule.

Conclusion and Discussion: We concluded that the targeting strategy of CTSS can reinvigorate IL-7, and enhance the anti-cancer effect of anti-PD-1 antibody in HNC. These results hinted us that targeting CTSS may modulate the tumor immunity to improve the anti-cancer effect of immune checkpoint therapy in HNC. (This study was supported by the following grants: NSTC113-2314-B-038-143 and the Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education)

P260

Tailored lipid-polymer nanoparticles for targeted therapeutic nucleic acid delivery to bone marrow

Mrs Ruba Almasri

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Tailored lipid-polymer nanoparticles for targeted therapeutic nucleic acid delivery to bone marrow

Ruba Almasri^{1,2}, Kai Chen¹, Haibo Jiang^{1,3}, Marck Norret¹, Killugudi Swaminathan Iyer¹, Clive Prestidge², Cameron Evans^{1*} School of Molecular Sciences, The University of Western Australia¹, 35 Stirling Highway, Crawley WA 6009, Australia; UniSA Clinical & Health Sciences, University of South Australia, Adelaide², 5000, Australia; Department of Chemistry, The University of Hong Kong³, Pok Fu Lam, Hong Kong, 999077 P. R. China

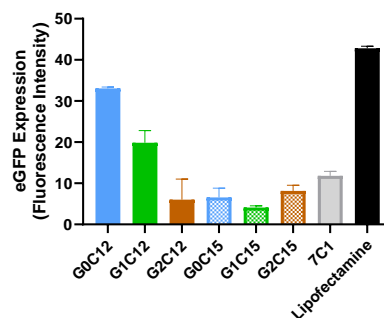
Introduction. The delivery of nucleic acid therapeutics to bone tissue is hindered by biological barriers and poor vascularization. Advances in lipid nanoparticle (LNP) technology have revealed that using PEI₆₀₀ substituted with C15 alkyl lipid (7C1) can achieve bone marrow-specific delivery of siRNA.¹ However, the polydisperse nature of PEI₆₀₀ poses challenges in reproducibility and targeting efficiency. This study explores the use of polyamidoamine (PAMAM) dendrimer-based polymer-lipid hybrids (PLHs) to enhance the bone marrow specificity of LNPs.

Aims. This research aims to design and synthesize PAMAM dendrimer-based PLHs with controlled architectures and evaluate their potential to improve the delivery of antisense oligonucleotides (ASOs) and eGFP plasmid DNA (pDNA) to bone marrow.

Methods. PAMAM dendrimers of varying generations (G0-G2) were conjugated with lipid tails (C12 or C15) and integrated into LNPs with different PEG surface densities. The LNPs were tested for their ability to complex and deliver ASOs and eGFP pDNA *in vitro*. Particle size analysis, gel retardation assays, and *in vitro* transfection studies in HEK293T cells were conducted to evaluate the performance of the formulations.

Results. Particle size was influenced by generation of PAMAM, alkyl lipid length and polymer lipid hybrid molar ratios. Gel retardation assays indicated effective complexation of pDNA and ASOs with LNPs, particularly at higher N/P ratios. *In vitro* transfection studies revealed that several PLH-LNP formulations matched or exceeded the delivery efficiency of the established 7C1 formulation.

Discussion. The findings suggest that PAMAM dendrimer-based LNPs have significant potential for enhancing targeted delivery of nucleic acid therapeutics to bone marrow. Future studies will focus on *in vivo* bone targeting efficiency using combinatorial DNA barcoding and single-cell sequencing to assess biodistribution and targeting efficacy.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P261

Lysine improves the aerosolization and stability of cannabidiol dry powder

Mrs Komal Komal

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Komal is a currently a PhD student at the School of Pharmacy, University of Otago, New Zealand. Her supervisors are Professor Shyamal Das and Professor Michelle Glass. She completed her Bachelor of Pharmacy (2014) and Master in Pharmacy (2018) from Kurukshetra University, Haryana, India. Her PhD research focuses on the inhaled delivery of cannabidiol (CBD) incorporated with various excipients for treating pulmonary diseases, including chronic obstructive pulmonary disease (COPD). Additionally, she has explored the combination of CBD with other therapeutic agents to enhance therapeutic outcomes.

Lysine improves the aerosolization and stability of cannabidiol dry powder

Komal Komal ¹, Michelle Glass ² and Shyamal C. Das ¹ ¹School of Pharmacy, University of Otago, Dunedin, New Zealand; ²Department of Pharmacology and Toxicology, University of Otago, Dunedin, New Zealand

Introduction: Cannabidiol (CBD), a phyto-constituent of cannabis has shown promising therapeutic outcomes against numerous diseases including seizures, cardiovascular diseases, chronic obstructive pulmonary disease, and asthma. However, the existing oral dosage form of CBD undergoes significant first-pass metabolism that minimizes its effectiveness. Delivery of CBD through inhalation can potentially ensure effective CBD concentration in the lungs and systemic circulation bypassing the fast-pass metabolism. A dry powder inhaler is considered one of the most effective modes of delivering drug through inhalation. This dry powder needs to be within the specific size range of 1–5 μm for deep lung delivery which is often difficult to aerosolize due to the highly cohesive nature of these micron-sized powder. Among different preparation techniques of inhalable dry powder, spray-drying is preferable as it is reproducible, scalable and cost-effective. Amino acids are often used in inhalable dry powder formulations due to their aerosolization-enhancing properties.

Aim: This study investigated the aerosolization, stability and cytotoxicity-enhancing properties of an amino acid namely lysine (LYS) for an inhalable cannabidiol dry powder developed by a spray-drying technique.

Methods: Cannabidiol dry powder was prepared in the presence/absence of lysine (C_{SD} and CL_{SD}), utilizing a spray-drying technique with the fixed feed concentration (0.8% w/v) in the cosolvent system of ethanol and water.

Results: The prepared inhalable dry powders were within the size range of 1–5 μm and crystalline in nature. LYS-free spray-dried cannabidiol (C_{SD}) showed irregular and flaky morphology whereas LYS-containing spray-dried cannabidiol (CL_{SD}) showed spherical morphology with dimples on the surface. CL_{SD} showed a better aerosolization profile than C_{SD} (ED: 90% vs 43% and FPF: 56% vs 27%) indicating more CBD deposition in the overall respiratory tract including the deep lung region. Both C_{SD} and CL_{SD} were found stable under low and high humidity (>15% RH and 53% RH) for one month while maintaining limited and comparable cytotoxicity (IC₅₀ >40 μM) in alveolar basal epithelial cells (A549). All these data indicate the suitability of the development technique.

Conclusion: Lysine improves CBD deposition in the lungs. The stability and cytotoxicity in cannabidiol powder for the presence of lysine was not significantly different than that without lysine.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P262

Analysis of Statins' Affinity towards PPAR Receptors: Multiple Docking and Neural Networks

Prof Igor Iezhitsa

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Igor Iezhitsa has over 25 years of experience in pharmacology, with a career dedicated to both academia and research. He earned his PhD in Pharmacology from Volgograd State Medical University (Russia) in 1998, followed by a Doctor of Biological Science (Dr. Sci. Biol.) degree from the same institution in 2008. From 1994 to 2000, Dr. Igor was instrumental in preclinical studies of a novel class of CNS stimulants at Volgograd State Medical University. Since then, he has conducted extensive screening and preclinical evaluation of new pharmacological compounds. In 2009, Dr. Igor joined the Faculty of Medicine at Universiti Teknologi MARA (UiTM), Malaysia, as an Associate Professor of Pharmacology. He was a key figure in establishing the Centre for Neuroscience (NeuRon) at UiTM in 2013, leading the center from 2015 to 2020. He currently serves as Professor of Pharmacology at the School of Medicine, International Medical University. Dr. Igor's research interests include neuropharmacology, neuroprotection, toxicology, and ocular pharmacology. He has published over 110 articles in indexed journals and authored five books and chapters.

Analysis of Statins' Affinity towards PPAR Receptors: Multiple Docking and Artificial Neural Networks

Pavel M Vassiliev¹, Maxim A Perfilev¹, Igor Iezhitsa², Renu Agarwal². ¹Lab for IT in Pharmacology & Computer Modelling of Drugs, Research Center for Innovative Medicines, Volgograd State Medical University, Russian Federation; ²IMU University, School of Medicine, Kuala Lumpur, Malaysia

Introduction: The objective of this *in silico* research is to determine the integral affinity of statins (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin) towards PPAR- α and PPAR- γ receptors using multiple docking methods combined with fully connected correlation artificial neural networks. The specific objectives include generating optimized 3D conformers for the statins, validating 3D models of PPAR receptors, creating docking spaces, conducting multiple docking, and establishing artificial neural networks to determine overall affinity.

Materials and Methods: The study utilized data on the 2D structures of the six statins and experimental X-ray crystallographic 3D models of PPAR- α and PPAR- γ receptors. Key software used includes ChemOffice for chemical structure processing, MarvinSketch for conformer construction, MOPAC2012 for conformation optimization, MSite for docking spaces construction, AutoDock Vina for multiple docking, CorrConv for neural network construction, and MS Office Excel for data processing. Calculations were performed on a supercomputer with a peak performance of ~ 31.2 teraflops. Sixty optimized conformers were generated for the six compounds, and docking simulations were conducted in 27 spaces of the 3D models of PPAR- α and PPAR- γ receptors using AutoDock Vina.

Results: The integral affinity values of the drugs towards PPAR- α and PPAR- γ receptors were determined using the energy values from neural fully connected correlation networks. Atorvastatin and fluvastatin showed the highest affinity towards PPAR- α , with atorvastatin's affinity being 2.80 times higher than fluvastatin's. For PPAR- γ , atorvastatin and pravastatin were the most active, with atorvastatin's affinity being 2.60 times higher than pravastatin's. Atorvastatin was 1.23 times more active towards PPAR- γ compared to PPAR- α . Other drugs showed significantly lower affinity, with simvastatin displaying almost no affinity for PPAR- γ .

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion / Conclusion: This study calculated the integral affinity of six statins towards PPAR- α and PPAR- γ receptors using fully connected correlation artificial neural networks based on multiple docking data. Atorvastatin showed the highest affinity for PPAR- α and PPAR- γ receptors.

P264

Intestinal epithelial cell EphB4 increases lipid absorption by promoting IL-22 secretion

Dr Xingfeng Liu

Poster presentations 1: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr Liu is an Assistant Research Fellow at the State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences, and Peking Union Medical College. Her research focuses on the pathogenesis and drug discovery for metabolic diseases, including obesity, diabetes, and non-alcoholic fatty liver disease (NAFLD), with an emphasis on identifying new drug targets and treatments for conditions like insulin resistance.

Intestinal epithelial cell EphB4 increases lipid absorption by promoting IL-22 secretion

Xingfeng Liu^{1,2,3,#}, Xiaowei Xing^{1,2,3,#}, Yibing Chen^{1,2,3}, Caiyi Xing^{1,2,3}, Shaocong Hou^{1,2,3}, Lijuan Kong^{1,2,3}, Yanjun Wan^{1,2,3}, Chunxiao Ma^{1,2,3}, Qijin Zhao^{1,2,3}, Qian Jiang^{1,2,3}, Wenjia Fan^{1,2,3}, Shengying Gu^{1,2,3}, Bing Cui^{1,3}, Pingping Li^{1,2,3}✉

State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College¹, Beijing, China. Diabetes Research Center of Chinese Academy of Medical Sciences², Beijing, China. CAMS Key Laboratory of Molecular Mechanism and Target Discovery of Metabolic Disorder and Tumorigenesis³, Beijing, China.

Introduction. Obesity is a global health problem. There are various factors that contribute to obesity, including diet, genetics, and lifestyle. The fundamental issue is that the intake of energy, particularly from lipid-related substances, exceeds its expenditure, leading to excessive fat accumulation in the body.

Aims. EphB4 in the intestine, particularly in the proximal small intestine, is upregulated in response to diet-induced obesity. This study focuses on how intestinal EphB4 contributes to the regulation of glucose and lipid metabolism during obesity development and its molecular mechanisms affecting intestinal lipid absorption.

Methods. To investigate the role of EphB4 in intestinal glucose and lipid metabolism, we created EphB4 intestinal epithelial-specific knockout mice. These mice were then subjected to a high-fat diet to induce obesity. We analyzed the regulatory effects of intestinal EphB4 on obesity and glucose-lipid metabolism using methods such as Western blot, ELISA, and real-time quantitative PCR to explore the underlying molecular mechanisms.

Results. Intestinal epithelial-specific knockout of EphB4 can inhibit the onset of obesity induced by a high-fat diet, reduce serum lipid levels, and improve glucose metabolic homeostasis. Further studies indicate that EphB4 mediates interactions between intestinal epithelial cells and immune cells, regulates the secretion of IL-22, and thereby affects intestinal lipid absorption, contributing to the regulation of glucose and lipid metabolism.

Discussion. The results of this study demonstrate that EphB4 in the intestine regulates intestinal lipid absorption. Combined with our previous findings that EphB4 in the liver is involved in insulin resistance induced by high insulin levels, these results suggest that EphB4 has potential as a target for therapeutic intervention in glucose and lipid metabolism disorders.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P265

Using nanobodies to facilitate drug delivery across the blood-brain barrier in gliomas

Mr Pranav Runwal

Poster presentations 2: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

I am an interdisciplinary PhD candidate at Monash University, collaborating with the Walter and Eliza Hall Institute of Medical Research and The Brain Cancer Centre. My research focuses on bioengineering nanobodies to cross the blood-brain barrier, aiming to improve therapeutic outcomes for brain cancer patients. I also serve as a lead teaching associate at the Monash Faculty of Pharmacy and Pharmaceutical Sciences. I have been involved in promoting the use of AI in education, facilitating workshops across six diverse Monash faculties, two national universities, and at national and international conferences. Additionally, I have designed AI-enhanced assignments, now implemented for final-year formulation science students at Monash University, further integrating innovative learning methodologies into the curriculum.

Using nanobodies to facilitate drug delivery across the blood-brain barrier in gliomas

Pranav Runwal ^{1,2,3}, Gabby Watson ^{1,3}, Duong Nhu ^{1,3}, Niva Jayakrishnan ^{1,3}, Guillaume Lessene ^{1,3}, Wai-Hong Tham ^{1,3}, Joseph Nicolazzo ^{2,3}, ¹Walter and Eliza Hall Institute of Medical Research, Australia, ²Monash Institute of Pharmaceutical Sciences, Australia, ³Brain Cancer Centre, Australia

Introduction. Glioblastoma multiforme (GBM), a highly aggressive brain cancer, has a mere 1% success rate in drug development due to significant challenges like the blood-brain barrier (BBB), which limits drug penetration through tight junctions and efflux transporters.^{1,2} Receptor-mediated transcytosis (RMT) by targeting the transferrin-1 receptor (TfR1) is being investigated as a potential solution to improve drug delivery across the BBB.³ Nanobodies, derived from camelid antibodies, are particularly suited for BBB crossing due to their increased stability, solubility, and ability to recognise unique epitopes compared to conventional antibodies.^{4,5}

Aims. This project focuses on developing nanobody-drug conjugates leveraging RMT for efficient anti-cancer drug delivery to GBM sites, addressing the critical challenge of drug resistance in brain tumors.

Methods. Nanobodies were expressed in a bacterial system, purified by size exclusion chromatography, fluorescently labelled with Alexa Fluor 647 via ion exchange chromatography, and binding properties were assessed using Bio-layer Interferometry (BLI).

Results. Nanobodies targeting human TfR1 were expressed, purified via bacterial expression, and isolated as pure, monomeric fractions using size exclusion chromatography. Fluorescent labelling with Alexa Fluor 647 (AF-647) at a 1:1 molar ratio was performed through ion exchange chromatography, preserving nanobody affinity for TfR1. Bio-layer Interferometry (BLI) demonstrated that the labelled nanobodies maintained binding affinities (0.2 nM to 49 nM) and exhibited cross-reactivity with mouse TfR1. BLI also showed that 6 out of 8 nanobodies did not interfere with transferrin (Tf) binding to TfR1, suggesting no disruption of iron transport.

Discussion. The nanobodies successfully retained TfR1 affinity after AF-647 labelling, allowing for tracking during transport studies. Their cross-reactivity with mouse TfR1 broadens potential in vivo applications. Crucially, the majority of nanobodies did not disrupt Tf binding, indicating minimal risk of interfering with iron transport. These properties position the nanobodies as promising candidates for targeted drug delivery across the BBB without off-target effects related to iron metabolism.

1. Cioffi G, Waite KA, Edelson JL, Kruchko C, Ostrom QT, Barnholtz-Sloan JS. Changes in survival over time for primary brain and other CNS tumors in the United States, 2004–2017. *Journal of Neuro-oncology*. 2022;160(1):209-219.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



2. Moujalled D, Southon AG, Saleh E, et al. BH3 mimetic drugs cooperate with Temozolomide, JQ1 and inducers of ferroptosis in killing glioblastoma multiforme cells. *Cell Death & Differentiation*. 2022;29(7):1335-1348.
3. Pulgar VM. Transcytosis to cross the blood brain barrier, new advancements and challenges. *Frontiers in neuroscience*. 2019;12:1019.
4. Jovčevska I, Muyldermans S. The therapeutic potential of nanobodies. *BioDrugs*. 2020;34(1):11-26.
5. Bannas P, Hambach J, Koch-Nolte F. Nanobodies and nanobody-based human heavy chain antibodies as antitumor therapeutics. *Frontiers in Immunology*. 2017;8:1603.

P266

A novel and targeted peptide drug conjugate for triple negative breast cancer

Ms Farhana Mollah

Poster presentations 1: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Farhana Mollah is a final-year PhD candidate within the Breast Cancer Targeting & Drug Delivery group at the University of Sydney's Faculty of Medicine and Health. Her research focuses on validating novel therapeutic candidates using 3D models for an aggressive breast cancer subtype, triple negative breast cancer. Additionally, she investigates the luteinising hormone-releasing hormone receptor in-depth to enhance targeted drug delivery.

A novel and targeted peptide drug conjugate for triple negative breast cancer

Farhana

Mollah^{1,2,3}, Barb Guild^{1,3}, Dinny Graham^{1,3,4}, Pegah Varamini^{1,2}. Fac of Medicine and Health, Univ of Sydney¹, Camperdown, NSW, Australia; Nano Institute, Univ of Sydney², Camperdown, NSW, Australia; Centre for Cancer Research, Westmead Institute for Medical Research³, Westmead, NSW, Australia; Breast Cancer Institute, Westmead Hospital⁴, Westmead, NSW, Australia.

Introduction. Triple-negative breast cancer (TNBC) accounts for 10-20% of breast cancers. There are limited effective targeted therapeutics for TNBC, and non-specific chemotherapy is the main method of treatment, leading to various damaging side effects. In many TNBC cases, the disease often recurs or progresses after an initial successful response, with future resistance to therapy. A major contributor to this disease progression is breast cancer associated fibroblasts (BCAFs), which signal to the tumour cells and their microenvironment to facilitate tumour growth, progression, invasion, and metastasis. Hence, TNBC is considered an unaddressed medical condition that urgently needs novel effective targeted therapeutics. A novel peptide drug conjugate (PDC), MLD5, was designed with a stable linker and cytotoxic payload, which targets a receptor that is selectively targetable in TNBC. For analysing the effectiveness of MLD5, three-dimensional (3D) preclinical models are needed as they can recapitulate the spatial dimension, cellular heterogeneity, and molecular networks of the tumour microenvironment more adequately than conventional two-dimensional (2D) models.

Aims. To evaluate the anticancer activity of MLD5 using 2D and 3D models of TNBC.

Methods. Antiproliferative and apoptosis induction activities of MLD5 were investigated. TNBC, BCAF and co-culture spheroids were generated using low attachment 96-well plates and treated with MLD5. Response to the treatment, was assessed in spheroids by spheroid morphology assessment, cell viability and invasion potential.

Results. MLD5 showed low half-maximal inhibitory concentration (IC₅₀) and showed significant apoptotic activity. It was observed that MLD5 was effective penetrating the spheroids, disintegrating the periphery, causing pyknosis and significantly reducing invasion.

Discussion. This project highlights the potential of the MLD5 PDC as a promising treatment for TNBC, particularly due to its specifically targeted action.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P267

Enhancing formulation stability of monoclonal antibodies with ionic liquids

Ms Miftahus Saadah

Poster presentations 2: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Miftahus is pursuing a PhD at the University of Sydney, School of Pharmacy. She is also a registered Indonesian pharmacist and a junior lecturer at the Faculty of Pharmacy, Universitas Gadjah Mada. Motivated by a desire to enhance the stability of biologics and minimise the reliance on cold chain logistics for biologics storage and distribution in her country, she intends to develop a stable room temperature formulation for therapeutic proteins, particularly monoclonal antibodies.

Enhancing formulation stability of monoclonal antibodies with ionic liquids

Miftahus Saadah, Veysel Kayser. Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia.

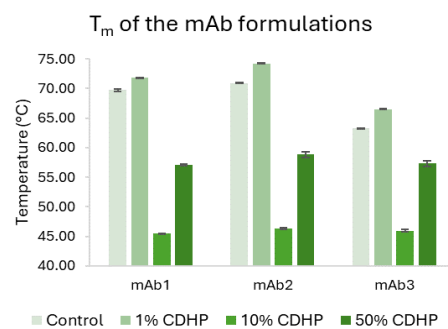
Introduction. Monoclonal antibodies (mAbs) are the most rapidly expanding class of biologics used for therapy and diagnosis. One of the significant challenges in mAb development is protein aggregation since it can lead to undesirable immunogenic reactions. Choline dihydrogen phosphate (CDHP) is a cholinium-based ionic liquid (IL) that has emerged as a promising candidate to produce stable biopharmaceutical formulations. Our group has been at the forefront of using ILs to improve mAb formulation stability. However, no research has been undertaken to evaluate how CDHP affects various mAbs. As a result, we evaluated CDHP's potential for stabilising a wide range of mAbs to prevent aggregation.

Aims. To investigate the impact of CDHP on various mAbs and determine the optimal concentration required to improve antibody stability against aggregation.

Methods. We prepared IgG1 (mAb1), IgG2/4 hybrid (mAb2) and IgG4 (mAb3) formulations with and without CDHP and tested their stability. Using different methods, we measured various characteristics to assess whether the IL approach can be broadly applied to stabilise mAbs.

Results. Adding 1% CDHP significantly increased the melting temperature (T_m) of mAb1 by 2.12 ± 0.15 °C ($P < 0.05$), mAb2 by 3.32 ± 0.05 °C ($P < 0.05$) and mAb3 by 3.30 ± 0.13 °C ($P < 0.05$) compared to formulations without CDHP. Under accelerated studies at high temperatures, the monomer content of all mAbs with 1% CDHP was higher than that of mAbs without CDHP.

Discussion. These T_m improvements are crucial for long-term storage conditions, which are vital to prevent degradation products such as protein aggregation. This is critical for the immunogenicity and efficacy of mAbs, which ultimately affect the therapeutic outcome of the medicine. Higher monomer content suggests higher mAb stability as there are more mAb in monomers rather than dimers or oligomers.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P268

Lipid-drug conjugates within supersaturated SNEDDS for improved oral delivery of Lopinavir

Miss Stephanie Stodulka

Poster presentations 1: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Lipid-drug conjugates within supersaturated SNEDDS for improved oral delivery of Lopinavir

Stephanie Stodulka¹, Clive Prestidge¹, Shane Hickey¹, Timothy Barnes¹, Paul Joyce¹. Clinical and Health Sciences, University of South Australia¹, Adelaide, SA, Australia.

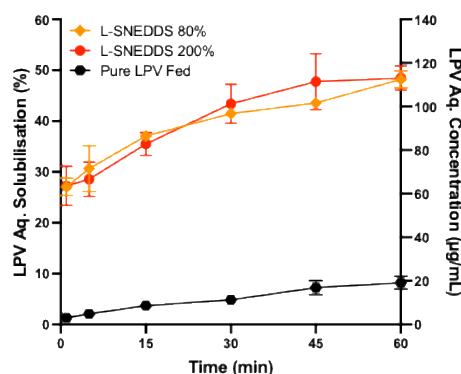
Introduction: Lipid-drug conjugates (LDC) enhance drug loading and overcome high metabolism, which are then loaded within self-nanoemulsifying drug delivery systems (SNEDDS) and supersaturated to enhance solubility and permeability, leading to improved oral bioavailability of Lopinavir.

Aims: To optimise a supersaturated SNEDDS formulation and develop a series of LDCs, characterise and perform *in vitro* release and digestion studies displaying enhanced solubilisation and drug loading.

Methods: A SNEDDS concentrate of lopinavir (200%) was heated at 60 °C for 48 hours to achieve a supersaturated formulation. Drug content was performed using the extraction method. Particle size was performed using Malvern Zetasizer. *In vitro* drug release and digestion were performed using a dissolution apparatus and a pH-stat apparatus. LDC synthesis was performed with esterification and purified with column chromatography.

Results: Supersaturation enhanced Lopinavir's drug solubility 1.8-fold from 129.8 mg/mL at 25 °C to 238.1 mg/mL at 60 °C. Supersaturation at 200% achieved drug loading of 17.7% and encapsulation efficiency of 85.3%. Particle size measured 239 nm. *In vitro* drug release improved dissolution from 5% for pure Lopinavir to 23.8% for supersaturated SNEDDS, and lipolysis enhanced solubilisation from 8.2% for pure Lopinavir to 48.4% for supersaturated SNEDDS (Figure above). The LDC was synthesised with butyric acid and purified with methanol in dichloromethane to create a completed prodrug with a molecular weight of 698.89 g/mol determined via mass spectrometry.

Discussion: Supersaturated SNEDDS increases Lopinavir's solubilisation to improve drug loading and outperforms pure Lopinavir during *in vitro* studies. Supersaturating Lopinavir both increases drug loads while stabilising solubilisation during intestinal digestion under fed conditions (Figure above).



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P269

Pharmacological activation of cannabinoid-sensing G-protein coupled receptor 55 promoted skin wound healing

Miss Nannaphat Suwannakul

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Nannaphat (JaJar) Suwannakul is a 3rd-year medical student studying at Princess Srisavangavadhana College of Medicine, Thailand. Although JaJar has always been passionate about cell biology, her interests flourished when she was introduced to dermatology in her second year of university. That unit covered a wide range of topics; however, the study of tissue scarring interests her the most. She was inspired to find an undiscovered substance that can enhance the wound healing processes of skin cells and began her research later that summer. Beyond dermatology, however, she also believes that integrating research into medicine allows physicians to apply cutting-edge scientific knowledge and enhances patient outcomes. Attending her first in-person science conference, she is thrilled to share her findings and how this discovery could be applied in medical practices.

Pharmacological activation of cannabinoid-sensing G-protein coupled receptor 55 promoted skin wound healing

Nannaphat Suwannakul¹, Pimngeon Chatkul^{1,2}, Pawin Pongkorpsakol^{1,2,*}. International Collaborative Medical Research Laboratory, Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy¹, Laboratory of Epithelial Tight Junction Pathophysiology², Bangkok, Thailand.

Introduction. G-protein coupled receptor 55 (GPR55) has been recognized as a cannabinoid-sensing receptor and is highly expressed in keratinocytes with unknown pharmacological impacts. In addition, cannabis was proposed to improve wound healing with unknown mechanism and its molecular drug target.

Aims. To investigate the effect of O1602 on keratinocyte wound healing and its underlying mechanisms.

Methods. Keratinocyte-like HaCaT cell line was used in this study as an *in vitro* model of keratinocytes to assess skin wound healing. Wound healing assay was performed to scrutinize pharmacological role of O1602 and its underlying mechanisms in vehicle-treated HaCaT cells and in HaCaT cells treated with various inhibitors of related intracellular signalling.

Results. We found that treatment with O1602 in HaCaT cells accelerated the rate of skin wound healing in HaCaT cells. Of note, neither mTOR inhibitor nor intracellular calcium chelator abolished the effect of O1602-induced wound healing. Moreover, the effect of O1602 on skin wound healing was partially suppressed by cotreatment with inhibitors of ERK, PKA, β -arrestin and PLC. Of particular importance, the effect of O1602-induced skin wound healing was fully suppressed by cotreatment with SIRT-1 inhibitor.

Discussion. Taken together, pharmacological activation of GPR55 by O1602 can be useful in promoting skin wound healing.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P270

Enhancing abiraterone pharmacokinetics with lipid-based formulations: addressing solubility and food-effect challenges

Mr Ali Taheri

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Enhancing abiraterone pharmacokinetics with lipid-based formulations: addressing solubility and food-effect challenges

Ali Taheri, Ruba Almasri, Anthony Wignall, Kristen E Bremmell, Paul Joyce, Clive A Prestidge. Centre for Pharmaceutical Innovation, UniSA, Adelaide, SA 5000, Australia

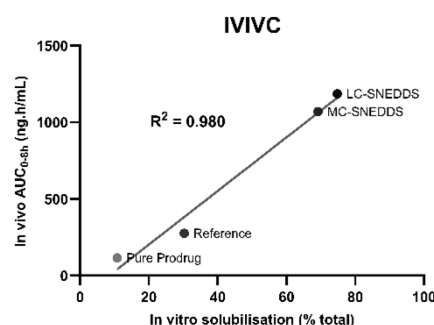
Introduction. Abiraterone acetate, a prodrug of abiraterone, is an effective anti-androgen for treating metastatic prostate cancer. However, its poor aqueous solubility restricts oral bioavailability to under 10% in fasted conditions. Additionally, its pharmacokinetics are highly variable and significantly influenced by a positive food effect, potentially impacting treatment safety and efficacy.

Aims. To develop a formulation strategy that enhances the fasted bioavailability of abiraterone and reduces its food effects by delivering the drug in a predissolved state.

Methods. Medium and long-chain self-nanoemulsifying drug delivery systems (MC-SNEDDS and LC-SNEDDS) were formulated with abiraterone acetate at 80% of its equilibrium solubility. The *in vitro* solubilisation performance was evaluated using a two-step, one-compartment gastrointestinal lipolysis model. *In vivo* pharmacokinetics were characterised in rats under fasted conditions and in pigs under both fasted and fed conditions.

Results. The SNEDDS formulations increased *in vitro* solubilisation by over 6-fold compared to pure abiraterone acetate and over 2-fold compared to the reference. In rats, both MC-SNEDDS and LC-SNEDDS, along with their enteric-coated (EC) forms, demonstrated enhanced bioavailability, with EC-LC-SNEDDS providing the highest performance, showing a 7.3-fold increase in abiraterone exposure compared to the reference. In pigs, EC-LC-SNEDDS improved fasted bioavailability and reduced food effects, with a fed-to-fasted AUC ratio of 108%, compared to 334% for the reference.

Discussion. Our findings suggest that the developed lipid-based formulations have the potential to overcome abiraterone's solubility-limited absorption and high PK variability, potentially offering improved outcomes for patients.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P271

Mechanistic insights into the zinc-sensing G-protein coupled receptor 39-promoted skin wound healing

Mr Ungkarit Wachapathana

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Ungkarit Wachapathana is a third-year medical student at Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy in Bangkok, Thailand. He is currently conducting research at the International Collaborative Medical Research Laboratory, focusing on pharmacological interactions of compounds with keratinocytes to develop potential innovative therapies for skin disorders.

Mechanistic insights into the zinc-sensing G-protein coupled receptor 39-promoted skin wound healing

Ungkarit Wachapathana¹, Pimngeon Chatkul^{1,2}, Pawin Pongkorsakol^{1,2,*}. International Collaborative Medical Research Laboratory, Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy¹, Laboratory of Epithelial Tight Junction Pathophysiology², Bangkok, Thailand.

Introduction. G-protein coupled receptor 39 (GPR39) has been recognized as a zinc-sensing receptor and is highly expressed in keratinocytes with unknown pharmacological impacts. GPR39 knockout in sebaceous gland contributed to delayed skin wound healing but its role in isolated keratinocytes is also unexplored. TC-G 1008 was reported as a specific agonist of GPR39 that can be used to mimic the pharmacological activity of GPR39 activation.

Aims. To investigate the effect of TC-G 1008 on keratinocyte wound healing and its underlying mechanisms.

Methods. Keratinocyte-like HaCaT cell line was used as an in vitro model to assess skin wound healing. Wound healing assay was performed to elucidate the pharmacological role of TC-G 1008 in vehicle-treated HaCaT cells and in HaCaT cells treated with various inhibitors of related intracellular signalling.

Results. We found that treatment with TC-G 1008 in HaCaT cells promoted the rate of skin wound healing measured by the distance of wound closure area. In addition, neither SIRT-1 inhibitor nor PLC inhibitor abolished the effect of TC-G 1008-induced wound healing. Moreover, mTOR inhibitor did not, however, interfere with the effect of TC-G 1008 on skin wound healing. Interestingly, the effect of TC-G 1008-induced skin wound healing could be fully interrupted by cotreatment with inhibitors of either ERK or PKA. Furthermore, chelating intracellular calcium by BAPTA also suppressed the effect of TC-G 1008 on skin wound healing as well.

Discussion. Collectively, pharmacological activation of GPR39 by TC-G 1008 in keratinocytes promoted skin wound healing, at least in part, via intracellular calcium-, PKA-, and ERK-dependent mechanisms. This study provides the proof-of-concept that pharmacological agonism of GPR39 in keratinocytes can enhance skin wound healing.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P272

Encapsulation of Hibiscus sabdariffa extracts in alginate-chitosan beads to preserve antioxidant properties

Dr Thilini Thrimawithana

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Thilini is a dedicated academic with a multifaceted career as a pharmacist, teacher, and researcher. Her research activities focus on improving chronic disease management among culturally and linguistically diverse (CALD) populations and optimising the quality use of complementary medicines. Her research aims to identify strategies to prevent and manage cardiometabolic diseases. Thilini employs a variety of methodologies, including qualitative interviews and intervention trials, to develop and implement strategies that enhance the quality of care provided to people from CALD backgrounds. Thilini is also interested in exploring innovative approaches to improving the quality use of complementary medicines, striving to bridge the gap between traditional and modern medicine. Her research endeavours focus on enhancing the understanding and application of complementary medicines through dosage form design, aiming to ensure their safe and effective integration into healthcare practices.

Encapsulation of Hibiscus sabdariffa extracts in alginate-chitosan beads to preserve antioxidant properties

Manisha Singh¹, [Thilini Thrimawithana](#)¹, Ravi Shukla¹ and Benu Adhikari¹ STEM College¹, RMIT University, Melbourne, VIC3083, Australia.

Introduction. *Hibiscus sabdariffa* extracts have been extensively studied for their role in the treatment of cardiometabolic diseases such as diabetes and hyperlipidemia. Although clinical trials of these extracts are promising¹, polyphenols in these extracts are known to degrade rapidly during storage and digestion.

Aims. This study aimed to develop a polyphenolic formulation using the complex coacervation method to improve stability and bioavailability of polyphenols extracted from *Hibiscus sabdariffa*.

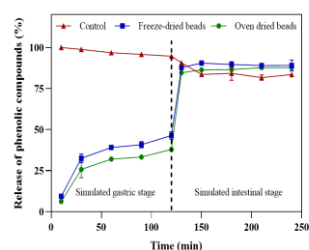
Methods. Sodium alginate mixtures with phenolic extract were prepared and this mixture was added dropwise to a CaCl₂ solution containing chitosan. The beads were on ice cold CaCl₂ solution for hardening. The beads were then dried (freeze drier and oven) and characterised to determine encapsulation efficiency, surface morphology, *in vitro* release, and stability.

Results. The combination of 3% w/v alginate, 0.2% w/v chitosan and 1% w/v extract provided highest encapsulation efficiency with a total polyphenol content of 92%. The alginate-chitosan matrix of the beads restricted the release of phenolic compounds into simulated gastric fluids (fig 1) and the beads improved the stability of the polyphenols.

Discussion. Freeze-dried beads provided higher rate of release, most likely due to the porous network of polymer formed by the freeze drying process, allowing for easier diffusion of encapsulated material from the matrix. The beads released the encapsulated polyphenols in intestinal fluids, due to the swelling and disintegration of alginate under neutral pH². In addition, polyphenols that were not encapsulated degraded rapidly in the media, with only 80% of the content remaining at 120 minutes of simulated digestion studies. This shows the stability enhancing properties of the polymer matrix.

¹Bule M et al (2020) Food Res Int 130: 108980

²Corstens MN et al (2017) J Funct Foods 34: 319-328.



kept
in

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P273

Cell cycle variation in drug-tolerant persister cells in non-small cell lung cancer

Miss Mo Zhou

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Zhou Mo is a first-year Ph.D. student at the Graduate School of Pharmaceutical Sciences, Osaka University, Japan, holding a bachelor's degree from Shenyang Pharmaceutical University, China. Zhou's research focuses on cancer drug tolerance and resistance, specifically investigating the diversity of drug-tolerant persisters (DTPs) in non-small cell lung cancer treated with the third-generation tyrosine kinase inhibitor Osimertinib. The goal is to elucidate the molecular mechanisms underlying drug-tolerant persister cells and propose therapeutic strategies to prevent drug resistance.

Cell cycle variation in drug-tolerant persister cells in non-small cell lung cancer.

Mo ZHOU¹, Yuya HAGA^{1,2}, Akihide NISHIMURA¹, Suzuno TANAHASHI², Kazuma HIGASHISAKA^{1,2,3}, Yasuo TSUTSUMI^{1,2,4,5}. Grad. Sch. Pharm. Sci., Osaka Univ.¹, Osaka, Japan; Sch. Pharm. Sci., Osaka Univ.², Osaka, Japan; IACS, Osaka Univ.³, Osaka, Japan; MEI Ctr., Osaka Univ.⁴, Osaka, Japan; OTRI., Osaka Univ.⁵, Osaka, Japan

Introduction. Epidermal growth factor receptor (EGFR) mutation is one of the most common oncogenic drivers in non-small-cell lung cancer (NSCLC) and EGFR tyrosine kinase inhibitors (EGFR-TKIs) have been approved as a first-line therapy. However, the inevitable development of drug resistance after months or years of treatment with EGFR-TKIs remains a significant concern in NSCLC. In this case, drug-tolerant persister cells (DTPs), which acquire tolerance in a mutation-independent manner after short-term drug exposure, are being investigated as a new target. It has been reported that, most DTPs remain arrested early in the course of drug treatment. However, understanding the variations in cell cycle dynamics during both DTPs formation and subsequent stages remains limited.

Aims. We aim to clarify the survival mechanisms of DTPs by exploring the variation in cell cycle during and after the DTPs formation.

Methods. The Fucci probe was induced into the EGFR-mutant non-small cell lung cancer cell line PC9, generating PC9-Fucci to enable the observation of dynamic cell cycle variation during and after the DTPs formation process. DTPs were established by treating PC9-Fucci with the third generation of EGFR-TKI Osimertinib at the concentration of 60 nM and 600 nM for 9 days. ImageJ and CellProfiler were used for quantitatively analysed the obtained fluorescence images.

Results. During the DTPs formation process, the cell counts gradually decreased, with most cells emitting red fluorescence, indicating cell cycle arrest in the G1 phase. Following DTPs formation, cells were cultured in both drug-containing and drug-free mediums for further observation. As a result, some cells regrew in drug-free medium at various time points, demonstrating the reversibility of DTPs after drug removal. On the other hand, some cells regained proliferative capability in drug-containing medium. In summary, these results illustrated the dynamic variations in the cell cycle of DTPs.

Discussion. For furtherly confirming the diversity in cell cycle of DTP formation, synchronous culture will be conducted. Besides, the detailed analysis of cell cycle variation of factors related to the diversity of DTPs will be analyzed.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P274

Australian polypharmacy trends by sex: A descriptive population-based study (2013-2023)

Ms Georgie Lee

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Georgie Lee is a PhD candidate and Research Officer at the University of Western Australia, specialising in the quality use of medicines. Her research focuses on pharmacoepidemiology, with particular attention to potentially suboptimal medication regimens. Using dispensing claims data from the Australian Pharmaceutical Benefits Scheme (PBS), Georgie's work aims to improve methods for defining and measuring exposure to polypharmacy, as well as to describe the patterns and implications of polypharmacy within the Australian population. Her current research is focused on refining indicators of suboptimal medicine use and understanding the longitudinal trajectories of medicine exposure over time.

Australian polypharmacy trends by sex: A descriptive population-based study (2013-2023)

Georgie Lee¹, Christopher Etherton-Beer², Julie A Pasco³, Osvaldo P. Almeida⁴, Erin Kelty⁵, Frank Sanfilippo⁵, Amy Page¹. Sch. Allied Health, UWA¹, Perth, WA, Aus; WACHA, UWA², Perth, WA, Aus; Sch. Med, Deakin Univ³, Geelong, VIC, Aus; Med Sch., UWA⁴, Perth, WA, Aus; Sch. Pop & Global Health, UWA⁵, Perth, Aus.

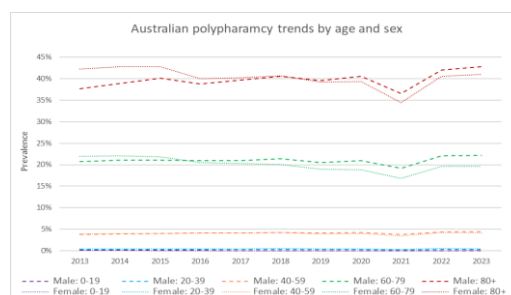
Introduction. Polypharmacy, the concurrent use of multiple medicines, is often considered an indicator of potentially suboptimal regimens. Trends research shows varying rates of growth and decline in polypharmacy across age groups; however, less is known about sex-specific patterns.

Aims. To describe polypharmacy trends stratified by sex and age in the Australian population.

Methods. We estimated annual polypharmacy prevalence using a nationally representative 10% random sample of Australian patients eligible for medicines subsidised by the Pharmaceutical Benefits Scheme (PBS). PBS-listed medicines dispensed between January 1, 2013 – December 31, 2023, were considered. Polypharmacy was defined as receiving ≥ 5 regularly dispensed medicines. Australian estimated residential population was used as the denominator to calculate polypharmacy prevalence by year, stratified by age and sex. Tests of proportions measured group differences.

Results. Between 2013 and 2023, Australian polypharmacy prevalence rose from 6.1% to 6.9%. In 2013, rates were higher among females, relative to males in middle age (3.9% vs 3.8%, $p < .001$), early older (22% vs 20.7%, $p < .001$) and later older age (42.8% vs 41%, $p < .001$). More rapid increases among males saw their prevalence surpass that of their female counterparts by 2023, among adults in middle (4.5% vs 4.1%, $p < .001$), early older (22.2% vs 19.6%, $p < .001$) and later older age (42.8% vs 41%, $p < .001$). The 2021 rate decline was present across age and sex strata.

Discussion. Over the last decade, disproportionate polypharmacy growth was observed among males. While females had higher rates initially, by 2023, prevalence was greater among males from middle age and up. The prevalence dip in 2021 was consistent across the population and was likely pandemic related. Further investigation into the medicines implicated in sex-specific trends may be beneficial for future deprescribing initiatives.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P275

Sedative and anticholinergic medication use in older people with dementia in Australia.

Mr Edward Chun Yin Lau

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Sedative and anticholinergic medication use in older people with dementia in Australia.

Edward C.Y. Lau¹, Sarah Hilmer², Kenji Fujita², Christine Lu^{1,2}, Yun-Hee Jeon³, Edwin C.K. Tan¹. Sydney Pharmacy School, The University of Sydney¹, Camperdown, NSW, Australia; Kolling Institute, The University of Sydney², St. Leonards, NSW, Australia. Susan Wakil School of Nursing and Midwifery, The University of Sydney³, Camperdown, NSW, Australia.

Introduction. Sedative and anticholinergic medications have been shown to be associated with poorer outcomes, such as worsening cognitive function, in older people. This is of particular concern in older people living with dementia. However, national estimates of prevalence of sedative and anticholinergic medication use in people living with dementia, and the sociodemographic factors associated with their use, are currently lacking in Australia.

Aims. To estimate the prevalence and risk factors for sedatives and anticholinergics use in Australians with dementia.

Methods. This study utilised linked 2021 Census and Pharmaceutical Benefits Scheme (PBS) data. People aged 65 or above in 2021 with linked PBS and Census data were included in this study. Dementia was defined as self-reported dementia diagnosis in 2021 and/or having at least one dispensing of an antidementia drug between 2016 and 2021. Main outcomes were sedative and anticholinergic medication use defined using (i) the Drug-Burden Index (DBI) (dispensing of at least one DBI drug), and (ii) the Anticholinergic Cognitive Burden Scale (ACB) (ACB score ≥ 3). Prevalence was calculated by 5-year age strata. Self-reported comorbidities and sociodemographic factors were included in binary logistic regression models to explore their association with these outcomes.

Results. Of the 177,809 people with dementia included, over half of them were using at least one DBI drug. Highest use was found in those aged 65-69, with two-thirds using at least one DBI drug. Similarly, anticholinergic burden was highest in those aged 65-69 (19%). Prevalence of DBI drug use and anticholinergic burden declined with increasing age. Factors associated with DBI drug use and high anticholinergic burden were largely consistent; those who lived in non-private dwellings and required assistance with core activities were at increased risk of DBI drug use and high anticholinergic burden, while older age, higher socioeconomic status and higher education level were associated with lower risk. Antidementia medication use was associated with lower risk of high anticholinergic burden.

Discussion. Over half of people with dementia were exposed to sedative and anticholinergic medications, with risk being higher in certain sociodemographic groups. Regular review and ongoing monitoring are required to ensure appropriate use of these drugs in this vulnerable population.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P276

Antidepressants for pain in older adults: a systematic review with meta-analysis

Dr Sujita Narayan

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr Sujita Narayan is a Research Fellow at the Institute of Musculoskeletal Health, Faculty of Medicine and Health, University of Sydney. She is an early career researcher and her main research interests are patient safety and quality use of medicines in older people. Sujita has gained experience in conducting pharmacoepidemiological research examining the quality use of medicines in older adults. Her previous work explored the trends in the utilisation of preventive and potentially inappropriate medicines in the older population, factors associated with adverse health outcomes and reducing unnecessary or harmful medicines as older adults approach end-of-life. Sujita's current work focuses on the utilisation, efficacy and safety of commonly prescribed medicines to manage pain conditions in older adults. She's particularly interested in the use of antidepressants and opioids, and the evidence surrounding their use in people aged 65 years and older.

Antidepressants for pain in older adults: a systematic review with meta-analysis

Sujita W Narayan^{1,2}, Vasi Naganathan^{3,4}, Lisa Vizza¹, Martin Underwood⁵, Rowena Ivers⁶, Andrew McLachlan², Linyi Zhou¹, Ramnik Singh¹, Shunyu Tao¹, Xiao Xi¹, Christina Abdel Shaheed¹

The Univ of Sydney and Sydney Local Health District¹, Institute for Musculoskeletal Health, Sydney, NSW, Australia. The Univ of Sydney², Sydney Pharm School, Faculty of Medicine and Health, Sydney, NSW, Australia. Centre for Education and Research on Ageing³, Dept of Geriatric Medicine, Concord Repatriation General Hosp, Concord, New South Wales, Australia. Concord Clinical Sch, Faculty of Medicine and Health, Univ of Sydney⁴, Sydney, New South Wales, Australia. Warwick Clinical Trials Unit, Warwick Medical Sch, Univ of Warwick⁵, Coventry, CV4 7AL, UK. Graduate Sch of Medicine, Faculty of Science, Medicine and Health, Univ of Wollongong⁶, Wollongong, NSW, Australia.

Introduction: In many countries, pain is the most common indication for use of antidepressants in older adults.

Aim: To review the evidence from randomised controlled trials on the efficacy and safety of antidepressants, compared to all alternatives for pain in older adults (aged ≥ 65 years, including mean/median age ≥ 65 years).

Methods: Trials published from inception to 1 February 2024, were retrieved through a comprehensive search of 12 databases: MEDLINE, Embase, CINAHL, PsycINFO, Cochrane Library, International Clinical Trials Registry Platform, Global Health, African Journals Online, Latin American and Caribbean Health Sciences Literature, Index Medicus for the Eastern Mediterranean Region, South East Asia Journal of Medical Sciences, and the China National Knowledge Infrastructure.

Results: Fifteen studies (N=1,369 participants) met our criteria for inclusion. The most frequently studied antidepressants were duloxetine and amitriptyline (6/15 studies each) followed by nortriptyline, imipramine, and escitalopram (one trial each). Pain related to knee osteoarthritis was the most studied (6/15 studies). For knee osteoarthritis, antidepressants did not provide a statistically significant effect for the immediate (0 to 2 weeks) term (-5.6, 95% CI: -11.5 to 0.3) but duloxetine provided a statistically significant, albeit a very small effect in the intermediate (≥ 6 weeks and ≤ 12 months) term (-9.1, 95% CI: -11.8 to -6.4). Almost half (7/15) of the studies reported

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



increased withdrawal of participants in the antidepressant treatment group versus the comparator group due to adverse events.

Discussion: For most chronic painful conditions in older adults, the benefits and harms of antidepressant medicines are unclear. This evidence is predominantly from trials with sample sizes of <100, have disclosed industry ties, and classified as having unclear or high risk of bias. (PROSPERO ID: CRD42023408204)

P277

STOPPFrail medication use in aged care: comparison across Asia, Oceania and Europe

Ms Shin Liau

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Shin is a pharmacist and research fellow at the Centre for Medicine Use and Safety (CMUS) at Monash University. Her research focuses on optimising medication management for frail older populations, including community-dwelling individuals with dementia and aged care residents. Driven by a passion for enhancing the quality use of medicines, she aims to advance ageing research by reducing unnecessary and potentially inappropriate medication use, thereby mitigating medication-related harms in older Australians. In addition to her research, Shin serves as Chair of the Australian Association of Gerontology (AAG) Victorian Student and Early Career Group and as a member of the Australian Deprescribing Network (ADeN) committee.

STOPPFrail medication use in aged care: comparison across Asia, Oceania and Europe

Shin J Liau¹, Meng Zhao², Shota Hamada³, Marta Gutiérrez-Valencia⁴, Agathe D Jadcak⁵, Li Li², Nicolás Martínez-Velilla⁴, Nobuo Sakata³, Peipei Fu², Renuka Visvanathan⁵, Samanta Lalic¹, Victoria Roncal-Belzunce⁴, J Simon Bell¹. Centre for Medicine Use and Safety, Monash Univ¹, Melbourne, VIC, Australia; Cheeloo College of Medicine, Shandong Unive², Jinan, SD, China; Institute of Medicine, Univ of Tsukuba³, Tsukuba, Japan; Navarre Institute for Health Research (IdiSNA)⁴, Pamplona, NA, Spain; Adelaide Medical School, Univ of Adelaide⁵, Adelaide, SA, Australia.

Introduction. Existing studies that have applied the Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail) criteria predominantly focus on hospital and palliative care settings, with few conducted in residential aged care services.

Aims. To compare the prevalence of STOPPFrail medications stratified by frailty status among Australian, Chinese, Japanese, and Spanish residents living in residential aged care services.

Methods. Secondary cross-sectional analyses of data across four cohort studies (n=1,142; 31 nursing homes). Medication data were extracted from resident records. Frailty was assessed using the FRAIL-NH scale (non-frail 0-2; frail 3-6; most-frail 7-14). Chi-square tests and prevalence ratios (PRs) were used to compare STOPPFrail medication use across cohorts.

Results. In total, 85% of non-frail, 96% of frail, and 91% of most-frail residents received ≥ 1 STOPPFrail medication. Overall, the most prevalent STOPPFrail medications were antihypertensives (53-73%), vitamin D (0-53%), statins (11-39%), aspirin (14-26%), proton pump inhibitors (2-32%), and diabetes medications (12-24%). Overall use of antihypertensives (PR 1.15 [95%CI, 1.06–1.25]), statins (PR 1.78 [95%CI, 1.45–2.18]), aspirin (PR 1.31 [95%CI, 1.04–1.64]), and diabetes medications (PR 1.3 [95% CI, 1.00–1.72]) had a higher prevalence among non-frail and frail residents compared to most-frail residents. Prevalence of antihypertensives was higher with increasing frailty in China and Japan, but lower with increasing frailty in

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Australia. Diabetes medication use was less prevalent with increasing frailty in China and Spain, but was similar across frailty groups in Australia and Japan.

Discussion. There were overall and frailty-specific variations in prevalence of different STOPPFrail medications across cohorts. This may reflect differences in prescribing cultures, application of clinical practice guidelines in the nursing home setting, and clinician or resident attitudes towards deprescribing.

P278

Clinical outcomes associated with drug-related hospitalisations in people with dementia

Dr Mohammed Salahudeen

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Clinical outcomes associated with drug-related hospitalisations in people with dementia

Anum S Zaidi¹, Gregory M Peterson¹, Colin M Curtain¹, Mohammed S Salahudeen¹. School of Pharmacy and Pharmacology, University of Tasmania¹, Hobart, TAS, Australia.

Introduction. The annual incidence of adverse drug reaction (ADR)-related hospitalisations among people with dementia increased by nearly 20% over 10 years. ADRs can result in significant negative consequences, such as prolonged hospital stays, increased morbidity and mortality rates, and financial burdens on patients and the healthcare system.

Aims. To determine the clinical impact of ADRs in patients with dementia, including length of stay, all-cause and ADR-related rehospitalisations, and mortality.

Methods. This case-control, propensity score-matched study utilised administrative data of people with dementia admitted to major public hospitals in Tasmania, Australia, from July 2010 to December 2019. ADR-related hospitalisations were identified using diagnosis-based and external cause codes.

Results. Two equal-sized groups of cases and controls (n=1,304) were produced using propensity score matching. The length of hospital stay was significantly greater for people with an ADR index admission compared to non-ADR index admission (median [IQR]: 9 [4-18] vs. 6 [2-12]; p < 0.001). In-hospital mortality and combined in-hospital and post-hospital mortality within 30, 60, and 90 days were higher for people with dementia whose index admission was ADR-related (in-hospital: HR 1.40, 95% CI 1.11-1.77, p < 0.001; 30 days: HR 1.25, 95% CI 1.05-1.49, p < 0.001; 60 days: HR 1.27, 95% CI 1.08-1.49, p < 0.001; 90 days: HR 1.29, 95% CI 1.10-1.50, p < 0.001). Subsequent ADR admission within 30, 60, and 90 days of index discharge was 9 to 10 times greater for people with dementia. Acute renal failure was the most common ADR at both index and subsequent admissions.

Discussion. These results emphasise the importance of safe prescribing and vigilant monitoring in individuals with dementia to mitigate adverse outcomes associated with ADRs.

Zaidi AS, et al. (2024) *Expert Rev Clin Pharmacol*. 17(1):73-78.

Zaidi AS, et al. (2024) *Drug Saf*. doi: 10.1080/17512433.2023.2294007

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P279

Indonesian medication adherence instruments' validity and reliability for diabetes and hypertension: review

Dr Riana Rahmawati

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Riana Rahmawati, PhD, is a lecturer at the Faculty of Medicine, Universitas Islam Indonesia, in Yogyakarta, Indonesia. She earned her medical degree and a master's degree in Drug Management and Policy from Universitas Gadjah Mada and completed her PhD in Pharmacy at the University of Technology Sydney. Her research focuses on pharmacoepidemiology, the use of medications and herbal remedies in patients and communities, and pharmacology education, with numerous publications in reputable journals and books. She is actively involved in efforts to improve medication literacy, medication adherence, and hypertension management in Indonesia.

Indonesian medication adherence instruments' validity and reliability for diabetes and hypertension: review

Riana Rahmawati¹, Dyah Aryani Perwitasari^{1,2}. Pharmacology Department, Faculty of Medicine Universitas Islam Indonesia¹, Sleman, Yogyakarta, Indonesia; Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Ahmad Dahlan², Yogyakarta, Indonesia

Introduction. A valid and reliable instrument to measure medication adherence in patients with type 2 diabetes mellitus (T2DM) and hypertension is important both in routine clinical care and research settings.

Aims. This review aims to identify and evaluate studies that report the validity and reliability of medication adherence instruments for patients with T2DM and hypertension in Indonesia.

Methods. A comprehensive search was conducted using PubMed, EBSCO, ScienceDirect, Google Scholar, and the Digital Reference Garba (GARUDA). We included articles published in English or Indonesian in the last ten years, recruiting patients with hypertension and/or T2DM, and assessing the validity and reliability of Indonesian version of medication adherence instruments. Peer-reviewed articles as well as grey literature (e.g., theses, conference proceedings) were included in this review. The methodological quality of the studies was assessed using the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist.

Results. Six studies met the inclusion criteria, with 3 instruments for T2DM patients and 3 for hypertension. The Medication Adherence Rating Scale and Hill Bone Compliance Scales were used for both T2DM and hypertension patients. The Indonesian versions of medication adherence questionnaires that have demonstrated good validity and reliability include the Diabetes Self-Management Instrument and Hill Bone Compliance Scale for T2DM patients, as well as the Medication Adherence Self-Efficacy Scale Revised (MASES-R) and Adherence Starts with Knowledge for hypertension patients.

Discussion. This review highlights the availability of valid and reliable medication adherence instruments for patients with T2DM and hypertension in Indonesia. These instruments are crucial for clinical practice and research, facilitating the detection and management of adherence problems and thereby enhancing health outcomes. The findings underscore the need for continued efforts to validate and refine these instruments to ensure their effectiveness in diverse populations.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P280

Medication use among the elderly: Survey from an urban area in Indonesia

Dr Riana Rahmawati

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Riana Rahmawati, PhD, is a lecturer at the Faculty of Medicine, Universitas Islam Indonesia, in Yogyakarta, Indonesia. She earned her medical degree and a master's degree in Drug Management and Policy from Universitas Gadjah Mada and completed her PhD in Pharmacy at the University of Technology Sydney. Her research focuses on pharmacoepidemiology, the use of medications and herbal remedies in patients and communities, and pharmacology education, with numerous publications in reputable journals and books. She is actively involved in efforts to improve medication literacy, medication adherence, and hypertension management in Indonesia.

Medication use among the elderly: Survey from an urban area in Indonesia

Riana Rahmawati¹, Pharmacology Department, Faculty of Medicine Universitas Islam Indonesia¹, Sleman, Yogyakarta, Indonesia.

Introduction. Elderly individuals are more prone to developing comorbidities, which can significantly impact their health and overall well-being. Understanding the prevalence and management of these comorbidities is crucial for improving healthcare services for older populations.

Aims. This study aimed to examine and present data related to comorbidities, medication used, and access to healthcare services among the elderly within an urban community. The data will provide valuable insights into the healthcare needs and challenges faced by older individuals in this setting.

Methods. A survey was conducted in an urban sub-district in Yogyakarta, Indonesia, in February 2024, involving people aged 60 years or older who were resident of the district and willing to participate. Descriptive analysis and chi-square test were applied.

Results. Data were compiled from 1,147 participants, with the majority being female (54.1%). The average age was 67.9 years (SD 6.5, range 60-98). More than half of the respondents had a low education level (n=631, 55%). The prevalence rates were as follows: hypertension 37.8%, hypercholesterolemia 19.6%, diabetes mellitus 13.6%, uric acid 12.6%, heart disease 7.4%, rheumatoid arthritis 3.7%, tuberculosis 0.7%, and mental disorders 0.9%. Eighty-eight respondents lived alone (7.2%). Loneliness was reported by 370 individuals, with 27.8% experiencing it often. Most elderly accessed primary healthcare facilities (61.8%), followed by hospitals (16.6%) and private physicians (11.5%). Routine medications were received by 88.5% for diabetes, 78.6% for hypertension, and 66.2% for hypercholesterolemia. Female respondents and those with social insurance were more likely to take routine medication ($p=0.013$). No significant association was found between education level, type of work, or income and taking routine medication.

Discussion. This study highlights a high prevalence of non-communicable diseases among the elderly. Medications are generally accessible, especially for females and those with social insurance. These findings can inform healthcare policies to improve health outcomes for older adults in urban communities.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P281

Anabasine in urine: distinguishing conventional cigarette use at individual and population level

Miss Min-Tz Weng

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Min-Tz Weng is a second-year PhD student at the School of Pharmacy, The University of Queensland. She holds a Bachelor's in Pharmacy and a Master of Pharmaceutical Industry Practice. Her PhD research focuses on nicotine metabolism during pregnancy.

Anabasine in urine: distinguishing conventional cigarette use at individual and population level

Min-Tz Weng¹, Qiuda Zheng², Shakti Shrestha¹, Yao Deng¹, Coral E Gartner³, Wenqing Fan¹, Phong K Thai², Kathryn J Steadman¹. Sch of Pharm, Univ of Queensland¹, Brisbane, QLD, Australia; Queensland Alliance for Env Health Sci, Univ of Queensland², Brisbane, Australia; Sch of Pub Health, Univ of Queensland³, Brisbane, QLD, Australia.

Introduction. Minor tobacco alkaloids, including anatabine and anabasine, could serve as valuable biomarkers for distinguishing between conventional cigarettes (CCs) and pharmaceutical grade nicotine-containing products. However, as certain nicotine vaping products (NVPs) also incorporate minor tobacco alkaloids, developing an improved calculation for their presence becomes essential in effectively discerning between the two groups. Furthermore, there is no available data for the excretion factor of anabasine to distinguish people who smoke CCs from people who use NVPs at the population level.

Aims. This study aimed to explore the optimal cut-off value for minor alkaloids and the excretion factor of anabasine.

Methods. A total of 74 participants were enrolled: 22 people who smoked CCs, 22 people who used NVPs, and 30 people who had never smoked or vaped. Quantity of CC and NVP use were documented over a 3-day period. 24-hour urine samples were collected on Day 3 and analysed using LC-MS/MS to quantify the nicotine, cotinine (COT), 3-hydroxycotinine (3HC), anabasine and anatabine. Receiver operating characteristic (ROC) analysis was used for a cut-off value of minor tobacco alkaloids. Excretion factors among 22 people who smoked CCs were calculated using a published equation with slight modifications (Zheng et al. 2023).

Results. There was a significant correlation ($r = 0.89$, $P < 0.001$) between the number of cigarettes consumed and the level of nicotine metabolites detected, while there was little correlation ($r = 0.058$, $P = 0.80$) for individuals who use NVPs. Using the anabasine to COT+3HC ratio produced sensitivity and specificity values of 81.82% and 90.91% in the ROC analysis. The average excretion factor of anabasine was calculated.

Discussion. The anabasine to COT+3HC ratio has potential for use in distinguishing between people who smoke CCs and people who use NVPs at an individual level. The excretion factor for anabasine will be used in predictive modelling for population-level nicotine product use.

Zheng Q et al (2023) Environ Sci Technol 57(21):7958-7965.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P282

Sodium-glucose co-transporter-2 inhibitors and non-genitourinary infections in diabetes: systematic review and meta-analyses

Mrs Maria Jose Alfonso Arvez

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Maria José Alfonso Arvez is a Paraguayan pharmacist and Ph.D. candidate at Monash University, Australia, specializing in pharmacoepidemiology and health economics. She has extensive experience in pharmacovigilance and public health, having served in leadership positions at Paraguay's Ministry of Health and currently working as an international consultant for the Pan American Health Organization.

Sodium-glucose co-transporter-2 inhibitors and non-genitourinary infections in diabetes: systematic review and meta-analyses.

Maria Jose Alfonso Arvez¹, George SQ Tan¹, Miriam T. Y. Leung¹, Zanfina Ademi¹, PhD, J. Simon Bell, PhD¹. Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Melbourne, VIC, Australia

Introduction. People with diabetes are at increased risk of infection and mortality. Emerging evidence suggests sodium-glucose co-transporter 2 (SGLT2) inhibitors have pleiotropic effects that may protect against certain infections.

Aims. We systematically reviewed real-world evidence on the association between SGLT2 inhibitors and non-genitourinary infections among adults with type 2 diabetes.

Methods. Medline, Embase, Scopus, and Google Scholar were searched from January 1, 2012, to March 18, 2024 for observational studies in adults with type 2 diabetes published in English. The exposure was SGLT2 inhibitors and comparators were non-users or users of other glucose-lowering medications. Studies reporting outcome estimates for specific non-genitourinary infections were included. Screening, data extraction and quality assessment (ROBINS-I) were conducted independently by two investigators. The study was prospectively registered with PROSPERO (CRD42023492265).

Results. From 6827 records, 32 studies were included in qualitative synthesis and 14 in meta-analyses. There was no association with COVID-19-related mortality in seven studies (OR 0.91; 95% CI: 0.57–1.46) or COVID-19-related hospitalisation in three studies (OR 0.90; 95% CI: 0.67–1.20). There was reduced pneumonia in three studies (HR 0.61; 95% CI: 0.57–0.66) and reduced pneumonia-related mortality in two studies (HR 0.49; 95% CI: 0.35–0.67). There was reduced sepsis in three studies (HR 0.45; 95% CI: 0.30–0.68). Overall, there was no evidence of publication bias but serious risk of bias in 17 studies.

Discussion. Real-world data suggest SGLT2 inhibitors are associated with a lower risk of pneumonia, pneumonia-related mortality and sepsis. Given the high burden of infection in adults with type 2 diabetes, the association between SGLT2 inhibitors and these and other infection-related outcomes deserves further research.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P283

Priorities for medication management information resources for people with dementia and carers

Dr Mouna Sawan

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Mouna is an early career NHMRC Dementia Centre Research Collaboration (DCRC) Research Fellow in medication management and dementia at the School of Pharmacy, Faculty of Medicine and Health, University of Sydney.

Mouna has focused her research on a national and global health challenge, reducing the burden of medication-related harm in people with dementia. Medication-related harm can result in negative outcomes, high rates of hospitalisation and mortality, particularly in people with dementia. Her research program is focused on working in partnership with people with dementia, carers, health care professionals, national consumer organisations, and relevant industries to build an evidence base and develop innovative and sustainable interventions to improve health service delivery and outcomes.

Priorities for medication management information resources for people with dementia and carers through community action

Karen Watson¹, Jacqueline Wesson², Amanda Cross³, Natali Jokanovic⁴, Joanne Lo⁵, Alexander Clough⁵, Mouna Sawan⁵
Sydney Nursing School, Univ. of Sydney¹; School of Health Sciences, Univ. of Sydney², Centre for Medicine Use and Safety, Monash Univ.³, Parkville, Vic; The Alfred Hospital and Monash Univ⁴, Melbourne, Vic, NSW, Australia; Sydney Pharmacy School, Univ. of Sydney⁵, Camperdown, NSW

Introduction. People with dementia (PWD) and their carers face several challenges managing medications safely. As information resources to support PWD and carers in medicines management are developed, it is important to identify the priorities of end-users and broader stakeholders throughout the design process.

Aims. To generate a set of priorities for medication management resources for PWD and carers.

Methods. Community-based participatory research (CBPR) was used to establish the Medication Management Consortium, a 23-member collaboration between the research team, the project's Research Advisory Group, and Partner Organisations. A comprehensive list of priority statements was compiled through a systematic review and focus groups with PWD (n=2), carers (n=3), healthcare professionals (n=8), advocates and professional organisations (n=9). These priorities were rated by a Delphi panel (round 1, n=23; round 2, n=16) on a nine-point Likert scale during two sequential rounds of questionnaire distribution. The Delphi panel comprised of participants with dementia, carers, healthcare professionals, and representatives of national consumer organisations. Priority statements were eligible for inclusion if ≥78% of participants rated it as important to be included.

Results. The Delphi panel was presented with 49 priority statements identified from the systematic review and stakeholder focus groups. After the initial survey round, 26 statements were accepted verbatim, 19 statements were reworded for clarity and 19 new statements were added based on participant feedback. Following the second survey round, final consensus was reached on 56 statements.

Discussion. This study used robust methodology to develop a set of community-centred priorities for medication management resources for PWD and carers. The identified priorities can be used by consumer and professional organisations, policy makers and researchers to develop medication management resources that address the unique needs of PWD and carers.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P284

Public benefit-risk assessment of vaccines: development and validation of methodological filters

Dr Hiba El Masri

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Hiba EL Masri graduated with a Doctor of Pharmacy (PharmD) from the Lebanese University. She worked in hospital settings and in the pharmaceutical industry, in Lebanon and Saudi Arabia. She had recently completed her PhD in the School of Pharmacy, University of Queensland, entitled *Dynamics of patient-based benefit-risk assessment and information seeking for medication decision-making in chronic disease*. Hiba's research is focused on the quality use of medicine, with an interest in patients' perspectives.

Public benefit-risk assessment of vaccines: development and validation of methodological filters for use in PubMed and Embase

Hiba EL Masri¹, Dima Elmasri², Samantha Hollingworth¹, Christine Dalais³. School of Pharmacy, The University of Queensland¹, Brisbane, QLD, Australia; L'Ecole Doctorale des Sciences et des Technologies, Lebanese University², Beirut, BEY, Lebanon; University Library, The University of Queensland³, Brisbane, QLD, Australia

Introduction. Understanding public benefit-risk assessment (BRA) of vaccines is important in the context of an increasing focus on the uptake of vaccines. Currently, literature searching for relevant evidence is challenged by the lack of standardised terminology and inconsistent indexing.

Aims. To develop and validate both generic and highly sensitive search filters for use in PubMed and Embase to retrieve studies reporting on the public BRA of vaccines.

Methods. We adopted an iterative and rigorous process to ensure an optimal performance by 1) hand searching gold standard sets for PubMed and Embase; 2) developing a candidate search term bank; 3) refining the search filter in PubMed; 4) validating the final filter in PubMed; 5) translating and adapting the filter to Embase, and 6) validating the adapted filter in Embase. We then tested the relative recall of the developed search filters by reproducing the search strategy of a relevant published systematic review.

Results. We created search filters in PubMed and Embase for the retrieval of studies reporting on public BRA of vaccines. We quantitatively appraised their performance metrics against previously identified gold standards sets. The search filter in PubMed had a sensitivity of 98.9% and a precision of 1.7%. The search filter in Embase had a sensitivity of 98.6% and a precision of 1.3%. The relative recall of the filters was 100.0% in PubMed and 94.4% in Embase.

Discussion. To facilitate improved vaccine coverage, we need to understand how the public assess the benefits and risks of vaccines and identify barriers to uptake. These generic and highly sensitive methodological search filters can be used with limited bibliographic skills, to retrieve studies reporting on public BRA of any vaccine.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P285

Predictors of Hospitalisation and Mortality in People with Dementia using Antipsychotics

Mr Timothy Josh Tan

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Predictors of Hospitalisation and Mortality in People with Dementia using Antipsychotics

Timothy Josh D Tan¹, Edward CY Lau¹, Trong H Le², Christine Y Lu^{1,3,4}, Edwin CK Tan^{1,3}. The University of Sydney School of Pharmacy, The University of Sydney¹, Sydney, NSW, Australia; Hanoi University of Pharmacy, Hanoi University², Hanoi, Vietnam; Kolling Institute, The University of Sydney and The Northern Local Health District³, Sydney, NSW, Australia; Department of Pharmacy, Royal North Shore Hospital⁴, St Leonards, NSW, Australia.

Introduction. Antipsychotics are used as part of the pharmacological management of behavioural and psychological symptoms of dementia. While antipsychotics have been associated with increased risk of adverse outcomes, predictors of these outcomes have been under-studied.

Aims. To identify factors associated with the risk of hospitalisation and mortality in antipsychotic users with dementia.

Methods. Four databases (Embase, Medline, PsycINFO and Web of Science) were searched from 2010 using keywords and Medical Subject Heading (MeSH) terms across four different concepts including dementia, older adults, antipsychotics, and outcomes (hospitalisation or mortality). Screening, data extraction and quality assessment were done by two authors independently.

Results. Several factors associated with the risk of hospitalisation and mortality were identified. Antipsychotic-related factors associated with mortality risk included the type of antipsychotic (e.g. typical vs atypical, adjusted hazards ratio (aHR): 1.50, 95%CI 1.10, 2.10), higher doses (aHR: 1.69, 95%CI 1.53, 1.88) and a short duration of use (1-30 days, aHR: 2.10, 95%CI 1.60, 2.90). Patient-related factors included older age (aHR: 1.05, 95%CI 1.01, 1.08), heart disease (aHR: 1.19, 95%CI 1.09, 1.30) and concomitant benzodiazepine use (aHR: 2.19, 95%CI 1.83, 2.63). Antipsychotic-related factors associated with hospitalisation risk included the type of antipsychotic (e.g. atypical vs. typical, aHR: 1.17, 95%CI 1.08, 1.27), higher dose (adjusted odds ratio (aOR): 1.19, 95%CI 1.09, 1.31), being a new user (aOR: 3.07, 95%CI 2.84, 3.32) and short duration of use (e.g. 1-30 days, adjusted incident rate ratio (aIRR): 3.01, 95%CI 1.40, 6.49). Patient-related factors included older age (aHR: 2.41, 95%CI 1.24, 4.70), female sex (aOR: 1.42, 95%CI 1.33, 1.51) and concomitant benzodiazepine use (aHR: 1.55, 95%CI 1.29, 1.86).

Discussion. This review identified several factors associated with risk of hospitalisation and mortality in antipsychotic users with dementia. Clinicians should consider these risk factors when contemplating antipsychotic prescribing in people living with dementia.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P286

Prevalence and factors of potentially inappropriate medication use in people with dementia.

Mr Edward Chun Yin Lau

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Prevalence and factors of potentially inappropriate medication use in people with dementia.

Edward C.Y. Lau¹, Sarah Hilmer², Yun-Hee Jeon³, Christine Lu^{1,2}, Kenji Fujita², Edwin C.K. Tan¹. Sydney Pharmacy School, The University of Sydney¹, Camperdown, NSW, Australia; Kolling Institute, The University of Sydney², St. Leonards, NSW, Australia. Susan Wakil School of Nursing and Midwifery, The University of Sydney³, Camperdown, NSW, Australia.

Introduction. People with dementia are high users of medications; however, some medications may be potentially inappropriate, increasing the risk of adverse outcomes.

Aims. To estimate the prevalence and risk factors associated with the use of potentially inappropriate medications (PIMs) in people with dementia.

Methods. Linked 2021 Census and Pharmaceutical Benefits Scheme (PBS) data were used in this cross-sectional study. People with dementia aged 65 or over in 2021 were included. Dementia was defined based on self-reported dementia diagnosis in the 2021 Census or any dispensing of an antidementia medication between 2016 and 2021. PIMs were defined using 2023 Beers Criteria and the 2024 Australian list of PIMs (AUSPIM). Age, gender, socioeconomic level, education, geographical remoteness, country of birth, language spoken at home, living arrangement, Aboriginal and/or Torres Strait Islander status, need for assistance with core activities and self-reported medical conditions were included in a logistic regression model to explore factors associated with increased likelihood of using PIMs.

Results. A total of 177,809 people with dementia were included in this study (median age 84 [interquartile range: 78-89], 59% female). Overall, half were using at least one PIM according to the Beers Criteria (49%) and AUSPIM (51%). After stratification by age, the prevalence of Beers criteria medications and AUSPIM were highest in those aged 85-89 (50%) and 90-94 (54%), respectively. Factors associated with the use of PIMs were consistent across the two criteria. People with dementia who were female, with higher socioeconomic level and higher education level were less likely to use PIMs while people with dementia who were living in non-private dwellings, required assistance with core activities and have other comorbidities were more likely to use PIMs.

Discussion. One in two people with dementia were using PIMs, with risk higher in certain sociodemographic groups. Clinicians should carefully balance the risks and benefits when prescribing PIMs to ensure equitable and quality use of medications in this vulnerable population.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P287

Translating evidence to practice: pharmacist-led deprescribing and the SaferMedsNL initiative.

Dr Justin Turner

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Dr Justin Turner has extensive experience providing patient care and leading research across aged care, primary care, tertiary care and academia in Australia, Europe and North America. His research seeks to answer the question, "How can we optimise medication use in older adults?" Dr Turner's research is driven by a passion for improving medication management and reducing medication-related harm.

Dr. Turner completed his Master of Clinical Pharmacy at the University of South Australia and his PhD at Monash University. He then undertook a Postdoctoral Fellowship at the University of Montreal, where he focused on designing, implementing, and evaluating evidence-based deprescribing interventions at a population level. Notable achievements during his time in Canada include conducting the first nationwide survey on deprescribing, leading a randomized controlled trial on opioid reduction, and instigating policy changes to incentivize pharmacists to deprescribe. His leadership in the SaferMedsNL initiative educated and engaged residents of Newfoundland and Labrador about the risks of medication-related harm and the importance of deprescribing.

As an inaugural member of the Australian Deprescribing Network (ADeN) and Co-Director of the Canadian Appropriate Medication Use and Deprescribing Network (CADeN), Dr. Turner has been at the forefront of deprescribing internationally. Dr Turner has been an investigator on successful grants and scholarships totalling over \$10 million and received awards for research excellence from both the Canadian Geriatrics Society and the American Geriatrics Society.

Dr. Turner's current research seeks to adapt international best practices in patient-led deprescribing to the contexts of Australia, Canada, and the United States. His work continues to influence health policies and clinical practice, leading to safer and more effective medication use for older adults globally.

Translating evidence to practice: pharmacist-led deprescribing and the SaferMedsNL initiative

Justin P Turner^{1,2}, Kelda Newport³, Cara Tannenbaum⁴, Deborah V. Kelly³. Centre for Medicines Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences¹, Monash University, VIC, Australia. Faculté de Pharmacie, Université de Montréal², QC, Canada School of Pharmacy, Memorial University of Newfoundland³, NL, Canada. Faculté de Médecine, Université de Montréal⁴, QC, Canada

Introduction: Newfoundland and Labrador (NL) has among the highest rates of potentially inappropriate medications (PIMs) in Canada, specifically chronic use of sedatives and proton pump inhibitors (PPIs). The SaferMedsNL intervention adapted the D-PRESCRIBE trial to the contexts of NL via stakeholder engagement. New funding was provided for pharmacists to identify PIMs and initiate deprescribing conversations with patients and healthcare providers.

Aims: To evaluate the changes in medication across NL for people who did or did not receive the pharmacist deprescribing intervention.

Methods: Prescription claims data for all NL adults from 2019 to 2021 were analysed to identify prescription and pharmacist deprescribing intervention claims. Propensity score matching assessed changes in mean daily defined doses

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



(DDD) for chronic sedative or PPI users who did or did not receive the deprescribing intervention. Sub-analysis investigated age categories.

Results: Reductions in DDD varied across medication classes and age groups. A significant reduction in PPI DDD was observed after 3 months, increasing to a 30% reduction at 10 months. The intervention group continued to have significantly lower DDD until the end of the 40-month follow-up. No significant reduction in sedative DDD was observed in the all-ages analysis. However, among adults aged ≥ 70 , sub-analysis indicated a significant impact of the intervention, with PPI DDD reducing by 20% and sedative DDD reducing by 12% during the follow-up period.

Discussion: The evidence-based D-PRESCRIBE trial was effectively adapted and scaled up at a population level, leading to reductions in PIM use. The reductions observed in older adults are important because this age category is most susceptible to adverse drug events. Further research should investigate the differences in effect observed between medication classes and across age groups.

P288

Quantifying Polypharmacy and Medicines Use in Hospital

Miss Lorna Pairman

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Lorna is an intercalated MBChB/PhD student at the University of Otago, currently between fifth and sixth year of medical school, completing a PhD in the field of clinical pharmacology. Her PhD focuses on linking hospital prescribing data to other data sources to measure appropriate medicines use. Her current project illustrates how small definitional changes can influence results by using routinely collected prescribing data to quantify medicines use during hospital admissions. Lorna is a co-chair of the ASCEPT Student Forum, a committee member on the ASCEPT New Zealand forum, and the Editor-in-Chief of the New Zealand Medical Student Journal.

Quantifying Polypharmacy and Medicines Use in Hospital

Lorna Pairman¹, Paul Chin^{1,2}, Richard McNeill², Matthew Doogue^{1,2}. Department of Medicine, University of Otago¹, Christchurch, New Zealand; Department of Clinical Pharmacology, Health New Zealand², Christchurch, New Zealand.

Introduction. Medicines are the most common form of treatment in healthcare. During hospital admission changes to medicines are common. However, few studies quantify medicine use and polypharmacy using hospital prescribing data, and fewer still consider medicine type and chronicity of use. Furthermore, significant heterogeneity in existing definitions limits comparisons between studies.

Aims. To quantify polypharmacy and medicines use in a tertiary hospital.

Methods. Prescribing and inpatient data from 01/07/2022 to 01/07/2023 was extracted from a data warehouse. The number of medicines at admission and discharge, as well as changes to medicines use (medicines initiated or ceased) were determined for each patient admission. Medicines were grouped as long-term, short-course, or *pro re nata* (PRN). Descriptive statistics, proportions, and odds ratios were used to quantify medicines use and patient outcomes.

Results. There were 56,202 admissions of 41,099 patients over the study period. The median patient was on 7 (IQR 4-11) medicines at admission, and 9 (IQR 6-12) at discharge. Of the 515,731 medicines at discharge, 38% were 'long-term', 16% were 'short course', and 46% were 'PRN'. Of the 194,087 long-term medicines, 94% were 'systemic' and 6% were 'non-systemic'. 84% of patient admissions had five or more medicines on discharge and 34% admissions had five or more long-term medicines on discharge. For each admission an average of 4.4 (SD 5.5) medicines were initiated, 2.4 (SD 3.2) were

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



ceased, and 0.8 (SD 1.4) had dose changes. The median patient was exposed to 11 (IQR 7-15) medicines, 13 (IQR 8-19) prescriptions, and had 27 (IQR 11-65) doses administered. The most common long-term medicines at discharge were omeprazole (22%), docusate sodium + sennoside B (21%), and aspirin (19%). Having five or more long-term medicines on discharge was associated with adverse drug reaction occurrence (OR 2.6, 95% CI 2.4-2.8), readmission within 30-days (OR 1.4, 95% CI 1.3-1.5), and mortality within 6-months (OR 2.1, 95% CI 2.0-2.2).

Discussion. Patients were typically discharged on nine medicines, two more than on admission, but the minority were for long term use. For the small net change of two medicines, there were several changes made (four initiated, two ceased, one dose change). Medicine use in hospital is complex and not all medicines are equal. Common descriptors of medicine use fail to account for this. Unsurprisingly polypharmacy was associated with worse patient outcomes.

P290

Apocynin prevents cigarette smoke-induced impairments in synaptogenesis.

Miss Alina Akhtar

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Apocynin prevents cigarette smoke-induced impairments in synaptogenesis.

Alina Akhtar¹, Simone N. De Luca¹, Rana Alateeq¹, Stanley Chan¹, Ross Vlahos¹.

¹Centre for Respiratory Science and Health, School of Health and Biomedical Sciences, RMIT University, Melbourne, VIC, Australia.

Introduction: Chronic obstructive pulmonary disease (COPD) is a leading cause of death worldwide. Alongside the overexuberant pulmonary inflammation and oxidative stress, people with COPD have impaired learning and memory as well as anxiety disorders compared to healthy aged, matched individuals. We hypothesise that exposure to cigarette smoke (CS) causes lung inflammation and oxidative stress that “spills over” into the central nervous system driving dysfunction in neurons and microglia; the brains immune cells, leading to learning and memory deficits.

Aim: To investigate if prophylactic treatment with the NADPH oxidase 2 (NOX2) inhibitor; apocynin, can alleviate CS-induced inflammation and oxidative stress in the lungs and brain.

Methods: Male BALB/c mice were exposed to room air or CS for 24 weeks and co-administered with either apocynin (5 mg/kg, i.p.) or vehicle (0.01% DMSO/sterile PBS) treatments daily. Mice were euthanised and lung inflammation and oxidative stress was assessed (bronchoalveolar lavage fluid [BALF] cellularity and qRT-PCR). Brains were collected to assess neuroinflammation (microglial morphology), synaptogenesis, and neurogenesis.

Results: CS exposure caused an increase in BALF macrophages, neutrophils and lymphocytes ($p < 0.0001$). Apocynin reduced CS-induced increases in BALF macrophages and the expression of lung *Nox1* ($p < 0.005$), and *Nox2/Cybb* ($p < 0.005$). Exposure to CS reduced the area per cell of microglia in the CA1 of the hippocampus suggesting an amoeboid morphology ($p < 0.001$) and apocynin restored the profile to a ramified morphology similar to sham mice ($p < 0.0001$). CS exposure reduced the expression of synaptophysin in the hippocampus ($p < 0.0001$) and apocynin treatment prevented this impairment ($p < 0.001$).

Discussion: CS exposure caused BALF inflammation and increased oxidative stress in the lungs. Apocynin reduced CS-induced BALF inflammation, lung tissue oxidative stress and improved microglial and synaptogenesis profiles in the CA1 of the hippocampus. Thus, targeting NOX2 could be a novel therapeutic avenue to improve COPD and its extra-pulmonary comorbidities.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P466

Trends in hospital admissions from adverse drug reactions among older Australians

Miss Azizah Vonna

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

A PhD Candidate at the University of Tasmania, Azizah brings a decade of pharmacy expertise to her research. Her current work focuses on Quality Use of Medicines and Medicines Safety in older adult populations. As an academic staff member at Universitas Syiah Kuala, Indonesia, and former pharmacist at dr. Zainoel Abidin public hospital in Banda Aceh, Indonesia, she draws from extensive clinical and educational experience. Building upon her Master of Pharmacy qualification and practical healthcare background, she aspires to implement her research findings through collaborative healthcare approaches in the future.

Trends in hospital admissions from adverse drug reactions among older Australians

Azizah Vonna^{1,2}, Mohammed S. Salahudeen¹ & Gregory M. Peterson¹. School of Pharmacy and Pharmacology, Univ of Tasmania¹, Hobart, TAS, Australia; Department of Pharmacy, Univ Syiah Kuala², Banda Aceh, ACH, Indonesia.

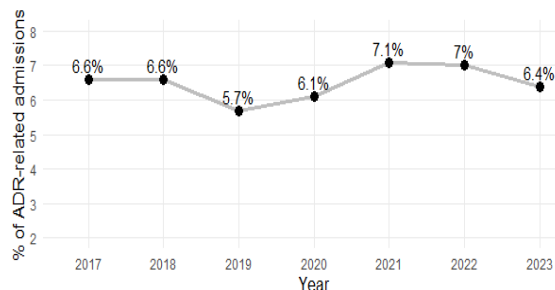
Introduction. While there was considerable research into adverse drug reaction (ADR)-related hospital admissions among older adults in the late 1990s and early 2000s, such studies have become less common in recent years (Lim et al, 2022). It is therefore difficult to know whether the occurrence of these admissions has changed over time.

Aims. To investigate trends in ADR-related admissions and associated risk factors among older Australian adults.

Methods. Using data from the Australian National Minimum Data Set (NMDS), we identified older adults (aged ≥ 65 years) admitted to Tasmanian public hospitals from 2017 to 2023 due to ADRs (using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM)). Trends were analysed using a trend analysis and risk factors were assessed using a regression model.

Results. A total of 28,293 out of 444,447 admissions (6.5%) were coded as ADR-related, with annual percentages relatively constant during the observation period ($p \geq 0.05$). Of all admitted patients, 9,238 (14.3%) experienced at least one ADR-related admission over the study period. Cancer, peptic ulcer disease, and musculoskeletal disease were associated with the highest risk, with adjusted odds ratios of 5.67 (95% CI: 5.32-6.05; $p < 0.0001$), 3.21 (95% CI: 2.58-4.00; $p < 0.0001$), and 2.98 (95% CI: 2.82-3.16; $p < 0.0001$), respectively.

Discussion. The rate of ADR-related hospitalisations remained stable during the observation period, though the overall percentage is notably higher than findings from similar studies using administrative data from the early 2010s (Lim et al., 2022). Despite an increasing focus on medicines safety, these findings suggest that significant improvements in reducing ADR-related admissions have yet to be achieved.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P290

Apocynin prevents cigarette smoke-induced impairments in synaptogenesis.

Miss Alina Akhtar

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Apocynin prevents cigarette smoke-induced impairments in synaptogenesis.

Alina Akhtar¹, Simone N. De Luca¹, Rana Alateeq¹, Stanley Chan¹, Ross Vlahos¹.

¹Centre for Respiratory Science and Health, School of Health and Biomedical Sciences, RMIT University, Melbourne, VIC, Australia.

Introduction: Chronic obstructive pulmonary disease (COPD) is a leading cause of death worldwide. Alongside the overexuberant pulmonary inflammation and oxidative stress, people with COPD have impaired learning and memory as well as anxiety disorders compared to healthy aged, matched individuals. We hypothesise that exposure to cigarette smoke (CS) causes lung inflammation and oxidative stress that “spills over” into the central nervous system driving dysfunction in neurons and microglia; the brains immune cells, leading to learning and memory deficits.

Aim: To investigate if prophylactic treatment with the NADPH oxidase 2 (NOX2) inhibitor; apocynin, can alleviate CS-induced inflammation and oxidative stress in the lungs and brain.

Methods: Male BALB/c mice were exposed to room air or CS for 24 weeks and co-administered with either apocynin (5 mg/kg, i.p.) or vehicle (0.01% DMSO/sterile PBS) treatments daily. Mice were euthanised and lung inflammation and oxidative stress was assessed (bronchoalveolar lavage fluid [BALF] cellularity and qRT-PCR). Brains were collected to assess neuroinflammation (microglial morphology), synaptogenesis, and neurogenesis.

Results: CS exposure caused an increase in BALF macrophages, neutrophils and lymphocytes ($p < 0.0001$). Apocynin reduced CS-induced increases in BALF macrophages and the expression of lung *Nox1* ($p < 0.005$), and *Nox2/Cybb* ($p < 0.005$). Exposure to CS reduced the area per cell of microglia in the CA1 of the hippocampus suggesting an amoeboid morphology ($p < 0.001$) and apocynin restored the profile to a ramified morphology similar to sham mice ($p < 0.0001$). CS exposure reduced the expression of synaptophysin in the hippocampus ($p < 0.0001$) and apocynin treatment prevented this impairment ($p < 0.001$).

Discussion: CS exposure caused BALF inflammation and increased oxidative stress in the lungs. Apocynin reduced CS-induced BALF inflammation, lung tissue oxidative stress and improved microglial and synaptogenesis profiles in the CA1 of the hippocampus. Thus, targeting NOX2 could be a novel therapeutic avenue to improve COPD and its extra-pulmonary comorbidities.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P291

Sexual Dimorphism in the Sugen-Hypoxia Mouse Model of Pulmonary Arterial Hypertension

Miss Chloe Landy

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Chloe is a PhD student in the Cardiovascular Pharmacology Lab at the Monash Institute of Pharmaceutical Sciences. Chloe completed her B.PharmSci(Adv)Hons in 2021. Her honours project explored the efficacy of novel FPR agonists in treating pulmonary arterial hypertension (PAH). Chloe's current research aims to identify whether a class of lipids known as specialised pro-resolving mediators (SPMs) are differentially expressed between the sexes in PAH.

Sexual Dimorphism in the Sugen-Hypoxia Mouse Model of Pulmonary Arterial Hypertension

Chloe Landy¹, Ting Fu¹, Ruby Tang¹, Miles J De Blasio¹, Kristy L Jackson¹, Owen L Woodman¹, Cheng Xue Qin¹. Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences¹, Parkville, VIC, Australia

Introduction. Pulmonary arterial hypertension (PAH) is an inflammatory vascular disease that ultimately results in right ventricular (RV) failure. Women with PAH have a better prognosis than men however underlying mechanisms, particularly as it relates to inflammation-resolution pathways, are poorly understood.

Aims. To compare inflammatory signalling in male (M) and female (F) mice using the sugen-hypoxia (SuHx) PAH model.

Methods. C57BL/6J mice were subjected to either hypoxia (10% O₂) with sugen (20mg/kg, sc, weekly in first 4 weeks) or normoxia (NmOx) with vehicle (0.5% carboxymethyl cellulose, 0.9% tween 80 and 0.4% benzyl alcohol in saline, sc) for 2 or 8 weeks (wk). Mice were anaesthetised (ketamine/xylazine/atropine, 100/20/1.2 mg/kg, ip) and RV systolic pressure (RVSP), a surrogate for pulmonary pressure in mice, was measured. RV hypertrophy (RV/LV+S) was assessed.

Results. SuHx mice exhibited significantly elevated RVSP and right ventricular hypertrophy. Female mice had a lower RVSP than males at 2 weeks after PAH induction but a higher RVSP at 8 weeks. Over time, RVSP increased in female SuHx mice but not in males. While RV/LV+S was not influenced by sex, it did increase significantly over time in both male and female SuHx mice, indicating progressive right ventricular hypertrophy in this model.

Discussion. The SuHx model effectively replicates sexual dimorphism observed in clinical setting of PAH. The substantial differences in RVSP between male and female mice warrants the need for further research into the underlying mechanisms contributing to sexual dimorphisms in PAH pathophysiology. This knowledge could pave the way for the development of sex-tailored therapies, enhancing the effectiveness of PAH treatment.

	2wk + M + NmOx	2wk + F + NmOx	8wk + M + NmOx	8wk + F + NmOx	2wk + M + SuHx	2wk + F + SuHx	8wk + M + SuHx	8wk + F + SuHx
RVSP	25.0±0.9 (7)	24.4±0.6 (11)	24.0±0.7 (11)	24.3±0.5 (11)	36.4±1.0 (12)****	30.6±1.0 (12)***/###	32.8±0.8 (12)****	37.4±2.4 (8)****/#/ †
RV/LV+S	0.34±0.01 (6)	0.28±0.01 (6)	0.31±0.01 (6)	0.33±0.01 (6)	0.41±0.01 (6)*	0.42±0.02 (6)****	0.49±0.02 (6)****/†	0.54±0.02 (4)****/ †

Mean ± SEM (n). *p<0.05, ***p<0.001, ****p<0.0001 compared to NmOx counterparts; #p<0.05, ###p<0.001 compared to male counterparts; †p<0.05 compared to 2-week counterparts

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P292

CXCL17 as a novel MRGPRX2 agonist: importance of cellular context

Miss Jie Ding

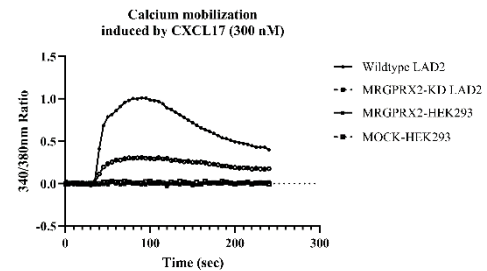
Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Jie is a final-year PhD candidate in the Department of Biochemistry and Pharmacology, The University of Melbourne. Under the supervision of A/Prof Graham Mackay in the Anti-Allergic Therapeutics Laboratory, her current research focuses on the role of orphan GPCR, MRGPRX2, in chronic inflammatory diseases and drug hypersensitivity reactions. She is investigating the novel mechanism of the new endogenous agonist CXCL17 on MRGPRX2 activation using GPCR assays, proteomics and high-throughput functional genomic screening.

CXCL17 as a novel MRGPRX2 agonist: importance of cellular context

Jie Ding, Graham A Mackay. Dept of Biochemistry & Pharmacology, University of Melbourne¹, Parkville, VIC, Australia.



Introduction. The Mas-related G protein-coupled receptor X2 (MRGPRX2) is selectively expressed on mast cells and is activated by diverse polycationic peptides. We have identified that CXCL17 acts as a novel endogenous agonist of MRGPRX2 in mast cell activation and demonstrated the clinical implication of CXCL17-MRGPRX2/MC pathway in psoriatic skin¹. However, the MRGPRX2 signalosome that leads to effective mast cell degranulation is not well understood.

Aims. To further characterise CXCL17-induced, MRGPRX2-mediated cellular activation mechanisms.

Methods. We used the human mast cell line LAD2 that natively expresses MRGPRX2, MRGPRX2 knockdown LAD2 cells generated by CRISPR-Cas9 technology and HEK293 cell line expressing human MRGPRX2. Calcium mobilization in response to CXCL17 and other MRGPRX2 agonists was measured using fura-2. CXCL17 binding to MRGPRX2, and downstream G protein-activation were determined using NanoBRET™ assays. Immunoprecipitation of LAD2 and MRGPRX2-expressing HEK293 cell lysates were conducted with an anti-MRGPRX2 antibody coupled to Dynabeads® with pull-down proteins identified by mass spectrometry.

Results. Compared to LAD2 mast cells, CXCL17 does not trigger Ca²⁺ mobilisation and Gq activation in MRGPRX2-transfected HEK293 cells (Fig 1). In immunoprecipitation studies, 76 proteins were identified within MRGPRX2 pull-downs in LAD2 mast cells with 40 proteins being uniquely expressed compared to MRGPRX2-expressing HEK293 cells. In addition, 19 proteins were increased upon MRGPRX2 activation in LAD2 mast cells.

Discussion. Our results show that MRGPRX2 activation by CXCL17 is cell context specific, suggesting that additional cellular components, perhaps unique to the mast cell, are necessary for productive receptor activation. The identified proteins immunoprecipitated with MRGPRX2 in LAD2 cells likely contribute to this mechanism and may serve as targets for novel mast cell inhibiting drugs.

¹Ding J et al (2024) Allergy doi:10.1111/all.16036.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P293

IL-21/IL-21R mediates fibrocyte activation in airway fibrosis of severe asthma

Dr Hong-Sheng Lee

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

IL-21/IL-21R mediates fibrocyte activation in airway fibrosis of severe asthma

H. S. Lee¹, B. C. Chen^{1,2}, K. Y. Lee^{1,4}, K. Y. Chen^{1,4}, H. P. Kuo^{1,5} and C. H. Lin^{1,3*}. Chen Wei-Tien Research Center of Thoracic Medicine¹, School of Respiratory Therapy², Graduate Institute of Medical Sciences³, Taipei Medical University (TMU), Taiwan (TW); Department of Thoracic Medicine, TMU-Shuang Ho Hospital⁴, TW; Department of Thoracic Medicine, TMU-Hospital⁵, TW.

Introduction. Interleukin 21 (IL-21) is a proinflammatory cytokine that has been shown to support T_H2 effector responses in asthma patients. CD34⁺/CD45⁺/collagen I⁺ fibrocyte activation is implicated in the pathogenesis of airway fibrosis in severe asthma (SA). However, little is known about the underlying mechanism of IL-21/IL-21 receptor (IL-21R) in the regulation of fibrocyte activation in airway fibrosis of SA patients.

Aims. To determine the role of IL-21/IL-21R mediates fibrocyte activation in airway fibrosis of SA patients and ovalbumin (OVA)-induced airway fibrosis in mice.

Methods. We used primary fibrocytes from SA to evaluate the pathological significance of IL-21/IL-21R. To elucidate the role of IL-21/IL-21R in fibrocyte activation and airway fibrosis, IL-21R knockout (KO) mice were used in OVA-induced airway fibrosis model. The role of STAT3 activation in IL-21R upregulation caused by IL-21 was also examined in human normal fibrocytes. Statistical data were shown as mean ± standard error.

Results. The serum level of IL-21 and IL-21R expression in fibrocytes from SA patients were higher than normal subjects. Treatment of anti-IL-21R antibody inhibited the capacity of proliferation and differentiation in fibrocytes from SA patients. In addition, IL-21R KO inhibited the capacity of proliferation and differentiation in fibrocytes from circulation and bronchoalveolar lavage fluid in OVA-induced airway fibrosis of mice. IL-21R KO suppressed fibrotic expression from lung tissue in OVA-induced airway fibrosis of mice. IL-21R KO protected the decline of lung function in OVA-stimulated airway fibrosis of mice. In human normal fibrocytes, IL-21 caused IL-21R expression, which was attenuated by transfection of STAT3 siRNA. Besides, IL-21 induced STAT3 phosphorylation and the recruitment of STAT3 to IL-21R promoter region, and further caused the increase in luciferase activity.

Discussion. Upregulation of IL-21R contributes to fibrocyte activation in airway fibrosis of SA patients and OVA-challenged mice. IL-21/IL-21R may be new therapeutic targets in the airway fibrosis of SA patients. We will subsequently explore the unmet medical needs of developing anti-IL-21R antibodies to address airway fibrosis in SA.

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P294

A novel pro-resolution therapy approach to treat pulmonary arterial hypertension

Miss Ting Fu

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Ting is a final-year PhD student at the Cardiovascular Pharmacology Laboratory of the Monash Institute of Pharmaceutical Science. She is supervised by Dr. Chengxue Helena Qin, with co-supervision from Professor Rebecca Ritchie, Associate Professor Barbara Kemp-Harper, and Dr. Elva Zhao. Ting's studies and research have been supported by the Monash Graduate Scholarship (MGS) and the Monash International Tuition Scholarship (MITS). Her doctoral research focuses on the regulation of formylpeptide receptors in cardiopulmonary diseases. She aims to understand the underlying mechanisms and identify novel therapeutic strategies to improve current treatments and outcomes for patients with cardiopulmonary diseases

A novel pro-resolution therapy approach to treat pulmonary arterial hypertension.

Ting Fu¹, Chloe Landy¹, Miles J De Blasio¹, Jaideep Singh¹, Anida Velagic¹, Owen L Woodman¹, Barbara Kemp-Harper², Peishen Zhao¹, Rebecca H Ritchie^{1,2}, Chengxue Qin^{1*}. ¹Drug Discovery Biology and ²Department of Pharmacology, Monash Univ, VIC; Australia.

Introduction. Chronic low-grade inflammation is a key contributor to the pathogenesis of pulmonary arterial hypertension (PAH). A crucial aspect of a self-resolving inflammatory response is its ability to limit the production of pro-inflammatory mediators and promote tissue healing. The nonselective formylpeptide receptor (FPR) agonist, Compound17b (Cmpd17b) has shown pro-resolution effects in the pulmonary vasculature *ex vivo*¹, but the impact of FPR agonists on PAH is not known.

Aim. To investigate the therapeutic effects of FPR agonist in PAH.

Methods. 9-week-old male

C57BL/6J mice were randomly allocated to either normoxia (21% O₂) or hypoxia (10% O₂) cohorts. The hypoxia cohort received subcutaneous injections of sugen 5416 (20mg/kg) weekly for 4 weeks and was exposed to hypoxia for 28 days. In this study, the sugen/hypoxia (SuHx) cohort was randomly divided into three groups: (i) treatment-vehicle, (ii) Cmpd17b (50 mg/kg/day), or standard clinical treatment (iii) sildenafil (0.3 mg/kg/day). The normoxia cohort received the treatment-vehicle (10% DMSO in 0.8% tween 80 in saline). Mice were culled and lungs were collected for analysis of gene expression by qPCR.

Results. SuHx mice displayed elevated right ventricular systolic pressure (RVSP) and elevation in lung weight and a higher RV/(LV+S), upregulated expression of the pro-inflammatory cytokine *mIl-6*. Cmpd17b not only lowered the RVSP in SuHx mice, but also downregulated pro-inflammatory cytokines *mIl-6* and *mTnf-α*, as well as the pro-fibrotic mediator *mCtgf* (Table).

Discussion. Our study demonstrated that Cmpd17b not only lowers the RVSP as current clinical treatment do, but also limits inflammation, which might be beneficial for preventing organ remodelling.

¹ Studley WR et al. (2023) Br J Pharmacol DOI10.1111.bph.16231.

	Normoxia + Vehicle	SuHx + Vehicle	SuHx + Cmpd17b	SuHx + Sildenafil
RVSP (mmHg)	29±1 (n=12)	40±2**** (n=12)	33±1 ⁵⁵⁵ (n=13)	34±1 ³⁵ (n=13)
RV/(LV+S) weight	0.33±0.01 (n=11)	0.47±0.02*** (n=7)	0.49±0.02 (n=10)	0.50±0.02 (n=10)
Lungs : tibia length (mg/mm)	14.7±0.6 (n=7)	21.6±0.9**** (n=7)	19.6±0.5 (n=10)	18.8±0.4 ⁵ (n=10)
<i>mIl-6</i> (fold increase)	1.0±0.2 (n=11)	1.9±0.3* (n=13)	0.6±0.1 ⁵⁵⁵ (n=11)	1.0±0.3 (n=10)
<i>mTnf-α</i> (fold increase)	1.0±0.2 (n=11)	1.8±0.5 (n=13)	0.5±0.1 ⁵ (n=11)	1.0±0.1 (n=10)
<i>mCtgf</i> (fold increase)	1.0±0.1 (n=11)	1.1±0.2 (n=13)	0.6±0.1 ⁵ (n=11)	0.4±0.1 ⁵⁵ (n=10)

*P<0.05, ***P<0.001, ****P<0.0001 vs Normoxia + vehicle; ⁵P<0.05, ⁵⁵P<0.01, ⁵⁵⁵P<0.001 vs SuHx + vehicle, (One-way ANOVA with Sidak's multiple comparisons test). RVSP: Right ventricular systolic pressure, RV: Right ventricular, LV: Left ventricular, S: Septum, *mIl-6*: Interleukin6, *mTnf-α*: Tumor necrosis factor-α, *mCtgf*: Connective tissue growth factor.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P296

Antiviral Effects of ANO6/TMEM16 inhibitors

Prof Min Goo Lee

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Antiviral Effects of ANO6/TMEM16 inhibitors

Ju-Ri Sim¹, Youngchae Lee¹, Wan Namkung³, Jae Myun Lee², Min Goo Lee¹

¹Department of Pharmacology, Brain Korea 21 Project for Medical Science, Yonsei University College of Medicine, Seoul 03722, Korea.

²Department of Microbiology and Immunology, Institute for Immunology and Immunological Diseases, Brain Korea 21 Project for Medical Science, Yonsei University College of Medicine, Seoul 03722, Korea.

³College of Pharmacy and Yonsei Institute of Pharmaceutical Sciences, Yonsei University, 85 Songdogwahak-ro, Yeonsu-gu, Incheon 21983, Korea.

Abstract

Enveloped viruses such as SARS-CoV-2 utilize class I fusion proteins to induce fusion between viral and host cellular membranes, enabling viral entry into the host cell. Furthermore, these enveloped viruses induce the formation of multinucleated cells (syncytia), which are thought to facilitate viral replication and evasion of the host immune system. However, the molecular mechanisms regarding syncytia formation during virus infection remain largely unknown. In a previous study, we have shown that some ANO6/TMEM16F inhibitors, phospholipid scramblase inhibitors, inhibit the host entry of SARS-CoV-2 [1]. Here, we show newer ANO6/TMEM16F inhibitors that have higher potency in inhibiting ANO6/TMEM16F-mediated cell surface exposure of phosphatidylserine, which is critical for viral fusion protein-induced syncytia formation. Treatment with these specific ANO6 inhibitors blocked PS externalization and the formation of syncytia induced by the viral fusion proteins. Importantly, ANO6 inhibitors strongly suppressed in vitro viral replication and alleviated virus-induced inflammation in an in vivo mouse model. These results provide mechanistic insights into the class I viral fusion protein-induced membrane fusion process and suggest a potential target for pharmacological intervention to protect against respiratory viral infections

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Reference

[1] Sim J-R, Shin DH, Park P-G, Park S-H, Bae J-Y, Lee Y, Kang D-Y, Kim YJ, Aum S, Noh SH, Hwang SJ, Cha H-R, Kim CB, Ko SH, Park S, Jeon D, Cho S, Lee GE, Kim J, Moon J-H, Kim J-O, Nam J-S, Kim C-H, Moon S, Chung YW, Park M-S, Ryu J-H, Namkung W, Lee JM, Lee MG (2022) Amelioration of SARS-CoV2 infection by ANO6 phospholipid scramblase infection. Cell Rep 40:111117

P297

Factors Influencing Antimicrobial Decision-Making in Respiratory Tract Infections

Ms Savannah Reali

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Savannah is a Clinical Pharmacist and PhD candidate at The University of Sydney. She graduated with a Bachelor of Pharmacy with First Class Honours and the University Medal from The University of Sydney in 2018. Savannah then completed her Pharmacy Internship at Prince of Wales Hospital in Randwick. Over the course of five years, she immersed herself in diverse clinical settings, honing her skills and expertise across a spectrum of specialties. This tenure culminated in her successful completion of the Advanced Pharmacy Australia (formerly Society of Hospital Pharmacists of Australia) Residency Program. Whilst at Prince of Wales Hospital, Savannah developed a passion for antimicrobial stewardship and began her PhD with a scholarship from The University of Sydney in 2023. Savannah's PhD thesis will focus on the optimisation of antimicrobial prescribing in respiratory tract infections in response to the escalating threat of antimicrobial resistance.

Factors Influencing Antimicrobial Decision-Making in Respiratory Tract Infections

Savannah Reali^{1,2,3}, Jin-Gun Cho^{4,5}, Jan-Willem Alffenaar^{1,2,3}, Parisa Aslani¹. School of Pharmacy, Faculty of Medicine and Health, The University of Sydney¹, Camperdown, NSW, Australia. Westmead Hospital², Westmead, NSW, Australia. The University of Sydney Institute for Infectious Diseases (Sydney ID), The University of Sydney³, Westmead, NSW, Australia. Department of Respiratory and Sleep Medicine, Westmead Hospital⁴, Westmead, NSW, Australia. School of Medicine, Faculty of Medicine and Health, The University of Sydney⁵, Camperdown, NSW, Australia.

Introduction. Respiratory tract infections are one of the most common indications for which antimicrobials are prescribed. However, non-compliance with treatment guidelines and inappropriate antimicrobial prescribing are a concern, as both are important drivers in the development of antimicrobial resistance. Hence, understanding factors that influence antimicrobial prescribing is vital for developing interventions to optimise prescribing.

Aims. This study aimed to identify factors that influence prescribers' and antimicrobial stewardship pharmacists' decisions around antimicrobial use in respiratory tract infections, and barriers and enablers to optimal antimicrobial prescribing.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Methods. Qualitative semi-structured interviews were conducted with antimicrobial stewardship pharmacists and prescribers practising in public and private hospitals in NSW. Interviews were audio-recorded and transcribed verbatim. Inductive thematic analysis as described by Braun and Clarke was used to analyse the data.

Results. Participants identified many factors influencing antimicrobial prescribing decisions including microbiological results, patient condition, imaging, patient allergy and immune status, and travel history. Physicians' antimicrobial prescribing behaviour was reported to be based on clinical experience and senior colleagues. Guidelines were perceived as useful resources, but it was acknowledged that they do not cover all patients and there were clinical circumstances where they were not appropriate. Fears and anxieties around patient deterioration and missing infections drove prescribing. This was particularly due to diagnostic uncertainty and the desire to cover for superimposed bacterial infections.

Discussion. Physicians are aware of antimicrobial resistance as a serious global health issue and strive to be judicious in their antimicrobial prescribing. However, increased uncertainty in the diagnosis and pathogenesis of respiratory tract infections and concerns for patient deterioration drove guarded antimicrobial prescribing.

P298

Bombesin 3 receptor: a novel target for the deadliest cancer

Ms Mariah Stavrou

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Mariah is a PhD candidate in A/Prof Nicola Smith's Orphan Receptor Lab at UNSW Sydney. She has been a member of ASCEPT since 2021 and has served on ASCEPT's student committee for 2 years. She has a keen interest in GPCRs, with a focus on taste receptors and the forgotten bombesin receptor, BB3.

Bombesin 3 receptor: a novel target for the deadliest cancer

Mariah R Stavrou¹, Zoe A Eastwood¹, Sara Ballouz², Nicola J Smith¹. Department of Pharmacology, School of Biomedical Sciences, UNSW Sydney¹, NSW, Australia; School of Computer Science and Engineering, UNSW Sydney², NSW, Australia.

Introduction. Despite significant treatment advances, lung cancer remains one of the biggest killers of Australians. Highly innovative strategies are urgently needed to target lung cancer with a limited side effect profile. Early evidence suggests that the orphan G protein-coupled receptor, bombesin 3 (BB₃), may be overexpressed in cancer and functionally absent in healthy tissue, presenting a unique opportunity for a biologically selective target for cancer.

Aims. First, to characterise expression of BB₃ and determine the extent of its biological selectivity in cancer. Then, to validate recently described synthetic ligands and the pharmacological properties of BB₃ that have otherwise been poorly characterised. Finally, to develop a highly disease-relevant model to measure the impact of BB₃ activity in cancer.

Methods. Gene expression data was mined from RNA-sequencing databases and extracted as transcripts per million RNA reads (TPM) for BB₃ and control genes. To measure constitutive and synthetic agonist activity at BB₃, HEK293 cells were co-transfected with BB₃ and luciferase reporter plasmids with and without agonist stimulation. A high-throughput GCaMP assay was used to measure increases in Ca²⁺ following BB₃ agonism. Human lung cancer organoids expressing BB₃ were incubated with BB₃ agonists and changes to disease phenotype and cell viability were measured.

Results. BB₃ mRNA was found exclusively in lung adenocarcinoma (LUAC), and not in adjacent healthy lung, other cancers and other healthy human tissue. BB₃ expression in LUAC was more prevalent (83%) than any other LUAC marker (<44%). BB₃ signals in the absence of ligand via the Gα_{q/11}, Gα_{12/13}, and Gα_s pathways, and agonism increases Ca²⁺. Lung cancer

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



organoids expressing BB₃ were assessed for morphological and molecular characteristics of cancer in the absence and presence of BB₃ ligands.

Discussion. The exclusive expression of BB₃ in LUAC offers the possibility of selective and targeted treatment in a disease with high resistance to chemotherapy and other clinically used drugs. Barriers to BB₃'s development as a LUAC target have been overcome with our characterisation of the receptor's pharmacology and development of a disease-specific model. This study awards us the opportunity to engineer targeted therapies that exploit BB₃'s unique pharmacology in lung cancer.

P300

Diesel exhaust particles trigger mast cell alarmin release in asthmatic airway epithelium

A/Prof Chih-Ming Weng

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Weng, Chih-Ming is an associate professor in school of Respiratory Therapy in Taipei Medical University. His work focuses specifically on the pathological change of epithelial immune microenvironment in lung and their impact on the lung chronic disease, such as asthma. His recent publication can be found in *Mucosal Immunology, Respirology and Allergy journal*.

Diesel exhaust particles trigger mast cell alarmin release in asthmatic airway epithelium

Chih-Ming Weng, PhD^{1,2}, Meng-Jung Lee, MSC¹, Han-Pin Kuo, MD, PhD^{1,3}

¹Pulmonary Medicine Research Center, Taipei Medical University, Taipei, Taiwan; ²School of Respiratory Therapy, Taipei Medical University College of Medicine, Taipei, Taiwan; ³Department of Bioscience Technology, Center of Nanotechnology, Chung Yuan Christian University, Taoyuan, Taiwan; ⁴Department of Thoracic Medicine, Taipei Medical University Hospital, Taipei, Taiwan

Introduction. Mast cells are implicated in the pathogenesis and severity of asthma in both children and adults. Pro-inflammatory mediators and cytokines released from activated mast cells are associated with evidence of Th2-skewed inflammation.

Aims. Human mast cells exposed to diesel exhaust particulate (DEP), through AhR canonical pathway, synthesized and released alarmins.

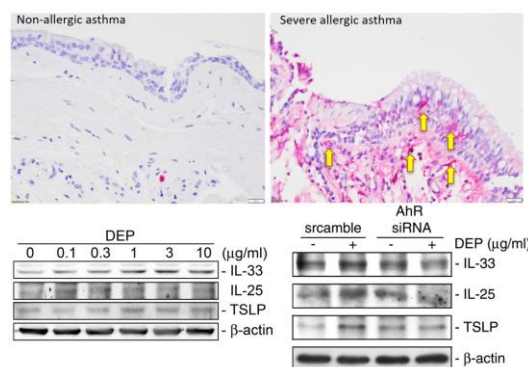
Methods. The IHC, western blot, and ChIP assay were performed to determine the effect of DEP on alarmin expression of human mast cells.

Results. The accumulation of mast cells in the airway wall of allergic asthma, as well as in air pollutant-challenged mice. DEP induced the release of IL-33, IL-25, and TSLP in HMC-1 via AhR or NF- κ B pathway.

Discussion. Mast cells release a broad spectrum of inflammatory cytokines and chemokines, which drive the immune responses (Galli et al., 2008). Mast cells may migrate to airway epithelium resulting in epithelial instability (Altman et al., 2019). Our results revealed that increased number of mast cells was found in the airway epithelium of allergic asthmatics or animals. Thus, mast cells in allergic asthmatic patients may be more susceptible to direct exposure to air pollutants, including DEP. that DEP induced mast cells to produce IL-33, IL-25 and TSLP at mRNA and protein levels through AhR.

Galli et al (2008) *Nat Rev Immunol* 8: 478-486

Altman et al (2019) *J Clin Invest* 129: 4979-4991



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P301

Pro-resolving FPR agonist Cmpd17b relaxes mouse and human pulmonary arteries

Mr William Studley

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Pro-resolving FPR agonist Cmpd17b relaxes mouse and human pulmonary arteries

William R Studley^{1,2}, Olivia N Young¹, Chloe Landy², Yi Chen³, Rebecca H Ritchie², Cheng Xue Qin², Jane E Bourke¹. Department of Pharmacology, Biomedicine Discovery Institute, Monash University¹, Clayton, VIC, Australia; Monash Institute of Pharmacological Sciences², Parkville, VIC, Australia; Victorian Heart Hospital³, Clayton, VIC, Australia

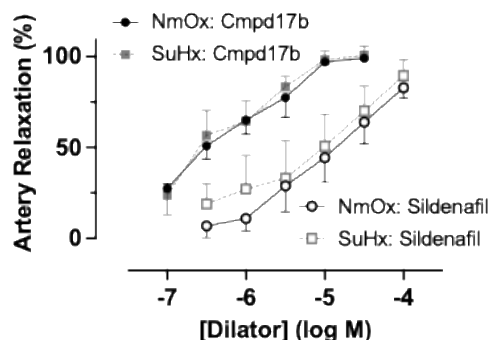
Introduction. New therapeutic approaches for pulmonary hypertension (PH) are urgently required to overcome the limited efficacy of current vasodilator therapy. The formyl peptide receptor (FPR) agonist Cmpd17b dilates pulmonary arteries from naïve mice under inflammatory conditions and exhibits pro-resolving effects *ex vivo* (Studley et al. 2023). The dual actions of Cmpd17b require validation in the gold-standard mouse model of PH and in human lung.

Aims. To compare beneficial actions of Cmpd17b with standard-of-care dilators using precision-cut lung slices (PCLS) from the validated Sugen/Hypoxia (SuHx) model of PH (mPCLS) and in human PCLS (hPCLS).

Methods. PCLS were prepared from agarose-inflated lungs from 9-week-old male C57BL/6J mice, either SuHx (20mg/kg Sugen 5416 weekly *s.c.*/4 weeks 10% O₂) or normoxic controls (NmOx, vehicle/21% O₂), or from non-diseased margins of human lung resections. Acute vasodilator responses to Cmpd17b, sildenafil or iloprost were visualised in serotonin (5HT)-constricted intrapulmonary arteries. hPCLS were treated overnight with TNF α +/- Cmpd17b to assay effects on IL-8 release with ELISA.

Results. In PCLS from NmOx and SuHx mPCLS, Cmpd17b induced relaxation with over 100-fold higher potency than sildenafil (pEC₅₀:7.8 \pm 0.8 vs 5.0 \pm 1.0, n=5-7 p<0.05). In hPCLS, 10 μ M Cmpd17b induced similar relaxation to iloprost, and inhibited TNF α -induced IL-8 secretion by 64% (n=8, p<0.05).

Discussion. Cmpd17b is a potent vasodilator of pulmonary arteries in PCLS from mice with PH and non-diseased human lung, and inhibits the secretion of a PAH-relevant inflammatory marker from PCLS. These findings support the development of FPR-based therapy against PAH.



Studley W et al (2023), Br J Pharmacol

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P302

Circadian Biology of Lung Cancer: Facilitated Through a Multiplexed, Perfused, Multi-Well Plate

Miss Jana Zielinski

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Jana graduated from the University of Melbourne in 2020 with a Bachelor of Science majoring in Pharmacology. She received her Honours degree in 2021 under the supervision of Prof. Alastair Stewart, with the thesis titled: "The Art and Artefact of Static Culture". Jana then began her PhD in 2022 with Prof. Alastair Stewart focusing on the characterisation of Casein Kinase 1 delta in circadian rhythm and cancer tumorigenesis. Her research goals include advancing the use of microphysiological systems for *in vitro* drug discovery. She was a general committee member of the ASCEPT student forum in 2023.

Circadian Biology of Lung Cancer: Facilitated Through a Multiplexed, Perfused, Multi-Well Plate

Jana L Zielinski^{1,2}, Xumei Gao^{1,2}, Alastair G Stewart^{1,2}. Dept of Biochemistry & Pharmacology, Univ of Melbourne¹, ARC Centre for Personalised Therapeutics Technologies², VIC, Australia.

Introduction. Disrupted circadian rhythm is associated with a variety of pathologies such as neurological disorders and cancer. There is emerging evidence linking tumour cell rhythmicity to mitotic genes enabling metastasis. Casein Kinase 1 Delta (CK1 δ) phosphorylates PER2 to regulate the circadian clock. Moreover, CK1 δ is implicated in many dysregulated signalling pathways that can trigger tumour progression. The rotary peristaltic multiplex pump (RPM2) allows for long-term *in vitro* circadian entrainment that has previously only been possible in *in vivo* circadian models (Gao et al, 2022).

Aims. To identify whether circadian entrainment demonstrates a CK1 δ -dependent influence on lung tumorigenesis.

Methods. The human lung adenocarcinoma cell line, A549, was transfected with human PER2::fluc using CRISPR-Cas9. 0-1000 nM, 2h cortisol incubation was used to induce circadian rhythm as measured by bioluminescence of PER2 expression. The CK1 δ/ϵ inhibitor PF670462 (0.1-10 μ M) and/or TGF- β (100 pM) were incubated post entrainment. The RPM2 was used to establish perfused multi-day circadian rhythm through daily cortisol (30 nM), 2h. Cell migration was measured with live cell microscopy (CM20, Olympus). Global and phospho-proteomes measured with LC-MS/MS Orbitrap Eclipse mass spectrometer over 24 hours of entrainment.

Results. Multi-day circadian entrainment was established *in vitro*. Global and phospho-proteomes were compared across the circadian day to identify the circadian proteome. PF670462 (3 μ M) increased PER2 expression in entrained and non-entrained cell and prevented ablation by TGF- β (100 pM) (n=5). FCS-induced cell migration was inhibited by PF670462 (3 μ M) and acted synergistically with cortisol (10-30 nM) for further inhibition (n=4).

Discussion. Disrupted circadian rhythm is a risk factor for cancer and its progression. Relevant *in vitro* models to study circadian entrainment may help unravel mechanisms behind functional phenotypes such as cell migration. Thus, identifying new potential drug targets and the potential to investigate their chrono-pharmacological actions.

Gao et al (2022) Comprehensive multiplexed superfusion system enables physiological emulation in cell culture: exemplification by persistent circadian entrainment. *Lab on a Chip*, 22(6):1137-1148

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P303

Complementary actions of casein kinase1d/e inhibitor PF670462 and tyrosine kinase inhibitor nintedanib

Dr Daniel Tan

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Complementary actions of casein kinase1d/e inhibitor PF670462 and tyrosine kinase inhibitor nintedanib

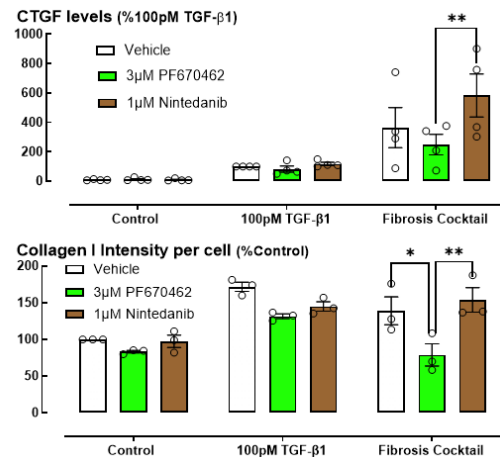
Meina Li^{1,2}, Daniel W S Tan^{1,2}, Qianyu Chen^{1,2}, Avanka Gunatilaka¹, Stephanie S Zhang¹, Bryan X Gao^{1,2}, Emma X Zhang^{1,2}, Shenna Langenbach¹, Alastair G Stewart^{1,2}. Dept of Biochemistry and Pharmacology, Univ of Melbourne¹, Parkville, VIC, Australia; ARC Centre for Personalised Therapeutics Technologies², Parkville, VIC, Australia.

Introduction. Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease with high healthcare and economic burden, and no cure available. Nintedanib is an FDA approved small molecule tyrosine kinase inhibitor for treatment of IPF, while PF670462 is a casein kinase 1 δ/ϵ inhibitor with anti-fibrogenic and anti-fibrotic activity.
Aims. To investigate the differential effects of PF670462 and nintedanib in various models of fibrogenesis in primary human lung fibroblast (LF).

Methods. LFs were incubated with TGF- β alone or a fibrosis cocktail (5 ng/ml TGF β 1, 400 pM PDGF, 5 μ M LPA and 1 U/ml Thrombin) and treated with either PF670462 or nintedanib. Fibrogenesis markers were examined by immunoassay and immunofluorescence at 72 h.

Results. The fibrosis cocktail showed marked increase in supernatant connective tissue growth factor (CTGF), interleukin-11 (IL-11) and plasminogen activator inhibitor-1 (PAI-1). IL-11 induced by the fibrosis cocktail was reduced by both PF670462 and nintedanib. However, the drugs demonstrated opposite effects on CTGF. Only nintedanib reduced fibrosis cocktail induced PAI-1 and only PF670462 reduced collagen I levels.

Discussion. The fibrosis cocktail presents a more complex in vitro model of fibrogenesis in ALF. PF670462 and nintedanib were shown to have differential effects on CTGF, PAI-1 and collagen I. There is a potential for PF670462 to work in combination with nintedanib, complementing each other for the treatment of IPF.



Keenan C R et al (2018) Frontiers in Pharmacology 10;9:738

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P304

Pirfenidone reduces poly I:C-induced inflammation in elastase treated precision cut lung slices

Dr Julia Chitty

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Julia completed her Bachelors of Science at Monash University in 2018, majoring in Pharmacology and Physiology. She then completed her Honours in Pharmacology in 2019 under the supervision of A/Prof Jane Bourke, Dr Belinda Thomas and Prof Phil Bardin. Julia began her PhD in this lab in 2020, focusing on pharmacological interventions to prevent the lung damage associated with viral induced exacerbations, which was conferred earlier this year. Julia is now working as a postdoc in the Bardin lab, continuing research on the project from her PhD'

Pirfenidone reduces poly I:C-induced inflammation in elastase treated precision cut lung slices.

JG Chitty^{1,2}, A Ali^{1,2}, PG Bardin^{1,3,4}, JE Bourke^{1,3}, BJ Thomas^{1,3}.

¹Centre for Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research, VIC, Australia. ²Pharmacology, Biomedicine Discovery Institute and ³Molecular and Translational Science, Monash University, VIC, Australia. ⁴ Monash Lung, Sleep, Allergy and Immunology, Monash Health, VIC, Australia

Introduction. Chronic obstructive pulmonary disease (COPD) ranks as the 3rd highest contributor to death globally, with acute exacerbations (AECOPD) a major contributor to mortality. Viral infections trigger over 50% of AECOPD and are amplified by the current standard-of-care COPD therapy, glucocorticoids (GCS). Pirfenidone (PFD), an anti-inflammatory, anti-fibrotic drug used for idiopathic pulmonary fibrosis, may offer a novel alternative. Herein, we utilised *ex vivo* precision cut lung slices (PCLS), a unique organotypic platform that maintains 3D lung architecture and all resident cells, to investigate effects of PFD in a model of AECOPD. Treatment with porcine pancreatic elastase (PPE) induces an emphysema-like phenotype, while poly I:C induces pro-inflammatory responses akin to viral exposure.

Aim. To determine whether PFD can reduce poly I:C-induced inflammation in elastase-treated PCLS.

Methods. Multiple PCLS were prepared from naïve mice and treated with PPE (2.5 µg/µl) or vehicle for 16 hrs, washed and media replenished, then left for a further 24 hrs to induce a COPD-like phenotype. PCLS were exposed to viral mimetic poly I:C (10 µg/µl) and treated with vehicle or PFD (500 nM) for up to 48 hr. PCLS and conditioned media were analysed for viability, histopathology, alveolar and inflammatory gene expression, and mediator production.

Results. MTT and LDH assays revealed PPE, poly I:C and PFD, alone or in combination, had no effect on PCLS viability. Treatment with PPE induced emphysema-like structural changes, including larger alveolar air spaces (control: 41.1 MLI, PPE: 55.6 MLI, $p < 0.01$) and decreased alveolar gene expression (*Aqp5*, *Sftpc*, *Rage*, $p < 0.01$). PPE-induced inflammatory gene expression (*Il-6*, *Il-8*, *Tnfα*, $p < 0.05$) and mediator release (*Il-6*, *KC*, $p < 0.01$) were further increased by poly I:C (*Il-6*: PPE *cf* PPE+poly I:C 1.5-fold, $p < 0.01$, *KC*: PPE *cf* PPE+poly I:C 2.2-fold, $p < 0.01$) and inhibited by PFD (genes *Il-6*, *Il-8* and mediators *Il-6*, *KC*, $p < 0.01$).

Discussion. Our study established an *ex vivo* PCLS model of AECOPD using PPE and poly I:C, resulting in an emphysema-like phenotype, reduced alveolar gene expression and increased inflammation. Treatment with PFD lowered inflammatory responses and may be a viable candidate as an alternative AECOPD therapy. Future studies will employ viral infection rather than poly I:C to establish the efficacy of PFD relative to the current standard GCS.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P305

Maternal Thirdhand E-vapour exposure impacts offspring lung health in experimental asthma model

Miss Andie Thorpe

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Andie Thorpe is a second-year PhD student at the University of Technology Sydney and the Woolcock Institute of Medical Research. Her research centres on the pulmonary effects of e-cigarette exposure, with a current focus on investigating the in-utero impacts of e-cigarette use and its implications for chronic respiratory diseases.

Maternal Thirdhand E-vapour exposure impacts offspring lung health in experimental asthma model

Andrew E Thorpe^{1,2}, Chantal Donovan^{1,2,3}, Richard Kim^{1,2,3}, Meng Wang^{1,2}, Xu Bai^{1,2}, Rochelle Yarrak¹, Hui Chen¹, Brian Oliver^{1,2}. School of Life Sciences, University of Technology Sydney¹, Sydney, NSW, Australia; Woolcock Institute of Medical Research, Respiratory Cellular and Molecular Biology², Sydney, NSW, Australia; University of Newcastle, Immune Health Program, Hunter Medical Research Institute³, Newcastle, NSW, Australia

Introduction. Women of childbearing age (14 - 45) comprise the highest demographic of e-cigarette usage globally, with little regulation around exposure, due to the perception that e-cigarettes are harm-free. Third hand exposure to e-cigarette vapour has been shown to cause negative biologic effects including immune regulatory and pulmonary effects [1, 2]. **Aims.** To determine the impact that in utero exposure on foetal health outcomes specifically chronic respiratory diseases including asthma.

Methods. 6-week-old Female Balb/c mice were exposed to third hand e-vapour encompassing a variety of e-cigarette usage behaviours (Low power (LP)& High power (HP), +/- nicotine (NIC)) for 15 weeks; inclusive of pre-exposure, gestation, and weaning periods. Female offspring from maternal (m) exposed mice were intraperitoneally administered ovalbumin (OVA) followed by intranasal OVA challenges (12,13 & d33,34) to induce experimental asthma. At the endpoint (d35), lung function analysis was conducted with a methacholine challenge to test for airway hyperresponsiveness and bronchoalveolar lavage fluid was collected to measure airway inflammation.

Results. Maternal third hand e-vapour exposure affected offspring lung health. Airway hyperresponsiveness was observed mLP-NIC vs mSHAMOVA (P<0.001). Airway inflammation was increased in high power setting groups regardless of nicotine concentration mHP-NIC and mHP+NIC vs mSHAMOVA (P<0.05). These findings were confirmed by histological inflammation scoring.

Discussion. Nicotine and non-nicotine containing e-cigarettes can produce harmful effects at a third-hand exposure level. These findings indicate the potential public health impact that third hand e-cigarette exposure can have during pregnancy and maternal exposure on respiratory health outcomes.

[1] Thorpe, A.E., et al., Third-Hand Exposure to E-Cigarette Vapour Induces Pulmonary Effects in Mice. *Toxics*, 2023. 11(9): p. 749. [2] Chen, H., et al., Evidence from a mouse model on the dangers of thirdhand electronic cigarette exposure during early life. *ERJ Open Research*, 2020. 6(2): p. 00022-2020.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P306

Targeting CXCR3 with SCH546738 reduces disease features in severe asthma

Dr Madison Coward-Smith

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Targeting CXCR3 with SCH546738 reduces disease features in severe asthma

Madison Coward-Smith¹, Chantal Donovan^{1,2,3}, Jessica Tolentino¹, Eyla Oxborrow¹, Andrew E. Thorpe^{1,3}, Brian GG Oliver^{1,3}, Richard Y Kim^{1,2,3}. School of Life Sciences, University of Technology Sydney¹, Sydney, NSW, Australia. School of Biomedical Sciences and Pharmacy, University of Newcastle², Newcastle, NSW, Australia. Woolcock Institute of Medical Research³, Sydney, NSW, Australia.

Introduction: Severe asthma is the major unmet clinical need in asthma management. Despite recent advances in biologics, many patients are unable to gain disease control and/or experience side effects, necessitating more effective therapies. Targeting CXCR3, a chemokine receptor present on T cells, with TAK-779 (non-selective CXCR3 and CCR5 antagonist) improves disease features in asthma, however, whether selectively targeting CXCR3 with SCH546738 (a selective CXCR3 antagonist) to reduce CCR5-modifying side effects remains unexplored.

Aim: To assess the effects of intranasal administration of SCH546738 in a clinically relevant mouse model of severe asthma.

Methods: Female BALB/c mice ($n=8$ /group) were sensitised to ovalbumin (Ova; intraperitoneal) on day 0 (or saline control), followed by intranasal Ova challenges (days 12-13) to induce experimental asthma. Mice were then infected with the bacteria, *Chlamydia Muridarum* (Cmu; day 14) or SPG control, which resolved prior to re-challenge with Ova (days 33-34) in the absence, or presence, of dexamethasone (DEX; 2mg/kg) to model inhaled corticosteroid therapy. Some groups of severe asthma (Ova/Cmu) mice were administered SCH546738 (intranasal; 10mg/kg) (days 32-34) in the absence or presence of DEX. On endpoints (day 35) *in vivo* invasive plethysmography was conducted to measure airway hyperresponsiveness and bronchoalveolar lavage was collected to measure airway inflammation.

Results: Treatment with SCH546738, but not DEX, in severe asthma suppressed airway hyperresponsiveness to methacholine and reduced airway inflammation (macrophages and lymphocytes) but had no effect on asthma-induced neutrophils or eosinophils.

Discussion: Treatment with SCH546738 in experimental severe asthma reduces normally intractable airway hyperresponsiveness and inflammation, warranting further investigation of its therapeutic utility in severe asthma.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P307

Targeting the chemokine receptor, CXCR3, SCH5436738 in asthma

Ms Jessica Tolentino

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Jessica Tolentino is a Honours student at the University of Technology Sydney. Her research focuses on asthma, with a primary focus on targeting the alpha-chemokine receptor, CXCR3, with a potent inhibitor to treat and manage asthma.

Targeting the chemokine receptor, CXCR3, with SCH546738 in asthma

Jessica Tolentino¹, Richard Y Kim^{1,2}, Eyla Oxborrow¹, Madison L Coward-Smith¹, Andrew E Thorpe^{1,2}, Brian GG Oliver^{1,2}, Chantal Donovan^{1,2}. School of Life Sciences, Univ of Technology Sydney¹, Sydney, NSW; Respiratory Cell and Molecular Biology, Woolcock Institute of Medical Research², Sydney, NSW.

Introduction. Asthma is a chronic inflammatory disease characterised by airway hyperresponsiveness (AHR), inflammation, and airway remodelling resulting in the permanent restructuring of the airways. T helper cells play critical roles in allergic asthma and their movements in the lung are coordinated by chemokines, cytokines, and their receptors. Targeting CXCR3, an alpha-chemokine receptor, with a potent CXCR3 inhibitor (SCH546738) prevents allergic inflammation and airway hyperresponsiveness, however the precise roles and the potential for therapeutic targeting of CXCR3 for the treatment and management of allergic asthma remains unclear.

Aim. To characterise the roles of targeting CXCR3 on lung inflammation and AHR in asthma.

Methods. Mice (n=8/group) were administered ovalbumin (Ova; 50µg) i.p. (day 0; or saline control) to induce allergic sensitisation. Mice were then challenged with Ova i.n. (or saline control) (days 12-15) to induce allergic asthma. Some mice were treated (days 11-15) with a CXCR3 inhibitor (or vehicle), SCH546738 (SCH; 10mg/kg). Endpoint analysis (day 16) included lung function measurements to assess AHR in relation to increasing doses of methacholine, airway inflammation measured in bronchoalveolar lavage fluid, and flow cytometry on lung single cell suspensions to detect and analyse the characteristics of immune cells.

Results. Ova-treated mice (Ova/veh; experimental asthma) had AHR compared to the Sal control. Administration of SCH in Ova-treated mice (SCH/Ova) significantly decreased AHR compared to Ova/veh (vehicle-treated controls). Ova-treated mice had increased airway inflammation compared to Sal/veh reflected by a significant increase in the total leukocytes detected. SCH/Ova-treated mice had decreased airway inflammation compared to Ova/veh. Ova also increased the number of immune cells present in lung tissue compared to Sal/veh. SCH/Ova-treated mice also increased in the number of immune cells compared to Ova alone.

Discussion. Inhibiting the alpha-chemokine receptor, CXCR3, with SCH546738 reduces AHR, decreases airway inflammation, and increases lung immune cells. These data highlight the need for further exploration of its potential therapeutic application in the treatment and management of allergic asthma.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P308

Soft-Cultured Lipofibroblasts Produce an Antifibrogenic Secretome

Mr Avanka Gunatilaka

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Soft-Cultured Lipofibroblasts Produce an Antifibrogenic Secretome

Avanka Gunatilaka^{1,2}, Asres Berhan¹ Alastair Stewart^{1,2}. ¹Department of Biochemistry and Pharmacology, ²ARC Centre for Personalised Therapeutics Technologies, The University of Melbourne, Parkville, VIC, Australia

Introduction. Idiopathic Pulmonary Fibrosis (IPF) is a progressive disease in which the lung parenchyma undergoes irreversible remodelling. We previously demonstrated that in a permissively soft microenvironment myofibroblasts, notable drivers of the remodelling and fibrogenesis, undergo differentiation to a lipofibroblast-like phenotype that is resistant to TGF- β -induced fibrogenesis. Intriguingly, these soft-cultured lipofibroblasts can condition culture media with antifibrogenic mediator(s) that potently and dose-dependently reduce basal and TGF- β -induced fibrogenesis.

Aims. This study seeks to characterize the conditioned media's antifibrogenic actions and ascertain the antifibrotic mediator(s) being produced by the lipofibroblasts.

Methods. Human pulmonary fibroblasts were cultured in a 2D stiff (monolayer) or 3D soft (spheroid) microenvironment and conditioned media collected from spheroids cultures was used to bioassay fibroblasts in a stiff monolayer in the presence or absence of TGF- β . Antifibrogenic activity was assessed by readouts at protein and message levels, and by functional assays such as a collagen gel compaction assay.

Results. Fibroblast monolayers treated with lipofibroblast-conditioned media (LipoCM) had reduced expression of α -SMA and Collagen 1 compared to vehicle, both at baseline and, strikingly, following 48-hour incubation with 100pM TGF- β . Fibroblasts treated with LipoCM failed to remodel collagen gels in the presence or absence of TGF- β . Preliminary benchmarking experiments show LipoCM inhibiting fibrogenesis with superior efficacy to existing antifibrotics, pirfenidone and nintedanib.

Discussion. This study revealed that a mechanopharmacology paradigm can be employed to drive pulmonary fibroblasts to produce an antifibrogenic secretome. The secretome contains novel antifibrogenic mediators that show promising efficacy and may complement existing drugs which have limited efficacy and tolerability issues in patients with IPF. This work also suggests that lipofibroblasts *in vivo* contribute to homeostasis within the lung, in a protective mechanism that may be impaired by lung stiffening. In ongoing work, we intend to assess the ability of LipoCM to resolve existing fibrotic lesions and regenerate damaged alveolar epithelial cells as a means of restoring physiological lung architecture and function.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P309

HIF-1 α mediates mitochondrial damage of FLS in rheumatoid arthritis by down-regulating ALKBH7

Prof Lingling Zhang

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Lingling Zhang, MD, Professor, doctoral supervisor. The director of the Institute of Clinical Pharmacology of Anhui Medical University, the academic technology leader of Anhui Province, the top talent of universities in Anhui Province, and the high-level C-class talent of Anhui Province. Act as the director of the Chinese Pharmacological Society, the vice chairman of the Clinical Pharmacology Committee of the Chinese Pharmacological Society, and the chairman of the clinical pharmacology committee of the Anhui Pharmacological Society. Research interests are anti-inflammatory immunopharmacology, clinical pharmacology and cellular immunotherapy development. Gained four National Natural science funds and more than ten provincial funds. Published more than 200 papers (including more than 80 SCI papers). Won the Anhui Youth Science and Technology Award, the first prize of Anhui Province Science and Technology Award, the Chinese Pharmacological Society SERVIER Young Pharmacologists Award, the first prize of the second and third Anhui Industrial Innovation Competition, the first prize in the third Grand Final of the Yangtze River Delta Translational Medicine Innovation and Entrepreneurship Competition, the third prize in Industrial Innovation Competition of the first Hefei "Kechuang Cup", and one invention patent. Won the honorary titles of the most beautiful scientific and technological worker in Anhui Province, the Model of the teacher's ethics of the postgraduate tutor in Anhui Province, the famous teacher of postgraduate education and teaching in Anhui Province, and the "Excellent Instructor" of the "Internet +" College Student Innovation and Entrepreneurship Competition in Anhui Province.

HIF-1 α mediates mitochondrial damage of FLS in rheumatoid arthritis by down-regulating ALKBH7

Lingling Zhang*, Han Wang, Xianzheng Zhang, Yuchen Zhao, Tianjing Zhang, Jiemin Zhao, Qingtong Wang, Wei Wei. Institute of Clinical Pharmacology, Anhui Medical University, Key Laboratory of Anti-inflammatory and Immune Medicine, Ministry of Education, Anhui Collaborative Innovation Center of Anti-inflammatory and Immune Medicine, Hefei, Anhui, China.

Introduction. Rheumatoid arthritis (RA) is an autoimmune disease characterized by synovial hyperplasia and progressive joint destruction. Fibroblast-like synoviocytes (FLS), as effector cells of RA, have been shown to directly cause local cartilage destruction and synovial inflammation in the joint. Compared with healthy people, the infiltrated immune cells, high levels of inflammatory factors and dysfunction of vascular endothelial cells in the synovial tissue of RA patients led to the formation of a hypoxic microenvironment in the synovial tissue, and the level of hypoxia-inducible factor-1 α (HIF-1 α) was significantly increased. Studies have shown that HIF-1 α can regulate the expression of multiple protein molecules to promote joint inflammation, angiogenesis and cartilage destruction in RA patients.

In previous studies on the relationship between abnormal activation of FLS and hypoxia, we also found that compared with OA-FLS, more mitochondria were damaged in RA-FLS, mainly manifested as mitochondrial swelling, ridge disappearance and mitochondrial membrane rupture. Damaged mitochondria turn the mitochondrial matrix, especially, mitochondrial DNA (mtDNA) is released into the cytoplasm and is sensed by cyclic GMP-AMP (cGAS) and catalyzes ATP and GTP synthesis

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



of cyclic GAMP (cGAMP). Subsequently, cGAMP binds to the stimulator of interferon genes (STING), resulting in conformational changes in STING, activating the IFN regulatory factor 3 (IRF3) and NF- κ B signaling pathways, leading to inflammation and even autoimmune diseases. These findings suggest that mitochondrial damage due to hypoxia may be a key factor in the abnormal activation of RA-FLS, but the molecular mechanism of mitochondrial damage caused by hypoxia is currently unclear. Notably, as a mitochondrial matrix-resident protein, ALKBH7 is mainly involved in mitochondrial homeostasis regulation by mediating mtRNA demethylation levels. The depletion of ALKBH7 leads to increased misprocessing of polycistronic mtRNAs and decreased mitochondrial protein translation levels, resulting in mitochondrial homeostasis imbalance. So does HIF-1 α as a transcription factor cause mitochondrial damage by downregulating the expression of ALKBH7?

Aims. HIF-1 α triggers mitochondrial damage by downregulating the expression of ALKBH7 with target manner thereby promoting FLS activation.

Methods. In this study, the Collagen-induced arthritis (CIA) model established by hif-1 α +/- mice, adjuvant arthritis (AA) model established by Wistar rats and FLS were used as the research objects, and the role of HIF-1 α in the pathological process of CIA mice was evaluated by small animal ultrasound, X-ray, flow cytometry, safranin-fast green staining and hematoxylin-eosin staining. The relationship between hypoxia, mitochondrial damage and abnormal activation of FLS was studied by RNA-Seq, CUT-Tag, plasmid overexpression, small interference and western blotting to clarify the molecular mechanism of HIF-1 α mediating mitochondrial damage leading to abnormal activation of FLS through targeted inhibition of ALKBH7 expression, which provided a theoretical basis for further revealing the pathological process of RA, discovering the early characteristics of RA course, and realizing early diagnosis and early targeted therapy.

Results. The expressions of HIF-1 α , cGAS and STING proteins in synovial tissues of RA patients and AA rats were significantly increased. It was found that hypoxia and abnormal activation of cGAS-STING signal existed in FLS. Hypoxia leads to mitochondrial damage, abnormal activation of cGAS-STING signal and FLS. The protein and mRNA levels of cGAS and STING in FLS were significantly increased after hypoxia treatment. At the same time, hypoxia can significantly up-regulate the mRNA levels of inflammatory cytokines TNF- α , IL-1 β , IL-6 and chemokines CXCL8, CXCL9, CXCL10 and CXCL11 in FLS. Silencing HIF-1 α inhibits mitochondrial damage, abnormal activation of cGAS-STING signaling and FLS induced by hypoxia. The clinical symptoms were improved and the clinical score was reduced in CIA mice with HIF-1 α knockout. HIF-1 α knockout could significantly improve the blood flow signal and cartilage injury of the knee or ankle joint of CIA mice. The pathological changes of the knee and ankle joints of CIA mice, such as synovial hyperplasia, inflammatory cell infiltration, pannus and cartilage damage HIF-1 α knockout were significantly improved. HIF-1 α knockout significantly reduced the serum levels of inflammatory cytokines TNF- α and IL-1 β and decreased the ratio of Th17/Treg. The expression of cGAS and STING in the synovial tissues of the knee and ankle joints of the HIF-1 α knockout mice was significantly lower than that of the CIA mice. HIF-1 α could bind to ALKBH7 promoter to inhibited the expression of ALKBH7. Silencing ALKBH7 promoted abnormal activation of FLS and cGAS-STING signaling. Silencing ALKBH7 promoted the proliferation and migration of FLS, increased the levels of inflammatory cytokines TNF- α and IL-1 β and chemokines CXCL8, CXCL9 and CXCL10 in FLS, the protein expressions of cGAS and STING in FLS were significantly up-regulated after ALKBH7 silencing. Low levels of ALKBH7 trigger mitochondrial damage in FLS by downregulating the expression of UQCRC2. Overexpression of ALKBH7 significantly inhibited hypoxia-induced abnormal activation of FLS and cGAS-STING signaling. Overexpression of ALKBH7 significantly inhibited the migration ability of FLS, inhibited the up-regulation of inflammatory cytokines and chemokines mRNA levels in FLS induced by hypoxia and significantly inhibited the up-regulation of cGAS and STING protein and mRNA levels caused by hypoxia.

Discussion. RA-FLS is characterized by hypoxia, mitochondrial damage, and abnormal activation of cGAS-STING signaling. Hypoxia promotes abnormal activation of FLS by inducing mitochondrial damage and activating cGAS-STING signaling. Hypoxia-induced mitochondrial damage promoting abnormal activation of FLS is caused by up-regulation of HIF-1 α . HIF-1 α downregulates the expression of ALKBH7 by binding to the ALKBH7 promoter site, resulting in mitochondrial damage. The down-regulation of ALKBH7 mediates mitochondrial damage mainly by affecting the expression of UQCRC2.

Supported by the National Natural Science Foundation of China (82204403, 82373878), Major Projects of Anhui Provincial Department of Education (2023AH040080).

*Corresponding author: Ll-zhang@hotmail.com

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P310

Targeting cAMP-specific phosphodiesterase to treat acute respiratory distress syndrome

Prof Tsong-Long Hwang

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Hwang's laboratory employs pharmacological approaches to elucidate the molecular mechanisms driving the inflammatory response of human neutrophils and to identify potential therapeutic targets for treating neutrophil-associated diseases, including acute respiratory distress syndrome, asthma, diabetics, liver injury and fibrosis, psoriasis, and arthritis. His research has identified drug-lead compounds that target critical receptors or molecules to regulate the neutrophilic inflammatory response, potentially contributing to the development of innovative therapies. Dr. Hwang has published over 496 research papers and holds 40 patents. He has also initiated 20 industry-academia collaboration projects and facilitated four technology transfers with various companies, highlighting the significant medical applications of his research.

Dr. Hwang holds several key positions in academic organizations in Taiwan. He is the President of the Society for Free Radical Research-Taiwan, the President of the Taiwan Association for Traditional and Complementary Medicine, and the Director of the Pharmacological Society in Taiwan. Dr. Hwang served as the Convenor of the Division of Pharmacy and Chinese Medicine, Department of Life Sciences, Ministry of Science and Technology, Taiwan, from 2017 to 2019, assisting the government in promoting and advancing academic research. In 2019, Dr. Hwang was honored to be appointed as the Honorary President of The Society of Chinese Natural Medicine in Taiwan. Dr. Hwang was invited by Frontiers, a global academic publishing organization, to create a new journal titled Frontiers in Natural Products and to serve as its Field Chief Editor starting in 2022.

Tsong-Long Hwang_ASCEPT-APFP-APSA2024_Abstract.pdf (could not be inserted)

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P311

Therapeutic features of Cold Atmospheric Plasma in the Treatment of Atopic Dermatitis

Mr Jabborov Abdulaziz

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Therapeutic features of Cold Atmospheric Plasma in the Treatment of Atopic Dermatitis

Abdulaziz Jabborov¹, Na-hee Jeong¹, Young-ae Choi¹, Sang-hyun Kim¹. Department of pharmacology, School of Medicine, Kyungpook National University¹, Daegu, Republic of Korea.

Introduction. Drugs recently developed for the treatment of atopic dermatitis (AD) are difficult to access for individuals due to their high cost. Meanwhile, dexamethasone (Dexa), an immunosuppressant, is widely used due to its excellent cost-effectiveness despite various side effects.

Aims. In this study, we evaluated the effectiveness and elucidated the underlying mechanism of using the cold atmospheric plasma (CAP) patch device to obtain effective treatment efficacy while minimizing the side effects of Dexa.

Methods. AD-like skin lesions were induced on the back skin using 2,4-Dinitrochlorobenzene (DNCB)/Dermatophagoides farinae extract (DFE), followed by treatment with 0.025% Dexa, 10 times lower concentration than general usage, CAP or Dexa plus CAP.

Results. The phenotypical changes of AD were ameliorated in Dexa plus CAP group compared to single treated-group. And, the expression of Th2 cytokines, including IL-4 and IL-13, and skin barrier regulatory proteins, including PAR2, claudin-1, occludin, and ZO-1, in the lesional skin tissue were significantly reduced by the combination of CAP patch. Moreover, 14-3-3, a sodium channel-associated protein, also decreased by CAP application.

Discussion. Conclusively, our research suggests that the application of the CAP patch in conjunction with low-dose steroids effectively promotes their therapeutic efficacy in AD while mitigating the adverse effects.

McCartney P (2001) J J 56:23-33

Starr R et al (2005) Pharmacology of FAB-4, ed Ono Y. pp 12-23, Tokyo, Abbey Road Press

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P312

A novel coumarin-based MT compound exhibits anti-inflammatory activities in LPS-activated macrophages

Prof Ming-jen Hsu

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Ming-Jen Hsu is a Professor and Chair at the Department of Pharmacology, Taipei Medical University, and the current Secretary-General of The Pharmacological Society in Taiwan. He completed his Ph.D. at the Graduate Institute of Pharmacology, National Taiwan University. His research specializes in signal transduction, molecular pharmacology, and drug development, with a focus on hydroxamate-based compounds as potential therapeutic agents for inflammatory diseases and cancers.

*In collaboration with Prof. Wei-Jan Huang (Taipei Medical University), Dr. Hsu's team investigates the anti-inflammatory, anti-angiogenic, and anti-tumor effects of WMJ hydroxamate derivatives. He also collaborates with Professor Filippo Cottiglia (University of Cagliari) on studying natural compounds, including MAG benzofuran glycosides and MT coumarins, derived from *Magydaris tomentosa*, which demonstrate promising anti-inflammatory and anti-angiogenic properties. His recent work explores the role of MT116 in modulating protein phosphatase, deubiquitinases, and COX-2 degradation in LPS-activated macrophages, with a view to its application in treating chronic respiratory diseases.*

A novel coumarin-based MT compound exhibits anti-inflammatory activities in LPS-activated macrophages

Min-Jen Hsu^{1,2}, Shiu-Wen Huang^{1,2}, Hsiu-Chen Chen^{1,2}, Filippo Cottiglia³. Department of Pharmacology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan¹; Graduate Institute of Medical Sciences, College of Medicine, Taipei Medical University, Taipei, Taiwan²; Department of Life and Environmental Sciences, University of Cagliari, Cittadella Universitaria di Monserrato, Monserrato, Italy³

Introduction. Coumarins is a natural bioactive compound found in abundant medical plants, and its derivatives have been indicated with their versatile pharmacological activities, including the well-known anticoagulant Warfarin. Given the established low toxicity and occurrence of coumarins in various herbal remedies, further exploring their bioactivities and underlying mechanisms appears prudent.

Aims. To develop a novel pharmacological agent that could suppress abnormally activated macrophages, we evaluated the anti-inflammatory effects of novel natural coumarin-based compounds (MT compounds), extracted from the seeds of *Magydaris tomentosa*, and explored its underlying mechanisms.

Methods. RAW264.7 murine macrophages were stimulated by LPS in the absence or presence of MT compounds. Cyclooxygenase-2 (COX-2) expression and signaling molecules altered by MT compounds in LPS-stimulated macrophages were analyzed by immunoblotting, MTT, qRT-PCR, chromatin immunoprecipitation (ChIP), ELISA, and reporter assays. We also performed an endotoxemia model to evaluate MT compounds' *in vivo* anti-inflammatory effects.

Results. Among these compounds, MT116 treatment resulted in a significant decrease in both COX2 mRNA and protein expression. It was associated with the inhibitory effect of MT116 on both p38MAPK and CCAAT/enhancer-binding protein β (C/EBP β) phosphorylation and according to the observation of p38MAPK-mediated C/EBP β activation validated by previous studies, it suggests that MT116 probably dephosphorylates p38MAPK to suppress C/EBP β activity. Reduced C/EBP β activity by MT116 was further indicated via chromatin immunoprecipitation that MT116 inhibited LPS-induced C/EBP β binding upon the COX2 promotor region. Moreover, decreasing phosphorylation of p38MAPK and C/EBP β retarded

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



by MT116 was restored via cell transfection of dominant-negative mutant of MAPK phosphatase-1 (MKP-1-DN). MKP-1-DN could reverse MT116-associated decline in COX2 protein expression as well. Intriguingly, MT116 treatment was also indicated with decreasing COX2 3'UTR luciferase and escalated COX2 degradation induced by LPS stimulation. Furthermore, MT116 significantly increased mice survival rates in an endotoxemia model.

Discussion. To conclude, MT116 dephosphorylated p38MAPK via MKP-1, which in turn deactivated C/EBP β to suppress C/EBP β binding on the COX2 promotor region, resulting in decreasing COX2 expression in LPS-activated macrophages. In addition to early transcriptional regulation, MT116 also participated in post-transcriptional and translational regulation of COX-2. The present study suggests that MT116 may be a potential lead for alleviating inflammatory diseases that are associated with abnormally activated macrophages.

P313

Myrmecodia platytyrea tuber extract modulates inducible enzyme expressions in lipopolysaccharide-activated murine macrophages

Dr Aisyah Jaafar

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Aisyah is a PhD candidate in Pharmacology at the Faculty of Pharmacy, Universiti Teknologi MARA, Malaysia. Her doctoral research explores the immunomodulatory potential of a traditional medicinal plant, which focuses on its effects and underlying mechanism against inflammation and oxidative stress. She earned her Bachelor's degree in medicine and surgery from Alexandria University, Egypt, and previously served as a medical officer. Currently, she is a trainee medical lecturer in the Department of Pharmacology, Faculty of Medicine, Universiti Teknologi MARA, where she continues to cultivate her passion and advance her research skills in Pharmacology.

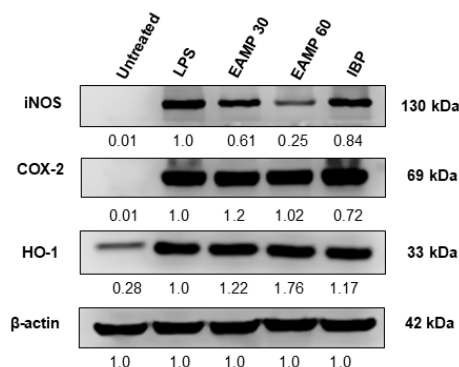
Myrmecodia platytyrea tuber extract modulates inducible enzymes expression in lipopolysaccharide-activated murine macrophages

Aisyah Jaafar^{1,2}, Fazleen Haslinda Mohd Hatta¹, Nurul Alimah Abdul Nasir², Aisyah Hasyila Jahidin¹, Mizaton Hazizul Hasan¹. Faculty of Pharmacy, Universiti Teknologi MARA¹, Puncak Alam, Selangor, Malaysia; Faculty of Medicine, Universiti Teknologi MARA², Sungai Buloh, Selangor, Malaysia.

Introduction. *Myrmecodia platytyrea* (Rubiaceae) has been traditionally utilised to boost the immune health. Our early findings indicated the immunomodulatory capacity of *M. platytyrea* tuber ethyl acetate extract (EAMP) against lipopolysaccharide (LPS)-induced inflammation. However, it is still not fully understood how it affects the inducible inflammatory and antioxidant enzymes in this context.

Aims. To investigate the effects of EAMP on inflammation via protein expression of inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and heme oxygenase-1 (HO-1) in LPS-activated RAW 264.7 cells.

Methods. RAW 264.7 cells were incubated with or without EAMP (30 and 60 $\mu\text{g}/\text{mL}$) or ibuprofen (200 μM) and induced with LPS for 24 h. The expression of iNOS, COX-2 and HO-1 was determined using Western blot and normalised with β -actin as the loading control.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Results. LPS-induced RAW 264.7 cells showed increased expression of iNOS ($p < 0.0001$), COX-2 ($p < 0.001$), and HO-1 ($p < 0.01$) compared to the untreated control. EAMP at both concentrations (30 and 60 $\mu\text{g}/\text{mL}$) significantly decreased LPS-induced iNOS expression by 39% and 75%, respectively. Meanwhile, LPS-induced HO-1 expression was markedly increased by 76% upon treatment with EAMP at 60 $\mu\text{g}/\text{mL}$. However, EAMP did not have a significant effect on LPS-induced COX-2 expression.

Discussion. EAMP may abate inflammation by attenuating iNOS and elevating HO-1 protein expressions. More research is needed to determine the role of HO-1 as a possible therapeutic target of EAMP against inflammatory immune response, which acts as the crosstalk between the antioxidant and inflammatory signalling pathways.

P314

Effect of *Myrmecodia platytyrea* extract on lipopolysaccharide-stimulated inflammatory mediators in murine macrophages

Dr Aisyah Jaafar

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Aisyah is a PhD candidate in Pharmacology at the Faculty of Pharmacy, Universiti Teknologi MARA, Malaysia. Her doctoral research explores the immunomodulatory potential of a traditional medicinal plant, which focuses on its effects and underlying mechanism against inflammation and oxidative stress. She earned her Bachelor's degree in medicine and surgery from Alexandria University, Egypt, and previously served as a medical officer. Currently, she is a trainee medical lecturer in the Department of Pharmacology, Faculty of Medicine, Universiti Teknologi MARA, where she continues to cultivate her passion and advance her research skills in Pharmacology.

Effect of *Myrmecodia platytyrea* extract on lipopolysaccharide-stimulated inflammatory mediators in murine macrophages

Aisyah Jaafar^{1,2}, Mizaton Hazizul Hasan¹, Fazleen Haslinda Mohd Hatta¹, Nurul Alimah Abdul Nasir², Aisyah Hasyila Jahidin¹. Faculty of Pharmacy, Universiti Teknologi MARA¹, Puncak Alam, Selangor, Malaysia; Faculty of Medicine, Universiti Teknologi MARA², Sungai Buloh, Selangor, Malaysia.

Introduction. *Myrmecodia platytyrea* is a traditional medicinal plant native to Southeast Asia, the Papua and Cape York, Australia. The tuber extracts possess anticancer, antidiabetic, and antimicrobial effects, attributed to the rich presence of flavonoids, alkaloids, terpenoids and polyphenols (Dirgantara et al, 2022). Nevertheless, the impact of its ethyl acetate extract on the inducible inflammatory enzymes and markers has not been thoroughly studied.

Aims. We evaluated the effect of *M. platytyrea* ethyl acetate extract on gene expression of inflammatory enzymes (iNOS and COX-2) and protein expression of inflammatory markers (NO and PGE2) in lipopolysaccharide (LPS)-induced murine RAW 264.7 macrophages.

Methods. RAW 264.7 cells were pre-treated with *M. platytyrea* extract or ibuprofen (drug control) for 1 h and induced with LPS for 4 h (gene expression study) or 24 h (protein analysis). The cells were harvested and RNA was extracted for gene expression study of iNOS and COX-2 using real-time qPCR. Meanwhile, culture media were collected for measuring NO level using Griess assay, and PGE2 level using enzyme-linked immunosorbent assay (ELISA).

Results. *M. platytyrea* extract at 30 and 60 $\mu\text{g}/\text{mL}$, and ibuprofen at 200 μM were shown to suppress LPS-stimulated iNOS expression from 49.38-fold to 29.93-fold ($p = 0.2873$), 16.92-fold ($p = 0.0449$) and 10.24-fold ($p = 0.0167$), respectively. Similarly, the LPS-stimulated NO production was significantly diminished by *M. platytyrea* extract (30 and 60 $\mu\text{g}/\text{mL}$) and

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



ibuprofen (200 μ M). However, treatment of the RAW 264.7 macrophages with *M. platytyrea* extract and ibuprofen had no significant effect on LPS-stimulated expressions of COX-2 and its metabolite, PGE₂.

Discussion. The current work elucidated the potential immunomodulatory impact of *M. platytyrea* extract for treating LPS-induced inflammation by inhibiting iNOS/NO expression but not COX-2/PGE₂ in murine macrophages, which requires future investigations into its cellular mechanisms of action.

Dirgantara et al (2022) Open Access Maced J Med Sci 10(F):97-103.

P315

Methyl eugenol improves ovariectomy-induced osteoporosis in rats and suppresses osteoclastogenesis in vitro

Prof Yen-mei Lee

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Methyl eugenol improves ovariectomy-induced osteoporosis in rats and suppresses osteoclastogenesis *in vitro*

Yen-Mei Lee, Yu-Hsuan Tseng. Department of Pharmacology, National Defense Medical Center, Taipei, Taiwan.

Introduction. Osteoporosis is classified by the WHO as the world's second most disease epidemiologically. Bone formation and resorption are mainly regulated by the interplay between osteoblast (OB) differentiation and osteoclast (OC) activation. With increasing age and menopause, the balance shifts to more bone resorption than bone formation. RANKL, the main stimulus of osteoclasts differentiation, is released by OB and can induce osteoclastogenesis via binding to its receptor RANK, leading to recruitment of TRAF6, and subsequent activation of MAPK and NF- κ B pathways in OC precursors. Pro-inflammatory cytokines and oxidative stress can enhanced RANKL-induced osteoclastogenesis. Methyl eugenol (MEG) is naturally present in angiosperms and has been proven to have anti-inflammatory, and antioxidant effects. The anti-osteoporotic effect of MEG has not been reported.

Aims. The aim of this study is to explore whether MEG can prevent ovariectomy (OVX)-induced osteoporosis in rats and reduce RANKL-induced osteoclastogenesis in macrophage RAW264.7 cells.

Methods. Eight-week-old Wistar female rats were bilaterally ovariectomized to induce osteoporosis. MEG 30 and 60 mg/kg was given by gavage for eight weeks, beginning at one week after OVX (once daily, six days a week). The inhibitory effect of MEG on osteoclastogenesis was examined in RANKL (50 ng/mL)-stimulated RAW264.7 cells.

Results. MEG 30 and 60 mg/kg significantly improved OVX-induced bone loss and the changes of bone morphology parameters. MEG 60 mg/kg reduced the plasma levels of OC marker TRAcP 5b and the TRAcP 5b-positive area in femurs. Furthermore, MEG significantly reduced RANKL-mediated OC differentiation evidenced by attenuation of TRAP activity and numbers of multinucleated OCs. The protein expression of RANK, TRAF6, NF- κ B p-p65, p-p38, NFATc1 were also reduce by MEG. In addition, MEG inhibited the protein expression of inflammatory cytokines TNF- α and IL-6, meanwhile, it increased the protein levels of antioxidant protein HO-1 and its transcription factor Nrf2 in OCs.

Discussion. MEG prevents estrogen deficiency-induced osteoporosis and inhibits RANKL-induced osteoclastogenesis by decreasing the activation of NF- κ B and p38 MAPK pathways. The anti-inflammatory and antioxidant effects of MEG may contribute to preventing bone loss.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P316

Coffea arabica pulp extract and its potential therapy to treat colitis

Mr Purit Kulworasreth

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Purit Kulworasreth is a 2nd year medical student at Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy, Bangkok, Thailand.

Coffea arabica pulp extract and its potential therapy to treat colitis

Purit Kulworasreth¹, Supisara Treveeravoot^{1,2}, Apiwan Arinno^{2,3}, Pawin Pongkorpsakol^{1,2,*}. International Collaborative Medical Research Laboratory, Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy¹, Laboratory of Epithelial Tight Junction Pathophysiology², Center of Excellence in Natural Products Chemistry (CENP), Department of Chemistry, Faculty of Science, Chulalongkorn University³, Bangkok, Thailand.

Introduction. Recovery of intestinal tight junction integrity is sufficient to treat colitis. Nowadays, no FDA-approved drug targeting intestinal tight junction recovery is clinically available. Although being considerable as an agricultural waste, *Coffea arabica* pulp exhibited several pharmacological activities. Indeed, our preliminary result indicated that *Coffea arabica* pulp extract (CPE) improved intestinal barrier function in T84 cell monolayers in a SIRT-1-dependent manner.

Aims. To demonstrate the *in vivo* mechanistic effect of CPE on intestinal tight junction assembly and its anti-colitogenic impacts in mice.

Methods. Dextran sulphate sodium (DSS)-induced colitis mouse model, pathohistological analyses, quantitative real-time PCR, H&E staining, PAS staining, immunofluorescence staining, and SIRT-1 activity assay were performed to investigate the effects of CPE in the treatment of experimental colitis.

Results. We found that CPE significantly reduced inflammation-induced decreases in body weight and colon length, disease activity index, and improved survival rate in DSS-induced colitis. Although CPE did not, however, suppress NF- κ B nuclear translocation and expression of cytokine transcripts including IFN, TNF, IL-1 β , and IL-6, it inhibited MLCK recruitment to perijunctional actomyosin ring in colon tissues of DSS-induced colitis mouse models. Of particular interest, H&E staining and PAS staining revealed that CPE suppressed immune cell infiltration and reduced PAS-positive staining. Similar to our preliminary results in intestinal epithelial cell line, CPE stimulated SIRT-1 activity in colon tissues of DSS-induced colitis mice in parallel with enhancing ZO-1 re-localization to apical junction region.

Discussion. Collectively, CPE is effective in the treatment of diseases related to intestinal tight junction disruption *in vivo* including colitis. In addition, this project can lead to sustainable development of agricultural wastes to be therapeutic nutraceuticals in the future.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P317

Pharmacovigilance-related regulatory obligations for the natural health products industry: a scoping review.

Ms Xin Yi Lim

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Xin Yi Lim, a registered pharmacist from Malaysia, is pursuing her PhD at the University of Auckland, New Zealand. Supervised by Prof Jo Barnes, A/Prof Shane Scahill, and Dr Sanya Ram, Xin Yi is examining the role of the natural health products (NHPs) industry in pharmacovigilance and the regulatory landscape for NHPs pharmacovigilance in New Zealand. The project also explores the potential for conducting active surveillance studies to collect comprehensive data on the use, benefits, and potential harms associated with specific NHPs. Despite being of 'natural' origin, NHPs are not without risks, yet safety monitoring (pharmacovigilance) for these products remains under-explored. With upcoming changes in New Zealand's legislative frameworks for NHPs, this research is timely. This project can help better understand the current and potential future contributions of the NHPs industry to pharmacovigilance for NHPs in New Zealand and identify key research and policy priorities, particularly concerning the NHPs industry.

Pharmacovigilance-related regulatory obligations for the natural health products industry: a scoping review.

Xin Yi Lim¹, Sanya Ram¹, Shane Scahill¹, Joanne Barnes¹. School of Pharmacy, University of Auckland¹, Grafton, AKL, New Zealand.

Introduction. The NHPs industry is a key stakeholder in pharmacovigilance (PV) for natural health products (NHPs). While regulations are often seen as an enabler for industry undertaking PV, there is limited consolidated information in published literature comparing the specific PV regulatory requirements for NHPs industry across different countries.

Aims. To undertake a scoping review of legislation to describe regulatory requirements for the NHPs industry regarding PV for NHPs in selected countries.

Methods. The top 30 countries, based on the World Health Organization's list of nations with the highest Current Health Expenditure in 2020, plus New Zealand (NZ), were identified. For these countries, publicly accessible regulatory instruments describing PV obligations for the NHPs industry and available in English at official governmental websites were accessed. European Union (EU) legislation was used as the overall reference for countries within the EU region.

Results. Regulations for ten countries/regions (Australia, Canada, EU, India, NZ, Republic of Korea, South Africa, Switzerland, UK, USA) were included. Definitions for NHPs and their categories varied across countries and, consequently, the regulatory obligations imposed on the industry also differed. Regulations from seven countries/regions specified timelines for mandatory reporting of suspected adverse reactions by industry for their products. Typically, the NHPs industry is required to report serious adverse reactions within 15 days of becoming aware. Four countries/regions (EU, India, UK, Republic of Korea) specified set timelines for Periodic Safety Update Reports submission.

Discussion. Regulatory obligations for the NHPs industry regarding PV for NHPs differed by country/region; typically, regulations emphasised the reporting of serious adverse reactions. Regulatory obligations also varied within certain countries/regions for different categories of NHPs. International harmonisation is desirable, but challenging.

Three distinct legislative approaches governing Natural Health Products (NHPs), illustrated by example countries/regions

Legislation	General legislation that include NHPs	General Act with specific legislation for NHPs	Separate legislation for different categories of NHPs
Example country/region	Australia	Canada	EU
NHPs categories	Complementary medicines	Natural health products	Therapeutic-type: Herbal & homeopathic medicinal products Food-type: Food supplements & novel food

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P318

Contributions of the natural health products industry to pharmacovigilance, a scoping review.

Ms Xin Yi Lim

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Xin Yi Lim, a registered pharmacist from Malaysia, is pursuing her PhD at the University of Auckland, New Zealand. Supervised by Prof Jo Barnes, A/Prof Shane Scahill, and Dr Sanya Ram, Xin Yi is examining the role of the natural health products (NHPs) industry in pharmacovigilance and the regulatory landscape for NHPs pharmacovigilance in New Zealand. The project also explores the potential for conducting active surveillance studies to collect comprehensive data on the use, benefits, and potential harms associated with specific NHPs. Despite being of 'natural' origin, NHPs are not without risks, yet safety monitoring (pharmacovigilance) for these products remains under-explored. With upcoming changes in New Zealand's legislative frameworks for NHPs, this research is timely. This project can help better understand the current and potential future contributions of the NHPs industry to pharmacovigilance for NHPs in New Zealand and identify key research and policy priorities, particularly concerning the NHPs industry.

Contributions of the natural health products industry to pharmacovigilance, a scoping review.

Xin Yi Lim¹, Sanya Ram¹, Shane Scahill¹, Joanne Barnes¹. School of Pharmacy, University of Auckland¹, Grafton, AKL, New Zealand.

Introduction. Industry parties are key players in pharmacovigilance, including natural health products (NHPs). However, in contrast to their counterparts in the pharmaceutical industry, the roles of the NHPs industry in pharmacovigilance and their contributions, particularly where not mandated, are not well explored.

Aims. To undertake a scoping review to collate and map global literature on the contributions of the NHPs industry towards pharmacovigilance for NHPs.

Methods. We searched seven international electronic journal databases (MEDLINE, EMBASE, CINAHL, AMED, IPA, PsycINFO, and Scopus) and selected local grey literature in New Zealand, up to March 2023, for articles reporting the contributions of the NHPs industry towards pharmacovigilance for NHPs, using pre-determined combined keyword and MeSH search strategies.

Results. Of the 2021 published articles identified, 30 articles that described both active and passive contributions of the NHPs industry to surveillance activities were included. In community-based surveillance, the NHPs industry mainly contributed through collection of spontaneous reports. Some companies undertook active surveillance for their products, though primarily limited to clinical settings. Of 59 grey literature articles found on the New Zealand Medsafe website, 18 described industry engagement, mostly involving the regulator's requests for product recalls due to adulterated products.

Discussion. The NHPs industry predominantly contributes to pharmacovigilance through passive surveillance. Active surveillance initiatives involving the NHPs industry were conducted in non-community settings, overlooking most NHPs use. Future studies could explore the potential of the NHPs industry in assuming a more prominent role in voluntarily undertaking pharmacovigilance for NHPs, particularly through proactive surveillance methods within community settings.

Table. Contents of articles discussing the NHPs industry's contributions to pharmacovigilance activities (N=30).

Contributions & roles	Number of studies, n (%)
Surveillance type	
Passive	17 (56.7)
Active	12 (40.0)
Others	2 (6.7)
Contributing role	
Product manufacturer	11 (36.7)
Funding	5 (16.7)
Research data	19 (63.7)
Surveillance system development	2 (6.7)
Risk minimisation plan	1 (3.3)

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P319

Identification of a novel proteasome inhibitor Xerophenone H and its anticancer effects

Prof Jinjian Lu

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Jin-Jian Lu is an Associate Professor in University of Macau and received his Ph.D. degree in Shanghai Institute of Meteria Medica, Chinese Academy of Sciences in 2009. Currently, Dr. Lu is mainly engaged in the discovery and mechanism study of anti-cancer compounds based on tumor microenvironment. He is also interested in studying the new targets and strategies for cancer therapy. He has been the recipient of more than 10 research grants funded by National Science Foundation of China, Science and Technology Development Fund Macao S.A.R and so on. Dr. Lu has published more than 200 scientific papers in the SCI journals including *J Hematol Oncol*, *Acta Pharm Sin B* and *Pharmacol Ther* (Total citations 10000+, H-index 54, Scopus). He is the editorial or youth editorial board member for 11 professional journals including *Transl Oncol* and *Chin J Nat Med*, and the referee for 100+ peer-reviewed journals. He was awarded as the 2nd Prize of Natural Science: Macao Science and Technology Awards (twice) and CNPHARS Annual Young Pharmacologists. (2/8/2024)

Identification of a novel proteasome inhibitor Xerophenone H and its anticancer effects

Wen-Yu Lyu^{1, #}, Jun Cao^{1, #}, Wei-Qing Deng¹, Mu-Yang Huang¹, Ting Li^{1, 2, *}, Li-Gen Lin^{1, 3, *}, Jin-Jian Lu^{1, 2, 3, *}

¹State Key Laboratory of Quality Research in Chinese Medicine, University of Macau, Macao SAR, China; ²MoE Frontiers Science Center for Precision Oncology, University of Macau, Macao SAR, China; ³Department of Pharmaceutical Sciences, Faculty of Health Sciences, University of Macau, Macao SAR, China.

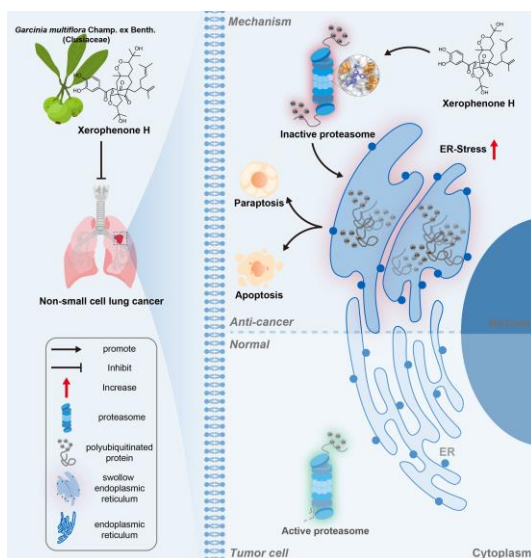
Introduction. Polycyclic polyisoprenylated acyl resorcinols (PPAPs) exhibit a unique chemical structure and a diverse range of pharmacological activities. This study identified a novel PPAP, Xerophenone H (XeH), derived from the fruit peel of *Garcinia multiflora* Champ. ex Benth. (Clusiaceae), and demonstrated its potential anti-lung cancer effect.

Aims. The objective of this study is to evaluate the anticancer effects of XeH on lung cancer and to elucidate the mechanism.

Methods. The *in vivo* efficacy of XeH was evaluated using a subcutaneous tumour model. XeH-induced cell death was confirmed using methods including TEM. The anticancer mechanism of XeH was further explored using RNA-seq and Western blot. Simultaneously, the target of XeH action was confirmed using molecular docking and CETSA experiments.

Results. XeH, as a novel proteasome inhibitor, exhibited anti-lung cancer activity both *in vitro* and *in vivo*. XeH directly interacted with the proteasome subunit PSMB5, thereby inhibiting the ubiquitin-proteasome degradation pathway, leading to apoptosis and paraptosis in lung cancer cells.

Discussion. The findings of this study indicate that XeH exerts anticancer effect by interacting with PSMB5. Further



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



investigation is required to determine whether XeH potentiate existing therapies and to elucidate its role in modulating the immune microenvironment.

Acknowledgement: This study was supported by the Science and Technology Development Fund, Macau SAR (File No. 0015-2022-A1 and 005/2023/SKL), University of Macau (File No. MYRG-GRG2023-00160-ICMS-UMDF), and the Internal Research Grant of the State Key Laboratory of Quality Research in Chinese Medicine, University of Macau (File No. SKL-QRCM-IRG2023-011).

P320

Discovery of Madecassoside as a pharmacological agent for skin wound healing

Miss Tadhi Sucharitakul

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Tadhi (Kati) Sucharitakul, is a second-year medical student at Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy, Bangkok, Thailand. She is currently working on a skin wound healing project at the International Collaborative Medical Research Laboratory, where she is developing her research skills and gaining insights that she hopes to apply in future clinical research.

Discovery of Madecassoside as a pharmacological agent for skin wound healing

Tadhi Sucharitakul¹, Pimngeon Chatkul^{1,2}, Pawin Pongkorpsakol^{1,2,*}. International Collaborative Medical Research Laboratory, Princess Srisavangavadhana College of Medicine, Chulabhorn Royal Academy¹, Laboratory of Epithelial Tight Junction Pathophysiology², Bangkok, Thailand.

Introduction. Wound is considered as one of the risk factors of infection. Delayed wound healing can be generally found in several diseases including type 2 diabetes mellitus. Therefore, searching for pharmacological agents that can promote skin wound healing has long been of interest. There are highly abundant of herbs in Thailand. Some bioactive compounds that can induce wound closure may be already available, but unexplored.

Aims. To screen and investigate the effects of bioactive compounds isolated from Thai herbs on keratinocyte wound healing and its underlying mechanisms.

Methods. Keratinocytes (HaCaT cell line) were used as a cell model to evaluate skin wound healing. Wound healing assay was performed to screen and investigate the effect of bioactive compounds from Thai herbs on wound healing and its underlying mechanisms in vehicle-treated HaCaT cells and in HaCaT cells treated with various inhibitors of related intracellular signalling.

Results. By screening, we identified that Madecassoside had ability to accelerate the rate of skin wound healing in HaCaT cells. Indeed, SIRT-1 inhibitor did not interfere with the effect of Madecassoside on skin wound healing. Surprisingly, Madecassoside treatment-induced skin wound healing was fully abolished by cotreatment with inhibitors of ERK and mTOR. Of particular importance, intracellular calcium chelation by BAPTA also suppressed the effect of Madecassoside on skin wound healing as well.

Discussion. Hence, Madecassoside was discovered here as a bioactive compound that can effectively enhance skin wound healing and its pharmacological mechanisms were also uncovered.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P321

Atopic dermatitis, Monotropein, Keratinocytes, Skin inflammation

Miss Inyoung Yang

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Monotropein mitigates atopic dermatitis-like skin inflammation

Inyoung Yang¹, Sang-Hyun Kim¹. Department of Pharmacology, School of Medicine, Kyungpook National University¹, Daegu, Republic of Korea

Introduction. Atopic dermatitis (AD) is a globally increasing chronic inflammatory skin disease with limited and potentially side-effect-prone treatment options. *Morinda officinalis* How roots, is known for its diverse pharmacological properties, specifically its potential to alleviate AD symptoms. Hence, this study reports the pivotal role of monotropein, a key component of *M. officinalis* roots, in alleviating AD symptoms and its therapeutic potential.

Aims. In the context of AD, our aim is to comprehensively explore the therapeutic potential of monotropein, the major iridoid glycoside of *M. officinalis* roots.

Methods. In this study, we investigated the pharmacological effects of monotropein on AD using a 2, 4-dinitrochlorobenzene (DNCB)/*Dermatophagoides farinae* extract (DFE)-induced AD mice and tumor necrosis factor (TNF)- α /interferon (IFN)- γ -stimulated keratinocytes.

Results. Oral administration of monotropein demonstrated a significant reduction in AD phenotypes, including scaling, erythema, and increased skin thickness in AD-induced mice. Histological analysis revealed a marked decrease in immune cell infiltration in skin lesions. Additionally, monotropein effectively downregulated inflammatory markers, encompassing pro-inflammatory cytokines, T helper (Th)1 and Th2 cytokines, and pro-inflammatory chemokines in skin tissues. Notably, monotropein also led to a considerable decrease in serum immunoglobulin (Ig)E and IgG2a levels. At a mechanistic level, monotropein exerted its anti-inflammatory effects by suppressing the phosphorylation of Janus kinase / signal transducer and activator of transcription proteins in both skin tissues of AD-induced mice and TNF- α /IFN- γ -stimulated keratinocytes. In conclusion, monotropein exhibited a pronounced alleviation of AD symptoms in the experimental models used.

Discussion. The findings suggest that monotropein holds promise as a functional ingredient or novel therapeutic agent for AD-like skin inflammation, paving the way for potential advancements in AD treatment strategies. Although clinical investigations have been conducted on *M. officinalis* root, monotropein alone has not been investigated, so it is important to verify efficacy and safety in human subjects.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P323

Excavating anti-epilepsy 3,4,5-trimethoxycinnamic acid derivatives inspired from Traditional Chinese Medicine *Polygala tenuifolia*

Dr Zefeng Zhao

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Zefeng Zhao is a lecturer of Shaanxi University of Chinese Medicine, served for Shaanxi Key Laboratory of Acupuncture & Medicine. Dr Zhao obtained his PhD degree from Northwest University in 2020 majored in Traditional Chinese Medicine. Dr Zhao is primarily engaged in drug discovery and research on mechanisms of actions in epilepsy. He excavated several precursors from Traditional Chinese Medicine and investigated the mechanisms of actions in curing epilepsy.

In the past years, Dr Du has published papers in *European Journal of Medicinal Chemistry*, *Bioorganic Chemistry*, *Food Chemistry*, *Medicinal Chemistry Research*, *Journal of Ethnopharmacology*, *Arabian Journal of Chemistry*. The research has been funded by National Natural Science Foundation of China.

Excavating anti-epilepsy 3,4,5-trimethoxycinnamic acid derivatives inspired from Traditional Chinese Medicine *Polygala tenuifolia*

Zefeng Zhao^{1,2}, Haifa Qiao¹, Xiaohui Zheng². Shaanxi Key Laboratory of Acupuncture & Medicine, Shaanxi University of Chinese Medicine, Xianyang, Shaanxi Province, PR China¹; School of Pharmacy, Northwest University, Xi'an, Shaanxi Province, PR China²

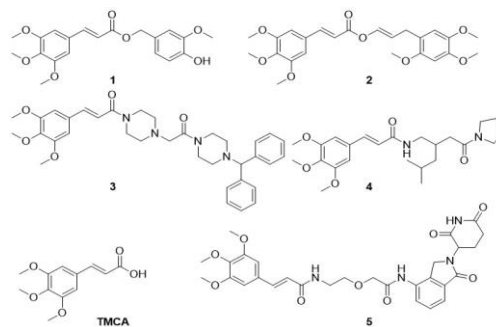
Introduction. 3,4,5-Trimethoxycinnamic acid (TMCA) isolated from Traditional Chinese Medicine (TCM) *Polygala tenuifolia* have been considered as effective ingredients which plays a role in anti-epilepsy effect interacting with GABA_A/benzodiazepine receptor complex [1].

Aims. Excavating novel anti-epilepsy TMCA derivatives through virtual screening and organic synthesis methods, ligands used for conjugates including vanillyl alcohol (1) from another TCM *Gastrodia elata*, asaronol (2) from TCM *Acori tatarinowii*, inspired from the compatibility of TCM [2,3]. Fragment of cinepazide (3), pregabalin (4) and proteolysis-targeting chimera moiety (5) are also considered.

Methods. Chemical methods including LC-MS and NMR are used to characterize the synthetic compounds. Anti-epilepsy activities are evaluated by electroshock, *sc*-pentylene tetrazole, electroencephalogram and behavioristics models. Docking analysis, enzyme kinetics and molecular biology methods are used to disclose the interaction between compounds and the targets.

Results. Several promising anti-epilepsy TMCA derivatives have been obtained, including compound 1 targeting GABA aminotransferase and compound 2 targeting lactate dehydrogenase.

Discussion. Above studies exemplified the rationality of developing candidates from TCM for epilepsy treatment.



Zhao Z et al (2019) *European Journal of Medicinal Chemistry* 173: 213-227

Zhao Z et al (2019) *Bioorganic Chemistry* 88: 102832

Bai Y et al (2019) *European Journal of Medicinal Chemistry* 183: 111650

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P324

Tenuifolin attenuates schizophrenia-like behaviors in mice

Prof Yonghe Zhang

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 1:15 PM - 2:10 PM

Biography:

Currently contributes to the field of neuropsychopharmacology as a faculty member. His research endeavors are centered on elucidating the neurobiological mechanisms associated with depression and exploring developments in antidepressant treatments. In addition, he serves in a leadership role as the Secretary General of the Chinese Pharmacological Society (CNPHARS) and Deputy Secretary of the China union of Life Science Societies.

Tenuifolin attenuates schizophrenia-like behaviors in mice

Su-Ying Cui¹, Qing Cao¹, Yong-He Zhang¹, Yong Jiang² & Peng-Fei Tu². Department of Pharmacology, Peking University¹, Beijing, China. State Key Laboratory of Natural and Biomimetic Drugs, Peking University², Beijing, China.

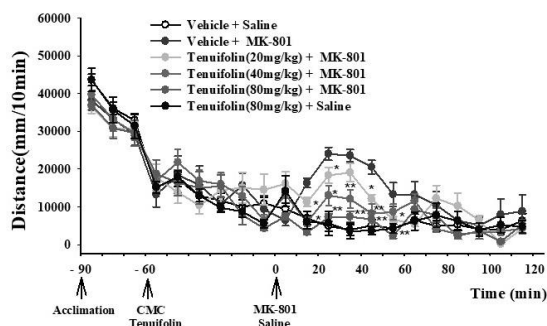
Introduction. Tenuifolin, a natural neuroprotective compound, is isolated from *Polygala tenuifolia* Willd, a medicinal herb with a profound history of therapeutic applications in treating mental disorders in China. The acute or chronic administration of MK-801, an NMDA receptor blocker, has been established as a validated animal model for simulating the positive, negative, and cognitive symptoms associated with schizophrenia.

Aims. The present study was aimed to examine the potential antipsychotic effects and the underlying mechanism of tenuifolin in MK-801-treated mice.

Methods. Positive symptoms, including sensorimotor gating deficit and hyperlocomotion, were assessed via the prepulse inhibition test and open field test. Negative symptoms, characterized by social withdrawal, were evaluated using social interaction tests. Cognitive deficits were measured by the novel object recognition test. Western blotting and HPLC were employed to determine the levels of glutamate decarboxylase (GAD), GABA, and monoamines.

Results. Acute MK-801 administration induced hyperlocomotion and prepulse inhibition deficits in mice, both reversed by tenuifolin treatment. Furthermore, tenuifolin ameliorated social withdrawal and cognitive deficits resulting from chronic MK-801 exposure. Notably, tenuifolin reversed MK-801-induced reductions in GAD and GABA levels and normalized monoamine levels in the prefrontal cortex, including dopamine, serotonin, and norepinephrine.

Discussion. These findings provide compelling evidence that tenuifolin exhibits multiple antipsychotic-like effects in an animal model of schizophrenia, suggesting a potential mechanism involving its modulation of GABA function in the prefrontal cortex.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P325

Effects of Salvianolic acid A on the heart failure

Prof Lianhua Fang

Poster presentations 1: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Fang LianHua, Ph.D., Professor and PI in Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College.

Main research filed is cardiovascular pharmacology and new-drugs discovery in related diseases.

Especially, research of drug targets for the cardiovascular diseases, Establishment of screening model of high-throughput screening, further evaluation of active compounds obtained from high-throughput screening, etc.

The member of the 11th council of the Chinese Pharmacological Society (CPS) and vice chairman of the crystal pharmacology special committee of the CPS and executive committee member of the Tonifying Drugs of the CPS, etc. Editorial board member of "Chinese Pharmaceutical Journal", "Acta Laboratorium Animalis Scientia Sinica", and "Pharmacology and Clinics of Chinese Materia Medica", etc.

Leaded 3 general projects of the National Natural Science Foundation of China; published over 150 academic papers; Authorized 14 China patents; Two monographs by the deputy editor in chief; Participated in the completion of preclinical research for four national Class 1 new drugs. Received second prize of Beijing Science and Technology Award, second prize and third prize of Chinese Medical Science and Technology Award, and third prize of Academic Works Award of the Chinese Association of Traditional Chinese Medicine.

Effects of Salvianolic acid A on the heart failure

Lianhua Fang, Awaguli Dawutia, Tianyi Yuan, Shoubao Wang, Yang Lu, Guanhua Du*.

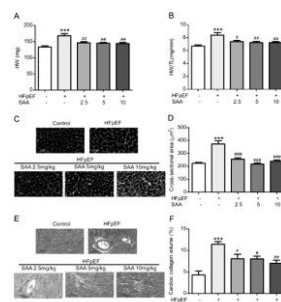
State Key Laboratory of Bioactive Substances and Functions of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.

Introduction. Heart failure with preserved ejection fraction (HFpEF) is a morbid, mortal, and common syndrome for which lack of evidence-based therapies. As a main active components of *Salvia miltiorrhiza* Burge, Salvianolic acid A (SAA) exerts good cardioprotective effects.

Aims. We investigated whether SAA possessed therapeutic activity against HFpEF and explored the potential mechanism.

Methods. HFpEF mice were established infusing a combination of high-fat diet (HFD) and N ω -nitro-L-arginine methyl ester (L-NAME) for 14 weeks. In the 10th week, the HFpEF mice were given SAA (2.5, 5, 10 mg/kg) via oral gavage for four weeks. The body weight, blood pressure, blood lipids, glucose tolerance, exercise performance, cardiac systolic/diastolic function, cardiac pathophysiological changes, and inflammatory factors were assessed.

Results. SAA reduced risk factors of HFpEF, such as body weight gain, glucose intolerance, lipid disorders, but not blood pressure, and increased exercise tolerance of HFpEF mice. Moreover, SAA not only relieved myocardial hypertrophy and fibrosis by reducing interventricular septal wall thickness, left ventricular posterior wall thickness, left ventricular mass,



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



heart index, cardiomyocyte cross-sectional area and cardiac collagen content, but also improved cardiac diastolic function via reducing E/E' ratio. On the other hand, SAA inhibited TLR2/TLR4-mediated Myd88 activation and its downstream molecules TRAF6 and IRAK4, which decreases the release of proinflammatory cytokines and mediators through NF- κ B and p38 MAPK pathways.

Discussion. SAA could attenuate obese and hypertension-induced cardiac dysfunction and cardiac inflammation in HFpEF mice, which provides evidence for SAA as a potential drug for treatment of HFpEF in clinic.

Acknowledgements. National Natural Science Foundation of China (No. 82073853), CAMS Innovation Fund for Medical Sciences (2021-I2M-1-005).

P327

The effect and mechanism of kaempferol targeting galectin-3 in anti-thrombotic stroke

Prof Yue-Hua Wang

Poster presentations 2: Cardiovascular, Clinical Pharmacology, Education, Medicines for Tropical Disease, Pharmaceutical Science, Pharmacoepidemiology, Respiratory and Inflammation, Traditional Medicines, Goldfields Event Space, December 2, 2024, 10:30 AM - 11:10 AM

Biography:

Researcher and doctoral supervisor at the Institute of Materia Medica, Chinese Academy of Medical Sciences. Main research areas include drug target confirmation, new drug discovery and drug efficacy evaluation, preclinical evaluation of new drugs, and mechanism of action research.

The effect and mechanism of kaempferol targeting galectin-3 in anti-thrombotic stroke

Man Liu, Ying-Lin Yang, Dong-Ni Liu, Yu-Fu Shang, Wen-Fang Zhang, Wan-Di Feng, Guan-Hua Du, Yue-Hua Wang. Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100050, China

Introduction. Kaempferol (KAE), a natural flavonoid in variety of plants and some of traditional medicines, has been increasingly investigated on its anti-inflammation and anti-oxidative effects. Although the anti-inflammatory effect of kaempferol is clear, its therapeutic target and potential molecular mechanisms on inflammation caused by cerebral stroke remain unclear. Galectin-3 (Gal3) and NLRP3 are reportedly involved in neuroinflammatory diseases.

Aims. To investigate kaempferol therapeutic effect and explore its potential mechanisms in thrombotic stroke.

Methods. The photothrombotic stroke (PTS) mouse model was used to evaluate the anti-stroke effects of KAE. Microglia BV2 cells transfected with Lgals3-shRNA was used to explore the mechanism. ELISA was used to detect the levels of inflammatory factors. Western blot and qPCR were used to analyze the levels of proteins linked to inflammation. RNA-Seq analysis was used to identify the differential expression genes. Molecular docking, immunofluorescence staining, and CO-IP and were executed to investigate the interaction between Gal3 and NLRP3.

Results. KAE could ameliorate brain injury, protect the neurons and BBB integrity, reduce neuroinflammation and oxidative stress by regulating multiple signaling pathways. At the same time, Gal3, as one of the targets of KAE to exert anti-stroke effects, is involved in the pathological process of thrombotic stroke, and knockdown of Gal3 is beneficial to reduce neuroinflammation and oxidative stress.

Discussion. This study provides experimental evidence for the mechanism of KAE in anti-thrombotic stroke and Gal3 as an anti-stroke target, and provides the theoretical basis for the development of compounds for treating stroke. Inhibition of Gal3 could alleviate neuroinflammation, which might associate with down-regulating NLRP3/cleaved caspase-1 signaling pathway.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P263

The role of RGS2 in ligand-mediated signalling of PAC1R splice isoforms

Miss Miaomiao Li

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Miaomiao Li is a Ph.D. candidate in the Drug Discovery Biology theme at Monash Institute of Pharmaceutical Science. She got her bachelor's degree from Shenyang Pharmaceutical University, China, and her master's degree from Shanghai Jiao Tong University School of Medicine, China. Her Ph.D. research focuses on investigating the regulation of the Pituitary adenylate cyclase-activating polypeptide type 1 Receptor (PAC1R) by intracellular accessory proteins, including the regulator of G protein signalling (RGS) proteins and β -arrestins. Driven by her passion for scientific innovation, she aims to advance our understanding of PAC1R regulation mechanisms and identify novel therapeutic targets for neurological disorders, such as migraine and post-traumatic stress disorder (PTSD).

The role of RGS2 in ligand-mediated signalling of PAC1R splice isoforms

Miaomiao Li¹, Laura J Humphrys¹, Samantha M McNeill¹, Patrick M Sexton^{1,2}, Denise Wootten^{1,2}, Peishen Zhao^{1,2}. Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Monash University¹, Melbourne, VIC, Australia; ARC Centre for Cryo-Electron Microscopy of Membrane Proteins (CCeMMP), Monash Institute of Pharmaceutical Sciences, Monash University², Melbourne, VIC, Australia.

Introduction. Pituitary adenylate cyclase-activating polypeptide type 1 receptor (PAC1R) belongs to the class B1 G protein-coupled receptor (GPCR) family and is a putative therapeutic target for several neurological disorders including migraine and post-traumatic stress disorder (PTSD). The PAC1R gene is subject to alternative splicing events that occur within the gene regions encoding the intracellular loop 3 (ICL3) and the N-terminal extracellular domain. Previous studies in our lab have revealed distinct in vitro signalling profiles are produced from these different isoforms, although the molecular mechanism is unclear. Potential contributors might be intracellular accessory proteins, such as regulator of G protein signalling (RGS) proteins, which can interact with GPCRs at the ICL3 region in a sequence-dependent manner. RGS proteins negatively regulate G protein signalling through GTPase activation. Among the 30 RGS proteins, RGS2 is co-expressed with PAC1R splice isoforms in multiple tissues, such as the brain and kidney. RGS2 is Gq selective, and is the only RGS protein that inhibits the cAMP pathway through a non-GTPase activating mechanism. Moreover, RGS2 has been suggested to be upregulated in patients with PTSD.

Aims. The current project aims to investigate the contribution of RGS2 protein to the diverse functions of PAC1R isoforms.

Methods. Ligand-induced intracellular calcium (iCa^{2+}) mobilization was assessed using Fluo-8 AM dye, while cAMP accumulation was measured using the CAMYEL sensor (cAMP sensor using YFP-Epac-RLuc).

Results. RGS2 overexpression showed minimal effect on PACAP27, PACAP38, and VIP-mediated cAMP signalling through PAC1nR, PAC1nR-hip, and PAC1nR-hop. More complex effects were observed with iCa^{2+} mobilization where RGS2 overexpression decreased the E_{max} or potency of all three ligand-induced iCa^{2+} mobilizations by PAC1nR and PAC1nR-hip, whereas it only reduced the potency of PACAP27 and PACAP38 induced iCa^{2+} mobilization on PAC1nR-hop.

Discussion. These results highlight the dynamic role of RGS2 in regulating the downstream signalling of distinct ligands on PAC1R isoforms. Further investigation is necessary to elucidate the underlying mechanisms.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P400

A promising MYLK4 Inhibitor for treating metastatic and drug-resistant colorectal cancer

Adj A/Prof Min-Wu Chao

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

MinWu Chao is an Assistant Professor at National Sun Yat-sen University in Taiwan. She teaches Pharmacology in the Post-Baccalaureate Medicine Program. Her research focuses on drug discovery and development in the field of cancer.

A promising MYLK4 Inhibitor for treating metastatic and drug-resistant colorectal cancer

Min-Wu Chao^{1,2,3}, Ming-Min Huang¹, Szu Lee⁴, Kai-Cheng Hsu^{5,6,7}, Shio-Lin Pan^{5,6,7},

¹ School of Medicine, College of Medicine, National Sun Yat-sen University, Kaohsiung, Taiwan

² Institute of Biopharmaceutical Sciences, College of Medicine, National Sun Yat-sen University, Kaohsiung, Taiwan

³ Doctoral program of clinical and experimental medicine, College of Medicine, National Sun Yat-sen University, Kaohsiung, Taiwan

⁴ School of Pharmacy, College of Pharmacy, Taipei Medical University, Taiwan.

⁵ Graduate Institute of Cancer Biology and Drug Discovery, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan

⁶ Ph.D. program for Cancer Molecular Biology and Drug Discovery, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan

⁷ TMU Research Center of Cancer Translational Medicine, Taipei Medical University, Taipei, Taiwan

Introduction. Metastatic colorectal cancer has a five-year survival rate of only 15%, with treatment options limited to traditional chemotherapy and VEGF/EGFR antibody drugs. More than half of the patients on long-term medication develop resistance, highlighting the urgent need for novel targeted therapies for metastatic and drug-resistant colorectal cancer.

Aims. MYLK (Myosin Light Chain Kinase) proteins regulate muscle contraction and are involved in cell adhesion, migration, and survival. MYLK has been found to be aberrantly expressed in multiple tumors. Our aim was to identify tern activity

Results. Our research identified that MYLK4 is highly expressed in colorectal cancer compared to normal tissues, with high MYLK4 expression correlating with poorer progression-free survival and shorter patient survival times. Knockout of the MYLK4 gene inhibits colorectal cancer cell survival, proliferation, and migration. Through computational simulations, we have identified the natural compound ellipticine as an effective MYLK4 inhibitor, with an IC₅₀ of 7.1 nM for MYLK4 enzyme inhibition. Ellipticine inhibits colorectal cancer cell survival and migration, remains effective against oxaliplatin-resistant cancer cells, and significantly reduces mice tumor growth.

Discussion. Overall, these findings suggest that the natural MYLK4 inhibitor ellipticine has the potential as a lead compound for developing treatments for metastatic and drug-resistant colorectal cancer.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P401

High-throughput pharmacokinetic predictions in early drug development

Dr Jeremy Jones

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Jeremy Jones is recognized as a leader in drug development and translational research with an historical focus in urologic oncology. He has over 20 years' experience leading and advising research projects, including as Assistant/Associate Professor of Cancer Biology and Medical Oncology at City of Hope Comprehensive Cancer Center, Director of Oncology at Terray Therapeutics, and as President of Jones Scientific Consulting. Dr. Jones now leads AI enabled drug design and development projects and services at Simulations Plus, a premier developer of drug discovery/development software and a leading provider of both preclinical and clinical pharmacometric consulting services.

High-throughput pharmacokinetic predictions in early drug development

Jeremy O Jones¹, Rafal Bachorz¹, Marcin Ratajewski², David Miller¹, Michael Lawless¹, Vladimir Chupakhin¹, Robert Fraczkiwicz¹. Cheminformatics, Simulations Plus Inc.¹, Lancaster, CA, USA; Institute of Medical Biology, Polish Academy of Sciences², Warsaw, Poland.

Introduction. The ability to quickly and accurately predict key PK properties based solely on chemical structure can aid in many arenas from drug development to toxicology. The High-Throughput Pharmacokinetic (HTPK) module in ADMET Predictor® (AP) achieves this task by integrating ADMET property estimates to solve a deterministic system of differential equations with respect to human, rat, or mouse physiology, based on a simplified version of the GastroPlus® Advanced Compartmental Absorption and Transit (ACAT) model. While the initial version of the HTPK module performed well, delivering very similar results to the full PBPK modelling predictions in GastroPlus, an updated version improves purely *in silico* PK predictions. HTPK can be used within the Artificial Intelligence-driven Drug Design (AIDD) module, which automates the drug design process by integrating the HTPK simulations and ADMET predictions with advanced generative chemistry algorithms to produce molecules that are active and lead-like.

Aims. To design potent RORy ligands with high predicted oral availability.

Methods. QSAR models for RORy agonists and inhibitors were developed in ADMET Modeler based on curated literature data. These QSAR models were used as optimization parameters along with other ADMET properties, synthesizability, and percent oral availability from the HTPK module within AIDD to design novel RORy ligands. After AIDD compound generation, we performed molecular docking calculations as well as similarity searches to Synthesis-on-demand (SoD) libraries and included this information in our Multi-Criteria Decision Analysis (MCDA) tool to select compounds for purchase and/or synthesis. Compounds were then tested in luciferase reporter and toxicity assays to determine their agonist or inhibitory activity.

Results. Combining HTPK, AIDD, and MCDA delivered novel, active RORy ligands with high predicted oral availability.

Discussion. RORy is involved in several diseases, including inflammation and cancer, and novel drugs targeting RORy may help with these conditions. While additional rounds of the Design/Make/Test/Analyze (DMTA) cycle must be undertaken to optimize our newly developed ligands, using HTPK and AIDD from the very initial stages of development can reduce the number and time of DMTA cycles, delivering drugs to patients faster and cheaper.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P402

Investigating the role of IA65 on thapsigargin-induced IL-6 gene expression via ORAI1

Ms Jihye Han

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Jihye Han is a 4th year pharmacy student at The University of Queensland. Her academic pursuit includes a supervised independent research project, which focuses on calcium signalling and gene transcription. She has also received multiple Dean's Commendation for Academic Excellence awards throughout her study. Outside of uni, Jihye works in a community pharmacy and enjoys going out for walks and watching wildlife documentaries. Her goal is to gain diverse experiences to expand my perspective and skill set, enabling her to provide valuable insights that enhance patient care.

Investigating the role of IA65 on thapsigargin-induced IL-6 gene expression via ORAI1

Jihye Han¹, Farzaneh Forouz¹, Sarah J. Roberts-Thomson¹, Gregory R. Monteith¹ and Mélanie Robitaille¹
Sch of Pharm, Univ of Queensland¹, Brisbane, QLD, Australia.

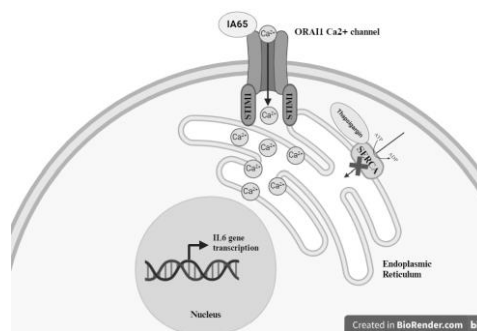
Introduction. Store-operated calcium entry (SOCE) is a central mechanism in maintaining cellular calcium balance. The ORAI1 calcium channel is the key channel regulating SOCE and its activation by thapsigargin is linked to the regulation of IL-6 gene transcription (Robitaille et al, 2022). IA65, a selective pharmacological enhancer of ORAI1 has been recently described (Azimi et al, 2020), but its effect on ORAI1-mediated gene transcription is unknown.

Aims. Our study aimed to assess the effect of IA65 on thapsigargin-induced IL-6 gene expression and its dependency on ORAI1 function.

Methods. ORAI1 protein expression was disrupted in MDA-MB-231 and MDA-MB-468 cells by CRISPR/Cas9. A submaximal concentration of thapsigargin was used to induce ORAI1-mediated SOCE. IL-6 gene expression level was quantified by RT-qPCR.

Results. Thapsigargin treatment increased IL-6 gene expression in an ORAI1 dependent manner. Addition of ORAI1 enhancer IA65 treatment did not change IL-6 gene expression.

Discussion. ORAI1 expression/function is altered in many diseases including asthma and cancer (Azimi et al, 2020). The discovery of the ORAI1 enhancer IA65 has opened up new opportunities to further investigate ORAI1 and its Ca²⁺ regulated mechanisms, including gene transcription. Although IA65 displays selectivity towards ORAI1 and weak inhibition of the ORAI3 isoform (Azimi et al, 2020), it is still poorly characterised. Our study demonstrated that IA65 treatment was ineffective at increasing thapsigargin induced IL-6 expression.



Azimi I et al (2020) ACS Pharmacol Transl Sci 3:135-147.

Robitaille M et al (2022) Int J Mol Sci 23:5867.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P403

ERRy loss promotes neuroendocrine differentiation in PTEN-deficient prostate cancer

Dr Ting Li

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Ting Li is currently a Research Assistant Professor at the State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, a position she has held since August 2023. Prior to joining the university, she earned her Bachelor's degree in Pharmaceutical Sciences from Wuhan University in 2012 and completed her doctoral studies at the University of Macau in 2018. Later that year, she began a five-year postdoctoral fellowship at the Rosalind and Morris Goodman Cancer Institute, McGill University, Canada.

Dr. Li has published 36 scientific articles with an h-index of 22 (Google Scholar). She is the first or corresponding author (including co-corresponding) of 15 papers in leading journals, including *Journal of Hematology & Oncology*, *Pharmacological Research*, *Acta Pharmacologica Sinica*, *Apoptosis*, and *Biochemical Pharmacology*.

Her research focuses on drug discovery and the development of strategies for aggressive neuroendocrine cancers by an interdisciplinary approach, integrating genetics, genomics, metabolomics, bioinformatics, and advanced *in vitro* and *in vivo* models.

ERRy loss promotes neuroendocrine differentiation in PTEN-deficient prostate cancer

Ting Li^{1,4,5,*}, Catherine R. Dufour¹, Lingwei Han^{1,2}, Mu-Yang Huang³, Jin-jian Lu^{3,4,5}, and Vincent Giguère^{1,2*}

¹ Goodman Cancer Institute, McGill University, Montréal, QC, H3A 1A3, Canada.

² Department of Biochemistry, Faculty of Medicine and Health Sciences, McGill University, Montréal, QC, H3G 1Y6, Canada.

³ State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao, China.

⁴ MoE Frontiers Science Center for Precision Oncology, University of Macau, Macao, China.

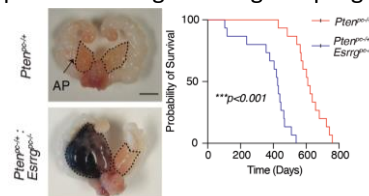
⁵ Department of Pharmaceutical Sciences, Faculty of Health Sciences, University of Macau, Macao, China.

Introduction. Increasingly effective therapies targeting the androgen receptor have paradoxically contributed to the incidence of neuroendocrine prostate cancer (NEPC). Although NEPC is the most lethal subtype of castration-resistant prostate cancer, the underlying mechanisms remain incompletely understood and effective treatments remain undiscovered.

Aims. Given the prominent roles that members of the nuclear receptor family play in developmental processes and cancer, we initially searched for genes encoding nuclear receptors in which their level of expression changes during PCa progression toward NEPC.

Methods. Several prostate-specific pre-clinical models includes genetically engineered mouse models (GEMMs) and cell lines, xenografts as well as organoids were applied.

Results. Loss of nuclear receptor ERRy expression promotes neuroendocrine differentiation of PTEN-deficient prostate adenocarcinoma.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion. This study delineates a novel nuclear receptor-dependent molecular mechanism driving lineage plasticity towards NEPC through downregulation of ERR γ signaling, thus offering new insights and possibilities into potential therapeutic approaches for PCa.

P404

6-methyl(sulfinyl)hexyl isothiocyanate and glycyrrhetic acid enhances cytotoxicity in glioblastoma cells

Miss Hafsa Hersi

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Hafsa Hersi, BBiomedSci (Hon.), is a PhD candidate at Bond University on the Gold Coast, currently in the final year of her doctoral studies. Her research focuses on cancer therapeutics derived from natural products, specifically investigating the in-vitro effects of 6-(Methylsulfinyl)hexyl isothiocyanate from Wasabi and glycyrrhetic acid from licorice root in the treatment of pediatric glioblastoma. This research is being conducted in collaboration with Meijo University, Nagoya, Japan. In addition to her research, Hafsa has extensive experience teaching various Biomedical Science and Medicine subjects, as well as training and mentoring students in laboratory-based research projects.

6-methyl(sulfinyl)hexyl isothiocyanate (6-MITC) and glycyrrhetic acid (GA) enhances cytotoxicity in glioblastoma cells

Hafsa Abdi Hersi¹, Oladayo Folasire¹, Katie Powell¹, Hideaki Yamaguchi², Anna Lohning¹.

Faculty of Health Science and Medicine, Bond University¹, Gold Coast, QLD, Australia; Department of Applied Biological Chemistry, Meijo University², Nagoya, Japan.

Introduction. Treating pediatric glioblastoma effectively remains a significant challenge, with limited success seen in children. 6-methyl(sulfinyl) hexyl isothiocyanate (6-MITC), isolated from Wasabia japonica (wasabi) and glycyrrhetic acid (GA) from liquorice root have been shown to possess anti-cancer properties. Selectivity is an important issue for cancer prevention and therapy. Understanding the effects of these natural compounds and their underlying mechanisms presents a promising avenue for developing new, more targeted chemotherapeutics with fewer side-effects.

Aims. To examine the selective cytotoxic effects of 6-MITC and GA on glioblastoma cells (U251-MG) and fibroblast cells (OUMS-36T-7).

Methods. Cytotoxicity was assessed after 24, 48 and 72 hours of incubation with 10 μ M 6-MITC and 50 μ M GA, using resazurin reduction assays to measure cell viability.

Results. The results indicate a greater than 50% reduction in the viability of U251-MG, glioblastoma cells, after 48 hours of treatment with 10 μ M 6-MITC and 50 μ M GA (n=6) ($p < 0.05$). Additionally, a greater selectivity in the U251-MG, glioblastoma cells (n=6) was notable compared to the control OUMS-36T-7 fibroblast cells (n=6) after 24, 48 and 72 hours of treatment with 10 μ M 6-MITC and 50 μ M GA ($p < 0.05$).

Discussion. These results suggest that the combinatorial 6-MITC and GA exhibit a selective time-dependent cytotoxicity against glioblastoma cells. This highlights their potential as candidates for developing more effective chemotherapeutic agents with fewer side-effects for patients. Lower concentrations such as those used in this study are noteworthy as they account for clinically relevant parameters such as bioavailability and toxicity.

10 μ M 6-MITC and 50 μ M GA

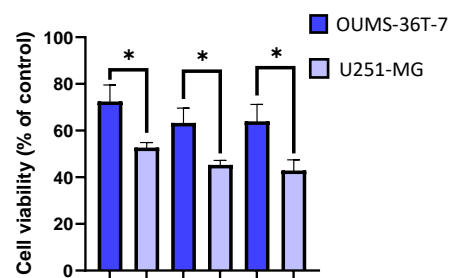


Figure 1. Effect of 10 μ M 6-MITC and 50 μ M GA treatment on OUMS-36T-7 fibroblast cells and U251-MG glioblastoma cells. Cells were treated with 10 μ M 6-MITC and 50 μ M GA for 24, 48, and 72 hours. Data represent mean viability \pm standard error of the mean (SEM).

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P405

Casein kinase 1 delta is a key mediator of TGF- β 1-induced pulmonary fibrosis

Dr Meina Li

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Casein kinase 1 delta (CK1 δ) is a key transducer of TGF- β 1-induced pulmonary fibrosis

Meina Li¹, Stephanie S. Zhang¹, Trudi Harris¹, Xin Li¹, Qianyu Chen¹, Shenna Y. Langenbach¹, Alastair G. Stewart¹.

¹ARC Centre for Personalised Therapeutics Technologies, Department of Biochemistry and Pharmacology, School of Biomedical Science, University of Melbourne, Parkville, VIC 3010, Australia

Introduction. Myofibroblasts are regarded as the key effector cells of the fibrogenic responses in idiopathic pulmonary fibrosis (IPF). Transforming growth factor-beta (TGF- β 1) is the main pro-fibrotic mediator characterized to date in IPF. Our previous work demonstrated that casein kinase CK1 δ/ϵ inhibitor, PF670462 attenuates the fibrogenic effects of TGF- β 1 in pulmonary fibrosis.

Aims. In this study, we investigated the potential contribution of CK1 δ/ϵ in regulating the molecular mechanisms underlying TGF- β 1-induced fibrosis.

Methods. Global proteomics was used to broadly assess TGF- β 1-induced response in human primary pulmonary fibroblasts. *In vitro* TGF- β 1-induced fibrogenesis was assessed by RT-qPCR, ELISA and western blotting. TGF- β 1 signal transduction was determined by western blotting and immunofluorescence staining. The potential contribution of CK1 δ/ϵ in these setting settings was ascertained using pharmacological (PF670462) and genetic (siRNA) inhibition.

Results. Using global proteomics and siRNA-based genetic approaches, we now demonstrate that PF670462 achieves comparable anti-fibrogenic effects to the ALK5 inhibitor, but via different targets. CK1 δ -targeting siRNA sequences, but not CK1 ϵ , have similar effects to PF670462, with respect to attenuate TGF- β 1-induced myofibroblast activation and ECM deposition, indicating the significance of on-target anti-fibrotic effects of PF670462. However, TGF- β 1 induction of fibrogenic mediators, including IL-11 and CTGF, is inhibited by PF670462 by actions that appear to depend on the Smad rather than the CK1 δ pathway.

Discussion. Thus, CK1 δ plays a critical role as a non-canonical signal mechanism required for selected fibrogenic effects of TGF- β 1. Precise modulation of TGF- β 1 signalling by inhibitors of CK1 δ may offer new therapies for IPF.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P406

Dendritic cell extracellular vesicle mimetics show potential for activating CD4⁺ T cells

Miss Eleanor Mills

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Eleanor is a 2nd year PhD candidate in the Department of Pharmacology at Monash University's Biomedical Discovery Institute. After completing her Honours degree in 2022, she commenced her PhD in 2023 under the supervision of Dr Mark Del Borgo, Associate Professor Meredith O'Keeffe and Professor Max Cryle. Combining her background in immunology and pharmacology, she is researching the use of dendritic cell-based extracellular vesicle mimetics for indications in vaccination and cancer. She hopes to develop a platform for utilising the innate ability of dendritic cells to transfer antigen to promote an immune response tailored to the target disease.

Dendritic cell extracellular vesicle mimetics show potential for activating CD4⁺ T cells

Eleanor M Mills¹, Meredith O'Keeffe², Mark P Del Borgo¹. 1. Dept of Pharmacol, Monash Univ, Clayton, VIC, Australia. 2. Dept of Biochem & Molec Biol, Monash Univ, Clayton, VIC, Australia.

Introduction. Vaccination may provide an alternative treatment for diseases that resist current therapies, and an emerging vaccination platform are extracellular vesicles (EVs). EVs are non-replicative representations of their parent cell, and dendritic cell EVs possess functional antigen presentation molecules that can activate and mobilise allogenic T cells against a pathogen. Extrusion is an emerging technique where the cellular membrane is disrupted at ~37°C, forming spherical particles (EV mimetics (EVMs)) with considerably greater yield than naturally derived EVs. Dendritic cell EVMs (DCEVMs) are yet to be explored for antigen-presentation capability.

Aims. The aim of this study is to assess the ability of peptide-pulsed DCEVMs to activate OTII (CD4⁺ T) cells.

Methods. 2x10⁶ cells/ml MuTuDC were pulsed with/without 0.1µg/ml OVA 323-339 and with 0.008µm diABZI for 4hrs, before extrusion of half to form DCEVMs. DCEVMs were analysed for size and concentration via nanoparticle tracking analysis, and 10³ MuTuDCs or DCEVMs (10⁷, 10⁸ or 10⁹ particles) were incubated with 50³ OTII cells for 72hrs. Cells were stained with CTV, anti-CD69-FITC, anti-CD366-PECy7, anti-CD196-BV605, and anti-Vα2-A700 for flow cytometry.

Results. 2x10⁵ MuTuDC/ml resulted in ~1.22x10¹⁰ DCEVMs/ml, with a median size of ~136nm (n = 6 batches (11 measuring positions per batch)). ~67.5% of viable Vα2⁺ OTII cells exposed to DCs/DCEVMs had proliferated (CTV⁺), with 84.6% viable Vα2⁺ OTII cells proliferated when exposed to 10⁹ peptide-pulsed DCEVMs. CD69 expression increased by 16.2-fold when OTII cells were incubated with 10⁹ DCEVMs; a 3.3x greater increase than intact MuTuDCs. CD196 and CD366 expression also increased 9.7- and 24.5-fold when exposed to 10⁹ DCEVM, respectively. However, an average fold change of 2.0 is seen in lower DCEVM concentrations (10⁷ & 10⁸).

Discussion. This is the first report of *ex vivo*-like DCs being formulated into particles, providing a closer representation of DCs found *in vivo*. Due to the intricacies of DC:T cell interactions, it was expected that DCEVMs would require the supplementation of cytokines to activate CD4⁺ T cells. This study provides preliminary evidence that contrasts this, as proliferative cells (CTV⁺); markers of activation (CD69⁺); and markers suggestive of differentiation to T_H1 and T_H17 (CD366⁺ & CD196⁺, respectively) were elevated when OTII cells were incubated with 10⁹ DCEVM, compared to DC. This interaction is dose-dependent, as increases in these endpoints are not to a similar degree for 10⁷ or 10⁸ DCEVM.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P407

Nanoformulations for the Treatment of Biofilm-Associated Bacterial Infections

Mr Yuzhang Li

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

I am Yuzhang Li, a PhD student at the University of Queensland. My research focuses on developing compound nanoformulations to treat biofilm-associated bacterial infections. I aim to enhance the effectiveness of antimicrobial treatments by refining therapeutic strategies and exploring innovative solutions. I deeply value collaboration and enjoy connecting with fellow researchers in related fields. I look forward to engaging with others to exchange insights. I am also interested in exploring opportunities to bridge the gap between academic research and industrial applications.

Nanoformulations for the Treatment of Biofilm-Associated Bacterial Infections

Yuzhang Li¹, Jaya Seneviratne², Jared Miles¹, Ben Ross¹, Amirali Popat¹, Zyta Ziora³, Peter Moyle¹. Sch of Pharm¹, Sch of Dent², Inst for Mol Biosci³, Brisbane, QLD, Australia

Introduction. Biofilms are complex microbial aggregates that adhere to biotic or abiotic surfaces and contribute to antibiotic resistance and chronic infections. Combating biofilm-related infections often requires recurrent antibiotic treatments, which promote the development of resistant bacterial strains. The discovery of antivirulence compounds that target biofilms at sub-minimum inhibitory concentration (sub-MIC), thereby reducing the risk of resistance, is crucial. However, this approach faces challenges like overcoming poor biofilm penetration. Nanoformulation techniques can be used to enhance the delivery of these agents into biofilms, potentially leading to more effective antibiofilm treatments.

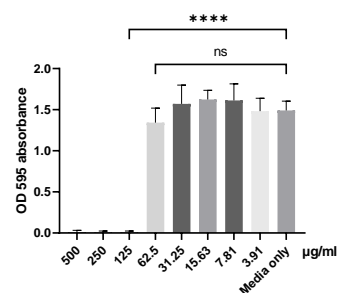
Aims. Screening the MIC and biofilm eradication activities of compounds from literatures against disease-associated bacteria. Formulate nanoparticles to evaluate their loading capacities and delivery efficacy. Modify nanoparticle surfaces with antimicrobial peptides (AMPs) to evaluate opportunities for synergy.

Methods. Crystal violet staining, dynamic Light Scattering (DLS), Size Exclusion Chromatography (SEC), solid phase peptide synthesis (SPPS), minimum inhibitory concentration (MIC).

Results. A library of compounds was screened, with some showing biofilm inhibition activity. Most selected compounds were insoluble in aqueous conditions, requiring DMSO to aid their solubilization. The nanoparticle formulations improved their dispersion in water, resulting in homogeneous, small particles around 13 nm. The AMPs are successfully synthesized in high purity and could be incorporated into the nanoparticles.

Discussion. Targeting biofilm with antivirulence compounds provides novel means to inhibit biofilms. Nanoformulation improves the dispersion of these compounds. Additionally, surface functionalization with AMPs provides affinity to bacterial cell membranes, offering synergistic effects towards bacterial biofilms.

Biofilm inhibition assay of compound X against *S. aureus*



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P408

Distinct fingerprint of formyl peptide receptor 2 agonists: the secret to bias?

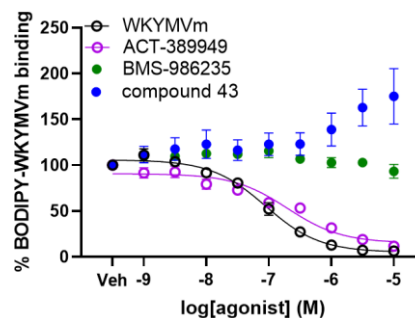
Ms Cheng Peng

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Distinct fingerprint of formyl peptide receptor 2 agonists: the secret to bias?

Cheng Peng, Elizabeth A. Vecchio, Anh T. N. Nguyen, Mia De Seram, Ruby Tang, Owen L. Woodman, Peter Keov, Lauren T. May, Peishen Zhao, Rebecca H. Ritchie, Cheng Xue Qin. Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, VIC, Australia.

Introduction. Formyl peptide receptor 2 (FPR2) is a G protein-coupled receptor (GPCR) that is important in resolving inflammation in cardiovascular diseases. A role for signalling bias has been proposed as FPR2 interacts with a chemically diverse range of ligands and produces different functional outputs. For instance, the small molecule FPR2 agonist ACT-389949 has ceased further clinical development, likely due to rapid tachyphylaxis. In contrast, BMS-986235 and compound 43 have both demonstrated protective effects in preclinical models of myocardial infarction. The complex biology of FPR2 has hindered drug discovery efforts. **Aims.** We aimed to test the hypothesis that structurally distinct ligands have different mechanisms of action at FPR2 which govern biased signalling. **Methods.** Concentration-response curves to G protein and β -arrestin coupling, receptor trafficking and second messenger signalling were performed with FPR2 ligands (compound 43, BMS-986235, ACT-389949 and WKYMVm peptide), in HEK293A cells. $\text{Log}(\tau/K_A)$, a composite measure of efficacy and functional affinity, was derived from bias analysis using WKYMVm as the reference ligand. Competition binding was performed by co-incubating the Nanoluc-FPR2-HEK293A with BODIPY-WKYMVm (31.6 nM) and unlabelled ligands (1 nM - 10 μ M) for 2 hrs at 4°C. Inhibitory concentration-response curves were fitted to the one site - Fit K_i equation, data presented as mean \pm SEM. **Results.** Overall, ACT-389949 shared a similar profile with WKYMVm. However, BMS-986235 and compound 43 were roughly 5- to 50-fold biased away from β -arrestin recruitment and trafficking ($n=5-7$, $p<0.05$), whilst being 35- to 60-fold biased towards cAMP inhibition and pERK1/2 relative to WKYMVm ($n=5-7$, $p<0.05$). Not surprisingly, both WKYMVm and ACT-389949 competitively inhibited the percentage probe (BODIPY-WKYMVm) binding with similar affinities ($n=5$, K_i : 26 nM, 79 nM respectively). Interestingly, BMS-986235 and compound 43 did not compete with the probe, suggestive of alternative binding modes. **Discussion.** ACT-389949 shared a similar binding mode and biased signalling fingerprint with WKYMVm, which is distinctly different from that of BMS-986235 and compound 43.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P409

A new paradigm for mRNA display selection by sequence space analysis

Mr Tommy Lu

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

A new paradigm for mRNA display selection by sequence space analysis

Tommy Y Lu^{1,2}, John Chen³, Colin Jackson^{2,3}, Richard Payne^{1,2}. School of Chemistry, University of Sydney¹, Sydney, NSW, Australia; Australian Research Council Centre of Excellence for Innovations in Peptide and Protein Science²; Research School of Chemistry, The Australian National University³, Canberra, ACT, Australia

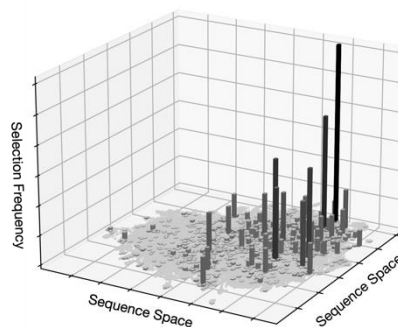
Introduction. mRNA display is a screening technique that can select peptides against a drug target through iterative binding and amplification cycles. This method is used in drug discovery where sequences that enrich for the target can be optimised for therapeutic use. Taking the most enriched peptides as the top hits is the current conventional approach. Yet this method is fallible, as false or non-specific hits can arise due to insufficient screening, random distribution and inherent biases in the initial library. We propose that investigating sequence space can assist in verifying high affinity ligand selection across selection rounds.

Aims. Establish benchmarks for deep sequencing data quality and mRNA display selections across rounds. Assess these benchmarks across multiple studies to ascertain the quality of hits identified under the current standard of display selection.

Methods. A pipeline was developed to extract, clean, and unify deep sequencing data. A sequence space model was designed by evaluating the complementarity of embedding and dimensionality reduction methods. Models of theoretical distribution and random selection were employed as a baseline to quantify and characterise round selection.

Results. Sequence space benchmarks effectively delineated between datasets by metrics of quality. This highlighted key areas of improvement for studies that obtained low quality or unexpected results. Correlation between quality of round selection and biological properties of tested hits affirm the significance of the established benchmarks.

Discussion. The inadequacy of selection in several studies demonstrates the necessity of improved rigour in mRNA display deep sequencing screens. Sequencing across more rounds with deeper reads would ensure higher quality and preserve the consistency of enrichment. Observed biological correlations posit the potential for improved peptide hits with greater affinity for their drug targets.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P410

An in-vitro model to assess drug holiday regimes in resistance to dabrafenib

Mrs Anika Nagarajan

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

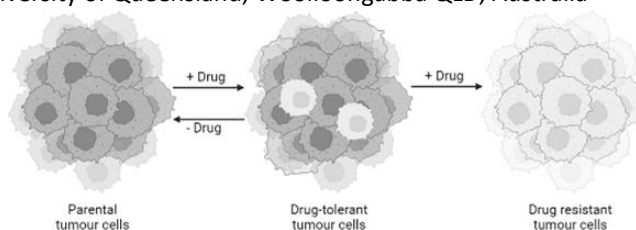
Biography:

Anika Nagarajan is a fourth-year Pharmacy (Honours) student majoring in Clinical and Experimental Therapeutics at the University of Queensland. She is an accomplished student with a passion for enhancing people's lives through actively promoting and offering quality patient-centred care. She holds a GPA of 6.8 and has earned 5 Dean's commendation for academic excellence awards, as well as the esteemed UQ Scholarship, "Pharmacy Interest Women's Group Prize". Anika holds practical experience as a pharmacy student with United Chemists, and placement experience at Mater and Royal Brisbane and Women's Hospital, and rural areas including Chinchilla. She enjoys mentorship and facilitating welcoming learning environments. Anika has held such positions, including volunteering as a Pharmacy Peer Mentor at UQ and is eager to explore the wide range of opportunities available in pharmacy to elevate her skill set and she is committed to positively contributing to the pharmacy field.

An in-vitro model to assess drug holiday regimes in resistance to dabrafenib.

Anika Nagarajan¹, Farzaneh Forouz¹, Sarah J. Roberts-Thomson¹, Gregory R. Monteith¹, Helmut Schaidler² and Mélanie Robitaille¹. ¹School of Pharmacy and ²Frazer Institute, The University of Queensland, Woolloongabba QLD, Australia

Introduction. The advent of molecularly targeted therapies, such as BRAF inhibitors for melanoma (e.g., dabrafenib), represents a major advance in the treatment of this once intractable disease. However, the success of these agents is eventually limited by the development of acquired resistance. Indeed, a small population of cells evades the effects of targeted therapies by entering a reversible slow proliferation state that allows cancer cells to survive drug therapy before the development of permanent resistance (Menon *et al.* 2015). The reversibility of the tolerance stage is exploited clinically using "drug holiday regimes". Eventually drug holidays become less and less effective and irreversible drug resistant cancer cell colonies begin to form (Song C *et al.*; Menon D *et al.* 2023).



Aims. To develop a melanoma *in vitro* model of drug holiday regimes.

Methods. 451Lu melanoma cells were exposed intermittently to cycles of submaximal concentrations of dabrafenib followed by drug holiday periods. Expression of known tolerance markers ABCB5 and SOX4 (Menon *et al.* 2015) were assessed at different time points by RT-qPCR.

Results. Both ABCB5 and SOX4 mRNA expression increased during dabrafenib exposure periods and returned to basal expression levels after the drug holiday periods.

Discussion. Drug holiday periods are exploited clinically to delay the development of resistance but are not sufficient to totally prevent resistance. Our new *in vitro* model may allow the identification of drug targets associated with the transition to drug resistance when cells are intermittently exposed to dabrafenib.

Menon *et al.* (2015) *Oncogene*34(34):4545

Menon *et al.* (2023) *Drug Resist Updat.* 2023 Nov;71:100993

Song C *et al.* (2017) *Cancer Discov*7 (11):1248-1265

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P411

Tomentosenol A, isolated from bee propolis, inhibits TGF- β 1/SMAD3 signalling in human fibroblasts

Ms Lisa Randall

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Lisa is a third year PhD candidate in the School of Health, Biomedicine discipline. Her PhD studies are centred around pharmacology, examining the cellular mechanisms of a novel, proposed anti-fibrotic compound isolated from the propolis produced by the Australian Stingless bee, *Tetragonula carbonaria*. This compound is Tomentosenol A. Her studies have enabled her to gain experience in a broad range of biochemical and molecular laboratory techniques, cell culture and animal models. She presents her findings wherever possible, winning the best poster presentation at the 2023 Australian Society for Medical Research, Post-Graduate Student Symposium. She represented the University of the Sunshine Coast and the Centre for Bioinnovation at the 2023 AusBiotech conference and is currently finalising her first research paper for submission for publication. She is a student member of ASCEPT, ASMR and APSA. In 2024 she has been accepted to present papers at the ASCEPT, APFP & APSA Joint Congress and the UniSC Research Conference.

Tomentosenol A, isolated from bee propolis, inhibits TGF- β 1/SMAD3 signalling in human fibroblasts

Lisa J Randall^{1,4}, Sarah Bajan^{1,2}, Trong T Tran^{3,4}, Robert J Harvey^{1,4}, Fraser D Russell^{1,4}. School of Health, UniSC¹, Sippy Downs, QLD, Australia; School of Biotechnology and Biomolecular Sciences, UNSW², Sydney, Australia; School of Science, Technology and Engineering, UniSC³; Centre for Bioinnovation, UniSC⁴, Sippy Downs, QLD, Australia.

Introduction. We isolated and purified a meroterpenoid from Australian stingless bee propolis, called tomentosenol A (Tom A). Tom A inhibited TGF- β 1-stimulated proliferation, migration and differentiation of human fibroblasts (Hamilton et al, 2022), suggestive of an anti-fibrotic compound. The mechanism of action Tom A is to be determined.

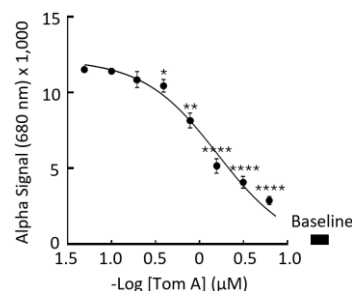
Aim. To examine the mechanism of action of Tom A in cultured adult human dermal fibroblasts and HEK293 cells, with a focus on the SMAD2/3 signalling pathway.

Methods. Normal adult human dermal fibroblasts were activated with TGF- β 1 (10 ng/mL) in media containing DMSO (control), Tom A (0.05-6.25 μ M), SIS3 (SMAD3 inhibitor; 10 μ M) or GW788388 (TGF- β R1 inhibitor; 1 μ M). Cell lysates were quantified for phosphorylation of SMAD3 (AlphaLISA assay), SMAD signalling (HEK293 cells expressing a SMAD3 reporter gene), and pro-fibrotic gene transcription (RTqPCR; *ACTA2*, *COL1A1*, *COL3A1*, *CCN2*).

Results. TGF- β 1 increased SMAD3 phosphorylation from baseline levels (Figure). Tom A (IC₅₀, 64.0 nM, n=3), SIS3 and GW788388 inhibited TGF- β 1-stimulated SMAD3 phosphorylation. Tom A and SIS3 partially inhibited TGF- β 1-stimulated SMAD3 reporter gene expression, while the combination of Tom A and SIS3 abolished the increased expression. TGF- β 1 upregulated smooth muscle alpha actin (*ACTA2*), collagens 1A1 and 3A1 (*COL1A1*, *COL3A1*) and connective tissue growth factor (*CCN2*) transcription and this was reversed by 6.25 μ M Tom A.

Discussion. The findings indicate inhibition of TGF- β 1/SMAD3 signalling by Tom A. As this pathway is implicated in tissue fibrosis, Tom A is a compound that can be developed as a novel therapeutic approach for management of hypertrophic scars caused by deep dermal injuries that are associated with surgery, trauma, and burns.

Hamilton et al (2022) Antioxidants, 11:1604.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P412

Anti-proliferative effects of HDAC8 PROTAC on HSCC cells via endoplasmic reticulum stress

Mr Phurinut Somchai

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Phurinut graduated high school from Benchama Maharat and is now studying at the Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

Anti-proliferative effects of HDAC8 PROTAC on HSCC cells via endoplasmic reticulum stress

Somchai P¹, Chotitumnavee J², Settacomkul R³, Yukihiro Itoh⁴, Takayoshi Suzuki⁴, Vivithanaporn P³. Faculty of Medicine Ramathibodi Hospital, Mahidol University¹, Bangkok, TH; Department of Pharmacology, Faculty of Dentistry, Mahidol University², Bangkok, TH; Chakri Naruebodindra Medical Institute, Faculty of Medicine Ramathibodi Hospital, Mahidol University³, Samut Prakan, TH; SANKEN, Osaka University, Mihogaoka, Ibaraki-shi, Osaka 567-0047, JP⁴.

Introduction. Hypopharyngeal squamous cell carcinoma (HSCC) has a high mortality rate. HDAC8, an enzyme that catalyzes the deacetylation of histone and non-histone proteins, plays a role in cancer progression. HDAC8 is overexpressed in oral squamous cell carcinoma (OSCC). We hypothesized that HDAC8 level is associated with the progression of HSCC. Proteolysis targeting chimera (PROTAC) proteins degrade specific proteins; therefore, it has significant advantages over conventional protein inhibitors. PROTAC can suppress all functions of targeted proteins because it degrades targeted proteins from the cell. The preliminary data on cell viability of HDAC8 PROTAC using MTT assays showed the IC₅₀ against FaDu cells is approximately 1.202 μ M. Therefore, we selected the concentrations

0.5 and 2.5 μ M, the lower and higher concentrations than the IC₅₀ value, to determine cell proliferation activity.

Aims. We compare the prohibition of cell proliferation and endoplasmic reticulum stress (ER) stress markers of HDAC8 PROTAC, HDAC8 inhibitor, Vorinostat (SAHA), Pomalidomide and Cisplatin on FaDu cell line.

Methods. FaDu cells were stained with Deep Red staining and the percentage of mean fluorescence intensity (MFI) was measured by flow cytometry. The increase in MFI indicates the inhibition of cell proliferation. The expression of ER stress marker mRNA was measured using real-time PCR.

Results. The percentage of mean deep red intensity of FaDu after exposed to HDAC8 PROTAC is 10 times higher than HDAC8 inhibitor and 5 times higher than SAHA under the same concentration of 2.5 μ M for 72 h. Real-time PCR shows increased ER stress-related genes such as XBP1s, CHOP, and ATF4 after exposed to HDAC8 PROTAC.

Discussion. HDAC8 PROTAC inhibits cell proliferation and induces ER-stress gene expression. Taken together, the present study shows that HDAC8 PROTAC is a potent therapeutic agent for HSCC.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P413

Utilising bioluminescence resonance energy transfer to elucidate novel pharmacology of AT₁-LOX-1 heteromer

Mr Julyan Tan

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Hi, my name Julyan and I'm a PhD candidate in the School of Biomedical Sciences at the University of Western Australia, and based at Harry Perkins Institute of Medical Research. My research focus is on novel receptor heteromers formed between G protein-coupled receptors and scavenger receptors, and their role in the receptor biology of atherosclerosis.

Utilising bioluminescence resonance energy transfer to elucidate novel pharmacology of the AT₁-LOX-1 heteromer

Julyan Tan¹, Kevin DG Pflieger^{1,2,3}, Elizabeth KM Johnstone^{1,2,4}. ¹Molecular Endocrinology and Pharmacology, Harry Perkins Institute of Medical Research and Centre for Medical Research, The University of Western Australia, Nedlands, WA, Australia; ²Australian Research Council Centre for Personalised Therapeutics Technologies, Melbourne and Perth, VIC and WA, Australia; ³Dimerix Limited, Fitzroy, VIC, Australia; ⁴School of Biomedical Sciences, The University of Western Australia, Nedlands, WA, Australia.

Introduction. G protein-coupled receptors can form receptor heteromers with, and transactivate, non-GPCR partner receptors to induce novel changes in pharmacology, signalling and intracellular trafficking.¹ There is evidence to suggest angiotensin II type 1 (AT₁) receptor and lectin-like oxidised low-density lipoprotein receptor-1 (LOX-1) form a heteromer – this represents an exciting area of research with implications for atherogenic signalling.²

Aims. This study aimed to provide further evidence for the heteromerisation between LOX-1 the AT₁ receptor and investigate any pharmacological and signalling changes that arise from the formation of this heteromer.

Methods. Use of the Receptor-Heteromer Investigation Technology (Receptor-HIT) through a bioluminescence resonance energy transfer (BRET) platform.³ Receptor-HIT detects a BRET signal between a luciferase-labelled receptor, and a fluorophore-labelled interacting protein that is recruited to an unlabelled partner receptor. This BRET signal informs proximity of receptors and provides insights into pharmacological changes such as G protein-signalling.

Results. LOX-1 produced Receptor-HIT signals indicative of heteromerisation when co-transfected with AT₁. LOX-1 co-transfection selectively altered mini-G protein coupling of AT₁ receptor, increasing mG_s but not mG_s_q coupling.

Discussion. These findings support the existence of the AT₁-LOX-1 heteromer, providing evidence for close proximity and interaction of the protomers, and suggesting distinct GPCR signalling activity in the AT₁-LOX-1 heteromer.

1. Dale NC, Johnstone EKM, Pflieger KDG. *Front Endocrinol (Lausanne)*. 2022.
2. Takahashi T, Huang Y, Yamamoto K, et al. *iScience*. 2021.
3. Pflieger KD, Eidne KA. *Nat Methods*. 2006.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P415

Discovering a Novel DYRK1A Inhibitor and Its Impact on Alzheimer's disease

Dr HuangJu Tu

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

HuangJu Tu is a postdoctoral fellow at Taipei Medical University. His research focuses on neuroscience and cancer biology.

Discovering a Novel DYRK1A Inhibitor and Its Impact on Alzheimer's disease

Huang-Ju Tu¹, Chao-Shiang Peng², Tony Eight Lin¹, Kai-Cheng Hsu^{1,2,3}, Wei-Chun HuangFu^{1,2,3}, Shio-Lin Pan^{1,2,3}

¹ Graduate Institute of Cancer Biology and Drug Discovery, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan

² Ph.D. program for Cancer Molecular Biology and Drug Discovery, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan

³ TMU Research Center of Cancer Translational Medicine, Taipei Medical University, Taipei, Taiwan

Introduction. The enzyme DYRK1A plays a crucial role in various physiological processes. Dysregulation of DYRK1A is implicated in severe neurodegenerative disorders such as Alzheimer's disease (AD). Despite the progress in identifying DYRK1A inhibitors, achieving selectivity has remained a significant challenge.

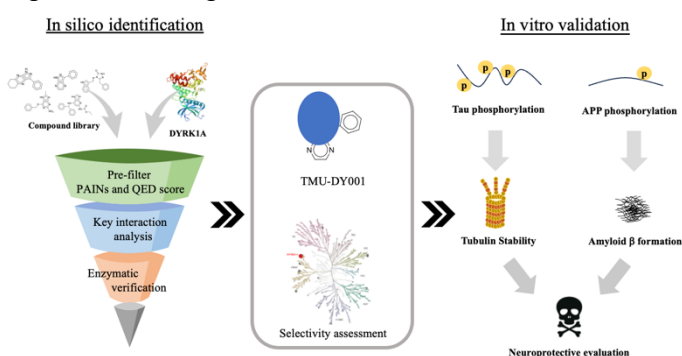
Aims. Our aim was to identify novel selective inhibitors that not only inhibits DYRK1A activity but also presents a novel therapeutic avenue for AD by modulating key pathological processes.

Methods. We used structure-based virtual screening to identify the potential DYRK1A inhibitors. Western blotting and tubulin binding assay were used to evaluate the effects of inhibitors in tau pathology and A β formation. Neuroprotective effects of DYRK1A inhibitors were examined by MTT assay.

Results. We successfully identified TMU-DY001 as a

highly selective DYRK1A inhibitor. TMU-DY001 effectively reduced tau phosphorylation at multiple sites, leading to enhanced tubulin stability. Additionally, TMU-DY001 decreased APP phosphorylation and A β formation. Finally, TMU-DY001 provided a neuroprotective effect by reversing A β -induced neurotoxicity.

Discussion. Our research highlights the critical role of selective DYRK1A inhibitors in treating Alzheimer's disease and presents a promising starting point for the development of targeted therapies.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P416

Characterisation of the pro-atherosclerotic orphan G protein-coupled receptor, GPR146

Mr Brendan Wilkins

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Brendan recently completed his PhD in the laboratory of Nicola Smith at UNSW Sydney. He is now a Lecturer in the Department of Pharmacology in the School of Biomedical Sciences at UNSW Sydney. Brendan has a special interest in G protein-coupled receptors, particularly those that do not yet have an identified endogenous ligand which are termed “orphans”. Brendan is the chair-elect of the ASCEPT Equity, Diversity, and Inclusion Committee and is committed to improving the visibility of the ASCEPT LGBTQIA+ community.

Characterisation of the pro-atherosclerotic orphan G protein-coupled receptor, GPR146

Brendan P Wilkins¹, Jack Zhang¹, Asuka Inoue², Marianne Martinello³, Blake Cochran¹, Rowena Bull³, Nicola J Smith¹. School of Biomedical Sciences, UNSW Sydney¹, NSW, Australia; Graduate School of Pharmaceutical Sciences, Tohoku University², Sendai, Japan; The Kirby Institute, UNSW Sydney³, NSW, Australia.

Introduction. GPR146 is an orphan G protein-coupled receptor that has a convincing pro-atherosclerotic role through upregulation of the cholesterol biosynthesis pathway. Inhibition of this receptor may be particularly useful with treatment-refractory familial hypercholesterolaemia. However, the molecular pharmacology of this receptor remains understudied. Proinsulin C-peptide and foetal bovine serum (FBS) are proposed activators of GPR146, although the pairing with C-peptide has not yet been reproduced by an independent research group and the active component in FBS has not yet been identified.

Aims. The aim of this study was to validate previously proposed ligands for GPR146.

Methods. C-peptide and FBS were tested using the following assays: reporter gene assays to investigate G_s, G_{ai/o}, G_{αq/11}, and G_{α12/13} signalling; a NanoBIT assay for β-arrestin recruitment; and Western blot or a BRET1-based biosensor for ERK1/2 phosphorylation (pERK1/2). A panel of 58 human sera was screened at GPR146 using Western blot probed for pERK1/2; the threshold for “hit” selection was set at ±2xSD. Human sera identified as “hits” were then further characterised using G protein- and arrestin-deficient HEK293A cells.

Results. Neither C-peptide nor FBS activated GPR146 in any assays tested (n=5); assay validity was confirmed by multiple positive controls. An overall increase in pERK1/2 was observed in response to human serum in GPR146-expressing cells compared to cells not expressing GPR146 (P<0.0001, paired t-test). 47/58 human serum samples elevated pERK1/2, with 5 surpassing the upper hit threshold indicating activation of GPR146.

Discussion. In this study, previously proposed ligands for GPR146 were not reproduced, indicating that C-peptide is not, and FBS does not contain, the endogenous ligand for GPR146. Instead, human serum was identified as an activator of GPR146. Future studies with human serum may identify the endogenous ligand for GPR146.

Yu et al. 2019. Cell. 179(6):1276-1288.e14.

Yosten et al. 2013. J Endocrinol. 11;218(2):B1-8.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P417

Pharmacological evaluation of beta-endorphin analogues: opioid-based bivalent peptides targeting multiple opioid receptors.

Mr Yifan Wang

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Yifan Wang is a PhD student at the University of Queensland's School of Pharmacy in Drug Discovery, specializing in analytical chemistry, quality control, biotechnology and pharmaceutical research. Yifan has previously worked as a Design Director at Beijing Jing-Meng Cell Bio-technology Co.Ltd. He holds a Bachelor of Science from China Pharmaceutical University with a major in Marine Pharmacy and a Master of Pharmaceutical Industry Practice from the University of Queensland. His research and professional pursuits are motivated by a dedication to advancing the field of pharmaceutical sciences and enhancing the processes involved in drug development.

Pharmacological evaluation of beta-endorphin analogues: opioid-based bivalent peptides targeting multiple opioid receptors.

Yifan Wang¹, Danial Saifuddin¹, Karnaker Tupally¹, Harendra Parekh¹, Peter J. Cabot¹. School of Pharmacy, The University of Queensland¹, Brisbane, QLD, Australia.

Introduction. Pain represents a global public health problem. The WHO analgesic ladder categorises opioids as the major treatment for moderate and severe pain. There are three main subtypes of opioid receptors: the mu-opioid receptor (MOPr), the delta-opioid receptor (DOPr), and the Kappa-opioid receptor (KOPr). Classic painkillers activate the MOPr to relieve the pain by blocking the pain signal transmission. Since the adverse effects of clinical opioids have become a severe problem for safe and effective drug use, the potential of new medicines based on endogenous opioid peptides (EOP) without adverse effects is an alternative to traditional small molecule opioids. Specifically, β -endorphin 1-31 (BE1-31) is highlighted as a potent analgesic targeting the MOPr. This study focuses on designing and assessing novel peptides using functional fragments of BE1-31 with a bivalent or dual pharmacophore. Lead bivalents in the series designed and reported in this study are BVE13-003 and BVE13-523.

Aims. Design, synthesise and characterise bivalent forms of BE1-31 analogues as bivalent peptides. Evaluate synthesised peptide libraries' pharmacological efficacy, potency and selectivity against MOPr, DOPr and KOPr.

Methods. Peptides are synthesised via the solid-phase peptide synthesis (SPPS). The cAMP inhibition of peptides is used to assess efficacy, potency, and selectivity in HEK293 cells overexpressing MOPr, DOPr, and KOPr.

Results. From the panel of bivalents screened, BE1-13 and BVE13-523 showed lower potency (IC_{50}) than fentanyl for MOPr ($0.19 \pm 0.02 \mu M$, $8.48 \pm 5.85 \mu M$ and $7.89 \pm 1.61 nM$, respectively, $n=3$, t-test, $P < 0.05$). BVE13-003 showed promise compared to BVE13-523 ($64.11 \pm 11.76 nM$, $n=3$, t-test, $P < 0.05$).

Discussion. BVE13-003, as the bivalent form of BE1-13, showed enhanced activity compared to BE1-13. It is consistent with Biphalin reported by Lipkowski, A. W et al. A dual pharmacophore connected by a linker is considered to increase drug concentration at local sites and plays a synergistic role in improving the possibility of targeting the receptors. The different linkers provide different lengths and abilities to target receptors. Although not all bivalents showed improvements, the relationship needs to be explored by expanding the library of bivalents prepared with varying-length linkers. Meanwhile, the peptides should be assessed IC_{50} in DOPr and KOPr to confirm the selective for MOPr.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P418

Activation and allosteric modulation of the human GLP-1R by small-molecule ligands

Dr Xin Zhang

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Dr Xin (Cindy) Zhang received her PhD in 2021 and was awarded the 2021 Mollie Holman Medal for doctoral thesis excellence by Monash University for studies on the glucagon-like peptide-1 receptor (GLP-1R) in the lab of Profs. Patrick Sexton and Denise Wootten. She was then recruited as a Postdoctoral Fellow in the same laboratory on projects aligned to the Australian Research Council (ARC) Centre for Cryo-EM of Membrane Proteins (CCeMMP), and was recently awarded an ARC Discovery Early Career Researcher Award (DECRA) fellowship (2023-2026). Her research program incorporates cell biology, biochemistry, structural biology (in particular cryo-EM) and pharmacology to gain molecular insights into G protein-coupled receptors (GPCRs). Her particular interest is in the structure-function relationships of glucagon family GPCRs to understand how diverse ligands bind to and activate these receptors, which are clinically important drug targets for the treatment of type II diabetes and obesity.

Activation and allosteric modulation of the human GLP-1R by small-molecule ligands

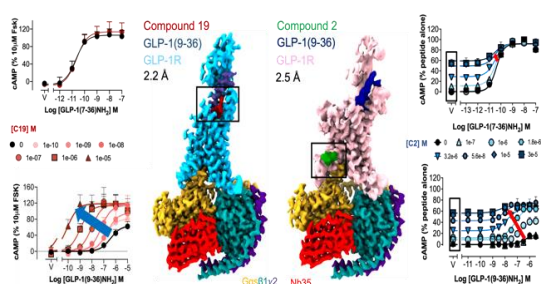
Xin Zhang^{1,2}, Hariprasad Venugopal³, Samantha McNeill¹, Matthew J. Belousoff^{1,2}, Patrick M. Sexton^{1,2}, Denise Wootten^{1,2}. Drug Discovery Biology¹, and ARC CCeMMP², Monash Institute of Pharmaceutical Sciences, and Ramaciotti Centre for Cryo-Electron Microscopy³, Monash University, Melbourne, VIC, Australia.

Introduction. The glucagon-like peptide 1 receptor (GLP-1R) is a well-established clinical target for type II diabetes and obesity. A variety of GLP-1R non-peptidic agonists and positive allosteric modulators (PAMs) have been identified, however, how they bind and modulate GLP-1R function is poorly understood.

Aims. Determine structures of GLP-1R-Gs complexes bound to different endogenous peptide agonist (GLP-1, GLP-1(9-36)NH₂, oxyntomodulin), biased small-molecule agonists (PF 06882961, CHU-128) or PAMs (compound 19, compound 2), and correlate these with their pharmacological profiles.

Methods. Structures of GLP-1R-Gs complexes were determined using cryo-electron microscopy (cryo-EM). Pharmacological profiles were assessed using assays of well-studied downstream signalling (cAMP production and calcium mobilisation) and regulatory (arrestin recruitment, internalisation) events.

Results. The binding site for PF 06882961 exhibits substantial overlap with that of endogenous peptide agonists within the receptor core. In contrast, CHU-128 displays limited overlap, which aligns with its divergent pharmacological properties (Deganutti et al 2022, Zhang et al 2020). Surprisingly, compound 19 engages at the extracellular side of the receptor, while compound 2 binds to the intracellular end. This correlates with the probe dependent properties of these PAMs, which differently modulate the metabolite signalling of endogenous peptides (Figure 1).



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion. Structural differences can be correlated to functional data revealing molecular insights into activation and modulation of small-molecule ligands. These findings will facilitate rational structure-based discovery of non-peptidic drugs targeting the GLP-1R and other related class B1 G protein-coupled receptors.

Deganutti G*, Liang YL*, Zhang X* et al (2022) Nat Commun 13:92; Zhang X et al (2020) Mol Cell 80:1–16

P419

Identification of anti-inflammatory ligands of GPCRs from natural products

Prof Richard Ye

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Richard Ye is a Presidential Chair Professor and Associate Dean of Biomedical Research & Innovation at School of Medicine, The Chinese University of Hong Kong (CUHK) in Shenzhen, China. He received a Ph.D. in cell and integrative biology from Washington University in St. Louis and established his lab at The Scripps Research Institute and University of Illinois, where he worked on gene cloning and pharmacological characterization of formyl peptide receptors. His lab focused on innate immunity and host defense when he joined Shanghai Jiao Tong University as Dean of School of Pharmacy in 2010. In recent years, Prof. Ye's lab used cryogenic electron microscopy to investigate the structural and functional correlation of G protein-coupled receptors including CXCR4, KSHV-GPCR, succinate receptor 1 and FPR1. He has published more than 230 research papers and is a Clarivate Highly Cited Researcher. Besides lab research, Prof. Ye serves as Associate Editor of Pharmacological Reviews.

Identification of anti-inflammatory ligands of GPCRs from natural products

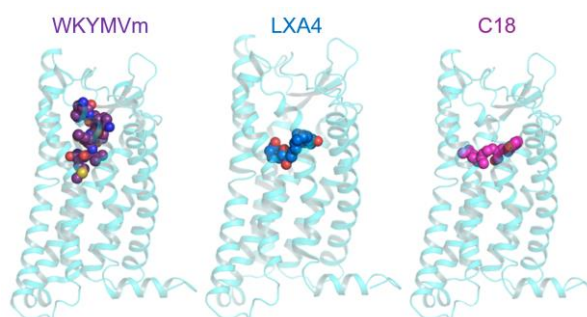
Qiwen Liao¹, Minghua Qiu², Richard D. Ye¹. Kobilka Institute of Innovative Drug Discovery, School of Medicine, The Chinese University of Hong Kong¹, Shenzhen, China; Kunming Institute of Botany, Chinese Academy of Science², Kunming, Yunnan, China

Introduction. Natural products such as herbal medicine have been widely used for treatment of inflammatory diseases. GPCRs such as FPR2 provide established and potential targets for anti-inflammatory therapies.

Aims. The present study explores structural information from solved GPCR structures for the discovery of anti-inflammatory agents from natural sources.

Methods. For ligand preparation, a natural product nuclear magnetic resonance (NMR) database was established. For receptor modeling, structural models based on PDB were prepared. Previously reported anti-inflammatory agents such as lipoxin A4 (LXA4) and the C18 compound from *Ganoderma* (figure on the right) were used as reference controls. After molecular docking, selected compounds were subject to functional assays either alone or together with an inflammatory agent targeting the same cell/receptor.

Results. A comparison with the full agonist WKYMVm found different ligand insertion pose, but anti-inflammatory ligands showed characteristic horizontal or transversal pose in the transmembrane ligand binding pocket. No binding outside the pocket has been found yet. In functional assays, none of the



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



tested natural compounds showed strong agonistic activity, but partial agonism was found in selected compounds. Competition with agonist was found with most compounds with some also displaying anti-inflammatory activity when applied alone.

Discussion. The combined use of NMR database, molecular docking based on solved receptor structure models, and functional assays together provide a more accurate and efficient approach for identification of anti-inflammatory agents from natural products.

P420

The role of RGS2 in regulating GLP-1R function

Miss Yanxi Chang

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Nancy (Yanxi Chang) is a third-year Ph.D. candidate at the Monash Institute of Pharmaceutical Sciences, Monash University, Melbourne, Australia. Her research focuses on Drug Discovery Biology, specifically in RGS protein fine tuning GLP-1R function. Nancy earned her B.S. and M.S. in Chinese Materia Medica in China.

The role of RGS2 in regulating GLP-1R function

Yanxi Chang¹, Sam M McNeill¹, Patrick M Sexton^{1,2}, Denise Wootten^{1,2}, Peishen Zhao^{1,2}.

Drug Discovery Biology, Monash University¹, Melbourne, Vic., Australia; ARC Centre for Cryo-Electron Microscopy of Membrane Proteins (CCeMMP), Monash University², Melbourne, Vic., Australia;

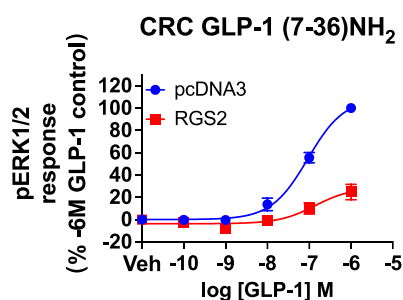
Introduction. The GLP-1R is an incretin receptor that plays an important role in glucose homeostasis and energy balance. It is a well-established drug target for treating T2DM and obesity, but current drugs have sub optimal clinical efficacy and unwanted side effect profiles. This may be due to lack of understanding of how GLP-1R works under disease conditions. Regulators of G protein signalling proteins (RGS) are intracellular proteins that act as negative regulators of G protein signalling, and RGS expression levels are dynamically regulated under pathological conditions. However, the role of RGS proteins in regulating GLP-1R signalling is unexplored. This project focuses on RGS2, a RGS protein that has been demonstrated to correlate with metabolic disorders.

Aims. To investigate the effects of RGS2 on GLP-1R receptor expression and downstream signalling.

Methods. Receptor cell surface expression was quantified using flow cytometry. Real-time ligand-mediated cAMP production was measured using a cAMP biosensor (Glosensor). Intracellular calcium (iCa²⁺) mobilization was assessed with Fluo-8 dye, while phosphorylated ERK (pERK) activation was measured using a YEN biosensor.

Results. Our findings indicate that RGS2 overexpression significantly decreases agonist-mediated GLP-1R intracellular calcium (iCa²⁺) mobilization and phosphorylated ERK (pERK) signalling, but has little or no effects on cAMP signalling. Moreover, these effects were not attributed to changes in receptor surface expression.

Discussion. Our research provides valuable insights into the roles of RGS2 in modulating GLP-1R signalling in a pathway dependent manner. Future experiments will be dedicated to investigate the molecular mechanisms that govern the observed effect.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P421

Targeting peripheral mu and delta receptors with bivalent opioid peptides

Mr Junkai Zhang

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Junkai Zhang is a PhD candidate at the University of Queensland's School of Pharmacy, focusing on molecular biology, drug discovery, and pharmaceutical formulation. His academic journey began with a Bachelor of Pharmacy from Jining Medical University, where he majored in chemistry and pharmacology, followed by a Master of Pharmaceutical Industry Practice from the University of Queensland. His doctoral research aims to advance pharmaceutical sciences through the development of innovative strategies to improve drug formulation and quality assurance. Junkai is committed to contributing to the body of knowledge in pharmaceutical science and to addressing critical challenges in drug development and healthcare delivery.

Targeting peripheral mu and delta receptors with bivalent opioid peptides

Junkai Zhang¹, Mélanie Robitaille¹, Danial Saifuddin¹, Benjamin P Ross¹, Peter J Cabot¹. Sch of Pharm, Univ of Queensland¹, Brisbane, QLD, Australia.

Introduction. Misuse and addiction to opioid drugs are now so widespread that it constitutes a major public health crisis known as the global opioid pandemic. Opioid peptides are effective for pain relief, mediated through their activation of opioid peptide receptors (OPs), which are G-protein coupled receptors (GPCRs), including mu (MOP) and delta (DOP) subtypes (Pasternak, 2004). GPCRs function as transmembrane protein receptors in dimers, where two GPCRs are in proximity (Prinster et al, 2005). β -endorphin and enkephalin (ENK) are endogenous opioid peptides for MOP and DOP. Bivalent opioids, which are opioid ligands containing two pharmacophores (Smith et al, 2023), are interesting because endogenous opioid peptides as pharmacophores produce potent analgesia without side effects, which may help alleviate the global opioid epidemic.

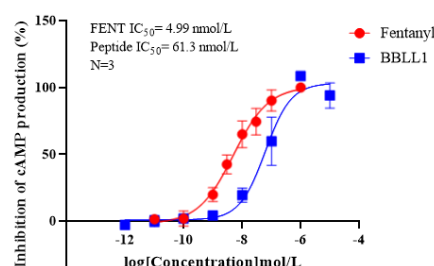
Aims. To design and synthesise bivalent peptides selective to MOP and DOP and examine the pharmacological potency and efficacy of the synthesised bivalent peptides and controls against established cell lines.

Methods. Peptides were assessed for OPs efficacy and potency in HEK293 cell lines overexpressing MOP and DOP respectively. cAMP modulation was measured via AlphaScreen cAMP assay.

Results. Our bivalent peptide BBLL1 comprising β -endorphin 1-7 (BE1-7) and Leu-ENK showed comparable efficacy and a lower potency on the cAMP inhibition curve compared to MOP agonist fentanyl. The IC₅₀ values of fentanyl and BBLL1 were not significantly different, 9.3 \pm 5.9nmol/L and 6.9 \pm 2.7nmol/L, respectively (n= 3, P>0.05, unpaired t test).

Discussion. The bivalent peptide BBLL1 significantly inhibits intracellular cAMP production in comparison to the parent peptide (Leu-ENK and BE1-7). β -endorphin is a potent MOP agonist and Leu-ENK also has a partial agonism for MOP, allowing the bivalent peptide to produce subnanomolar potencies.

cAMP modulation for agonist on MOP overexpressing cell



Pasternak GW (2004) Neuropharmacology 47 Suppl 1:312-23. Prinster SC et al (2005) Pharmacol Rev 57(3):289-98. Smith MT et al (2023) J Med Chem 66(6):3746-84.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P422

Designing novel bivalent opioid peptides targeting kappa and nociceptin opioid receptors.

Mr Muhaimin Habib

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Muhaimin Habib is a PhD student at the University of Queensland's School of Pharmacy in Drug Discovery, specializing in analytical chemistry, quality control, and pharmaceutical formulation. With a solid background in the pharmaceutical industry as a qualified chemist and pharmacologist, Muhaimin has previously worked as a Quality Control Analyst at DBL Pharmaceuticals Ltd. and as a Clinical Trial Associate at IQVIA. He holds a Bachelor of Science from Monash University with a major in chemistry and pharmacology and a Master of Pharmaceutical Industry Practice from the University of Queensland. His research and professional endeavors are driven by a commitment to advancing pharmaceutical sciences and improving drug development processes.

Designing novel bivalent opioid peptides targeting kappa and nociceptin opioid receptors.

Muhaimin Habib¹, Mélanie Robitaille¹, Danial AP Saifuddin¹ & Peter J Cabot¹. School of Pharmacy, The University of Queensland¹, Woolloongabba, QLD 4102, Australia

Introduction. The opioid crisis is a significant societal challenge, with many individuals prescribed opioid analgesics for acute and chronic pain, raising global concerns due to widespread repercussions and adverse effects. Opioids reduce pain signal transmission through the inhibition of cyclic adenosine monophosphate (cAMP) production by acting on opioid receptors (OPRs) in both the central nervous system (CNS) and peripheral nervous systems (PNS). However, this can lead to addiction and other side effects with CNS. OPRs, including Mu-OPr (MOPr), Delta-OPr (DOPr), Kappa-OPr (KOPr), and Nociceptin/Orphanin FQ-OPr (NOPr), distributed throughout the CNS and PNS. Dynorphin (Dyn) and Nociceptin/orphanin FQ (N/OFQ), selective endogenous opioid peptides originating from the nervous system target KOPr and NOPr respectively within the PNS; the drawback is their susceptibility to enzymatic metabolism, which hampers *in vivo* potency. A strategy implemented using bivalent constructs of Dyn1-7 and N/OFQ1-13 (most potent fragments of Dyn and N/OFQ) linked with stable linker targeting KOPr/NOPr simultaneously. The constructs were further evaluated for enhanced potency.

Aims. To develop stable bivalent constructs incorporating analogues of Dyn and N/OFQ, designed to target both KOPr and NOPr utilizing various linker compositions to enhance stability and potency over monovalent counterparts.

Methods. The bivalent peptide DyNo; construct of Dyn1-7 and N/OFQ1-13 fragments with the linker was synthesized using solid-phase peptide synthesis. CHO_{NOPr} cells were used to assess the cAMP modulation of DyNo. Potencies were probed using IC₅₀ values from concentration curves for NOPr.

Results. Synthesized peptides were validated for *in vitro* assessments, achieving purities >90% in HPLC analysis. The IC₅₀ values of DyNo and N/OFQ1-13 were not significantly different in NOPr, 12.44±1.06 nmol/L and 6.88±2.63 nmol/L respectively; (n=3; P>0.05, unpaired *t*-test).

Discussion. In cAMP assay experiments, no significant differences were observed between DyNo and N/OFQ1-13 in CHO_{NOPr} cells for cAMP modulation. DyNo's interaction with CHO_{NOPr} cells resulted in a cAMP inhibitory concentration curve that closely paralleled that of N/OFQ1-13, with minimal variance in efficacy and potency suggesting NOPr's selectivity for its endogenous peptide N/OFQ1-13 and inactivity for Dyn1-7 fragment of DyNo.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P423

Influence of medium composition and dimensionality of culture on tumour cell characteristics

Ms Xiaodan Zhang

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Xiaodan(Emma) Zhang, a final-year PhD candidate at the mechano-pharmacology lab at the department of Biochemistry and Pharmacology, University of Melbourne. Xiaodan is working on optimisation of *in vitro* conditions for breast cancer drug screening. melbourne medium (MM), a new physiologically relevant medium developed by our group, was prepared and contrasted with conventional cell culture medium (CM) throughout her project. She is a recipient of the 2022 “Chinese Government Award for Outstanding Self-financed Students Abroad”, and she's a member of the EDI committee of ASCEPT.

Influence of medium composition and dimensionality of culture on tumour cell characteristics

Xiaodan Zhang^{1,2}, Tianhong Cheng^{1,2}, Ellie Cho³, Alastair Stewart^{1,2}. Department of Biochemistry and Pharmacology, The University of Melbourne¹, VIC, Australia; ARC Centre for Personalised Therapeutics Technologies², Melbourne, VIC, Australia; The Biological Optical Microscopy Platform (BOMP), The University of Melbourne³, VIC, Australia.

Introduction. Melbourne medium (MM), a plasma-like physiological medium developed by our group, is contrasted with hyper-nutritional conventional cell culture medium (CM) and Human Plasma-Like Medium (HPLM) for influence on the breast cancer cell proteome and cell migration. The influence of medium composition and 3D vs. 2D culture on cell proteome and drug effectiveness was also explored.

Aims. To use global proteomics to study protein expression profiles in *in vitro* breast cancer models established using MCF-7 and MDA-MB-231 cells in 2D and 3D, to compare the effectiveness of selected breast cancer drugs in different experimental conditions, and to explore the influence of medium composition on breast cancer cell migration.

Methods. The protein expression profiles in MDA-MB-231 and MCF7 cells in 2D and 3D (MM vs. CM vs. HPLM) were established by global proteomics. Acridine orange and ethidium bromide (AO/EB) staining was used in combination with Operetta high content imaging for viable and non-viable cell numeration in 2D conditions. A new 3D viability assessment using Propidium iodide and Hoechst 33342 staining, Zeiss LSM 900 Airyscan2 Confocal live cell imaging system and Imaris software was established for 3D viability assessment. Scratch-wound healing assay was used to study the migration of MCF-7 and MDA-MB-231 cells in the 3 different media.

Results. In MDA-MB-231, 284 and 71 proteins were found to be upregulated in CM compared to MM in 2D and 3D, respectively; 199 and 198 proteins were downregulated in CM compared to MM in 2D and 3D, respectively. The results for MCF-7 cells showed similar trends. Several drugs including paclitaxel, doxorubicin showed differences in drug effectiveness between CM and MM groups in both cell lines. However, the differences were reduced after adding FCS to the media. Medium composition has a larger influence on drug potency in 2D than that in 3D culture. Medium composition has significant influence on cell migration ability, where both cell lines had higher migration speed in MM and CM compared to that in HPLM.

Discussion. Cell migration, proteome profiles and the effectiveness of breast cancer drugs were greatly influenced by medium composition. Dimensionality of culture had significant impact on cell proteome and effectiveness of drugs.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P424

Targeted PAK1/PAK4 inhibition normalizes vasculature and boosts gemcitabine effectiveness in pancreatic cancer

Mr Arian Ansardamavandi

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Arian Ansardamavandi is a PhD candidate at the University of Melbourne, Department of Surgery, Austin Precinct, supervised by Dr. Hong He and Professor. Mehrdad Nikfarjam. With over ten years of research experience in cancer biology, including at the prestigious Pasteur Institute, Arian's work has focused on advancing therapeutic strategies within this field. Since beginning his PhD in December 2021, he has concentrated on enhancing treatment efficacy in pancreatic cancer through the inhibition of p21-activated kinases (PAK), aiming to improve vascular normalization and modulate the tumor microenvironment. His research investigates immune cell activation, particularly involving T cells, dendritic cells, and M1/M2 macrophages, to foster an effective anti-tumor response. Arian has authored five ISI journal publications so far, with his most recent work, "PAK in Pancreatic Cancer-Associated Vasculature: Implications for Therapeutic Response," contributing valuable insights into the potential for targeted therapeutic responses in cancer treatment. For a full list of publications, please visit his Google Scholar profile.

Targeted PAK1/PAK4 inhibition normalizes vasculature and boosts gemcitabine effectiveness in pancreatic cancer

Arian Ansardamavandi¹, Mehrdad Nikfarjam^{1,2}, Hong He¹

¹Dept of Surgery, Austin Precinct, Univ of Melbourne, Heidelberg, VIC, Australia; ²Dept of Hepatopancreatic-Biliary Surgery, Austin Health, Heidelberg, VIC, Australia.

Introduction Angiogenesis drives the progression of solid tumors, including pancreatic cancer. Anti-angiogenesis therapies, though intended to starve tumors, may restrict the delivery of chemotherapeutic agents like gemcitabine, exacerbating tumor aggression. This has resulted in minimal improvements in overall survival rates among pancreatic cancer patients.

Aims To investigate the roles of PAK1 and PAK4 inhibition on tumor vascularity, vascular normalization, and the effectiveness of gemcitabine in pancreatic cancer mouse models.

Methods We used mouse models with selective PAK1 and PAK4 inhibition. Vascularity and normalization were assessed using IHC for CD31, CD34, NG2, and PDGFRB. Gemcitabine efficacy was evaluated in PAK1 and PAK4 knockout models.

Results PAK1 KO reduced tumor vascularity, as assessed by CD31 and CD34 staining, and increased vascular normalization, demonstrated by enhanced pericyte coverage. However, the reduction of tumour growth by gemcitabine was modest in PAK1 KO tumour. In contrast, PAK4 KO did not alter tumor vascularity but significantly enhanced vascular normalization, as evidenced by improved pericyte coverage, and increased the reduction of tumour growth by gemcitabine, resulting in a 92% reduction in tumor weight.

Discussion PAK1 inhibition reduces tumor vascularity and promotes vascular normalization through increased pericyte coverage, while PAK4 inhibition significantly enhances gemcitabine efficacy via improved vascular normalization without altering vascularity. These findings highlight the potential of targeting specific PAK isoforms to optimize treatment strategies in pancreatic cancer.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P425

The effects of different resistance mechanisms on *Pseudomonas aeruginosa* response to meropenem

Ms Dominika Fuhs

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dominika is a PhD candidate at the Monash Institute of Pharmaceutical Sciences. Her PhD research focuses on the development of novel mechanism-based mathematical models that can describe and predict full time-courses of bacterial growth and resistance emergence to combat multidrug-resistant bacteria that can cause life-threatening infections. She's passionate about investigating ways to treat resistant bacterial "superbugs" by optimising dosing regimens of currently available antibiotics in the fight against antimicrobial resistance."

The effects of different resistance mechanisms on *Pseudomonas aeruginosa* response to meropenem

Dominika T. Fuhs¹, Sara Cortés-Lara², Jessica R. Tait¹, Kate E. Rogers¹, Carla López-Causapé², Wee Leng Lee¹, Roger L. Nation¹, Antonio Oliver², Cornelia B. Landersdorfer¹. Monash Institute of Pharmaceutical Sciences, Monash University¹, Parkville, Vic, Australia. Servicio de Microbiología, Hospital Universitario Son Espases-IdISBa², Palma de Mallorca, Spain.

Introduction. Meropenem (MEM) is used against *Pseudomonas aeruginosa* (PA) infections, but resistance mechanisms reduce its effectiveness. Mechanism-based mathematical models (MBMs) address limitations of PK/PD indices, such as the time free antibiotic concentration exceeds the pathogen's min. inhibitory conc. ($fT_{>MIC}$).

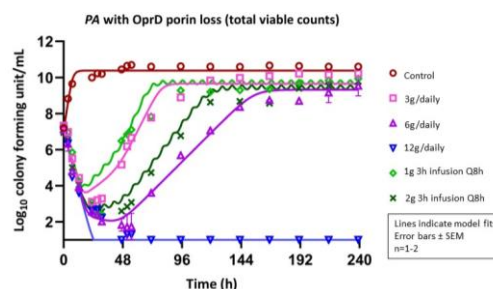
Aims. Characterise the effects of different baseline resistance mechanisms on bacterial killing and resistance emergence; evaluate whether $fT_{>MIC}$ can predict these effects; develop a novel MBM.

Methods. We conducted 10-day hollow-fibre infection model (HFIM)

studies using seven isogenic PA strains with OprD porin channel loss, MexAB-OprM efflux pump over-expression, AmpC β -lactamase over-expression, and the combinations thereof. The HFIM simulated MEM PK for critically-ill patients with normal renal function ($t_{1/2, MEM}=1.5h$). All viable counts on drug-free, 3 \times MIC and 5 \times MIC MEM-containing agar across all strains, five clinically relevant regimens and control (n=90 profiles) were modelled simultaneously.

Results. $fT_{>MIC}$ could not explain the differences in bacterial response between strains. For example, regimens achieving $\geq 98\%$ $fT_{>1\times MIC}$ suppressed regrowth and resistance of one strain, while even 100% $fT_{>5\times MIC}$ failed to achieve this against two other strains, despite all three of these having the same MIC. In contrast, the MBM well characterised all bacterial outcomes of all seven strains with the same model structure and without estimating strain-specific drug effect parameters (observed vs individual-fitted $r^2=0.98$, observed vs population-fitted $r^2=0.96$, Fig. shows one strain).

Discussion. The resistance mechanisms were described by their effects on the estimated MEM concentration in the periplasmic space, which led to different bacterial outcomes, even for strains with the same MIC. The developed MBM is the first model to directly translate all major mechanisms of MEM resistance in PA and their complex interplay.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P426

Antenatal hypoxia or dexamethasone alter hepatic Cytochrome P450 activity in ovine offspring

Ms Millicent Bennett

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Millicent (First Class Honours in Biomedical Research, and top 2% of cohort) is a PhD Candidate investigating how decreased oxygen, and maternal medications during pregnancy including antenatal corticosteroids, impact the programming of drug metabolism for the offsprings' lifetime. She is utilising established preclinical models developed at the University of Cambridge and the University of South Australia to explore hepatic cytochrome P450 activity, which are responsible for the phase I metabolism of approximately 80% of clinical medications. Millicent completed an internship at the Future Industries Institute focussing on material chemistry on a project with industry collaboration. These experiences have added to her diverse background and inspired her interest in cross-disciplinary research. She is currently collaborating with a Neonatologist and Researcher from the Women's and Children's to explore how antenatal steroids affect placental cytochrome P450 activity.

Antenatal Hypoxia or Dexamethasone Alter Hepatic Cytochrome P450 Activity in Ovine Offspring

Millicent GA Bennett¹, Ashley S Meakin¹, Kimberley J Botting², Youguo Niu², Sage G Ford², Michael P Murphy³, Michael D Wiese¹, Dino A Giussani^{2*}, Janna L Morrison^{1*}. Clinical and Health Sciences, University of South Australia¹, Adelaide, SA, Australia; Department of Physiology, Development and Neuroscience, University of Cambridge², Cambridge, United Kingdom; MRC Microbiology Unit, University of Cambridge³, Cambridge, United Kingdom. *equal contribution

Introduction. Chronic hypoxia *in utero* leads to fetal growth restriction (FGR), increased risk of premature birth and respiratory distress syndrome (RDS). Current prophylactic treatment to prevent RDS is antenatal corticosteroid (ACS) treatment; however, ~50% of women given ACS give birth more than 7 days after administration and despite established benefits, recent evidence points to negative outcomes due to this overexposure. Babies born pre-term are at greater risk of non-communicable diseases requiring medication likely to be metabolised by hepatic Cytochrome P450 enzymes (CYP). We have previously reported that CYP3A activity was decreased in the fetus and 21-day old lamb in response to chronic hypoxaemia *in utero*, demonstrating that CYP activity is altered due to FGR in early life.

Aims. To determine if ACS or hypoxemia *in utero* programs altered fetal and young adult offspring hepatic CYP activity.

Methods. Ewes carrying singletons were randomly allocated to normoxic (N) or hypoxic (H) (11% O₂) pregnancy from 105-138dGA (Term=150dGA). Dex (12mg IM) or vehicle (S; saline IV) was administered at 115 and 116 dGA, equivalent to 28 weeks gestation in humans. Ewes carrying male fetuses were humanely killed at 138±2 dGA, while female fetuses lambed spontaneously and were humanely killed at 9 months (9mo; sexual maturity). Hepatic microsomes were isolated and CYP activity was determined using established functional assays.

Results. Chronic hypoxia decreased birthweight ($n_N=20$, $n_H=19$; $P=0.0342$) but increased weight at 9mo ($n_N=20$, $n_H=19$; $P=0.0492$). Hepatic CYP2B6 activity was increased in the fetus exposed to hypoxia ($n_N=22$, $n_H=18$; $P=0.0019$) but decreased in 9mo lambs exposed to Dex ($n_S=18$, $n_{Dex}=21$; $P=0.0174$) and was worsened by exposure to hypoxia ($P_{Intx}=0.0446$). Conversely, Dex decreased CYP3A activity in the fetus ($n_S=15$, $n_{Dex}=25$; $P=0.0142$) and 9mo lamb ($n_S=18$, $n_{Dex}=21$; $P=0.0497$), but hypoxia during pregnancy did not alter activity.

Discussion. Chronic hypoxia and ACS during pregnancy have differential effects on hepatic CYP activity in offspring. ACS may compound developmental programming of disease risk by impairing offspring liver drug metabolism mediated by CYP enzymes.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P427

Effect of oxycodone, polypharmacy, deprescribing on pain, function, cognition and molecular changes.

Dr John Mach

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr John Mach is a Research Fellow and Laboratory Manager who leads the basic science branch of the Laboratory of Ageing and Pharmacology, Kolling Institute, University of Sydney and Royal North Shore Hospital. He studied his undergraduate BSc with Honours in pharmacology at UNSW and earned his PhD at USYD, supervised by Professor Sarah Hilmer, using preclinical models to investigate risk of drug induced liver injury in old age. His work now focuses on utilising preclinical models to understand the risks of multiple concurrent medicines in old age, aiming to inform optimal medication use for older people. He strives to understand the mechanism, and identify risk factors and biomarkers that modulate an older individuals functional wellbeing.

The effect of oxycodone, polypharmacy, and deprescribing on pain, function, cognition and molecular changes.

John Mach¹, Bryony Winters¹, Carina Blaker¹, Yo Otsu¹, Neda Assareh¹, Kevin Winardi¹, Matt McKay¹, Mark Molloy¹, Roderick Peel¹, Charlie W Gregson¹, Sarah Hilmer¹. Kolling Institute, Northern Sydney Local Health District and Faculty of Medicine and Health, University of Sydney, St Leonards, NSW, Australia.

Introduction. Opiates are commonly prescribed to older people to treat chronic non-cancer pain. However, long term use of opiates is associated with tolerance, addiction, loss of efficacy and adverse events. Thus, deprescribing (reducing or cessation) opiates is a clinical priority across many disciplines (geriatric medicine, pain management and rheumatology). However, there is little data on opiate tolerance/withdrawal and deprescription in aged populations.

Aims. To assess the effect of chronic oxycodone (in monotherapy and in polypharmacy; use of 5 or more medications, which is common in old age), and deprescribing oxycodone on pain, physical and cognitive function in middle-aged, osteoarthritic mice.

Methods. At 12 months of age, osteoarthritis was induced in male and female C57BL mice (n=12-15 per group). Upon injury, mice were administered either control, oxycodone monotherapy or in a polypharmacy regimen (oxycodone, citalopram, simvastatin, oxybutynin, and metoprolol). After 6 weeks of treatment, deprescribing oxycodone commenced for oxycodone and polypharmacy groups. Behavioural testing was conducted at baseline, after 6 weeks of treatment and at the end of study at 12 weeks. This study measured pain, mobility, activities of daily living, anxiety and cognition. Proteomic analysis was conducted on the CA1 hippocampus.

Results. Preliminary results demonstrate in male mice only, oxycodone caused cold allodynia, which was reversible by deprescribing oxycodone. Polypharmacy reduced mobility and activities of daily living. For females, polypharmacy increased anxiety. Deprescribing oxycodone did not reverse any of the impairments induced by polypharmacy. No statistical significance was observed with cognition with any treatment. Compared to control, polypharmacy caused hippocampal proteomic changes and deprescribing oxycodone did not reverse all changes and introduced novel ones.

Discussion. In a clinically relevant middle-aged mouse model of osteoarthritis, we demonstrate some opioid effects appear in monotherapy only and can be reversed. In polypharmacy, oxycodone deprescribing did not reverse impairment, was tolerable and caused novel changes in the hippocampus proteome.

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P428

CFTR modulator bidirectional transport through CLEFF4 monolayers, evidence of P-gp substrate affinity

Dr Andrew Crowe

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

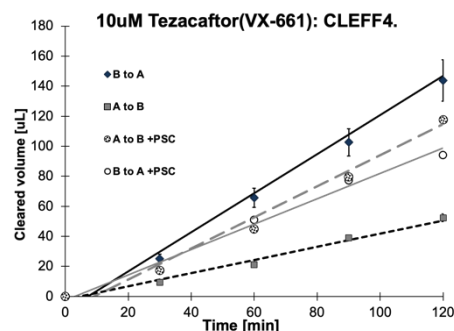
CFTR modulator bidirectional transport through CLEFF4 monolayers, evidence of P-gp substrate affinity

Andrew Crowe^{1,2}. Curtin Medical School, Curtin University¹, Perth, WA, Australia and Curtin Health Innovation Research Institute (CHIRI), Curtin University², Perth, WA, Australia.

Introduction. Cystic Fibrosis (CF) is a clinical manifestation of mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene leading to a Chloride transport protein that does not function adequately. One of the current drug therapies for CF is the CFTR modulator class of drug, that restores functionality to the CFTR protein. **Aims.** As these are a relatively new class of drug, very little is known about their affinity for the efflux system, P-glycoprotein (P-gp). As there are new studies suggesting CFTR drugs can traverse sensitive sites causing problems, such as within the brain, or into a developing foetus or secretion into breast milk, this small study was done to explore P-gp mediated efflux of the 4 main CFTR modifiers currently in use today. **Methods.** The rapid CLEFF4 sub clone of

Caco2 cells used for P-gp efflux and diffusion characteristics of drug movement across human epithelial barriers was used at 6 days of growth to determine apparent permeabilities (P_{app}) from bi-directional transport of 4 CFTR modulators. These being, Ivacaftor, Elexacaftor, Lumacaftor and Tezacaftor. These drugs were used at the lowest concentration possible that could still be measured by optimised UV-HPLC methods using an Agilent 1100 series HPLC, which allowed 10-20 micromolar concentrations to be used. **Results.** Only Tezacaftor was shown to be a P-gp substrate in this study with P_{app} of 12×10^{-6} cm/sec shown in the apical (Ap) to basolateral (Bas) direction and 36×10^{-6} cm/sec in the reverse direction (see Fig). When P-gp was inhibited by PSC-833, transport increased to over 28×10^{-6} cm/sec in apical direction and reduced to 23×10^{-6} cm/sec in the reverse. This reduced the efflux ratio from 3.0 to 0.8.

Discussion. Tezacaftor is affected by P-gp, such that high P-gp levels in tissue barriers will reduce drug concentrations. However, Elexacaftor and Lumacaftor are unaffected and would have likely higher concentrations in the brain, testes and access to a foetus, increasing adverse effects compared to Tezacaftor. Ivacaftor was not measurable through even empty filter inserts suggesting it would be difficult to interpret any direct movement of this drug in vivo or in vitro.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P429

Effect of allyl isothiocyanate in the paediatric ALL cell line REH

Dr Suong Ngo

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr Suong Ngo has been a member of ASCEPT since 1999 and actively contributed to ASCEPT Annual Scientific Meetings, AGMs and Education Forum, Symposium. Suong has been working closely with Fellow ASCEPT educators on developing the core concepts of pharmacology education and is part of the Australian and New Zealand Core Concepts Group (CC-PEG) (White et al., 2021; Santiago, Davis et al., 2021, Guilding et al., 2023) and was one of the attendees at the Inaugural Core Concepts of Pharmacology Education Workshop, held at Monash University Prato Centre, Italy in July 2022 as part of the IUPHAR Education project. Her current research focuses on the anti-cancer stem cell effects of cruciferous vegetables' constituents. Overall, she has published over 50 research papers in high quality specialised scientific journals, including in *BJP* and *JPRP*. Suong is a Committee Member of the ASCEPT Equity, Diversity and Inclusion Committee.

Effect of allyl isothiocyanate in the paediatric ALL cell line REH

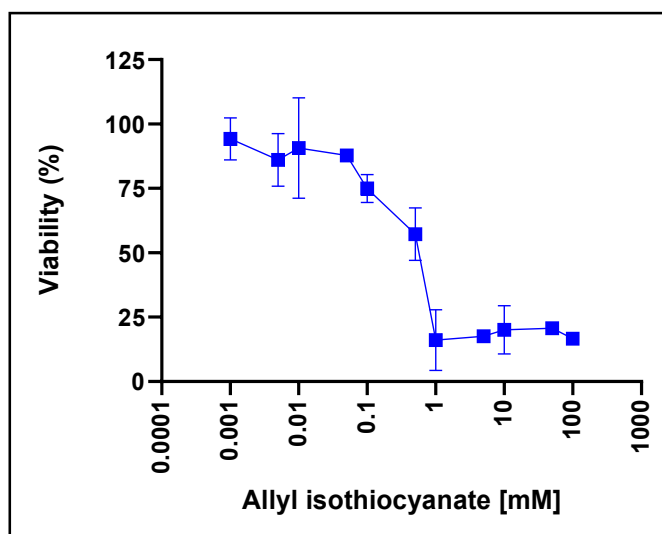
Suong N T Ngo¹, Lauren Thurgood², Robyn Meech². The University of Adelaide¹, Roseworthy Campus, Adelaide, SA, Australia. College of Medicine and Public Health, Flinders University², Adelaide, SA, Australia

Introduction. Acute lymphoblastic leukaemia (ALL) is the most common cancer in Australian children. Most young children with ALL initially respond well to drug therapy, however, 20% of these children later will experience relapse. Following relapse, the median survival time is 7.5 months¹. Whilst the mechanisms of relapse are still unknown, recent evidence suggests the existence of leukaemic stem cells which often remain quiescent and subsequently replenish the blast population. Developing new drugs for paediatric ALL is currently warranted. The current study reported the anti-leukaemic effect of allyl isothiocyanate in paediatric cell REH, with an ongoing aim to further explore its mechanism in ALL stem cells.

Methods. A standard cytotoxic study protocol was used to examine REH cell viability (%) after 72h incubation with allyl isothiocyanate (conc range 0.0001-10000mM).

Results, Discussion. Allyl isothiocyanate was found to induce cell death in a concentration-dependant effect, with an identified IC₅₀ = 0.3mM in the paediatric ALL cell line REH at 72-hours (see attached figure). This is the first study which reported the cytotoxic effect of isothiocyanate compounds from cruciferous vegetables (e.g. brocolini) in paediatric ALL. Further preclinical study on the potential role of isothiocyanates and allyl isothiocyanate in paediatric ALL and their action mechanisms are warranted.

[1] Pham NT, Tran KH, Nguyen TKH (2020). *Cureus*. 12(7): e9238.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P430

LC-MSMS bioanalytical method for PBT2 and doxycycline quantification in mouse plasma microsamples

Mr Viet Tin Pham

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Viet Tin Pham is a Ph.D. student at the School of Biomedical Sciences, University of Queensland. His major research interests include *in vivo* pharmacokinetic/pharmacodynamic (PK/PD) analysis of antimicrobial agents in murine infection models and bioanalysis of murine plasma microsamples. Viet Tin's current research focuses on the preclinical development of an antibiotic adjuvant for treating multidrug-resistant bacterial infections."

LC-MSMS bioanalytical method for PBT2 and doxycycline quantification in mouse plasma microsamples

Viet T. Pham¹, Suzanne Parker², Steven C. Wallis², Helen Won², Mark J. Walker³, Maree T. Smith¹. School of Biomedical Sciences, The Univ of Queensland¹, Brisbane, QLD; Univ of Queensland Centre for Clinical Research, The Univ of Queensland Brisbane², QLD; Institute for Molecular Bioscience, The Univ of Queensland³, Brisbane, QLD.

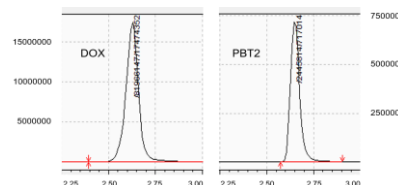
Introduction. PBT2 in combination with doxycycline (DOX) is a potential antimicrobial therapy for treating drug resistant bacterial infections. Bioanalytical methodology to simultaneously quantify PBT2 and DOX concentrations in mouse plasma samples is required to support pharmacokinetic (PK) and *in vivo* PK/pharmacodynamic (PD) studies.

Aims. To develop and optimise an LC-MSMS bioanalytical method for quantification of PBT2 and DOX concentrations in small volumes of mouse plasma, suitable for a murine PK study using a serial sampling approach.

Methods. The plasma sample volume analysed was 5 μ L. Doxycycline- $^{2}\text{H}_3$ was used as the internal standard. The mobile phase was a gradient of 0.1% formic acid in water (A) and 0.1% formic acid in acetonitrile (B) run from 10% to 90% (as %B) across a runtime of 3.5 min. Six different stationary phases were tested for optimal retention of analytes. Quantification was performed using a Shimadzu UHPLC-MSMS 8050 with electrospray ionization, using multiple reaction monitoring (MRM) at 445.0>>428.2 for DOX, 448>>431.2 for DOX- $^{2}\text{H}_3$, and 272.75>>156.00 for PBT2.

Results. Significant peak tailing and fronting were observed for DOX with most columns tested. This issue was resolved using an InfinityLab PoroShell 120 CS-C18 to minimize the silanol effect, delivering satisfactory peak shapes for both DOX and PBT2. The method provided linear calibration lines for the concentration ranges of 2-2000 ng/mL for PBT2 ($r^2 = 0.9943$) and 25-10000 ng/mL for doxycycline ($r^2 = 0.9978$). The accuracy of all calibration standards for PBT2 and DOX was within 15%. From preliminary matrix tests performed, EDTA plasma demonstrated a matrix enhancement effect while heparinised plasma exerted a matrix suppression effect for both DOX and PBT2, but both were offset by equivalent changes to the internal standard.

Discussion. This LC-MSMS bioanalytical method is suitable to quantify PBT2 and doxycycline concentrations in mouse plasma microsamples, thereby enabling PK and PK/PD studies for this drug combination. This methodology will support serial blood sampling in mice and so reduce numbers of mice used to develop well-defined PK profiles.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P431

Synergistic combination therapy of aztreonam and ciprofloxacin against resistant *Pseudomonas aeruginosa* strains

Miss Charlotte Picton

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Charlotte Picton is an honours student studying antibacterial resistance at the Monash Institute of Pharmaceutical Sciences, Monash University, Australia. Her studies focus on investigating how different genetic mutations in bacteria affect antibiotic treatment regimens and utilising combination therapy to overcome treatment challenges. She previously completed a Bachelor of Pharmaceutical Science at Monash University.

Synergistic combination therapy of aztreonam and ciprofloxacin against resistant *Pseudomonas aeruginosa* strains

Charlotte A Picton¹, Jessica R Tait¹, Kate E Rogers¹, Wee Leng Lee¹, Han B Le¹, Carla López-Causapé², Roger L Nation¹, Antonio Oliver², Cornelia B Landersdorfer¹. Drug Delivery, Disposition and Dynamics, Monash University¹, Parkville, VIC, Australia; Instituto de Investigacion Sanitaria Illes Balears², Palma De Mallorca, BALEARIC ISLANDS, Spain.

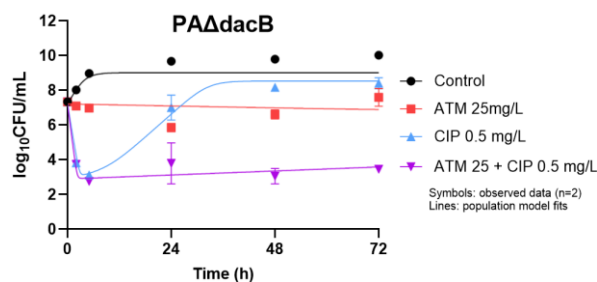
Introduction. Effective use of antibiotics is crucial for successful treatment and suppression of antibiotic resistance.

Aims. To investigate the efficacy of aztreonam (ATM) and ciprofloxacin (CIP) combination therapy on mutant *Pseudomonas aeruginosa* (Pa) strains with defined resistance mutations and clinical isolates.

Methods. The PAO1 wild type reference strain, its five isogenic strains (PA Δ dacB, PA Δ DDh3 and PA Δ DDh2Dh3 with *AmpC* β -lactamase hyperproduction caused by different mutations, and PA Δ mexR and PA Δ mexZ with MexAB-OprM and MexXY-OprM efflux pump overexpression, respectively), and three multidrug-resistant (MDR) clinical paediatric isolates (ICU-11, FQSE15-0803 and FQSE06-1104) were investigated in 72-h static concentration time kill studies. Clinically relevant concentrations of CIP and ATM were studied. Bacterial viable counts were determined, and a mechanism-based mathematical model developed.

Results. For all strains except PA Δ mexR, synergy (≥ 2 -log₁₀ difference from most effective monotherapy) was observed with clinically achievable ATM concentrations (ATM 6.4 mg/L for strains FQSE15-0803 and FQSE06-1104 from paediatric patients with CF, and ATM 25 mg/L for all other strains) plus CIP 0.5 mg/L (Fig. shows one strain). For PA Δ mexR, ATM 25 mg/L plus CIP 1 mg/L resulted in synergy. All monotherapies failed, except for 1 mg/L CIP against PA Δ DDh2Dh3 and 25 mg/L ATM against FQSE06-1104 which both successfully suppressed resistance. The mechanism-based mathematical model described the data well.

Discussion. Combination therapy of CIP and ATM successfully killed bacteria and inhibited regrowth over 72-h in the wildtype strain, isogenic strains, and MDR clinical isolates when most monotherapies failed to do so. Further investigation of this promising synergistic combination is warranted.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P432

Mechanism-based modelling predicts antibiotic effect on *Pseudomonas aeruginosa* where PK/PD indices cannot

Ms Alice Terrill

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Alice is a second-year PhD candidate at Monash University focusing on the optimisation of dosing regimens of antibiotics to overcome the antimicrobial resistance crisis. She has been the Student Representative of both the Population Approach Group of Australia and New Zealand (PAGANZ) and the ASCEPT Drug Disposition and Response Special Interest Group. She is passionate about connecting with people and sharing science.

Mechanism-based modelling predicts antibiotic effect on *Pseudomonas aeruginosa* where PK/PD indices cannot

Alice E Terrill¹, Kate E Rogers¹, Carla López-Causapé², Wee Leng Lee¹, Roger L Nation¹, Jiangning Song³, Antonio Oliver², and Cornelia B Landersdorfer¹. Monash Institute of Pharmaceutical Sciences, Monash University¹, Parkville, VIC, Australia; Instituto de Investigación Sanitaria Illes Balears², Palma De Mallorca, BALEARIC ISLANDS, Spain; Monash Biomedicine Discovery Institute and Department of Biochemistry and Molecular Biology, Monash University³, Clayton, VIC, Australia.

Introduction. PK/PD indices are based on minimum inhibitory concentrations (MICs) and link bacterial response to antibiotic exposure. The index for ciprofloxacin (CIP) (a fluoroquinolone) is the ratio of free drug area under the concentration-time curve to MIC over 24h ($fAUC/MIC$) and for meropenem (MER) (a carbapenem) it is the percentage of time the free concentration remains above the MIC (or a multiple of MIC) over 24h ($\%fT_{>MIC}$).

Aims. To evaluate if the effect of CIP and MER alone and in combination on isogenic strains of *P. aeruginosa* could be predicted by PK/PD indices or depended on resistance mechanisms present.

Methods. Seven isogenic *P. aeruginosa* strains: PAO1 (wild-type reference strain), PA Δ AD (*ampD* knockout/*ampC* overexpression), PAOD1 (*oprD* mutation/loss of porin OprD), PA Δ mexR (*mexR* knockout/*MexAB-OprM* upregulation), PA Δ AD Δ mexR, PAOD1 Δ mexR and PAOD1 Δ AD (combinations of these resistance mechanisms) were used. MICs were determined in triplicate. Strains were exposed to MER (1-64mg/L) and CIP (0.5-4mg/L) alone and in combination, in static concentrations over 72h. Mechanism-based mathematical modelling (MBM) was performed.

Results. MICs were 1-16 mg/L for MER and 0.125-1 mg/L for CIP. PK/PD indices did not predict bacterial response. 1-4x MIC and $fAUC/MIC$ of 48-384 for MER and CIP, respectively, were required to suppress regrowth across strains. PK/PD indices also could not predict combination therapies. An MBM was developed that described the bacterial response to antibiotic based on the resistance mechanisms. The model could predict mono- and combination therapies of MER and CIP. Including controls and biological replicates, 292 treatments were modelled.

Discussion. PK/PD indices alone did not predict the MER or CIP exposure required to suppress bacterial regrowth over 72h, indicating that mechanisms of resistance should be considered when optimising dosing. An MBM, accounting for different resistance mechanisms could predict the impact of double mutations and combination therapies.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P433

Extracellular vesicles are a broadly applicable liquid biopsy to characterize medicines exposure.

Prof Andrew Rowland

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Andrew Rowland is a Professor of Clinical Pharmacology at Flinders University. He leads a highly productive team of researchers at the forefront of advancing extracellular vesicle isolation and analysis for use with human biospecimens. Andrew's team are world leaders in the isolation and characterisation of tissue specific extracellular vesicles from blood and work closely with industry and clinicians to apply this technology to improve patient outcomes by enhancing drug efficacy and minimising harms. Andrew's 143 peer-reviewed manuscripts have been cited more than 6,500 times, reflecting the high impact of his research, Andrew's five-year field-weighted citation index of 7.74. Andrew holds leadership roles across multiple professional societies, including ASCEPT, where he serves on the society's Board of Directors and is actively involved in philanthropic initiatives, through organisations including Flinders Foundation, Starlight and Tour de Cure.

Extracellular vesicles are a broadly applicable liquid biopsy to characterise variability in exposure to medicines.

Andrew Rowland¹, Lauren A Newman¹, Michael J Sorich¹. College of Medicine and Public Health, Flinders University¹, Adelaide, SA, Australia.

Introduction: Differences in the abundance of hepatic drug metabolizing enzymes (DMEs) underpin variability in exposure and response to medicines and impact treatment efficacy and tolerability. Extracellular vesicles (EVs) contain protein cargo inherited from originating cells and may be useful for characterising differences in expression for proteins related to hepatic drug metabolism.

Aim: To quantify the absolute protein abundance for a panel of 14 DMEs in liver derived EVs and paired liver tissue homogenates.

Methods: Tissue homogenate and isolated EVs were prepared from eleven paired human liver tissue samples. Targeted liquid chromatography mass spectrometry was performed to quantify the absolute protein abundance for a panel of 8 cytochromes P450 (CYP), 4 UDP-glucuronosyltransferases (UGT) and 2 carboxylesterases (CES) in isolated EVs and paired homogenate. The association between paired EVs and homogenate was assessed as by linear regression analysis, with the strength of correlation reflected as the Pearson r coefficient.

Results: All DMEs were readily detected and quantified in all EV and homogenate samples. Strong correlations between paired EVs and homogenate were observed for all CYP, ranging from $r = 0.654$ (CYP2E1) to $r = 0.962$ (CYP2B6). Generally weaker correlations were observed for UGT and CES proteins, ranging from $r = 0.229$ (UGT2B7) to 0.722 (CES2). Correlation in protein abundance were impacted by the extent of extra-hepatic target expression. The association between EV and homogenate protein abundance was best described by linear regression in all cases.

Discussion: This study establishes the fundamental potential of liver derived EV protein abundance as a broadly applicable liquid biopsy to account for variability in exposure to medicines. The linear regression equations describing the relationship between the EV and tissue abundance may be used as a first step to calibrate EV protein results for applications such as individualised physiologically based pharmacokinetic models (virtual twins).

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P434

Fetal rat ocular development after in utero exposure to elexacaftor-tezacaftor-ivacaftor

Miss Yimin Zhu

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Fetal rat ocular development after in utero exposure to elexacaftor-tezacaftor-ivacaftor

Yimin Zhu¹, Holly R. Chinnery², Elena Schneider-Futschik¹. Dept of Pharmacology and Biochemistry, Univ of Melbourne¹, Parkville, VIC, Australia; School of Allied Health Optometry, Univ of Western Australia², Perth, WA, Australia.

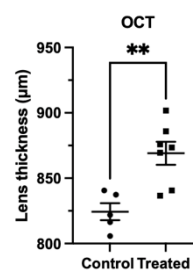
Introduction. Elexacaftor-tezacaftor-ivacaftor (ETI) is a highly effective modulator therapy for cystic fibrosis, however there are limited data to confirm its safety on fetal development when used during pregnancy. Recent reports of bilateral cataracts developing in newborns after exposure to ETI *in utero* highlight the need to analyse its potential risks on fetal ocular development.

Aim. This study aims to investigate whether *in utero* exposure to ETI will impact the development of fetal rat eyes.

Methods. This study assessed embryonic day 19 (E19) Sprague Dawley rats born to dams given ETI (6.7 mg/kg/day elexacaftor + 3.5 mg/kg/day tezacaftor + 25 mg/kg/day ivacaftor) orally during E12-E19 (n=6 dams) and the control group with sham treatment (n=2 dams). Fetal ocular tissue samples were collected and were investigated using histological analysis, ex vivo optical coherence tomography imaging (OCT) and LC-MS.

Results. ETI was confirmed to maternally transfer into the fetal rat ocular tissues and plasma. There were no significant differences in the biometric parameters of anterior chamber depth, vitreous chamber depth, lens capsule thickness, corneal thickness, and axial length measured. Similarly, the hyper-reflective features and cell counts within the anterior chamber of the two experimental groups were comparable. While there was no compelling evidence of significant lens pathology arising such as lens opacity, the presence of lens cavities was observed in both groups within histology and OCT images. In particular, the median individual lens cavities area was significantly higher within the ETI-exposure rats' eyes ($p < 0.0001$) measured on the histology sections. Furthermore, OCT measurements indicate an increase in the lens thickness in comparison to the control group ($p < 0.01$).

Discussion. Our results suggest that *in utero* exposure to ETI during E12-E19 does not significantly alter fetal ocular development. However, considering the lens-related observations in our studies, further investigation to confirm the nature of these phenomena and to ensure the safety of ETI during prenatal exposure is crucial.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P435

Medicine policies and innovation: a comparison of Australia, Malaysia and China

Dr Orin Chisholm

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Orin is the program director for the postgraduate programs in Pharmaceutical and Medical Device Development at the University of Sydney. She has academic appointments with UNSW and Arizona State University, USA, as well as Board appointments with ARCS Australia and the Association of Graduate Regulatory Educators (USA). Orin developed and delivers the Pharmaceutical and Therapeutics Specialisation course within the NSWHealth Commercialisation training program at CICADA Innovations. Orin received The Organisation for Professionals in Regulatory Affairs (TOPRA), UK award for excellence in regulatory education in 2017; became a Senior Fellow of the Higher Education Academy (UK) in 2018 and was elected a Fellow of the Regulatory Affairs Professionals Society (RAPS), USA in 2021. Her research focuses on regulatory science, workforce development and pharmaceutical policy. Orin is also a regulatory consultant and has been the regulatory responsible person for bringing several new medicines to the Australian and New Zealand markets.

Medicine policies and innovation: a comparison of Australia, Malaysia and China

Jane Lyn Yeong¹, Bill Zhou², Brendan Shaw^{1,2} and Orin Chisholm¹. School of Pharmacy, Faculty of Medicine and Health, The University of Sydney¹, Sydney, NSW, Australia. Shawview Consulting², Sydney, NSW, Australia

Introduction. Health is an essential need for everyone and access to medicines is supported within countries through their medicine policies. However, the adoption of medicine policies differs across countries, particularly countries of different economic development. We therefore compared policies from Australia (high income economy) with China and Malaysia (middle income countries) to determine the integration of medicine policies in different economies in our region.

Aims. To identify the role of National Medicine Policies (NMP) in Australia and Malaysia, and Essential Medicines Lists (EML) in Malaysia and China, in facilitating the entry of new therapeutic products into these countries.

Methods. Medicine policies were retrieved from the government website and reviewed. The US Food and Drug Administration (FDA) lists of new molecular entities approved between 2016-2020 were used as the reference of innovative medicines. Regulatory agencies and reimbursement lists of each country were accessed to obtain relevant data on adoption of innovative therapies by each country.

Results. The contents of each countries' main policies were compared. Australia and Malaysia both have a NMP, while China relies on broader health policies and an EML. Malaysia also has an EML. Of the 228 new medicines registered by the US FDA between 2016-2020, Australia had 116 approved and 65 reimbursed; China had 82 approved and 51 reimbursed and Malaysia had 63 approved and 10 reimbursed.

Discussion. Australia's policy supports adoption and access to innovative medicines, while Malaysia and China are still refining their processes with Malaysian policies focusing on providing access to affordable basic essential medicines. China's healthcare system has greatly improved after recent reforms, particularly for reimbursement of new medicines.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P436

Navigating the Challenges of Cell and Gene Therapies- Nonclinical and Manufacturing Considerations

Ms Sharleen Menezes

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Navigating the Challenges of Cell and Gene Therapies– Nonclinical and Manufacturing Considerations

Sharleen Menezes¹, Sweta Kumar², Melisa Anggraeni³, Felicity Grzeski⁴, Reshma Ganapathi³. Drug Development Consulting, Novotech Clinical CRO, Sydney, NSW, Australia¹; Bengaluru, India², Brisbane, QLD, Australia³, Melbourne, VIC, Australia⁴.

Introduction. Given the on-going advancement in cell and gene therapies (CGTs), the considerations for nonclinical and chemical, manufacturing and controls (CMC) evaluation required for their clinical trial entry are naturally evolving. The Asia Pacific region stands out in driving the global effort for their development, incentivising the conduct of clinical trials in Australia. CGT trials are preceded by nonclinical studies and CMC strategies to provide robust efficacy and safety data, and production methods in support of its clinical indication. For the development of these products, a 'one size fits all' concept does not apply. Rather, a case-by-case approach needs to be adopted.

Aim: To highlight the contextual nature involved in developing CGTs and provide insights into some key considerations on the nonclinical and CMC of these therapies in order to advance to specifically designed and tailored clinical trials.

Discussion: A CGT nonclinical program generally contains pharmacology, toxicology and biodistribution studies. Study design should be customised and consider the characteristics of the product including method of delivery, mechanism of action (MOA), target disease and treatment regimen. A major challenge is identifying a relevant animal species or disease model that allows for adequate safety and efficacy evaluation, prompting the use of animal-derived analogous or surrogate comparators. Translational barriers to development include potential tumorigenicity, and specific to gene therapies, off-target effects which require a thoughtful approach to study design and incorporation of study endpoints. Key CMC considerations include raw materials, manufacturing, analytical methods, and chain of custody. Manufacturing CGTs involves complex processes with accelerated timelines, unclear modes of action, and challenges in scaling up and standardisation. Displaying product suitability in formulation and container is critical, while analytical methods must be robust, accounting for sample and reference standard availability. Often, multiple assays are required to elucidate MOA. Adequate characterisation data is needed to support these methods, and finally, critical elements of chain of custody encompass sample tracking, packaging, and shipping, storage and validation of equipment, and documentation.

Conclusion: Challenges remain that limit the widespread translation of CGTs. The diversity of CGTs necessitates a product-specific testing and production strategy to ensure successful entry into clinical trials.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P437

Machine Learning tool for Pharmacokinetic and Pharmacodynamic model prediction using RsNLME-Pydarwin.

Dr Chandramouli Radhakrishnan

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Machine Learning tool for Pharmacokinetic and Pharmacodynamic model prediction using RsNLME-Pydarwin.

Chandramouli Radhakrishnan¹, Mark Sale¹, Keith Neiforth¹, Bernd Wendt¹, James Craig¹, Michael Tomashevskiy¹ Certara¹, NJ, USA.

Introduction. The advent of Machine Learning (ML) tools in clinical data analysis has revolutionised the field. Among these tools, pyDarwin (Li, X. et al. 2024) stands out for its unique ability to explore the model space and uncover robust and parsimonious models, particularly in scenarios where traditional modelling falls short. PyDarwin, an R package combined with Certara's NLME engine (RsNLME), is a prime example of this innovative approach.

Aim. Evaluation of a population pharmacokinetic analysis using pyDarwin, a tool for ML-based approaches.

Methods. This study employed pyDarwin, an open-source Python package (Command line), to select an ML-based model for RsNLME. This practical tool offers a range of algorithms, including GA, GP, RF, gradient-boosted random tree, particle swarm optimisation, and exhaustive search. We used pyDarwin to identify the number of compartments and absorption models and test covariate relationships and covariances between parameters, which are crucial in population pharmacokinetic analysis.

Results. Pharmacokinetic analysis was conducted using pyDarwin—RsNLME using simulated datasets. The search identified a more robust and parsimonious model than the traditional approach.

Discussion. RDarwin simplifies creating and executing machine learning-based model searches using pyDarwin. For more details, visit PyDarwin: <https://certara.github.io/pyDarwin/html/index.html>.

Li, X., et al. (2024). "pyDarwin: A Machine Learning Enhanced Automated Nonlinear Mixed-Effect Model Selection Toolbox." *Clinical Pharmacology & Therapeutics* 115(4): 758-773.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P438

Novel 96-Well Plate-Compatible Device for Studying GPCRs in a Fluid Flow System.

Miss Renate Roeterink

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Renate Roeterink is a Ph.D. candidate in Biomedical Engineering at the University of Melbourne, enrolled in a joint program with KU Leuven. With a background in biology and biofabrication, she is interested in combining applied molecular biology with microfluidic systems to explore mechanosensitive ion channels and G-Protein Coupled Receptors (GPCRs).

A Novel 96-Well Plate-Compatible Device for Studying GPCRs in a Fluid Flow System.

Renate M.A. Roeterink^{a,b}, Alaa Abdul-Ridha^b, David J Collins^{a,d}, Daniel J Scott^{b,c}. Department of Biomedical Engineering, University of Melbourne^a, Melbourne, VIC, Australia. The Florey Institute, University of Melbourne^b, Melbourne, VIC, Australia. Department of Biochemistry and Pharmacology, University of Melbourne^c, Melbourne, VIC, Australia. The Graeme Clark Institute, The University of Melbourne^d, Melbourne, VIC, Australia.

Introduction. G-protein coupled receptors (GPCRs) are crucial membrane proteins involved in numerous physiological processes and are key drug targets. However, many GPCRs remain untargeted due to challenges in developing selective drugs. Conventional static cell culture systems fail to replicate the dynamic chemical and mechanical conditions found in vivo. This limitation often results in a poor understanding of ligand-GPCR binding, leading to sub-optimal drug candidates and hindering drug discovery.

Aims. This study aims to investigate the effects of mechanical stimuli and varying fluid flows on GPR68, a proton-sensing and mechanosensitive orphan GPCR.

Methods. We created a novel 96-well plate-compatible device that enables dynamic fluid flow over cultured cells, replicating mechanical stimuli and chemical gradients. The 3D-printed device directs fluid flow radially over cells in a 96-well plate, creating a micro-physiological environment.

Results. Our studies demonstrated that shear stresses significantly affect GPR68's ability to sense protons, indicating that mechanical forces can modulate receptor sensitivity and function.

Discussion. The application of this novel 96-well plate-compatible device represents a significant advancement in the study of GPCR signaling and drug discovery. This adaptable system offers a broader application for studying drug-target interactions under conditions that closely resemble physiological environments, ultimately facilitating more accurate and efficient drug discovery efforts.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P439

Impact of medicines demand forecast accuracy on medicines shortages in Sri Lanka

Miss Nimmi Dilsha

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

I am a PhD candidate at QUT, as well as a registered pharmacist and higher education academic in Sri Lanka. My research interests are centered on pharmacy practice-based research.

Impact of medicines demand forecast accuracy on medicines shortages in Sri Lanka

Rajapaksha AN Dilsha¹, Esther Lau^{1,2}, Marea Patounas¹, Anne T Matthias³, Rohini Fernandopulle⁴, Lisa Nissen². Queensland University of Technology, Brisbane, Australia¹ University of Queensland, Brisbane Australia²; University of Sri Jayewardenepura, Colombo, Sri Lanka³ General Sir John Kotelawala Defence University, Colombo, Sri Lanka⁴

Introduction. Medicines shortages are a multifactorial global issue, and are inadequately addressed in developing countries (Shukar et al., 2021). In Sri Lanka (SL), the number of medicines required for the upcoming year (medicines demand forecasting) is performed manually in State sector hospitals. Inaccurate medicines demand forecasting is a claimed factor that contributes to medicines shortages (Wijegunasekara, 2021), but has not been studied in SL.

Aims. This study evaluated the impact of medicines demand forecasting accuracy on medicines shortages in SL state hospitals.

Methods. Secondary data of 17 cardiovascular medicines, from 13 state hospitals (2016-2022) recorded in the computerised inventory control system of medicines distribution (called Medical Supplies Division's Management Information System) was analysed.

Results. Over the 7 years, an average of 41.2% of the medicines were out-of-stock and 81.2% of medicines were overestimated each year. Overall, the out-of-stock period in medicines per annum appeared to increase while the annual forecast accuracy of medicines declined from 2016 to 2022, as with the graphical presentation in trend analysis. However, 93.8% of medicines showed a statistically insignificant association ($p>0.05$) between the stock-out-period and forecasted accuracy in linear regression.

Discussion. The forecast inaccuracy in overestimation creates unrealistic financial demand for medicines purchases, which is challenging to meet given SL's economic background. This results in the disruption of steady supply in the centralised medical supply system in the State sector, causing stockouts. Thus, forecast inaccuracy could indirectly impact medicines shortages with the absence of direct statistical associations, and it requires further evaluation. Therefore, technology to improve demand forecasting is warranted in SL medicines shortage management.

Shukar S et al. (2021) Front Pharmacol 12:693426

Wijegunasekara JHR (2021) JDDT 11(1):3-7

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P440

CASK mediates oxidative stress-induced microglial cell death via p38 and Ca²⁺ influx

Mr Keith Jun Hao Cheong

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Keith is a full-time research assistant at the Graduate Institute of Pharmacology, National Taiwan University, holding a Master degree in Pharmacology from National Taiwan University and a Bachelor's degree in Medical Biotechnology from Sunway University. Highly enthusiastic and driven by a passion for scientific discovery, Keith has developed a strong foundation in both theoretical knowledge and practical lab skills, particularly in the fields of pharmacology, biotechnology, and molecular biology. During Keith's research in graduate programme, he focused on dissecting the novel functional role of CASK in H₂O₂-induced cell death and inflammation in microglial through using different molecular biology technique. Besides, during his undergraduate studies, he participated in a final year project on the development of a vaccine for SARS-CoV-2, further demonstrate their ability to apply scientific principles to pressing global health challenges.

CASK mediates oxidative stress-induced microglial cell death via p38 and Ca²⁺ influx

Keith Jun Hao Cheong^{1,2}, Wan-Chen Huang³, Wan-Wan Lin^{1,2} *. ¹Department of Pharmacology, College of Medicine, National Taiwan University, 100233 Taipei, Taiwan. ²Graduate Institute of Medical Sciences, Taipei Medical University, 110301 Taipei, Taiwan. ³Institute of Cellular and Organismic Biology, Academia Sinica, 115 Taipei, Taiwan

Introduction:

CASK (Calcium/Calmodulin-Dependent Serine Protein Kinase) is a multidomain scaffold protein that plays an indispensable role in controlling neural activity. Despite the beneficial roles of microglia in maintaining brain homeostasis and serving as immune sentinels, microglia-mediated neuroinflammation and microglial cell death resulting from stimulation by toxic molecules can foster the progression of neuronal death and neurodegeneration.

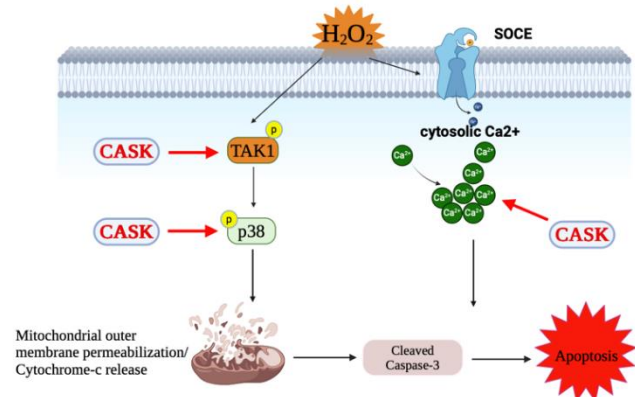
Aims:

Human RNAseq revealed that CASK is ubiquitously expressed in microglia. However, the functional role of CASK in microglia remains unclear.

Materials and Methods:

Murine BV2 microglial crCTL and crCASK cell lines were generated using the CRISPR-Cas9 approach. H₂O₂ (100 μM) was used to study cell death. PI and Annexin V/PI staining were employed to determine the cell cycle and cell death, respectively. mRNA and protein expressions were measured by real-time PCR and immunoblotting, respectively. Cellular Ca²⁺ influx, ROS production, and mitochondrial membrane potential (MMP) assays were conducted using flow cytometry and/or immunofluorescence.

Results:



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



We found that crCASK inhibits H₂O₂-induced BV2 microglial cell death, while pan-caspase inhibitor zVAD fully blocks H₂O₂-induced cell death, suggesting apoptosis as the mode of death. Consistent with the protective effect of crCASK, we observed that crCASK significantly inhibits MMP loss, mitochondrial ROS production, and caspase-3 activation under H₂O₂ challenge. Additionally, we observed that crCASK inhibits H₂O₂-induced p38 phosphorylation but enhances H₂O₂-induced AKT and AMPK phosphorylation. Interestingly, we found that only the p38 inhibitor SB203580 protects cells against H₂O₂-induced mitochondrial dysfunction, apoptotic cell death and caspase-3 activation in crCTL but not in crCASK. This implies that CASK promotes oxidative stress-induced cell death via the enhancement of p38 phosphorylation. Previous studies showed that H₂O₂ can induce Ca²⁺-dependent apoptosis in different cell types. Here we found that the TRPM2 inhibitor 2-APB significantly reversed H₂O₂-evoked cell death. Immunofluorescence data using Fluo-8 also revealed that the crCASK significantly inhibited cytosolic Ca²⁺ influx after the depletion of ER Ca²⁺ store through the blockage of SERCA using thapsigargin. Moreover, flow cytometry results revealed that increased cytosolic Ca²⁺ was inhibited by crCASK but not by SB203580.

Discussion:

CASK mediates BV2 microglial apoptosis upon H₂O₂ treatment via increasing the activation of p38, thereby leading to mitochondrial dysfunction and apoptotic cell death. Additionally, CASK promotes Ca²⁺-dependent cell death by enhancing the activation of the calcium channel TRPM2 and store-operated calcium entry (SOCE). These findings strongly suggest that targeting CASK could be a potential therapeutic strategy for CNS disorders.

P441

Investigating benzodiazepine and vinpocetine sensitivity of GABAA variants in patients with epilepsy

Ms Taegan Charles

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Taegan Charles is currently completing a Bachelor of Science (Honours) in Pharmacology, having previously earned a Bachelor of Science in Medical Science (Neuroscience) at the University of Sydney. As a 2024 ARCS Student Scholarship recipient, Taegan has a strong background and interest in neuroscience and neuropharmacology. Her experience in science communication and media allows her to excel at translating complex scientific concepts for lay audiences, with her current Honours work centring on the benzodiazepine and vinpocetine sensitivity of GABAA receptor variants found in patients with epilepsy. This research addresses the current deficit for treatment strategies of pharmacoresistant epilepsy and examines the potential of vinpocetine as an adjunct treatment. Taegan has gained international research exposure through the Dalyell Scholars Travel Scholarship, which allowed her to study at the University of Florida. This experience expanded her scientific network and provided valuable insights into global research practices. She has also presented her work at the SIG Drug Symposium (2024) showcasing her findings thus far and demonstrating her commitment to advancing the discourse surrounding the pharmacoresistance of GABAAR variants in epilepsy.

Investigating benzodiazepine and vinpocetine sensitivity of GABA_A variants in patients with epilepsy

Taegan Charles¹, Han Chow Chua¹ Mary Chebib¹, Philip K. Ahring¹, Vivian W. Y. Liao¹. Brain and Mind Centre, The University of Sydney¹, Sydney, NSW, Australia

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Introduction: GABA_A receptors (GABA_ARs), the primary inhibitory ion-channels of the mammalian brain, play a crucial role in maintaining normal brain function. Genetic missense variants of this receptor are known to cause epilepsy. Since drugs that enhance GABA transmission are commonly used as anti-seizure medications, it is important to assess the sensitivity of benzodiazepines, such as diazepam, in patients with mutations in the primary and secondary benzodiazepine binding sites (α +/ γ 2- in the extracellular domain and β +/ α - transmembrane domain respectively). This holds significance in the field of precision medicine as it may prevent clinicians from administering benzodiazepines to non-responders. Recently, vinpocetine has emerged as a GABA_AR enhancer and has shown superior effect in treating patients with pharmacoresistant GABA_AR-associated epilepsy. However, the pharmacological profile of vinpocetine and its binding site on the GABA_AR remain elusive.

Aims: This project therefore has two aims: **1.** To investigate whether GABA_AR benzodiazepine-binding site variants (*GABRA1*: Y187N, A188D, M263I, I255F, *GABRB3*: L310I, *GABRG2*: T94S, R183Q) have reduced sensitivity to diazepam. **2.** To determine whether vinpocetine can effectively modulate the variant receptors that have reduced diazepam sensitivity.

Methods: Site-directed mutagenesis followed by receptor concatenation was performed to introduce, insert, and assemble the mutation and subunits respectively. This was followed by RNA transcription and two electrode voltage clamp physiology on *Xenopus laevis* oocytes subjected to varying concentrations of GABA, diazepam and vinpocetine.

Results: We demonstrated that some variants have reduced sensitivity to diazepam, while vinpocetine effectively modulates these receptors, indicating an alternative primary binding site to benzodiazepine. Furthermore, variants in the secondary benzodiazepine binding site showed reduced vinpocetine sensitivity, suggesting that vinpocetine may exert its primary effect via the transmembrane GABA_AR binding site.

Discussion: These results have direct clinical translation, specifically on precision medicine, where clinicians will be able to mitigate trial and error approach of prescribing anti-seizure medication. In addition, patients who have variants in the primary benzodiazepine binding site will have the option of being treated with vinpocetine.

P442

Cholinergic muscarinic type 4 receptor is the dominant driver of Xanomeline's efficacy

Dr Christopher (KH) Choy

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Christopher Choy is a postdoctoral researcher in the Drug Discovery Biology lab at Monash University's Institute of Pharmaceutical Sciences. He earned his PhD in Pharmacology from the University of Melbourne and specialises in neuropharmacology and preclinical drug discovery. His recent work focuses on muscarinic acetylcholine receptor modulation for schizophrenia treatment and the development of animal models for schizophrenia. He is one of the recipients of a recent NHMRC Ideas Grant and has co-authored over 20 publications, garnering more than 800 citations (H-index: 16). Additionally, he is a dedicated mentor to early-career researchers and research students.

Cholinergic muscarinic type 4 receptor is the dominant driver of Xanomeline's efficacy

KH Christopher Choy, Jasmin Li, Arthur Christopoulos & Celine Valant. Analytical & Structural Neuropharmacology Lab, Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Parkville, VIC

Introduction. Antipsychotics, whilst effective in suppressing positive symptoms, remain completely ineffective for treating negative symptoms and cognitive deficits as seen in patients suffering from schizophrenia. Hence there is an unmet need

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



for new therapeutics with broader spectrum of action. Xanomeline, a cholinergic muscarinic type 1 (M1) and type 4 (M4) receptors preferring agonist, has recently emerged as a new non-dopaminergic antipsychotic that successfully passed Phase III clinical trial. We hypothesised that Xanomeline produces its effect mainly via acting on M4 receptor due to recent preclinical studies showing that compounds targeting this receptor subtype (e.g., M4 positive allosteric modulators) already demonstrated therapeutic potential.

Aims. We validate this hypothesis using M4 receptor knockout (KO) mice in behavioural tests.

Methods. We conducted open-field locomotor activity (LMA) and prepulse inhibition (PPI) of acoustic startle tests in wild type and M4 KO mice ($n = 7 - 15/\text{gender/genotype}$), with a NMDA non-competitive blocker, MK-801, as the psychotomimetic, which induced locomotor hyperactivity, and disruption of PPI.

Results. In LMA test, Xanomeline (1 or 10mg/kg) significantly reversed hyperactivity in the wildtype mice. In contrast, in M4 KO mice, only the highest dose of Xanomeline (10mg/kg) could reverse the MK-801 effect. In PPI test, Xanomeline dose-dependently rescued the disruption of PPI in wildtype animals, but its effect was completely abolished in the KO mice, even at the highest dose.

Discussion. We demonstrated the action of Xanomeline involves different balance of M1/M4 receptors engagement. For instance, in LMA Xanomeline requires predominantly M4 with some M1 activity, but in PPI, only M4 activity is necessary. Next, we will investigate the role of M4 receptors in learning and memory tests to elucidate Xanomeline's therapeutic potential on cognitive deficits in the treatment of schizophrenia.

P443

Unravelling the mechanisms for internalisation and subcellular trafficking of the M4 receptor

Miss Yingshan Dong

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Yingshan Dong is an Honours student in the Drug Discovery Biology Theme at the Monash Institute of Pharmaceutical Science. She completed her Bachelor of Pharmaceutical Science at Monash University, where she developed a keen interest in pharmacology. Following her undergraduate studies, Yingshan pursued Honours in Analytical and Structural Neuropharmacology under the supervision of Celine Valant and Vi Pham. Her Honours project aims to unravel the mechanisms underlying the internalisation and subcellular trafficking of the M4 receptor. Her research interest focuses on G protein-coupled receptors, particularly on muscarinic receptor signalling and trafficking. In the future, Yingshan aspires to pursue a PhD in a related field.

Unravelling the mechanisms for internalisation and subcellular trafficking of the M₄ receptor

Yingshan Dong¹, Vi Pham¹, Asuka Inoue², Arthur Christopoulos¹, Celine Valant¹. Drug Discovery Biology, Monash Institute of Pharmaceutical Science¹, Parkville, VIC, Australia; Graduate School of Pharmaceutical Sciences, Tohoku University², Sendai, Miyagi 980-8578, Japan.

Introduction. The M₄ muscarinic acetylcholine receptor (M₄ mAChR) has become an emerging therapeutic target for the treatment of various neurological disorders, including schizophrenia and Alzheimer's disease. However, underlying

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



mechanisms of M₄ mAChR internalisation and trafficking, and how they affect drug responses, remain unclear. Mechanistic understanding of agonist-mediated M₄ mAChR regulation is essential for development of new therapeutics.

Aims. This study aims to characterise the ligand-induced trafficking profile of the M₄ mAChR, and address the role of G proteins, G protein-coupled receptor kinases (GRKs) and β -arrestins in M₄ mAChR internalisation.

Methods. Parental HEK293A cells and different CRISPR/Cas9-edited cell lines with selected deletions of the endogenous β -arrestins, G-proteins, or GRKs were transiently co-transfected with the Rluc8-tagged human M₄ mAChR and different GFP-tagged biosensors located in distinct cellular compartments (CAAX, FYVE, Rab4 and Rab11). The bioluminescence resonance energy transfer (BRET) assay was utilized to quantify internalization and subcellular trafficking of the M₄ receptor following stimulation with different agonists (ACh, iperoxo, and two clinical candidates, xanomeline and emraclidine).

Results. All ligands promoted a concentration-dependent and rapid internalisation of the M₄ receptor into early endosomes with different efficacies before it traffics through recycling pathways. Knockout of G-proteins or non-visual GRK2/3/4/5/6 significantly affected the internalisation of the M₄ mAChR by reducing the E_{max} and potencies of the ligands. Moreover, β -arrestins, G-proteins and GRKs are found to be critical in trafficking of the M₄ receptor from the cell membrane to the early endosome.

Discussion. The data suggest that internalisation and subcellular trafficking of the M₄ mAChR is regulated by G-proteins, GRKs and β -arrestins. This finding provides novel insights into the ligand-mediated M₄ mAChR internalisation and trafficking which could be potentially targeted for the design of optimally efficacious drugs to treat neurological diseases.

P444

Neural projection from intralimbic cortex to nucleus accumbens regulates methamphetamine reinstatement

Prof Po-Wu Gean

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Gean obtained his PhD in the Department of Pharmacology and Toxicology, University of Texas at Galveston in 1986 by establishing the amygdala slice preparation to investigate epileptic mechanisms. He is the Chair professor of Pharmacology at National Cheng Kung University, Taiwan and Former-President of the Pharmacological Society in Taiwan. Currently, Dr Gean is primarily engaged in researches of neuropsychiatric disorders, drug addiction and learning and memory.

Neural projection from intralimbic cortex to nucleus accumbens regulates methamphetamine reinstatement

Po-Wu Gean, Hsueh-Heng Liu, Yu-Qi Shen. Department of Pharmacology, National Cheng Kung University, Tainan City, Taiwan.

Introduction. Methamphetamine (MeAM) is one of the most abused drugs in Taiwan that cause serious substance use disorders. Psychologists use extinction-like exposure therapy to help people overcome drug seeking behavior. However, there is still a high rate of reinstatement after abstinence.

Aims. In the present study, we used conditioned place preference (CPP) as a rewarding model to investigate the neural circuits responsible for extinction and reinstatement of MeAM-associated memory.

Methods. The mice were administered with MeAM for 5 days to induce CPP. Then, they were given saline in the MeAM-paired chamber for 6 days (extinction training). On following day, they were injected a low dose of MeAM for priming-induced reinstatement. Chemogenetic manipulations were used to selective activation or inhibition of neural circuits.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Results. Repetitive chemogenetic inhibition of the basolateral amygdala (BLA)-nucleus accumbens core (NAc core) pathway resulted in extinction-like reduction of the MeAM-related memory that can be reinstated by MeAM priming. Conversely, activation of this circuit after extinction training failed to recall the original MeAM memory. Anisomycin (Ani) was infused into NAc core after extinction training and re-test next day revealed that extinction of MeAM memory was blocked in Ani-treated group. hM4Di-mediated inhibition of intralimbic cortex (IL)-NAc core suppressed reinstatement whereas inhibition of prelimbic cortex (PL)-NAc core had no effects on reinstatement.

Discussion. These results suggest the engram of MeAM CPP memory may reside in the NAc core and inhibition of IL-NAc core pathway suppresses reinstatement of MeAM CPP memory.

P445

Understanding the interplay of STING and TOLLIP in driving secondary injury post-TBI.

Miss Amelia Fryer

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Amelia is in the final year of her PhD with the Neuropharmacology research group in the Department of Biochemistry and Pharmacology at the University of Melbourne. Her research focuses on CNS innate immunity and understanding the cGAS-STING pathway and its role in driving neuroinflammation and neurodegeneration in traumatic brain injury (TBI). She has first-authored two publications during her candidature, the most recent of which was published in May in the British Journal of Pharmacology titled 'Pharmacological inhibition of STING reduces neuroinflammation-mediated damage post-traumatic brain injury.'

Understanding the interplay of STING and TOLLIP in driving secondary injury post-TBI.

Amelia L Fryer¹, Amar Abdullah², Juliet M Taylor¹ and Peter J Crack¹ Dept of Biochem and Pharmacol, Univ of Melbourne¹, Parkville, VIC, Australia; Dept of Biol Sci, Sunway University², Selangor, Malaysia

Introduction. Traumatic brain injury (TBI) is a major cause of death and disability worldwide with limited pharmacological interventions available to slow the inflammation and neurodegeneration that ensues post-injury. Our lab has demonstrated the cGAS-STING pathway as a key driver of neuroinflammation-mediated neurodegeneration in TBI and other neuropathologies. Known to be a regulator of type-I interferon production, there is increasing evidence for additional roles for STING in mediating cell death and ER-stress. Toll interacting protein (TOLLIP), is an endogenous negative regulator of TLR signaling with roles in misfolded protein trafficking. Recently, TOLLIP has been identified to regulate STING activity, by stabilising STING at its resting state on the ER.

Aims. This study aims to evaluate the role of TOLLIP in regulating STING and ER-stress activity in the CNS post-TBI.

Methods. 10–12-week-old male C57Bl/6 mice anaesthetized with an ip injection of ketamine (100mg/kg)/xylazine (10mg/kg) and were exposed to brain injury using the controlled-cortical impact model (CCI). 30-minutes post-injury, mice were administered a single iv 750nmol dose of the STING inhibitor, C-176 or saline (vehicle). Analysis was conducted 2 and 24-hours post-TBI (n=7-9 mice for each treatment group).

Results. Western blot analysis revealed a significant reduction in the expression of TOLLIP and total STING in the cortex 24h-post TBI and not 2h-post TBI in both C-176 (0.65 ± 0.08 , n=9 p<0.0001) and vehicle-treated mice (0.65 ± 0.10 , n=9

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



$p < 0.0001$) when compared to sham (1.55 ± 0.15). C-176-treated mice alone exhibited significantly increased phosphorylation of the unfolded protein response (UPR) regulator IRE1- α (6.14 ± 1.24 , $p < 0.001$ $n=9$) compared to both sham (1.00 ± 0.12) and vehicle-treated TBI mice (1.37 ± 0.28). Striatal mRNA expression levels of its downstream mediator *Xbp1* were also elevated at 24h-post TBI when compared to sham mice (C-176= 1.24 ± 0.11 ; sham= 1.03 ± 0.08 , $p < 0.05$ $n=9$).

Discussion. Together these findings suggest TOLLIP and its stabilising activity on resting-state STING is lost-post TBI with the pharmacological inhibition of STING increasing activation of the IRE1-XBP1 branch of the unfolded protein response. This study provides novel mechanistic insight into the regulation and activity of STING post-TBI in mice.

P446

Mechanism underlying lactate release from astrocytes in brain ischemic tolerance

Dr Yuri Hirayama

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Mechanism underlying lactate release from astrocytes in brain ischemic tolerance

Yuri Hirayama¹, Schuichi Koizumi^{2,3}, Naohiko Anzai¹. Dept. Pharmacol., Grad. Sch. Med., Chiba Univ.¹, Chiba, Japan; Dept. Neuropharmacol., Interdisciplinary Grad. Sch. Med., Univ. Yamanashi², Yamanashi, Japan; GLIA center, Univ. Yamanashi³, Yamanashi, Japan.

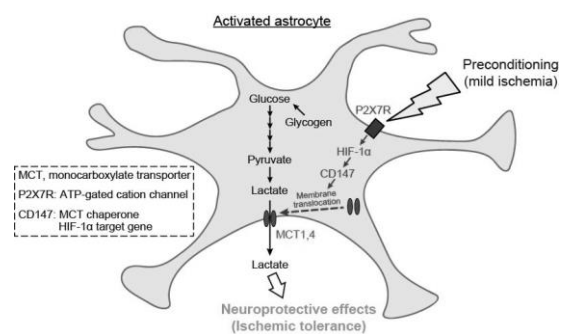
Introduction. Brain ischemic tolerance refers to an endogenous neuroprotective phenomenon whereby a non-lethal ischemic episode, termed preconditioning (PC), induces resistance to a subsequent severe ischemic injury. We have previously reported that PC activates astrocytes and subsequently upregulates P2X7 receptors (P2X7Rs), thereby leading to ischemic tolerance. However, the downstream signals of P2X7Rs that are responsible for PC-induced ischemic tolerance remain unknown.

Aims. To clarify a molecular mechanism underlying astrocytic P2X7R-mediated ischemic tolerance.

Methods. In *in vivo* experiments, unilateral transient focal ischemia was induced in mice by right middle cerebral artery occlusion (MCAO). Using an MCAO mouse model combined with a microdialysis technique, we measured extracellular lactate levels by inserting a probe into the ipsilateral striatum. In *in vitro* experiments, we used primary cultures of astrocytes.

Results. Extracellular lactate levels during severe ischemia were significantly increased in mice who experienced PC; this increase was dependent on P2X7Rs. In addition, the intracerebroventricular injection of lactate protected against cerebral ischemic injury. In *in vitro* experiments, although stimulation of astrocytes with the P2X7R agonist BzATP had no effect on the protein levels of monocarboxylate transporter (MCT) 1 and MCT4 (which are responsible for lactate release from astrocytes), BzATP induced the plasma membrane translocation of these MCTs via their chaperone CD147. Importantly, CD147 was increased in activated astrocytes after PC, and CD147-blocking antibody abolished the PC-induced facilitation of astrocytic lactate release and ischemic tolerance.

Discussion. Our findings suggest that astrocytes induce ischemic tolerance via P2X7R-mediated lactate release.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P447

Dissecting the role of differential phosphorylation in mGlu5 signalling and regulation

Dr Shane Hellyer

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr Hellyer is a senior postdoctoral fellow in the Endocrine and Neuropharmacology Laboratory at the Monash Institute of Pharmaceutical Sciences (MIPS) in Melbourne, Australia. He is an emerging independent researcher with an interest in G protein-coupled receptors (GPCRs), and how they contribute to the pathology of neurological disorders. Dr Hellyer has established a track record in analytical GPCR pharmacology, including biased agonism and modulation of Class C GPCRs in recombinant cells and primary brain cell cultures

Dissecting the role of differential phosphorylation in mGlu5 signalling and regulation

Shane D Hellyer¹, M.A. McInness¹, C.L. Lo¹, Z.F. Tan¹, K Yao¹, S Je¹, S Dalsgaard Seiersen², L Dwomoh³, B Hudson³, S Bradley³, K.J. Gregory^{1,4}. Monash Inst. Pharm. Sci¹, Parkville, VIC; Novo Nordisk², Copenhagen, Denmark; Uni. Glasgow³, Scotland; ARC Centre for Cryo-Electron Microscopy of Membrane Proteins⁵, Monash Uni, Parkville, VIC, Australia

Introduction. Metabotropic glutamate receptor 5 (mGlu₅) plays a key role in important neurobiological processes and is implicated in multiple CNS disorders (Gregory et al, 2020). Through pleiotropic signalling, mGlu₅ interacts with multiple kinases, such as Ca²⁺/calmodulin kinase 2 (CaMKII) and protein kinase C (PKC) which also regulate mGlu₅ activity. However, little is known about how kinase interactions with mGlu₅ affect signalling and regulatory processes in response to chemically divergent mGlu₅ activators.

Aims. To assess the effects of mutating kinase interaction domains within mGlu₅ on acute mGlu₅ signalling and receptor desensitisation in response to structurally and functionally diverse mGlu₅ agonists

Methods. 15 novel and known mGlu₅ phosphorylation sites were mutated to alanine individually or in combination; mutant and wild type rat mGlu₅ were stably transfected in HEK293A cells. Receptor expression was determined by radioligand binding. Two orthosteric (glutamate, DHPG) and two allosteric (VU0424465, VU0409551) agonists were tested using Ca²⁺ mobilisation assays. Pharmacological parameters were derived using operational and kinetic models of agonism.

Results. mGlu₅ phosphorylation site mutations differentially affected ligand potency, E_{max} and time to peak in a mutation and ligand dependent manner. VU0409551 potency was not significantly affected by any mutation, with the exception of a known CaMKII phosphorylation site. Allosteric, but not orthosteric, agonists displayed concentration-dependence in time to peak, with known PKC phosphorylation sites significantly delaying time to peak.

Discussion. Here we reveal kinases differentially pattern canonical mGlu₅ signalling, with notable difference between orthosteric and allosteric agonists. Our data highlight the importance of rigorous characterisation of mGlu₅ pharmacology, especially with regards to unappreciated aspects such as receptor-kinase interactions.

Gregory KJ., Goudet C (2020) Pharmacol Rev 73:521-69

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P448

Neuroprotective effect of astaxanthin nanoemulsion in middle cerebral artery occlusion stroke model.

Prof Igor Iezhitsa

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Igor Iezhitsa has over 25 years of experience in pharmacology, with a career dedicated to both academia and research. He earned his PhD in Pharmacology from Volgograd State Medical University (Russia) in 1998, followed by a Doctor of Biological Science (Dr. Sci. Biol.) degree from the same institution in 2008. From 1994 to 2000, Dr. Igor was instrumental in preclinical studies of a novel class of CNS stimulants at Volgograd State Medical University. Since then, he has conducted extensive screening and preclinical evaluation of new pharmacological compounds. In 2009, Dr. Igor joined the Faculty of Medicine at Universiti Teknologi MARA (UiTM), Malaysia, as an Associate Professor of Pharmacology. He was a key figure in establishing the Centre for Neuroscience (NeuRon) at UiTM in 2013, leading the center from 2015 to 2020. He currently serves as Professor of Pharmacology at the School of Medicine, International Medical University. Dr. Igor's research interests include neuropharmacology, neuroprotection, toxicology, and ocular pharmacology. He has published over 110 articles in indexed journals and authored five books and chapters.

A preliminary study on the concentration of astaxanthin nanoemulsion for its neuroprotective potential in a rat model of permanent middle cerebral artery occlusion (pMCAO).

Anis Syahirah Mohd Shafie^a, Siti Norsyafika Kamarudin^{a*}, Meor Mohd Affandi Meor Mohd Redzuan^b, and Rosfaiizah Siran^c
^a Department of Pharmacology, Faculty of Medicine, Universiti Teknologi MARA, 47000 Sungai Buloh, Selangor, Malaysia.

^b Department of Pharmacy, Faculty of Pharmacy, Universiti Teknologi MARA, 42300 Puncak Alam, Selangor, Malaysia.

^c Neuroscience Research Group, Faculty of Medicine, Universiti Teknologi MARA, 47000 Sungai Buloh, Selangor, Malaysia.

Introduction. Astaxanthin (ATX), a naturally occurring orange-reddish pigment in the microalgae *Haematococcus pluvialis*, is well-known for its antioxidant and anti-inflammatory benefits. The development of a nanoemulsion formulation enhances the ability of ATX to cross the blood-brain barrier. This pilot study examined the optimal concentration of ATX nanoemulsion to reduce infarct volume and improve neurological function in a rat model with permanent middle cerebral artery occlusion (pMCAO). **Aims.** Text to begin immediately following the heading and without additional line spacing. Do not bold or underline heading. **Methods.** Nine Sprague Dawley rats were divided into four groups, each receiving varying concentrations of ATX nanoemulsion: Group A (2%), Group B (5%), and Group C (10%). ATX nanoemulsion was administered orally for 7 days prior to and 3 hours following the pMCAO induction. Neurological function assessments and brain infarct volume measurements were performed 24 hours post-pMCAO. The rats were euthanized via cardiac puncture, and their brains were collected for infarct volume analysis. Data were analyzed using one-way ANOVA and post-hoc Tukey test, with significance set at $p < 0.05$. **Results.** Neurological scores and grid walking tests showed significant differences ($p < 0.05$) between Group A and Groups B and C ($p < 0.001$). The rotarod test scores for Group A were significantly higher ($p < 0.001$) compared to Groups B and C. Additionally, Group A's infarct volume was significantly lower ($p < 0.001$) than Groups B and C ($p < 0.05$). **Discussion.** This preliminary study demonstrated that a 5% concentration of ATX nanoemulsion is optimal, as it significantly enhanced neurological function and reduced infarct volume in the pMCAO rat model.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P449

Efficacy and Safety of Immunotherapies for Alzheimer's Disease: A Network Meta-Analysis

Prof Igor Iezhitsa

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Igor Iezhitsa has over 25 years of experience in pharmacology, with a career dedicated to both academia and research. He earned his PhD in Pharmacology from Volgograd State Medical University (Russia) in 1998, followed by a Doctor of Biological Science (Dr. Sci. Biol.) degree from the same institution in 2008. From 1994 to 2000, Dr. Igor was instrumental in preclinical studies of a novel class of CNS stimulants at Volgograd State Medical University. Since then, he has conducted extensive screening and preclinical evaluation of new pharmacological compounds. In 2009, Dr. Igor joined the Faculty of Medicine at Universiti Teknologi MARA (UiTM), Malaysia, as an Associate Professor of Pharmacology. He was a key figure in establishing the Centre for Neuroscience (NeuRon) at UiTM in 2013, leading the center from 2015 to 2020. He currently serves as Professor of Pharmacology at the School of Medicine, International Medical University. Dr. Igor's research interests include neuropharmacology, neuroprotection, toxicology, and ocular pharmacology. He has published over 110 articles in indexed journals and authored five books and chapters.

Efficacy and Safety of Immunotherapies for Alzheimer's Disease: A Network Meta-Analysis

Rida Rabab Chowdhury, Htet Htet, Igor Iezhitsa, Heethal Jaiprakash, Renu Agarwal, IMU University, School of Medicine, Kuala Lumpur, Malaysia

Introduction: Alzheimer's disease (AD) is characterized by cognitive decline, and existing treatments offer limited relief. Immunotherapy holds promise by targeting amyloid plaques and potentially reversing cognitive decline. This study aimed to systematically review existing literature and conduct a network meta-analysis (NMA) to assess the therapeutic benefits and potential harms of immunotherapies for AD.

Methodology: This study was registered with INPLASY and followed PRISMA NMA guidelines. Predetermined PICO criteria were utilized, and an extensive database search was conducted on Ovid MEDLINE, the COCHRANE library, and PUBMED, employing specific keywords with appropriate MeSH terms. English publications up to December 2022 were included. Study selection, data extraction, methodological quality assessment, and data analysis were independently conducted by two investigators using COVIDENCE, Stata 18, and Rev Man Web software. Outcome measures focused on cognitive improvement assessed through ADAS-cog and MMSE scales.

Results: A total of 19 studies were included with 9944 participants in the intervention arm and 8617 participants in the control arm. Methodological quality assessment indicated an overall low risk of bias, with unclear bias in certain domains in some studies. Regarding cognitive improvement with ADAS-cog outcome, aducanumab was found to be the highest ranking among 8 interventions, followed by lecanemab and crenezumab. For the outcome measure using MMSE scale, aducanumab was found as the highest ranking followed by solanezumab and control/ACC-001. Headache was the most reported adverse effect at 19%, followed by overarching respiratory symptoms at 16%.

Discussion/ Conclusion: Monoclonal antibodies such as aducanumab, lecanemab, crenezumab, or solanezumab were observed as the most effective in improving cognition. Efficacy and safety for the long-term management of AD with monoclonal antibodies should be observed in future studies.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P450

New fundamental therapeutics for Alzheimer's disease utilizing unused parts of medicinal plants.

Miss Jae-Won Jung

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Jae-Won Jung is a doctoral student at the Section of Neuromedical Science, Institute of Natural Medicine, University of Toyama. She is researching the development of new fundamental therapeutics for Alzheimer's disease (AD) by utilizing unused parts of medicinal plants. The goal of her research is to restore neural circuits and identify potential active components in these extracts, with the aim of contributing to the advancement of AD treatments.

New fundamental therapeutics for Alzheimer's disease utilizing unused parts of medicinal plants.

Jae-Won Jung, Chihiro Tohda. Section of Neuromedical Science, Institute of Natural Medicine, University of Toyama, Toyama City, Japan

Introduction. Currently, Alzheimer's disease (AD) treatments provide only temporary and symptomatic relief, and recent approved drugs show limited efficacies and risk of adverse events. Therefore, it is crucial to find new pharmaceutical substances that can effectively treat AD. For the fundamental recovery of cognitive function, reconstructing neural networks is essential. We have found that various medicinal plant extracts have the ability to reconstruct neural networks. However, the unused parts of medicinal plants, despite their potential activity, have been largely unexplored and discarded. **Aims.** The aim of this study is to identify potential activity from extracts of the unused parts of medicinal plants, with the goal of developing a novel therapeutic drug for AD.

Methods. In vitro studies, primary cultured cortical neurons (ddY mouse, E14) were treated with A β ₂₅₋₃₅ for 3 days to induce neurite atrophy. The plant extracts were post treated. Four days later, immunocytochemistry was performed to quantify the lengths of axons and dendrites. In vivo studies, post-onset 5XFAD transgenic mice and their wild-type littermates (6-8 months old were used). Target extracts were orally administered daily for 14 days, and behavioral tests related to memory function, such as object recognition and object location tests, were performed. A β plaques, hyperphosphorylated tau, and axonal regeneration in the brain were quantified.

Results. Nine plants (Ginseng Radix, Panacis Quinquifolia Radix, and so on) were selected, and the unused parts were extracted by different conditions and solvents. Eventually, 26 extracts were evaluated. In vitro studies narrowed the extracts which demonstrated high reproducibility of axonal and/or dendritic regrowth activity. At the next step, behavioral tests are performed on 5XFAD mice.

Discussion. In this abstract, the concrete names of extracts are not disclosed due to patent. After identifying effective extracts in vitro and in vivo, we identify active compounds that transfer to the brain after oral administration and investigate their molecular mechanisms for repairing neural circuits.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P451

Testosterone signaling in microglia: its roles for sex differences in Alzheimer's Disease

Prof Takashi Kanematsu

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Takashi Kanematsu is a professor in the Faculty of Dental Science at Kyushu University, Fukuoka Japan, where he has been since 2019. He has served as Chair of the Department of Cell Biology, Aging Science, and Pharmacology. His current research interests are in the field of Alzheimer's disease, especially the molecular mechanism of sex differences in its pathophysiology. He received his Ph.D. in Dental Science (Biochemistry) from the Kyushu University in 1994, after graduating from the Faculty of Dentistry, Kyushu University. He worked for two years as a postdoctoral fellow at Vanderbilt University, TN, USA (1995–1996), and then served as an associate professor in the Department of Biochemistry, Faculty of Dentistry, Kyushu University (1997–2008). During 2009–2018 he was Professor and Chair of the Department of Cellular & Molecular Pharmacology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima Japan.

Testosterone signaling in microglia: its roles for sex differences in Alzheimer's Disease

Haiyan Du¹, Akiko Mizokami², Tomomi Sano¹, Takashi Kanematsu¹. Department of Cell Biology, Aging Science and Pharmacology¹, and OBT Research Center², Faculty of Dental Science, Kyushu University, Fukuoka, Japan

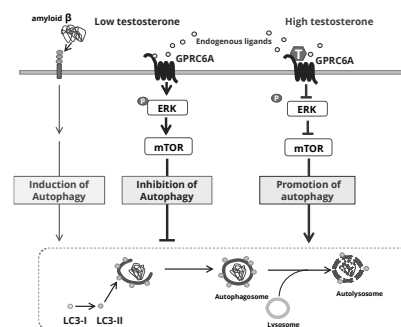
Introduction. Men have lower Alzheimer's disease (AD) rates than women, potentially linked to testosterone's influence. Microglia, primary innate immune cells in the brain, contribute to the clearance of aggregated proteins such as amyloid beta ($A\beta$) through phagocytosis and lysosomal degradation, including autophagy. We hypothesized that testosterone acts protectively against AD by enhancing autophagic activity in microglia, potentially reducing the incidence of AD in men.

Aims. The aim of this study is to focus on the role of testosterone in regulating autophagic activity in microglia through non-genomic testosterone signaling via the G protein-coupled receptor, class C, group 6, subtype A (GPRC6A).

Methods. The 5x FAD AD model mice and the mouse microglial cell line MG6 were used. LC3-II and p62 were used as indicators for selective autophagy. GPRC6A signaling was inhibited pharmacologically with an allosteric antagonist and genetically with shRNAs.

Results. Brain sections from male and female 5xFAD mice showed that autophagy is suppressed in female microglia. Testicular removal from male mice also suppressed microglial autophagy, indicating the contribution of testosterone to autophagic activity. Testosterone suppressed ERK phosphorylation in MG6 cells, inhibiting mTOR activation and promoting $A\beta$ -induced autophagy. MG6 cells were able to engulf extracellular $A\beta$, which colocalized with the autophagosome marker LC3, and this process was enhanced in the presence of testosterone. Genetic knockdown and pharmacological inhibition of GPRC6A restored ERK phosphorylation. These results suggest that testosterone-GPRC6A signaling enhances $A\beta$ -induced autophagy in microglia, potentially contributing to lower AD susceptibility in men.

Discussion. The study emphasizes the role of testosterone in microglial autophagy, potentially lowering AD risk in men. Targeting GPRC6A signaling or hormone replacement therapies may offer therapeutic or preventive benefits.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P452

CASK mediates UVA-induced Muller cell apoptosis via regulating AMPK and Ca²⁺ trafficking

Dr Vladlen Klochkov

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

My PhD research focused on evaluating the GSK3 β inhibitory activity of 3,5-disubstituted indoline-2-one derivatives as potential therapeutic agents for type 2 diabetes mellitus and acute inflammation. After defending my PhD, I moved to Taiwan and joined Prof. Chi-Ming Chan and Prof. Wan-Wan Lin's project as a postdoctoral researcher. Our work explored the role of AMPK in diabetic retinopathy. My specific research focused on investigating the role of the CASK protein and AMPK in the effects of UVA light on retinal Müller cells.

CASK mediates UVA-induced Muller cell apoptosis via regulating AMPK and Ca²⁺ trafficking

Klochkov Vladlen¹, Duen Yi Huang², Wan Wan Lin^{2,3}, Chi Ming Chan^{1,4}. Department of Ophthalmology, Cardinal Tien Hospital¹, New Taipei City 23148, Taiwan; Department of Pharmacology, College of Medicine, National Taiwan University², Taipei 100233, Taiwan; Graduate Institute of Medical Sciences, Taipei Medical University³, Taipei, Taiwan School of Medicine, Fu Jen Catholic University⁴, New Taipei City 242062, Taiwan.

Introduction. Calcium/calmodulin-dependent serine protein kinase (CASK) is a scaffold protein and involves in the retina diseases.

Aims. To dissect the role of CASK in UVA-induced Muller cell (rMC1) apoptosis under UVA stress.

Methods. We generated the stable CASK knockdown rMC1 cells by lentivirus and knockdown AMPK by siRNA. Annexin V/PI, mtSOX, MitoTracker, JC-1, LysoTracker, Fluo-3 and rhod-2 were used for flow cytometry.

Results. shCASK protects rMC1 cells from UVA-induced cell apoptosis, mitochondrial mass and MMP loss, and mtROS increase. UVA induces a biphasic effect on cytosolic Ca²⁺ level and a time-dependent increase in mitochondrial Ca²⁺ level. CASK silencing reduces basal mitochondrial and cytosolic Ca²⁺ levels and protects cells from UVA-induced changes. We found that TRPM2 inhibitor (2-APB), MCU inhibitor (Ru265), SOCE inhibitors (YM58483, MRS1845) and TRPML1 inhibitor (ML-SI3) can also decrease UVA-induced cell death. In addition, 2-APB and Ru265 can block cytosolic and/or mitochondrial Ca²⁺ changes. Moreover, UVA can upregulate lysosomal mass and this effect is reduced by shCASK. In contrast, TRPML1 activator (ML-SA1) can reduce CASK silencing-induced protective effect. We found that UVA can induce AMPK phosphorylation at T172 in both shCTL and shCASK cells; however, shCASK can also prolong AMPK phosphorylation at S485, suggesting the AMPK inhibition in UVA-treated shCASK cells. Pre-activation of AMPK by A769662 exerts a cell protection, while its post-treatment fails to exert such protection and even decreases the protective effect of CASK silencing. In addition, siAMPK can protect shCTL cells from UVA-induced apoptosis.

Discussion. We found a crucial role of CASK in UVA-induced Muller cells apoptosis and the involvements of AMPK activation and mobilization of intracellular Ca²⁺ trafficking in the mitochondrial dysfunction.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P453

Structural Insights into Positive Allosteric Modulation at the M₄ muscarinic acetylcholine receptor

Miss Michaela Kaoullas

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Structural Insights into Positive Allosteric Modulation at the M₄ muscarinic acetylcholine receptor

Michaela Georgia Kaoullas^{1,2}, Jesse Mobbs^{1,2}, Celine Valant^{1,2}, David Thal^{1,2}, Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences¹, Melbourne, VIC, Australia; ARC Centre for Cryo-Electron Microscopy of Membrane Proteins, Monash Institute of Pharmaceutical Sciences², Melbourne, VIC, Australia

Introduction. The M₄ muscarinic acetylcholine receptor has emerged as a clinically validated target for the treatment of schizophrenia. There remains a major challenge in selectively activating this receptor due to the highly conserved orthosteric binding domain that is shared amongst the muscarinic receptor subtypes. A promising approach to overcome this hurdle, is to target allosteric sites of the M₄R, which are spatially distinct from the orthosteric site and comprised of less-conserved residues. Understanding how positive allosteric modulators (PAMs) engage with and activate the M₄R is crucial to facilitate drug discovery efforts.

Aims. Probe the structure-activity relationship of the M₄R and a new generation PAM, XY6, to elucidate interactions that may underlie receptor engagement and positive allosteric modulation.

Methods. Using cryogenic electron microscopy, we determined an active state structure of the M₄R in complex with its cognate Gi1 protein, and co-bound to acetylcholine and XY6 (2.4 Å). We pharmacologically validated the interactions of XY6 at the M₄R and determined how allosteric site residues contribute to the binding affinity (pK_B), binding cooperativity (α), allosteric agonism (τ_B), and functional cooperativity (αβ) of XY6 with the agonist ACh. The structurally identified residues were replaced with alanine and stably expressed in cells lines (Flp-In CHO cells) for radioligand binding and BRET-based G protein activation assays.

Results. Mutations of residues Y89, F186 and W434 into alanine significantly impacted both the binding and functional abilities of XY6 at the M₄R. Importantly, XY6 now represents the highest affinity M₄R PAM (pK_B= 6.3 ± 0.2) and is the first to retain some activity at the aforementioned mutant residues.

Discussion. These findings suggest that all three aromatic residues are key contributors to XY6's allosteric modulation at the M₄R. Critically, our study indicates that XY6 is less sensitive to mutagenic alterations likely due to its unique binding mode and improved properties. These exciting findings represent an important milestone in drug discovery efforts for novel PAM scaffolds, which can inform future structure-activity relationship studies to enhance the development of both tool and therapeutically beneficial M₄R PAMs.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P454

Deprescribing benzodiazepine receptor agonists in people living with dementia: a systematic review

Miss Aisling McEvoy

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

I am a PhD candidate with the Centre for Medicines Use and Safety (CMUS) at Monash University's Faculty of Pharmacy and Pharmaceutical Sciences. My background as a hospital pharmacist in a large tertiary teaching hospital has allowed me to gain practical experience in both clinical and research settings. I completed my Masters of Pharmacy with Monash University in 2021, where I won Best Project Poster and Presentation for my cohort. I am excited to continue my research in investigating how benzodiazepine receptor agonists can be safely and effectively deprescribed in people living with dementia.

Deprescribing benzodiazepine receptor agonists in people living with dementia: a systematic review

Aisling M McEvoy¹, Aili V Langford¹, Darshna Goordeen¹, Shin J Liao¹, Emily Reeve^{1*}, Justin P Turner^{1*}. 1. Centre for Medicines Use and Safety, Monash Institute of Pharmaceutical Sciences, Parkville, VIC, Australia. *Joint senior authors

Introduction. Benzodiazepine receptor agonists (BZRAs) (benzodiazepines and z-drugs) can be beneficial for sleep if used short-term; however, they lack long-term efficacy and are associated with adverse events such as falls. Deprescribing can be especially beneficial in people living with dementia (PLWD) to reduce adverse events.

Aims. This review aimed to investigate; 1) how can BZRAs be safely and effectively deprescribed in PLWD, and 2) what is the effectiveness of patient-directed non-pharmacological interventions to support BZRA deprescribing in older adults with insomnia.

Methods. Systematic searches were executed in Embase, CENTRAL, Scopus, and Ovid Medline in January 2024. Randomised and non-randomised trials published in English were included. Screening, data extraction and risk of bias assessments were conducted independently by 2 authors. Outcomes of interest included the percentage of participants ceasing BZRAs at follow up, as well as changes in medication, sleep, and clinical outcomes.

Results. From 9,803 studies, 26 were included (7 addressing Question 1, and 19 for Question 2). For question 1, studies that focused on PLWD mostly utilised a multidisciplinary approach to deprescribe BZRAs and had a cessation rate between 0-70%. Nil adverse effects were reported, and some studies showed an improvement in quality of life.

Thirteen studies utilised patient or carer education to support deprescribing, delivered via written (n=9) and verbal (n=4) formats. Most of these studies focused on older adults (n=12) (Question 2). Deprescribing success varied across studies, however educational interventions resulted in more consistent reductions in BZRA use. Between ~50-92% of participants ceased BZRAs at follow up after receiving an educational intervention; the BZRA cessation rate for those in the comparator groups ranged from ~2-45%.

Discussion. Educating patients and their carers about the potential harms of BZRAs was shown to reduce BZRA use in older adults. Multidisciplinary interventions form the majority of current interventions to deprescribe BZRAs in PLWD but have inconsistent cessation success. Interventions to deprescribe BZRAs were overall less effective in PLWD than those conducted in older adults without dementia. Therefore, further research investigating alternative options may find more appropriate treatments for this population.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P455

Exploring sex-differences of metabotropic glutamate receptor 5 (mGlu5) negative allosteric modulators (NAMs).

Mr Jackson Kos

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Jackson completed a Bachelor of Pharmaceutical Science with Honours at Monash University in 2021. He is currently a PhD Candidate in the department of Drug Discovery Biology at the Monash Institute of Pharmaceutical Sciences. Jackson has a keen interest in glutamatergic signalling within the context of neurodegenerative and neuropsychiatric disorders

Exploring sex differences of metabotropic glutamate receptor 5 (mGlu₅) negative allosteric modulators (NAMs).

Jackson A Kos¹, Monica Langiu¹, Shane D Hellyer¹, Karen J Gregory^{1,2}. Drug Discovery Biology, Monash Inst. Pharm. Sci.¹, ARC Centre for Cryo-electron Microscopy of Membrane Proteins², Monash Univ., Parkville, VIC, Australia.

Introduction. Sex is an important biological variable affecting efficacy and safety of drug candidates. Drug effects in females and women remain poorly understood due to their limited inclusion in preclinical and clinical studies (Beery and Zucker., 2011). Consequently, approved medications often have smaller therapeutic windows in women, warranting withdrawal from the market (Lee., 2018). mGlu₅ NAMs are promising novel therapeutics for neurodegenerative disorders, although recent evidence suggests efficacy is sex-dependent (Abd-Elrahman et al., 2020). The molecular mechanisms underpinning these sex differences remain unsolved, limiting clinical translation.

Aims. Herein, we aimed to determine whether mGlu₅ NAMs demonstrate sex-dependent molecular pharmacology.

Methods. Male and female mouse embryos were isolated to produce single-sex hippocampal and cortical neuron cultures, with accuracy assessed by genotyping. We evaluated ten structurally diverse mGlu₅ NAMs to attenuate agonist-mediated mGlu₅ signalling in single-sex hippocampal and cortical primary neuron cultures. Affinity and cooperativity estimates for each NAM were quantified using an operational model of allosterism.

Results. Sex assignment was ~98% accurate (n=4 independent cultures, 90 embryos). Quisqualate potency and efficacy were consistent in both sexes and brain regions tested. Affinity and cooperativity estimates of mGlu₅ NAMs based on inhibition of quisqualate-mediated intracellular calcium mobilisation were consistent between sexes.

Discussion. We successfully established single-sex neuron cultures from two distinct brain regions. We did not detect sex differences in mGlu₅ NAM pharmacological parameters, suggesting transient signalling events may not contribute to preclinically observed sex differences. This study provides an *in vitro* framework to explore the molecular mechanisms of sex differences and inform translation of *in vitro* findings into preclinical studies. Further work will explore sex differences in long-term cellular processes and in response to pathological insults.

Abd-Elrahman et al (2020) Sci Signal 13(662):eabd2949

Beery and Zucker (2011) Neurosci Behav Rev 35(3):565-572

Lee (2018) BMB Rep 51(4):167-173

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P456

New myokine-mediated functional recovery in chronic phase of spinal cord injury

Prof Chihiro Tohda

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Dr. Chihiro Tohda was earned Ph.D. (Pharmaceutical Science) from Hokkaido University in 1994. She worked as a Research Fellowship for Young Scientists of JSPS and became an Assistant Professor in Research Institute for Wakan-yaku, Toyama Medical and Pharmaceutical University. She moved to Research Center for Ethnomedicines, Institute of Natural Medicine, Toyama Medical and Pharmaceutical University in 1996. From Nov. 1997, she worked at National Institute of Health (USA) for 4 months. She became an Associate Professor and Head of Division at of Neuromedical Science, Institute of Natural Medicine, University of Toyama in 2010, and a Full Professor and Head of Section of Neuromedical Science in 2017. Current Position is a Full Professor/Vice Director of Institute of Natural Medicine, University of Toyama.

She is engaged in research primarily focused on natural medicines, aiming to develop novel therapeutic approaches for refractory neurodegenerative diseases such as dementia, spinal cord injury, degenerative cervical myelopathy and glaucoma. She is also advancing clinical studies based on the outcomes of foundational research, with a keen awareness towards eventual societal implementation of our findings.

New myokine-mediated functional recovery in chronic phase of spinal cord injury

Chihiro Tohda, Atsushi Kodani, Takahiro Kikuchi. Section of Neuromedical Science, Institute of Natural Medicine, University of Toyama, Toyama, Japan.

Introduction. Chronic spinal cord injury (SCI) is quite difficult to cure. Although a lot of SCI studies have focused on the nervous system and inflammatory cells in the spinal cord, we targeted skeletal muscle atrophy, as a characteristic finding in the chronic SCI. A longitudinal study showed that skeletal muscle atrophy progresses in a time-dependent manner after injury in humans. Generally, the skeletal muscle is known to secrete some myokines responded by exercise. Although exercise slightly improves motor function in chronic phase, feasibility of exercise is limited under muscle atrophy condition.

Aims. We hypothesized that some myokines would be beneficial to motor function, and there are some beneficial myokines which are increased by drug stimulation not by exercise.

Methods. For drug screening, primary cultured skeletal myocytes were treated by plant extracts or compounds, and conditioned medium (CM) was collected. CM was treated to primary cultured neurons to evaluate axonal growth. For in vivo study, SCI mice were prepared by contusion at T12-13 level.

Results. *Cistanche tubulosa* extract and its active constituent, acteoside, induced the secretion of axonal growth factors from skeletal myocytes and proliferation of myocytes¹. Pyruvate kinase isoform M2 (PKM2) was identified as an acteoside-induced myokine¹. Extracellular PKM2 enhanced proliferation for cultured skeletal myocytes and axonal growth for culture neurons¹. Intramuscular injection of acteoside in chronic SCI mice recovered skeletal muscle mass and motor function¹. Sustained i.c.v. infusion (i.c.v.) of PKM2 significantly recovered motor function and density of raphespinal tracts in chronic SCI mice².

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion. We found that a small compound, acteoside, protected muscle atrophy and activated secretion of PKM2, a new myokine for axonal growth. PKM2 transferred to the central nervous system and improved descending tracts density and motor function in chronic SCI mice. This study proposes that both acteoside and PKM2 have potentials to recover motor function in chronic SCI.

(1) Kodani A et al (2019) J Neurotrauma 36(12):1935-1948, (2) Kikuchi T et al (2020) Sci Rep10(1):19475

P457

Evolution of 5-HT₃ receptors in animals and their moonlighting roles in mitochondria

Dr Santosh RamaBhadra Rao Tata

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Evolution of 5-HT₃ receptors in animals and their moonlighting roles in mitochondria.

Santosh T R B Rao¹, Ilona Turek¹, Julian Ratcliffe¹, Christine Kettle¹, Donna R Whelan¹, Helen R Irving¹ La Trobe Institute for Molecular Science, La Trobe University¹, P.O. Box 199, Bendigo, VIC Australia

Introduction. The 5-hydroxytryptamine 3 (5-HT₃) receptor is the only pentameric ligand gated cation selective channel in the serotonin receptor family. In humans heteromeric and homomeric 5-HT₃ receptors are formed by 5 subunits (A-E) where subunit A can form homomeric and heteromeric subunits with other subunits. 5-HT₃ receptors play key role in development, growth, and behaviour in animals. 5-HT₃ receptor specific antagonists are used to treat nausea, emesis, and irritable bowel syndrome and other gastrointestinal disorders.

Aims. To determine the (i) if 5-HT₃ receptors locate to mitochondria and (ii) 5HT₃ receptor subunit distribution throughout the animal kingdom.

Methods. 5-HT₃ receptor subunit protein sequences were subjected to BLAST searches on NCBI database with greater than 1000 species identified. These sequences were computationally analysed for conserved residues in the ligand binding and transmembrane domains and conserved peptide targeting sequences. HEK293T cells were transiently transfected with epitope and fluorescent protein-tagged subunits of human 5-HT₃ receptors and detected with fluorescence and transmission electron microscopy. Membrane potential and oxygen consumption assays were performed on isolated mitochondria or in whole cells.

Results. Multiple sequence alignment and phylogenetic analyses predicted that 5-HT₃ receptors are widely distributed in the animal kingdom including several lower species and gut parasitic species. Both A and E subunits localise at mitochondrial inner membrane forming A homomeric and AE heteromeric receptors. Localised A and E subunits influenced the membrane potential and mitochondrial oxygen consumption rates following treatment with agonist serotonin (enhanced) or antagonist ondansetron (inhibited).

Discussion. The presence of conserved 5-HT₃ receptor ligand binding sites in a wide range of species suggests that those species are likely to respond to 5-HT₃ receptor antagonists used to treat humans and has implications for organisms exposed to them in human ecosystems. The surprising localisation of 5-HT₃ receptors in mitochondrial inner membranes where they may have a moonlighting uncoupling function highlights the importance of investigating mitochondrial effects to improve efficacy and lower toxicity of 5-HT₃ receptor mediated treatments.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P458

CASK involves in methylglyoxal-induced mitochondrial calcium overload and dysfunction in Müller cells

Mr Chuin Shung Yeoh

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Yeoh Chuin Shung is a dedicated researcher with a master's degree in pharmacology from the Graduate Institute of Pharmacology, College of Medicine, National Taiwan University, where he is also currently posted at. He previously earned his bachelor's degree in biotechnology and bio-industrial science from National Cheng Kung University, Taiwan. Currently serving as a research assistant, Yeoh focuses on studying CASK and its critical role in calcium signalling and mitochondrial regulation of cell death. His work reflects a passion for uncovering molecular mechanisms that drive cellular processes and aims to contribute meaningfully to the fields of pharmacology and cell biology. Outside the lab, he remains committed to continuous learning and scientific discovery.

CASK involves in methylglyoxal-induced mitochondrial calcium overload and dysfunction in Müller cells

Chuin Shung Yeoh¹, Duen-Yi Huang¹, Ponarulsevam Sekar¹, Wan-Chen Huang², Wan-Wan Lin^{1,3} *. ¹Department of Pharmacology, College of Medicine, National Taiwan University, 100233 Taipei, Taiwan. ²Institute of Cellular and Organismic Biology, Academia Sinica, 115 Taipei, Taiwan. ³Graduate Institute of Medical Sciences, Taipei Medical University, 110301 Taipei, Taiwan.

Introduction. Diabetic retinopathy is a diabetic complication that affects vision and is one of the leading causes of blindness. Methylglyoxal (MGO) is a product of glycolysis in cells and is involved in the formation of advanced glycation end products (AGEs), whose accumulation is a key pathological event in DR. Müller cells are a type of glial cells found in the retina and are essential to the development, function and health of the retina. Calcium/calmodulin-dependent serine protein kinase (CASK) is a multidomain scaffold protein that plays a crucial role in neuronal development and is ubiquitously expressed in the brain as well as the retina.

Aims. To investigate the role of CASK in Müller cell death response during DR.

Methods. In this study, murine rMC1 Müller cells were used and CASK was silenced using short-hairpin RNA sequences delivered via a lentiviral vector.

Results. We found that MGO (100 µg/ml) treatment for 6 h induces rMC1 cell apoptosis, which is inhibited by zVAD, unaffected by olaparib, necrostatin-1, bafilomycin A1 and 3MA, but enhanced by BBGC. CASK is present in the nucleus, cytosol and mitochondria and its silencing confers a protective effect against MGO-induced caspase-dependent apoptosis. shCASK attenuates MGO-induced mitochondrial ROS generation, MMP loss, and oxidative phosphorylation inhibition. The death effect of MGO is blocked by ROS scavenger NAC and mitoTempo, suggesting the involvement of mtROS-dependent apoptosis. Furthermore, shCASK inhibits MGO-induced calcium increase in the cytosol and mitochondria. The inhibitors of endoplasmic reticulum (ER) stress, store operated Ca²⁺ entry (SOCE) channels, and TRPM2 channel attenuate MGO-induced cell death. Besides that, immunofluorescence analysis reveals that shCASK significantly inhibits cytosolic Ca²⁺ influx after the depletion of ER Ca²⁺ store through the blockage of SERCA using thapsigargin. Additionally, AMPK activators and p38 inhibitor prevent cell death and cytosolic calcium accumulation.

Discussion. In a nutshell, CASK plays a significant role in decreasing Müller cell survival upon MGO treatment, but further studies may be required to elucidate CASK as an ideal therapeutic target for diabetic retinopathy.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P459

Diosgenin improves cognition in Alzheimer's disease model mice and humans

Prof Chihiro Tohda

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Chihiro Tohda was earned Ph.D. (Pharmaceutical Science) from Hokkaido University in 1994. She worked as a Research Fellowship for Young Scientists of JSPS and became an Assistant Professor in Research Institute for Wakan-yaku, Toyama Medical and Pharmaceutical University. She moved to Research Center for Ethnomedicines, Institute of Natural Medicine, Toyama Medical and Pharmaceutical University in 1996. From Nov. 1997, she worked at National Institute of Health (USA) for 4 months. She became an Associate Professor and Head of Division at of Neuromedical Science, Institute of Natural Medicine, University of Toyama in 2010, and a Full Professor and Head of Section of Neuromedical Science in 2017. Current Position is a Full Professor/Vice Director of Institute of Natural Medicine, University of Toyama.

She is engaged in research primarily focused on natural medicines, aiming to develop novel therapeutic approaches for refractory neurodegenerative diseases such as dementia, spinal cord injury, degenerative cervical myelopathy and glaucoma. She is also advancing clinical studies based on the outcomes of foundational research, with a keen awareness towards eventual societal implementation of our findings.

Diosgenin improves cognition in Alzheimer's disease model mice and humans

Chihiro Tohda, Ximeng Yang, Yuna Inada. Section of Neuromedical Science, Institute of Natural Medicine, University of Toyama, Toyama, Japan.

Introduction. In Alzheimer's disease (AD), repairing neuronal circuits is very crucial to improve memory impairment. We have aimed to repair the neural network by natural medicines for development of a new therapeutic agent for AD, and focused on diosgenin which is known as a constituent of Yam (rhizome of *Dioscorea japonica* or *D. batatas*). Our previous studies provided solid evidence showing that administration of diosgenin to AD model mice (5XFAD) restored memory impairment.

Aims. This study revealed molecular mechanism of repairing of neural circuit by Diosgenin and evaluated effects of Diosgenin on cognitive function in humans.

Methods. To figure out Diosgenin mechanism, axon-growing neurons in the hippocampus connecting to the prefrontal cortex were selectively visualized, and transcriptome analysis was performed. For clinical studies, Diosgenin-rich Yam extract was treated to subjects.

Results. Diosgenin (p.o.) extended damaged axons successfully to the prefrontal cortex in 5XFAD mice. The axon-growing hippocampal neurons and naïve neurons were captured by laser microdissection to serve gene array. Genes of SPARC and Gal-1 were largely increased in axon-growing neurons. Overexpression of these genes in hippocampal neurons improved memory deficits and promoted accurate axonal reinnervation to the prefrontal cortex in 5XFAD mice^{1,2}. Aiming to social implementation of the basic study, effects of diosgenin in humans were evaluated. Taking advantage of Borderline of Pharmaceuticals to Non-pharmaceuticals in Japan, we optioned to perform clinical studies with Yam extract as more realistic and feasible approaches than those with diosgenin itself. A randomized, double blinded, crossover clinical study

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



for healthy subjects clarified upregulation of cognitive function by taking Yam extract for 12 weeks³. Furthermore, a specified clinical trial was conducted on subjects with mild cognitive impairment and mild AD. Results suggested certain effects of the diosgenin-rich Yam extract for cognition.

Discussion. Diosgenin recovered memory function in AD mice a via direction-specific axonal regeneration and improved cognition in humans.

(1) Mol Psychiatry 2023;28(6):2398-2411, (2) Mol Neurobiol 2023;60(3):1250-1266, (3) Nutrients 2017;9(10):1160.

P460

Safety and efficacy of methylenedioxymethamphetamine (MDMA)-assisted psychotherapy in post-traumatic stress disorder

Dr Alene Yong

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr Alene is a Research Fellow at the Centre for Medicine Use and Safety, Monash Institute of Pharmaceutical Sciences. She is currently working on clinical practice guideline development and research implementation. Previously, she has been involved in various public health projects, particularly in health financing and non-communicable disease service enhancement. She has experience using research methodologies such as evidence synthesis, qualitative research, and preference elicitation methods.

Safety and efficacy of methylenedioxymethamphetamine (MDMA)-assisted psychotherapy in post-traumatic stress disorder

Alene S J Yong¹, Suzie Bratuskins², Musa Sultani^{1,3}, Brooke Blakeley¹, Christopher G Davey⁴, J Simon Bell¹. Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Parkville, VIC, Australia; Neuromedicines Discovery Centre, Monash Institute of Pharmaceutical Sciences, Monash University², Parkville, VIC, Australia; School of Pharmacy, University of Nottingham³, Nottingham, United Kingdom; Department of Psychiatry, The University of Melbourne, Parkville, VIC, Australia⁴

Introduction. In July 2023, Australia became the first country to reclassify certain psychedelics to permit prescription of MDMA-assisted psychotherapy (MDMA-AP) for the treatment of post-traumatic stress disorder (PTSD).

Aims. To critically evaluate published and unpublished systematic reviews and meta-analyses on the safety and efficacy of MDMA-AP for PTSD.

Methods. Six bibliometric databases and grey literature were searched from inception to 9 May 2024 for systematic reviews on the safety and efficacy of MDMA-AP compared to psychotherapy alone among adults with PTSD. Quality assessment using the AMSTAR-2 tool was conducted independently by two investigators.

Results. Fourteen systematic reviews comprising 20 primary studies involving up to 353 participants were included. All reviews included studies of one-to-three sessions of 50-125mg MDMA-AP (some with supplemental dosage) compared to either 25-40mg of MDMA or inactive placebo with psychotherapy. Four of 14 reviews were deemed high quality. Meta-analyses reported substantial benefits of MDMA-AP in improving PTSD symptoms (SMD 0.8 to 1.3), response rate (RR 1.3 to 3.5), and remission rate (RR 2.3 to 2.9) compared to psychotherapy alone after one-to-three sessions of MDMA-AP. However, for reviews that assessed the certainty of evidence, the evidence was rated as low to very-low certainty due to high risk of bias, indirectness, and imprecision. There was moderate-quality evidence that MDMA-AP was associated with an increased odd of transient adverse events. However, reviews noted reliance on spontaneous rather than systematic adverse event reporting, discrepancies between adverse events reported in published studies and clinical trial registries, and a lack of long-term safety data.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion. Four high-quality systematic reviews suggest low to very-low certainty evidence for improvements in PTSD outcomes and moderate to very-low quality evidence for transient adverse events. Systematic reviews did not sufficiently evaluate or report on the psychotherapy session, supplemental dosage, intervention duration, and adverse events.

P461

Promoting microglial and macrophage uptake of amyloid- β proteins using diabodies

Dr Emma Van Der Westhuizen

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

I completed my PhD with Professor Roger Summers at the Department of Pharmacology, Monash University, where I characterised the ligand binding and signalling profiles of relaxin peptides at the human and mouse relaxin-3 receptors.

I undertook postdoctoral research with Professor Michel Bouvier at the Institute for Research in Immunology and Cancer, University of Montreal, Canada from 2008 to 2012. This work involved developing intracellular signalling fingerprints for clinically used drugs targeting the β 2-adrenergic receptors to better understand the links between intracellular signalling pathways and drug adverse effects, resulting in several publications in Mol Pharmacol, Nature Chem Biol and Nature Comms. This work was recently recognized as I was awarded the 2022 Early Career Researcher Award from the Monash University Faculty of Pharmacy and Pharmaceutical Sciences.

From 2013-2022, I undertook postdoctoral research with Professor Arthur Christopoulos at the Monash Institute of Pharmaceutical Sciences. Here I worked within a multidisciplinary team to develop and test novel allosteric modulators targeting the M1 and M4 muscarinic acetylcholine receptors, for the treatment of the symptoms of Alzheimer's disease and schizophrenia.

I moved to SVI in 2023, to develop and characterise new drug candidates for the treatment of Alzheimer's disease with Professor Michael Parker.

Promoting microglial and macrophage uptake of amyloid- β proteins using diabodies.

Emma T van der Westhuizen^{1,2}, Gabriela AN Crespi^{1,2}, Stefan J Hermans^{1,2}, Nancy C Hancock^{1,2}, Tracy L Nero², Michael W Parker^{1,2}. Structural Biology, St Vincent's Institute¹, Fitzroy, VIC, Australia; Dept Biochemistry and Pharmacology, Bio21 Molecular Science and Biotechnology Institute, The University of Melbourne², Parkville, VIC, Australia.

Introduction. Immunotherapy with amyloid-beta (A β) antibodies is the predominant strategy to treat Alzheimer's disease (AD) (Aljassabi et al., 2024). Coupling A β to the cell surface expressed triggering receptor expressed on myeloid cells 2 (TREM2) protein of microglial and macrophage cells (Colonna, 2023) may enhance A β phagocytosis and reduce toxic A β peptides and oligomers. This strategy may represent a new disease-modifying treatment for AD.

Aim. To develop diabodies with high affinity for A β and TREM2 that promote internalisation of A β into microglia without activating inflammatory responses.

Methods. Two A β -TREM2 diabodies were prepared using the Expi293F mammalian expression system. Microscale thermophoresis (MST) was used to determine the binding affinities (ρ K_D) of the diabodies for A β , and surface plasmon

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



resonance (SPR) was used to measure the affinities for TREM2. Flow cytometry was used to measure pH-Rodo-A β phagocytosis in mouse BV2 microglia and differentiated human THP-1 macrophages. Western blots were used to determine if the diabodies triggered inflammatory signalling in BV2 and differentiated THP-1 cells.

Results. Two TREM2-amyloid- β diabodies were generated and purified. A β and oligomeric (o)-A β affinities for diabody-1 (pK_D : A β = 5.7 ± 0.3 ; oA β = 5.4 ± 0.1 ; $n=3$) and diabody-2 (pK_D : A β = 4.5 ± 0.3 ; oA β = 6.4 ± 0.1 ; $n=3-4$) were in the micromolar range, whereas the affinities of diabody-1 (pK_D = 8.8) and diabody-2 (pK_D = 9.1) were in the nanomolar range for TREM2. A β phagocytosis was observed for both diabodies in differentiated human THP-1 cells, but only diabody 1 in mouse BV2 cells. Diabody-1 and diabody-2 did not increase the expression of tumor necrosis factor (TNF)- α , interleukin (IL)-6 or IL-1 β levels ($n=3$).

Discussion. The results suggest that our A β -TREM2 diabodies successfully bind to both proteins. When applied to cells that endogenously express TREM2 the diabodies promoted A β phagocytosis. The diabodies did not contribute to microglial inflammatory responses. Together these results suggest that coupling A β to a cell-surface protein with a diabody can improve uptake of toxic proteins into cells.

Aljassabi et al., (2024) J Alzheimers Dis. 98(3):755-772; Colonna (2023) Nat Rev Immunol 23: 580-594

P462

GABA-B receptor modulation in hPSCs-derived sensory neurons by baclofen and α -conotoxin Vc1.1

Dr Arsalan Yousuf

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

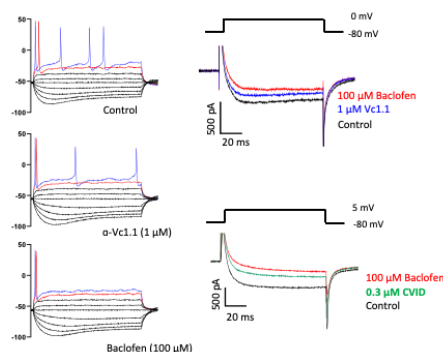
Arsalan Yousuf is Lecturer in Sydney Pharmacy School, University of Sydney. His research focusses on Pain signaling via membrane GPCRS and ion channels and hunting down small molecules and conotoxins. Arsalan has a background in neuroscience and electrophysiology techniques.

GABA_B receptor modulation in hPSCs-derived sensory neurons by baclofen and α -conotoxin Vc1.1

Arsalan Yousuf^{1,2}, Mitchell St Clair-Glover¹, Dominic Kaul¹, Mirella Dottori¹, and David J. Adams¹

¹ Molecular Horizons, Faculty of Science, Medicine and Health, University of Wollongong, Wollongong, NSW 2522 Australia. ² Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, NSW 2050 Australia.

Emerging strategies to develop, study and characterise human pluripotent stem cell (hPSC)-derived sensory neurons present a favourable alternative to study pain relief. In this study, hPSCs were differentiated into DRG sensory neurons using a chemical and transcription factor-driven approach. Molecular characterisation by immunocytochemistry and qPCR showed differentiated sensory neurons express key markers such as BRN3A, ISLET1, and PRPH, in addition to GABA_BR and ion channels including Cav2.2, GIRK, and HCN channels. Functional characterization of GABA_BR was carried out using patch clamp electrophysiology, with neuronal excitability studied under current clamp conditions in the absence and presence of GABA_BR agonists, baclofen and α -conotoxin Vc1.1. Both baclofen and Vc1.1 significantly reduced membrane excitability by hyperpolarizing the resting membrane potential by ~ 4 mV from -54 ± 4 mV ($n = 10$). In voltage-clamp mode, Vc1.1 and baclofen inhibited HVA Ca²⁺ channel currents by $\sim 25\%$ and 50% ($n = 8$), respectively, which



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



was attenuated by the GABA_BR antagonist CGP 55845. Hyperpolarization-activated current was inhibited by selective HCN antagonist ZD7288. Transient expression of human GABA_B receptor subunits together with HCN1/2 channels in HEK293T cells confirm that baclofen and Vc1.1 potentiate HCN-mediated K⁺ currents. Overall, this study reports GABA_BR modulation of HVA Ca²⁺ channels and membrane excitability in hPSC-derived sensory neurons by baclofen and Vc1.1, which could pave the way for future cell models to study analgesic compounds.

Hulme, A. J., McArthur, J. R., ... & Dottori, M. (2020). Molecular and functional characterization of Neurogenin-2 induced human sensory neurons. *Frontiers in Cellular Neuroscience*, 14(425).

P463

Dexmedetomidine retracts hippocampal astrocyte processes in vivo

Mr Shu Watanuki

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Shu Watanuki graduated from the School of Veterinary Medicine at Hokkaido University in 2023 and obtained a veterinary license. Currently, he is affiliated with the Laboratory of Pharmacology at the Faculty of Veterinary Medicine, Hokkaido University, where he conducts research on the central nervous system. As a second author, he contributed to the publication "Short-term memory impairment following recovery from systemic inflammation induced by lipopolysaccharide in mice" (DOI: 10.3389/fnins.2023.1273039). Additionally, he has received three awards at academic conferences in Japan.

Dexmedetomidine retracts hippocampal astrocyte processes *in vivo*

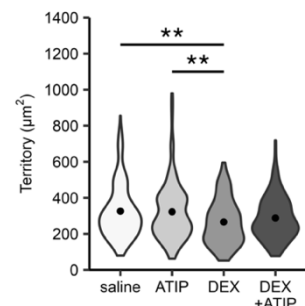
Shu Watanuki¹, Hinako Kaji¹, Yudai Nakano¹, Taisuke Kitano², Ryota Eguchi¹, Ken-ichi Otsuguro¹. Fac of Vet Med, Hokkaido Univ¹, Sapporo, HOKKAIDO, Japan; Sch of Basic Vet Med, Kitasato Univ², Towada, AOMORI, Japan.

Introduction. Astrocytes are characterized by complex morphology with numerous processes, which are related to the physiology and pathogenesis of the CNS. It is known that astrocyte morphology is altered by various transmitters. However, the effect of the α_2 -adrenoceptor agonist dexmedetomidine, which is commonly used as a sedative, on astrocyte morphology especially *in vivo* is unknown.

Aims. We investigated the effects of dexmedetomidine in rodent hippocampal astrocyte morphology.

Methods. Mice were injected with dexmedetomidine (1–100 μ g/kg, ip) and α_2 -adrenoceptor antagonist atipamezole (10 mg/kg, ip), and then brain slices were prepared after a certain time in the presence of isoflurane. In addition, acute hippocampal slices of rat brain were prepared and treated with dexmedetomidine (10 μ M, 90 min). Slices were stained with GFAP, an astrocyte marker, and morphological parameters of astrocyte were evaluated using an automated analysis tool (Sethi et al, 2021). In addition, cell volume was assessed by injecting lucifer yellow into astrocytes using microelectrodes.

Results. Dexmedetomidine decreased several astrocyte morphological parameters such as territory in a concentration-dependent manner, which peaked 3 h after injection. Some parts of this reduction were not observed in the presence of atipamezole. Dexmedetomidine also significantly decreased astrocyte volume assessed by lucifer yellow 3 h after injection. Conversely, dexmedetomidine did not change astrocyte morphology in acute hippocampal slices, i.e., under conditions that



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



suppress neural activity.

Discussion. It is suggested that dexmedetomidine retracts astrocyte processes via neuronal α_2 -adrenoceptors. However, atipamezole did not completely suppress this reaction, suggesting that mechanisms other than α_2 -adrenoceptors may be involved.

Sethi P et al. (2021) J Cell Sci. 134(12):jcs258430.

P464

Formononetin ameliorates chemotherapy-induced neurotoxicity in dorsal root ganglion neurons through Nrf-2/HO-1 pathway

Mr Yang-Chen Chang

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

My name is Yang-Chen Chang, and I am currently a third-year Ph.D. student at the Graduate Institute of Natural Products, School of Pharmacy, Kaohsiung Medical University, Taiwan. I initially entered the institute as a Bachelor's/Master's 4+1 combined degree program student. Due to my passion for scientific research and outstanding academic performance, I was selected for direct admission to the Ph.D. program in 2022.

*My research interest originated during my undergraduate studies when I joined Professor Yih-Fung Chen's laboratory for a special research project. My research mainly focuses on developing natural products to ameliorate chemotherapy-induced peripheral neuropathy. I have dedicated myself to this field with great enthusiasm and diligence for over five years of research experience. In April 2023, I successfully published my first first-author paper in *NeuroToxicology* (2023, 96, 118-128), a significant journal in the field of neuroscience. Currently, I am preparing my second first-author manuscript for publication, while another paper where I serve as the second author is under review.*

Formononetin ameliorates chemotherapy-induced neurotoxicity in dorsal root ganglion neurons through Nrf-2/HO-1 pathway

Yang-Chen Chang¹, Wan-Hsuan Lin¹, Yih-Fung Chen¹. Graduate Institute of Natural Products, College of Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan¹.

Introduction. Oxaliplatin and paclitaxel are the most commonly used chemotherapeutic agents causing significant neuropathy. No Food and Drug Administration (FDA)-approved therapy is now available to prevent or ameliorate chemotherapy-induced peripheral neuropathy (CIPN). Formononetin is an isoflavone possessing the antioxidant effect and has previously demonstrated neuroprotective potentials.

Aims. We aimed to research the neuroprotective potential and underlying mechanisms of formononetin against CIPN.

Methods. ND7/23 dorsal root ganglion (DRG) neurons were treated with or without the formononetin for 24 hours and then co-treated with paclitaxel (50 nmol/L) or oxaliplatin (10 μ mol/L) for another 24 hours. Cell viability, intracellular reactive oxygen species (ROS) levels, and apoptotic index were detected by resazurin assay, dihydroethidium (DHE) staining, and Annexin V/ propidium iodide (PI) staining, respectively. Protein expressions of the antioxidant defense mechanism (Nrf-2 and HO-1) and pro-apoptotic (PARP1 cleavage and Bax) and anti-apoptotic (BCL-2) pathways were

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



examined with immunoblotting. Cervical cancer SiHa cells and colorectal cancer HT29 cells were applied to investigate the interaction of formononetin with anticancer activities of oxaliplatin or paclitaxel.

Results. Formononetin at 20 and 40 $\mu\text{mol/L}$ significantly reduced the viability loss and ameliorated ROS overproduction in oxaliplatin- and paclitaxel-damaged ND7/23 DRG neurons, accompanied by the augmentation of the antioxidant defense Nrf-2/HO-1 pathway. Oxaliplatin induced apoptotic index and increase in Bax/BCL-2 ratio and PARP1 cleavage in ND7/23 DRG neurons, that were inhibited by the pre-treatment of formononetin. Additionally, formononetin did not affect the cytotoxicity of paclitaxel and oxaliplatin in cancer cells.

Discussion. In conclusion, formononetin demonstrated neuroprotective potential for preventing oxaliplatin- and paclitaxel-induced CIPN by alleviating oxidative stress and apoptosis. With its great antioxidant potential, formononetin exhibits stronger neuroprotective activities against oxaliplatin-induced oxidative stress and neurotoxicity than against paclitaxel.

P465

Vagus nerve stimulation ameliorates cortical spreading depression via activation of locus coeruleus

Ms Tzu-Chiao Wei

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Tzu-Chiao Wei has just completed her first year of master degree in pharmacology at National Yang Ming Chiao Tung University(NYCU), instructed by A/prof. Yen. She was honored with a scholarship award for academic excellence in her first year. In addition to academic pursuits, Tzu-Chiao is a licensed respiratory therapist with a specialization in critical care medicine and used to work as a Clinical Research Coordinator (CRC) in Cardiology Department at Taipei Veterans General Hospital

Her current research focuses on the preclinical study of migraine, which she has made some interesting discovery and is eager to share.

Vagus nerve stimulation ameliorates cortical spreading depression via activation of locus coeruleus

Jiin-Cheng Yen¹, Tzu-Chiao Wei¹ & Shih-Pin Chen^{2,3}. Inst Pharmacol¹ & Inst Clin Med², Natl Yang Ming Chiao Tung Univ, Taipei, Taiwan; Dept Neurol, Taipei Veterans General Hospital³, Taipei, Taiwan.

Introduction. Cortical spreading depression (CSD), suggesting to cause inflammatory responses and vascular changes in cerebral cortex, is the underlying mechanism of migraine aura and may serve as a therapeutic target of migraine. Vagus nerve stimulation (VNS) has been approved for the treatment of neurological disorders including migraine. We have previously demonstrated that VNS caused suppressive effect, associated with activation of the locus coeruleus (LC), on CSD frequency and cyclooxygenase-2 (COX-2) expression in cerebral cortex. However, the role of LC in VNS-elicited attenuation of CSD-induced neuroinflammation remains to be elucidated.

Aims. This study aimed to investigate whether auricular VNS (aVNS), a non-pharmacologic therapy approved for migraine treatment, could ameliorate the CSD-induced responses in cerebral cortex via LC-dependent mechanism.

Methods. Auricular VNS (five consecutive 2-minute stimulation at 25 Hz, 0.42 mA with 5 minutes apart) was delivered to unilateral auricular concha of C57BL/6 mouse (6-8 weeks) anesthetized by 4% isoflurane (maintained with 1.5%). CSD was induced by topical application of 300 mM KCl on skull thinned with an electric drill.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Results. Our results revealed that aVNS significantly suppress KCl-evoked CSD frequency (/h) (6.6 ± 0.5 vs. 4.2 ± 0.8 , $p < 0.05$) and attenuate CSD-induced increase of cortical COX-2 level (fold change of sham control) (0.93 ± 0.19 vs. 0.58 ± 0.12 , $p < 0.05$). In addition, aVNS could increase the number of cFOS⁺ neurons in LC (per 10000 μm^2) (1.9 ± 1.5 vs. 6.8 ± 0.3 , $n=2$). It suggests aVNS may attenuate CSD-induced neuroinflammation via activation of the LC. We further found that aVNS-elicited attenuation of CSD frequency and COX-2 expression could be inhibited by chemical lesion of the LC with intraperitoneal injection of DSP4. In conclusion, our results suggest aVNS may ameliorate KCl-evoked CSD generation and COX-2 expression via activation of LC-dependent pathway.

Discussion. Our previous study demonstrated that cervical VNS can attenuate CSD-induced increase of COX-2 expression in cerebral cortex via activation of the nucleus tractus solitarii (NTS) in rats. It requires further study on whether aVNS-triggered LC activation is mediated by NTS-dependent mechanisms.

P467

Economic impact of increasing TPMT testing rates prior to thiopurine drug therapy

Ms Bella Ianni

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Bella is a final year Bachelor of Pharmacy student at The University of Sydney. This year she completed her honours degree under the supervision of Professor Christine Lu and Dr Edwin Tan. Her research focuses on investigating the opportunity for pharmacogenetic testing implementation in Australia.

Economic impact of increasing TPMT testing rates prior to thiopurine drug therapy

Bella Ianni¹, Chin Hang Yiu^{1,2}, Edwin C K Tan^{1,2}, Christine Y Lu^{1,2,3}. Sydney Pharm School, The Univ of Sydney¹, Sydney, NSW, Australia; Kolling Institute², The Univ of Sydney and Northern Sydney Local Health District, Sydney, NSW, Australia; Dept of Pharm, Royal North Shore Hospital³, St Leonards, NSW, Australia.

Introduction. Testing *thiopurine methyltransferase (TPMT)* status to guide initial thiopurine drug dose is recommended to reduce the risk of moderate to severe, potentially fatal myelosuppression in intermediate and poor *TPMT* metabolisers.

Aims. This study aimed to measure current Australian *TPMT* testing utilisation rates based on self-reported ancestry, and predict the economic impact that increasing these rates to realistic and international standards may have on adverse drug reaction (ADR)-related hospitalisations.

Methods. Linked data including the Pharmaceutical Benefits Scheme, Medicare Benefits Schedule (MBS) and 2021 Census accessed at the Person Level Integrated Data Asset at the Australian Bureau of Statistics DataLab was utilised in this study. *TPMT* testing rates were estimated by determining *TPMT* testing incidence from 07/2011–12/2022 (MBS) amongst adult thiopurine drug users between 01/2020–12/2022 (PBS; Census). Average cost per hospitalisation was determined from the Australian Institute of Health and Wellness (\$5,527) and average cost of testing was derived from the MBS (\$43.70). Proportion of poor or intermediate metabolisers were derived from international pharmacogenomic guidelines and the literature was used to determine that 50% to 90% of poor or intermediate metabolisers are expected to experience ADRs. The economic impact of increasing testing rates to 50% was estimated using this data.

Results. The *TPMT* testing rate in Australia was found to be 32.5% amongst thiopurine drug users ($n=62,574$). We estimated that this rate captured only 34% of poor or intermediate metabolisers. Considering both increasing *TPMT* testing costs and

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



reduction in ADR-related hospitalisations, increasing the *TPMT* testing rate to 50% could lead to an overall saving of \$2.19-\$4.29 million per year.

Discussion. Improving the *TPMT* testing rate prior to thiopurine drug initiation could lead to a reduction in ADR-related hospitalisations and associated costs. Further research investigating *TPMT* phenotypes, the barriers to utilisation of established pharmacogenetic testing services as well as the incidence of thiopurine-induced ADRs in Australia is needed to evaluate real-world economic and clinical impact.

P468

Self-pharmacogenomic testing increases pharmacy student confidence for future delivery of pharmacogenomic services

Ms Toni Michael

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Toni is a PhD student at the University of Sydney, School of Pharmacy. Her research is focused on understanding factors which contribute to the variability in urate response to gout medications and ovarian response to IVF medications (supervised by Dr. Sophie Stocker). She has received two awards for oral conference presentations.

Self-pharmacogenomic testing increases pharmacy student confidence for future delivery of pharmacogenomic services

Toni Michael¹, Ruby Soueid¹, Pete Yeap¹, Fanfan Zhou¹, Stephen Hughes¹, Betty Chaar¹, Rose Cairns¹, Kellie Charles¹, Sophie Stocker¹. School of Pharmacy, Faculty of Medicine & Health, The University of Sydney¹, Sydney, NSW.

Introduction. The use of pharmacogenomic (PGx) testing in Australian healthcare settings is hindered by practitioners' poor confidence in interpreting and applying PGx test results. Pharmacists contribute to the implementation and delivery of PGx services. Integration of PGx in pharmacy degrees is needed, and may require innovative educational methods to develop students' confidence. Experiential methods, such as providing students with the opportunity to undergo their own PGx test, may help improve the confidence of future pharmacists in PGx service delivery.

Aims. To evaluate the impact of self-PGx testing on undergraduate pharmacy student confidence in PGx.

Methods. Second-year pharmacy students (N=258) completed a novel PGx education module that offered a free PGx test (myDNA Life Pty Ltd) to improve student familiarity with PGx testing. PGx test results were not included in learning activities. Students completed surveys with Likert-scale questions before and after the PGx module to assess self-reported confidence in applying PGx. Avatars were used to link results (N=128, 50%), which were assessed using descriptive statistics and paired T-tests.

Results. PGx testing was completed by 100 of 128 students (78%). Perceived confidence in designing a PGx-guided dose regimen improved by 58% in students that underwent PGx testing and 46% in students that didn't. Similarly, confidence in communicating PGx-guided recommendations to other healthcare professionals improved by 52% in students that underwent PGx testing and 46% in students that didn't. Further, confidence in counselling patients on the ethical implications of PGx improved by 38% in students that underwent PGx testing and 21% in those that didn't.

Discussion. This study suggests that innovative educational methods, in particular providing students with the opportunity to undergo PGx testing, can supplement pharmacy curricula by supporting confidence in applying new PGx knowledge. Students with the experience of PGx testing considered themselves competent to empathise with future patients who also undergo PGx testing. Exploration of integrating student PGx test results within other learning activities as part of the PGx education module is required.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P469

Elucidating Psychiatric Disorder, Antipsychotic, and Metabolic Syndrome Genetic Connection in GWAS

Mr Rory Shepherd

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Rory Shepherd is a Master's by Research student in Pharmacogenomics at the University of South Australia. Their research focuses on the genetic basis of antipsychotic-induced weight gain, specifically investigating the links between clozapine metabolism and metabolic syndrome in schizophrenia patients using Genome-Wide Association Studies. Rory's academic background includes a Bachelor of Health and Medical Science (Advanced) from the University of Adelaide. They have also earned a Postgraduate Diploma in Biostatistics. Currently, Rory is conducting research that combines pharmacogenomics, psychiatry, and metabolic health. Their work aims to uncover genetic factors influencing individual responses to clozapine treatment, potentially leading to more personalized and effective therapies for schizophrenia patients.

Elucidating Psychiatric Disorder, Antipsychotic, and Metabolic Syndrome Genetic Connection in GWAS

Rory Shepherd^{1,2,3}, David Stacey^{1,2,3}, Jack Janetzki², Wern Chern Chai², Scott Clark⁴, Elina Hypponen^{1,2,3}, Vijayaprakash Suppiah^{1,2}

¹Australian Centre for Precision Health, University of South Australia, ²UniSA Clinical and Health Sciences, University of South Australia, ³South Australian Health and Medical Research Institute, ⁴Faculty of Health and Medical Sciences, University of Adelaide

Introduction. Metabolic syndrome (MetS) and psychiatric disorders (PDs) share a complex relationship, with interactions between genetic, environmental, and lifestyle factors. Second-generation antipsychotics (SGA) can exacerbate metabolic disturbances in vulnerable individuals. Genome-wide association studies (GWAS) have become powerful tools for investigating the shared genetic underpinnings of these linked conditions.

Aims. This review aims to: (1) assess the GWAS literature for genetic connections between MetS and PDs; (2) assess the GWAS literature for genetic links between SGA induced MetS and PDs.

Methods. A systematic literature search was conducted using PubMed, Scopus, and Web of Science. Eligible studies included original research articles employing GWAS data and genetic-statistical techniques such as mendelian randomisation (MR). Publications were screened by two researchers individually before inclusion.

Results. Numerous studies have demonstrated significant genetic overlap between psychiatric disorders, particularly schizophrenia, bipolar disorder, major depressive disorder, and MetS or related metabolic comorbidities. Biological pathways implicated include dopamine and insulin signalling, lipid metabolism, glucose homeostasis, and inflammation. MR studies have suggested a potential causal effect of higher BMI and metabolic dysregulation on the risk of specific psychiatric symptoms, while the evidence for a causal effect of psychiatric disorders on metabolic traits remains inconsistent. GWAS of antipsychotic-induced weight gain have identified genetic loci and pathways involved in energy balance, adipogenesis, and insulin signalling.

Discussion. Understanding the shared genetic architecture between psychiatric disorders, antipsychotics, and MetS is crucial for developing targeted interventions. However, the complexity of these conditions and limitations of current GWAS methodologies present challenges. Future research should focus on integrating multi-omics data and employing advanced methods to model complex interactions between genetic, environmental, and clinical factors, leading to personalized risk prediction and treatment approaches.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P470

Implementing CYP2C19-guided clopidogrel therapy: a scoping review of pharmacogenomic testing services

Mr Tark Patel

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Tark is a 4th year undergraduate pharmacy honours student at the University of Sydney. His honours project this year focussed on CYP2C19-guided antiplatelet therapy and the value it can provide within clinical care. Tark has also worked across community and hospital pharmacy during the 4 years of his degree and is looking forward to internship next year as the next step towards becoming a registered pharmacist.

Implementing CYP2C19-guided clopidogrel therapy: a scoping review of pharmacogenomic testing services

Tark J. Patel¹, Eman Wehbe¹, Stephen Hughes¹, Asad E. Patanwala¹, Leonard Kritharides², Ronald Trent³, Sean Lal⁴, Sanjay Patel⁴, Sophie L. Stocker¹. Sch of Pharm, Uni of Sydney, NSW¹; Concord Repat Hosp, Sydney, NSW²; Dept of Medical Genomics, Royal Prince Alfred Hosp, Sydney, NSW³; Dept of Cardiology, Royal Prince Alfred Hosp, Sydney, NSW⁴.

Introduction. CYP2C19 testing helps personalise clopidogrel therapy and reduces the risk of a secondary myocardial infarction in poor metabolisers. However, a lack of understanding on how to best deliver such a service within hospital and community settings has been a major barrier to clinical implementation.

Aim. To identify and evaluate pharmacogenomic testing services to inform the design and delivery of CYP2C19 testing services in relation to clopidogrel therapy.

Methods. The SCOPUS, CINAHL, Medline, PubMed and EMBASE databases were searched from inception to 25th March 2024. The search strategy utilised “pharmacogenomic”, “community”, “hospital”, and “implementation model” terminology. Studies describing the implementation of a pharmacogenomic testing service for CYP2C19 and clopidogrel as the sole gene-drug pair or part of a wider panel of genes were included.

Results. Of the 2,455 articles screened, 37 were eligible for study inclusion (14 community, 22 hospital and 1 in both settings). A multi-disciplinary approach to service implementation was critical in all studies, with particular importance of pharmacist involvement alongside physicians, laboratory staff and nurses. Additionally, pre-implementation education and training for clinical staff was essential in most studies (22/37, 59%). This was delivered through a variety of methods including in-person training on point-of-care devices, online seminars and webinars, and educational resources linked within the electronic health records for clinicians to access. Although CYP2C19 test results were most commonly documented and reported electronically by the laboratory, they were infrequently integrated within clinical decision support systems to guide decision making at the point of prescribing.

Discussion. Pre-implementation training and education, a multidisciplinary team involving pharmacists, and electronic documentation and notification of results are common elements of CYP2C19 testing services for guiding clopidogrel therapy. The ability to access genotype results across various healthcare disciplines, and improved integration of genotype results within clinical decision support systems has the potential to further the practical application of CYP2C19 testing.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P471

Exploring the nicotine metabolite ratio among people who smoke or vape

Miss Min-Tz Weng

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Exploring the nicotine metabolite ratio among people who smoke or vape

Min-Tz Weng¹, Qiuda Zheng², Shakti Shrestha¹, Yao Deng¹, Coral E Gartner³, Wenqing Fan¹, Phong K Thai², Kathryn J Steadman¹. Sch of Pharm, Univ of Queensland¹, Brisbane, QLD, Australia; Queensland Alliance for Env Health Sci, Univ of Queensland², Brisbane, Australia; Sch of Pub Health, Univ of Queensland³, Brisbane, QLD, Australia.

Introduction. The nicotine metabolite ratio (NMR), calculated as the ratio of 3-hydroxycotinine (3HC) to cotinine (COT), indicates activity of CYP2A6 enzyme in metabolising nicotine. There has been limited consideration of variation in nicotine metabolism among people who use nicotine vaping products (NVPs).

Aims. This study aimed to explore NMR values in a cohort of individuals who either smoked tobacco or used NVPs.

Methods. A secondary analysis was conducted using data of 43 participants from a prospective observational study of 74 participants. Their 24-hour urine samples were analysed for 3HC and COT for calculation of NMR and comparison with participant gender, age, ethnicity, nicotine source, nicotine and its metabolites levels and nicotine product use (cigarettes or puffs per day).

Results. NMR values were higher in female participants than male participants. NMR values demonstrated a moderate correlation with cigarettes per day ($r= 0.5243$; $P= 0.0122$), but no association was observed with NVP puffs per day. Participants were categorised as either slower or faster metabolisers using a threshold value of 2.5, chosen because it evenly divided the cohort. Those with faster metabolism (higher NMR values) exhibited a higher total quantity of nicotine and its metabolites, as well as elevated COT and 3HC levels than their counterparts with slower metabolism (lower NMR values). There was no difference in NMR between people who smoked and people who used NVPs.

Discussion. Higher urine NMR values were observed in females and in individuals with higher total nicotine intake. NMR does not serve as a biomarker for distinguishing between people who smoke and people who use NVPs.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P472

The Australian Public's Current Thoughts on Pharmacogenomics

Miss Richelle Breed

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

The Australian Public's Current Thoughts on Pharmacogenomics

Richelle Breed^{1,2}, Joanne Voisey², Esther Lau³, Yasmin Antwertinger¹, Annalese Semmler¹. School of Clin Scien¹, Faculty of Health, Queensland Univ of Technology, Brisbane, QLD; Centre for Genomics and Personalised Health, School of Biomedical Sciences², Faculty of Health, Queensland Univ of Technology, Brisbane, QLD; School of Pharmacy³, Univ of Queensland, Brisbane, QLD

Introduction. Pharmacogenomics is the study of how a person's genetic makeup influences their response to medications. This knowledge allows for medication optimisation, by minimising adverse drug reactions and maximising therapeutic efficacy. While pharmacogenomic knowledge advances, the implementation into Australian clinical practice has been slow. For successful implementation, it's important to consider the current understandings and perceptions of pharmacogenomics from consumers. Within Australia, there's limited current insight into the thoughts and preferences of consumers regarding pharmacogenomics.

Aims. This study aimed to understand the general Australian public's current knowledge and perception of pharmacogenomics.

Methods. A mixed-method online survey with 54 questions was distributed via Qualtrics. Questions ranged from multiple choice, Likert scale and open-text options. A calculated sample size of 600 was needed to give a 95% confidence level with a 4% margin of error based on Australia's population size of 26 million in 2023. Descriptive and inferential statistics were used for quantitative data analysis, while thematic analysis was applied to qualitative data.

Results. Preliminary data from 781 participants was analysed. Most respondents (76.46%, n=591) had never heard of pharmacogenomics. Approximately 10% (n=77) of respondents were still unsure about pharmacogenomics and its benefits even after receiving a definition and blurb. This awareness and understanding of pharmacogenomics were further explored in focus groups/semi-structured interviews to identify themes.

Discussion. A previous study from over a decade ago found that the Australian public had limited awareness regarding pharmacogenomics, and this lack of awareness amongst the population was still evident in our current 2023/2024 survey (Haddy et al, 2010).

Haddy CA, Ward HM, Angley MT et al (2010) Res Social Adm Pharm 6:221-231.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P473

Utilisation and associated factors of TPMT testing among thiopurine users in Australia

Mr Chin Hang Yiu

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Benson is a PhD candidate at the Sydney Pharmacy School. His primary areas of research interest include clinical pharmacy, pharmacoepidemiology and health services research. He is also a registered pharmacist with experience in both community and hospital pharmacy.

Utilisation and associated factors of TPMT testing among thiopurine users in Australia

Chin Hang Yiu^{1,2}, Bella Ianni^{1,2}, Kenji Fujita¹, Edwin C.K. Tan², Sarah N. Hilmer¹ & Christine Y. Lu^{1,2,3}

Kolling Institute, Univ of Sydney & NSLHD¹, NSW, Australia; School of Pharmacy, Univ of Sydney², NSW, Australia; Dept of Pharmacy, Royal North Shore Hosp³, NSW, Australia

Introduction. Thiopurine drugs are metabolised by thiopurine methyltransferase (*TPMT*) and low *TPMT* activity can result in severe adverse drug reactions. The detection of genetic polymorphisms in *TPMT* gene is one of the current two pharmacogenetic (PGx) tests that are subsidised by the Medicare Benefits Schedule (MBS) in Australia.

Aims. To assess the prevalence of *TPMT* testing among thiopurine users, and explore factors associated with undergoing *TPMT* testing in Australia.

Methods. This retrospective cohort study utilised administrative data from the Pharmaceutical Benefits Scheme (PBS), MBS, and the 2021 Census, accessed via the Person Level Integrated Data Asset (PLIDA) at the Australian Bureau of Statistics (ABS) DataLab. Thiopurine users aged 18 years or above were identified using PBS data and exposure to *TPMT* testing was determined using MBS data. Multivariate logistic regression was performed to identify factors associated with *TPMT* testing.

Results. A total of 62,574 thiopurine users were identified between 2020 and 2022. Of these, 20,327 (32.5%) underwent *TPMT* testing (2011 – 2022). The most significant factor associated with *TPMT* testing was having at least one thiopurine medication prescribed by a medical specialist (adjusted odds ratio [aOR] 2.12, 95% CI 2.02 – 2.22), compared to having medication solely prescribed by general practitioners (GPs). Other significant factors included having no chronic health conditions (aOR 1.18, 95% CI 1.13 – 1.24) and a higher educational attainment (aOR 1.11, 95% CI 1.06 – 1.11). Compared to living in major cities, users living in remote areas were significantly less likely to undergo testing (aOR 0.49, 95% CI 0.39 – 0.60).

Discussion. The low utilisation of guideline-recommended *TPMT* testing in Australia is concerning. Our findings suggest the need for targeted interventions to improve *TPMT* testing and address disparities in testing.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P474

Utilisation and associated factors of HLA-B*5701 testing among abacavir users in Australia

Mr Chin Hang Yiu

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Benson is a PhD candidate at the Sydney Pharmacy School. His primary areas of research interest include clinical pharmacy, pharmacoepidemiology and health services research. He is also a registered pharmacist with experience in both community and hospital pharmacy.

Utilisation and associated factors of HLA-B*5701 testing among abacavir users in Australia

Chin Hang Yiu^{1,2}, Bella Ianni^{1,2}, Kenji Fujita¹, Edwin C.K. Tan², Sarah N. Hilmer¹ & Christine Y. Lu^{1,2,3}

Kolling Institute, Univ of Sydney & NSLHD¹, NSW, Australia; School of Pharmacy, Univ of Sydney², NSW, Australia; Dept of Pharmacy, Royal North Shore Hosp³, NSW, Australia

Introduction. Individuals carrying the human leukocyte antigen (*HLA*)-*B*5701* allele are significantly more likely to experience immune-mediated hypersensitivity reaction (HSR) of abacavir. The determination of *HLA-B*5701* status before initiating abacavir-containing therapy is one of the current two pharmacogenetic (PGx) tests that are subsidised by the Medicare Benefits Schedule (MBS) in Australia.

Aims. To assess the prevalence of *HLA-B*5701* testing among abacavir users, and to identify factors associated with its uptake in Australia.

Methods. This retrospective cohort study utilised administrative data from the Pharmaceutical Benefits Scheme (PBS), MBS, and the 2021 Census, accessed via the Person Level Integrated Data Asset (PLIDA) at the Australian Bureau of Statistics (ABS) DataLab. Abacavir users aged 18 years or above were identified using PBS data and exposure to *HLA-B*5701* testing was determined using MBS data. Multivariate logistic regression was performed to identify factors associated with *HLA-B*5701* testing.

Results. A total of 5,463 abacavir users were identified between 2020 and 2022. Of these, 1,411 (25.8%) underwent *HLA-B*5701* testing (2011 – 2022). Significant factors associated with its uptake included a younger age (adjusted odds ratio [aOR] per year 0.99, 95% CI 0.99 – 0.99) and male gender (aOR 1.67, 95% CI 1.37 – 2.08). Individuals who were born in Australia were more likely to undergo testing (aOR 1.27, 95% CI 1.08 – 1.51). Other factors such as comorbidities, income level, highest educational attainment and types of prescribers were not significantly associated with uptake of testing.

Discussion. The low utilisation of guideline-recommended *HLA-B*5701* testing in Australia is concerning. Our findings suggest the need for targeted interventions to improve *HLA-B*5701* testing and address disparities in testing.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P475

Drug interactions, adverse effects and pharmacogenomic implications of polypharmacy in cystic fibrosis

A/Prof Vincent Chan

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Vincent is a pharmacist and pharmacy academic with backgrounds in pharmacy, public health and biomedical sciences. He is currently the Assistant Associate Dean (Pharmacy) at RMIT University and also holds appointments at Austin Health and Queensland University of Technology. His research focuses on pharmacy practice/quality use of medicine, pharmacist roles and interventions, and pharmacotherapeutics.

Drug interactions, adverse effects and pharmacogenomic implications of polypharmacy in cystic fibrosis

Theeba Thiruchelvam^{1,2}, Chiao Xin Lim², Vijayaprakash Suppiah³, Vincent Chan², Geshani Jayasuriya¹, Peter Wark⁴, Courtney Munro⁵, Kingsley Coultard³

¹John Hunter Hospital, New Lambton, NSW; ²RMIT University, Melbourne, VIC; ³University of South Australia, Adelaide, SA; ⁴The Alfred Hospital, Melbourne, VIC; ⁵Murdoch Children's Research Institute, Parkville, VIC

Introduction: Cystic fibrosis (CF) is a genetic, multiorgan system disease with a high treatment burden. The recent introduction of CF transmembrane conductance regulator (CFTR) modulators has led to an increase in life expectancy and better health outcomes for people with CF (PwCF). However, drug-drug interactions (DDI) have become more prevalent with potential to negatively impact PwCF's quality of life. Exploring pharmacogenomic implications may help optimise prescribing for PwCF to maximise efficacy of medications and minimise adverse effects.

Aim: To

investigate the DDIs, adverse effects and pharmacogenomic implications of polypharmacy in PwCF.

Method: An audit of adverse effects of CFTR modulators – elexacaftor, tezacaftor and ivacaftor (ETI), and concomitant medications was conducted, using data from the FDA Adverse Event Reporting System (FAERS) database. All the medications were categorised as inhibitors, inducers, substrates of Cytochrome P-450 (CYP) enzymes, according to Flockhart drug interaction table.¹

Result: 10,500 case reports of ETI adverse events were collated from the FAERS database. ETI are substrates for CYP3A4/5 enzyme and Ivacaftor is an inhibitor of CYP2C9 and weak inhibitor of CYP3A4/5. Ninety concomitant medications which are metabolised by the CYP enzymes were identified. Both inhibitor and inducer medications of CYP3A4/5 enzymes were also ascertained.

Discussion: ETI is

the mainstay treatment for the majority of PwCF, therefore potential DDI may result in adverse effects and even treatment failure. Having identified potential DDI, this data can be used as basis to further explore the utilisation of pharmacogenomic testing for PwCF.

Reference: 1. Flockhart DA et al (Updated 2021) <https://drug-interactions.medicines.ie.edu/>. Accessed 29.05.24.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P476

The Pharmacogenomics of Cisplatin Induced Ototoxicity

Mr David Harman

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

The Pharmacogenomics of Cisplatin Induced Ototoxicity

David B Harman¹, Chiao Xin Lim², Vidya Menon³, Ganessan Kitchenadasse³, Vijayaprakash Suppiah¹. ¹UniSA Clinical and Health Sciences, University of South Australia, SA, Australia; ²School of Health and Biomedical Sciences, RMIT University, VIC, Australia; ³Flinders Medical Centre, Bedford Park, SA, Australia

Introduction. Platinum-based chemotherapy is one of the most common forms of treatment for many kinds of cancers in both adult and paediatric patients. It is well known that platinum-based treatment, especially cisplatin, has a high risk of ototoxicity resulting in irreversible hearing loss in many patients. By identifying genes which put a patient at higher risk of ototoxic side effects, genetic screening can be performed prior to treatment to better inform medication and dosage choices to preserve quality of life.

Aims. To analyse the literature to identify genetic variations with high levels of evidence supporting a significant influence on the likelihood of ototoxic side effects occurring from the use of cisplatin.

Methods. A literature review was conducted using the databases PubMed, Scopus and Web of Science using the terms “(cisplatin OR platinum) AND (ototoxicity OR “hearing loss”) AND (genetic OR pharmacogenomic)” returning 292 results on PubMed, 234 results on Scopus and 171 results on Web of Science. Results were then filtered to only include articles in the English language and duplicates were removed. Results were then filtered into only those relevant to the aims of the review.

Results. 42 studies were included in the final review. The genes/single nucleotide polymorphisms (SNPs) which had shown a statistically significant positive or negative association with ototoxicity and had been replicated in more than one study were gathered into a table i.e. ACYP2 rs1872328 (Drogemoller et al, 2018; Vos et al, 2016; Xu et al, 2015), TPMT rs12201199, rs1142345, rs1800460 (Pussegoda et al, 2013; Ross et al, 2009; Yang et al, 2013).

Discussion. The literature has shown that there is a significant genetic link to an increased chance of ototoxic side effects. The SNPs gathered from this literature view used in tandem with the genetic testing of patients prior to treatment with Cisplatin could provide a better understanding of a patient’s likelihood of developing hearing loss during treatment. Treatment plans could be better tailored and the quality of life of patients could be preserved.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P477

The development of an aggregated medication review taxonomy: a systematic scoping review

Mr Timothy Yeo

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

The development of an aggregated medication review taxonomy: a systematic scoping review

Timothy Z Yeo¹, Margaret Jordan^{1,2}, Rebekah J Moles¹ & Timothy F Chen¹, School of Pharmacy, Faculty of Medicine and Health, The University of Sydney¹, Camperdown, NSW, Australia, Faculty of Science, Medicine and Health, University of Wollongong², Wollongong, NSW, Australia

Introduction/Aim: An established and validated medication management review system is core to identifying, preventing and addressing drug-related problems (DRPs). This study aims to review current DRP classification systems on their content and validation, and to develop an aggregated medication review taxonomy for recommendations and interventions.

Method: A systematic search using MEDLINE, International Pharmaceutical Abstracts (Ovid), Web of Science, Scopus, and EMBASE was performed. Studies were eligible for inclusion if they outlined development or comparisons between DRP classification systems or reported measurement properties of systems for validation and reliability and had to be full-text articles in English language. The development of our aggregated taxonomy followed a systematic synthesis of current classifications in literature and clinical experiences of the research team.

Results: From the 699 included articles, 20 DRP classification systems were identified. The design of classifications was diverse, ranging from 8 to 97 categories organized into 3 main identifiable sections. 13 out of 20 systems reported the utilization of validity or reliability indices, primarily via metrics of Cohen's and Fleiss' kappa coefficients. Only 8 systems consisted of an 'interventions' classification, which served as the basis for the aggregated taxonomy. The final developed aggregated taxonomy consists of 4 main categories with 74 sub-categories for clinical coding.

Conclusion: The review underscores the need for standardized and validated DRP classification systems along with a current lack of robust recommendations and interventions classification. As such, the developed aggregated taxonomy for recommendations and interventions shows great potential for clinical use and is due for content validation and reliability testing in further studies.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P478

Impact of medicines shortages in a developing country, Sri Lanka

A/Miss Nimmi Dilsha

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

I am a PhD candidate at QUT, as well as a registered pharmacist and higher education academic in Sri Lanka. My research interests are centered on pharmacy practice-based research.

Impact of medicines shortages in a developing country, Sri Lanka

Rajapaksha AN Dilsha¹, Esther Lau^{1,2}, Marea Patounas¹, Anne T Matthias³, Rohini Fernandopulle⁴, Lisa Nissen^{1,2}. Queensland University of Technology, Brisbane, Australia¹; University of Queensland, Brisbane Australia² University of Sri Jayewardenepura, Colombo, Sri Lanka³, General Sir John Kotelawala Defence University, Colombo, Sri Lanka⁴

Introduction. Comprehending the implications of medicines shortages is crucial for addressing medicines shortages; but limited literature is found from developing countries (Shukar et al., 2021). The detailed evidence from healthcare professionals could address the complexity of the impact of medicines shortages on patients and healthcare professionals in developing countries, such as Sri Lanka, where there are limited research approaches to investigate the impact of medicines shortages.

Aims. This study explored healthcare professionals' perceptions of the impact of medicines shortages in Sri Lanka.

Methods. Healthcare professionals (n=38) working in State sector hospitals were interviewed. The interviews were transcribed and translated into English, and then analysed for thematic concepts using Leximancer.

Results. Healthcare professionals' perceptions of the impact of medicines shortages on patients were primarily clinical and economic factors (e.g. treatment failures, impact due to substitutions, out-of-pocket payments). The situational changeovers of patients' emotions (eg: anger, frustration) led to the assault of healthcare professionals by patients (e.g.: scolding and hitting). Other impacts on healthcare professionals were related to personal and work-related factors (e.g.: emotional constraints, additional workload and deviation from standard professional practice).

Discussion. The insight gained from health professionals highlights the requirement of multifaceted support for both healthcare professionals and patients. A legislative approach (e.g.: establishment of medicines shortages notification system, standardisation of substitution practices) could minimise the impact of medicines shortages on healthcare professionals. Alongside this, the enhancement of patient awareness of medicine shortages and medication/ disease management practices during medicine shortages could benefit patients. However, an investigation of patients' perspectives on medicines shortages is required to establish effective strategies to mitigate the impact of medicines shortages.

Shukar S et al. (2021) Front Pharmacol 12:693426

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P479

Evaluation of electronic partnered pharmacist medication prescribing: a multi-centre matched cohort study

Ms Hana Amer

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Hana Amer is a Senior Pharmacist at SA Pharmacy and PhD Candidate at the University of South Australia. Hana's PhD focuses on evaluating the effectiveness and economic consequences of collaborative pharmacist prescribing across SA public hospitals.

Evaluation of electronic partnered pharmacist medication prescribing: a multi-centre matched cohort study

Hana Amer^{1,2}, Sally B Marotti^{1,2}, Sharon Goldsworthy², Imaina Widagdo¹, Joshua M Inglis^{4,6}, Jacinta L Johnson^{1,2}, Matthew Pegoli², Ying Li Liang², Hayley Vasileff², Julian Zurauskas⁵, Lisa M Kalisch Ellett¹. University of South Australia¹, SA Pharmacy², Flinders Medical Centre⁴, Lyell Mc Ewin Hospital⁵. Adelaide University⁶. All sites: Adelaide, SA, Australia.

Introduction. Partnered pharmacist medication prescribing (PPMP) models have been implemented in Australian hospitals and involve credentialed pharmacists working closely with doctors and patients to develop patient medication plans and chart or prescribe medications. Most studies to date have been conducted in paper-based prescribing environments and data regarding the impact of PPMP using electronic medical records (EMR) is lacking.

Aims. To determine whether PPMP on admission is associated with a change in the rate and severity of medication discrepancies compared to independent medical prescribing in the setting of an EMR.

Methods. A matched cohort study was conducted using EMR data for 120 patients aged ≥ 18 years admitted to two South Australian public hospital acute medical units from September 2023 to March 2024. Each case (patient that received PPMP) was matched with one control (usual care) for admitting unit, sex, age, date of admission, triage category and number of medications taken prior to admission. The EMR was reviewed to identify medication discrepancies, which were defined as 'any unexplained difference between the documented medication history and medications charted on admission'. A sample of 40 cases and controls were reviewed by an independent expert panel of clinicians to determine the potential for harm associated with the discrepancies, using the Harm Associated with Medication Error Classification (HAMEC) tool. HAMEC scores ≥ 3 indicate potential for serious or severe harm.

Results. In the PPMP group, a total of 921 medication orders were prescribed on admission, compared to 731 medications in controls. In the PPMP group, seven unexplained discrepancies (0.8% of medication orders) were identified compared to 203 discrepancies (28% of medication orders) in the control group. No patients in the PPMP group had a HAMEC score of 3 or above (potentially serious or severe patient harm) compared to 8 of the 20 patients (40%) in the control group.

Discussion. There were fewer medication discrepancies per medication order prescribed in the PPMP group compared to usual care, and the potential for harm associated with discrepancies was rated lower in the PPMP group. Overall, the rates of discrepancies identified per medication order prescribed was lower than the rates reported in the literature for PPMP in paper-based prescribing settings.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P480

Prospective identification of medication harm in geriatric inpatients using a trigger tool

Dr Nazanin Ghahreman-Falconer

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Prospective identification of medication harm in geriatric inpatients using a trigger tool

Nazanin Ghahreman-Falconer^{1,2}, Jonathan Yong Jie Lam^{1,2}, Andre Wang¹, Michael Barras^{1,2}.

School of Pharmacy, The University of Queensland¹, Brisbane, QLD, Australia; Pharmacy Department, Princess Alexandra Hospital², Brisbane, QLD, Australia

Introduction. Medication harm (MH) causes patient morbidity and is a major healthcare burden. The prevalence of MH is often based on an incomplete, retrospective chart review or spontaneous reporting, reliant on busy clinicians. A practical and clinically relevant method to detect MH is required. A trigger tool (TT) offers a solution. This study aimed to evaluate a modified TT to prospectively detect MH and determine the prevalence and severity of MH in a geriatric population.

Methods. An international TT was peer evaluated and modified for use in a geriatric ward of a quaternary hospital. Patients were recruited over a 6-month period. The TT was applied to prospectively help identify MH, which was assessed for causality and severity. Positive predictive values (PPV) were estimated for each trigger to determine its sensitivity in identifying MH. Informed consent was obtained from all participants through completion of a written consent form, after a full explanation of the protocol design.

Results. Fifty patients consented, of which 16 (32%) patients experienced one or more MH events. A total of 257 triggers were activated (mean of 5.14 per patient) and 31 (12%) predicted an event. Of the 31 events, 19 (61.3%) events were rated as mild and 12 (38.7%) events were rated as moderate to severe. Most common events were bleeding/large bruising, major constipation, diarrhea, and vomiting. The triggers with the highest PPV included triggers T5 (bleeding/bruising), T9 (gastrointestinal disorders), and T11 (major constipation) with PPVs of 0.455, 0.238, and 0.286, respectively.

Discussion. A modified TT helped to detect MH in a geriatric population and will aid in identifying events in future studies.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P481

Pharmacist-led transition of care services in patients with cardiovascular disease

Dr Nazanin Ghahreman-Falconer

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Pharmacist-led transition of care services in patients with cardiovascular disease

Nazanin Ghahreman-Falconer^{1,2}, Keshia De Guzman^{1,2}, Holly Foot¹, Jared Miles¹, Neil Cottrell¹, Michael Barras^{1,2}.

School of Pharmacy, The University of Queensland¹, Brisbane, QLD, Australia; Pharmacy Department, Princess Alexandra Hospital², Brisbane, QLD, Australia

Introduction. Transition of care (ToC) is a critical time that requires effective management, especially for patients with cardiovascular disease, who have complex health needs. Pharmacists can play an integral role in improving medication safety and care coordination at ToC. This scoping review determined the types of pharmacist-led multidisciplinary ToC services and associated outcomes in patients with cardiovascular disease.

Methods. A systematic literature search of four databases; PubMed, Embase, CINAHL, and Scopus, was undertaken from inception until June 2023. Abstracts and full text were screened against eligibility criteria. Extracted data included study characteristics, ToC service descriptions, primary and secondary outcomes, limitations, and key findings. Study findings were synthesised narratively. The types of in-patient and post-discharge activities and their effect on patient outcomes were critiqued and presented

Results. Of the 1822 studies identified, 37 were included in the final review. The most common primary outcome reported was 30-day all cause readmissions (n=14). Pharmacist-led ToC services incorporated a diverse combination of inpatient and post-discharge activities. The most common in-patient activities included medication history and reconciliation, patient medication education, and medication review and optimisation. The most common post-discharge activities were medication review and optimisation, adherence assessments, and medication education. Multifaceted ToC services that involved inpatient and post-discharge activities demonstrated statistically significant changes in readmission rates and other patient reported outcomes.

Discussion. Future research should investigate the added value of post-discharge home visits, and culturally appropriate care, in cardiovascular ToC services. Policy makers should consider funding pharmacist-led ToC services that are evidence-based, and those which demonstrate positive outcomes for patients with cardiovascular disease.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P482

Electronic clinical pharmacy documents for quick and accurate clinical pharmacy performance measurement

Mr Huri Balikubiri

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Research: I am a Third-year PhD student enrolled at the University of South Australia. My research explores how clinical pharmacy governance can be informed and improved using routinely collected electronic data in Australian hospitals.

Personal History: I was born in the Democratic Republic of Congo and lived there until age five. I have grown up and currently live in Adelaide, South Australia.

Education: I completed the Bachelor of Pharmacy (Honours) program in 2020 at the University of South Australia for my undergraduate studies.

Occupation: I gained registration as a pharmacist in 2021 and I have been working as a rotational clinical pharmacist at the Modbury Hospital in South Australia since then.

Electronic clinical pharmacy documents for quick and accurate clinical pharmacy performance measurement

Huri Balikubiri¹, Anna Kemp-Casey¹, Andre Q Andrade¹, Richard Marotti². Clinical and Health Sciences, University of South Australia¹, Adelaide, SA, Australia; SA Pharmacy², Adelaide, SA, Australia

Introduction. Hospital-based clinical pharmacy services improve patient outcomes, reduce medication-related problems, and lower the cost of medication therapy. Measuring the provision of clinical pharmacy services is essential to ensuring quality. However, traditional methods are inefficient as they rely on manual reporting of performance measures.

Aims. This study examined the accuracy of using electronically generated clinical pharmacy progress notes, stored as files in hospital electronic medical record (EMR) systems, to measure the provision of clinical pharmacy admission, inpatient assessment, and discharge services.

Methods. A manual audit was performed on electronically generated clinical pharmacy progress notes completed by pharmacy staff for a random sample of 300 adults admitted to the three study hospitals between the 3rd of May and the 1st of November 2021. The audit identified the types of clinical progress notes completed, as indicated by the title of the progress notes, and the types of clinical pharmacy services documented within them. To determine the accuracy of utilising automated counts of different types of clinical pharmacy progress notes to indicate the completion of clinical pharmacy services, sensitivity, specificity, and positive predictive value were calculated using the manual audit as a gold standard.

Results. A total of 858 progress notes were audited, and 783 (91.3%) indicated the completion of clinical pharmacy admission, inpatient assessment, or discharge services. Automated counts of clinical pharmacy progress notes that were commonly utilised to document the completion of medication histories, medication chart reviews, and medication management on discharge demonstrated high specificity and positive predictive values (>98%) for admission, inpatient assessment, and discharge clinical pharmacy services, respectively. Sensitivity varied across types: medication history (98%), discharge medications (90%), and medication review (89%).

Discussion. Electronic clinical pharmacy progress notes provided an accurate measure of clinical pharmacy service provision in the study hospitals and can be used as reliable performance measures. Hospitals that utilise electronic clinical progress notes in EMRs may adopt a similar approach to derive accurate and effective performance measures.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P483

Feasibility and Acceptability of a Nurse-Pharmacist Post-Discharge Telehealth Heart Failure Service

Mr Joshua Bennetts

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Joshua is a clinical pharmacist and PhD candidate from the University of Newcastle. Joshua has a particular interest in cardio-oncology — an emerging field that focusses on mitigating cardiovascular disease secondary to cancer treatment. His research focusses primarily on pharmacist-led models of care to support people with cardiovascular disease and cancer as they transition between hospital and home.

Joshua has presented his research at national and international conferences and is an active member of the International Cardio-Oncology Society (IC-OS) pharmacist working group. Joshua is also a credentialed pharmacist who continues to provide domiciliary medication management review services for his community and has broad clinical experience across both hospital and community pharmacy.

Feasibility and Acceptability of a Nurse-Pharmacist Post-Discharge Telehealth Heart Failure Service

Joshua Bennetts^{1,2}, Cameron Robson³, Dawn McIvor³, Trent Williams³, Aaron Sverdlov^{2,3}, Doan Ngo^{1,2}. School of Biomedical Sciences and Pharmacy, University of Newcastle¹, Callaghan, NSW, Australia; Hunter Medical Research Institute², New Lambton Heights, NSW, Australia; Hunter New England Local Health District³, New Lambton Heights, NSW, Australia.

Introduction. Poor medication compliance, use of harmful medications and withdrawal of beneficial medications are common contributors to hospital readmissions and mortality for heart failure patients (HFPs). However, few studies have evaluated the implementation of a nurse-pharmacist model of care into a HFPs transition-of-care journey.

Aims. To determine the feasibility and acceptability of a nurse-pharmacist telehealth service for transition-of-care HFPs discharged from the John Hunter Hospital, Australia.

Methods. HFPs were referred to an existing telehealth service and offered medication reconciliation and education in addition to their usual care; a service we termed 'MedRec'. Primary outcomes were feasibility — measured by calculating recruitment and successful completion of a MedRec — and acceptability — measured by an investigator-developed survey. Secondary outcomes were medication-related issues detected during MedRec.

Results. In total 100 HFPs were offered a post-discharge MedRec. Mean age of patients was 68.5 years (± 14.2). HFPs were mostly male sex (62%). Pharmacist MedRecs were requested by 80% of HFPs. In total 62 MedRecs (77.5%) were performed; 9 HFPs declined MedRec during follow-up and an additional 9 HFPs were uncontactable. Mean time to MedRec following nurse referral was 10.98 days (± 9.74). At the time of MedRec, 25 recipients (40.3%) were experiencing drug-related toxicity or adverse events, 13 recipients (20.9%) were experiencing medication compliance issues, and undertreated comorbidities, such as symptomatic heart failure or chronic pain, was identified in 12 recipients (19.4%). Drug and/or disease management information was requested by 35 MedRec recipients (56.4%). Post-MedRec surveys were completed by 35 (56.5%) HFPs. All survey participants agreed that a telehealth MedRec was an acceptable form of education provision. Engagement with a pharmacist MedRec was perceived to ease anxiety associated with understanding medication-related changes and empowered greater medication self-management.

Discussion. A post-discharge nurse-pharmacist telehealth service is a feasible and acceptable model of care. Inclusion of a routine MedRec post-discharge may be an effective means of maintaining continuity of care for HFPs.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P484

Stakeholders' views on a virtual pharmacy discharge service for First Nations patient

Miss Bushra Haque

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Bushra is a 4th year pharmacy honours student at the University of Sydney. She is passionate about patient-centred and equitable healthcare and strives to improve culturally safe healthcare for First Nations peoples. She is currently undertaking an honours research project based in Dubbo to inform the culturally safe implementation of a transition of care program. She has worked in a small community pharmacy in Maroubra for almost 4 years and has found it extremely rewarding. Thank you to the Virtual Clinical Pharmacy Service team in the Western New South Wales Local Health District for their support and invaluable knowledge towards the project.

Stakeholders' views on a virtual pharmacy discharge service for First Nations patients

Bushra Haque¹, Siniti Herath¹, Kingston Yeung¹, Jonathan Penm¹. School of Pharmacy, University of Sydney¹, Sydney, NSW, Australia

Introduction. The transition from hospital to home remains a prominent issue that leads to negative health outcomes when not addressed appropriately. Risks of negative outcomes at these transitions for First Nations peoples may be inflated due to a lack of culturally safe healthcare (AIHW, 2024; Australian Commission on Safety and Quality in Health Care, 2024). As a result, a virtual transition of care stewardship (TOCS) pharmacist who facilitates a post-discharge Home Medication Review (HMR) is to be implemented in rural/regional New South Wales to increase patient safety regarding medications, and to reduce medication-related hospital readmissions.

Aims. To explore the thoughts, beliefs and perceptions of key stakeholders involved in First Nations peoples' healthcare on the implementation and cultural safety of a virtual TOCS pharmacist service that facilitates a post-discharge HMR for First Nations patients.

Methods. Semi-structured one-on-one interviews were conducted with key stakeholders including doctors, nurses, pharmacists, Aboriginal Health Workers, and allied health workers. All interviews were transcribed manually and analysed according to the methodology described by Bernard and Ryan.

Results. The study included 20 interviews with clinicians. Clinicians stressed the importance of informing the patient of what to expect, why the service will be used, and how it can assist them with managing their medications. Additionally, building rapport with First Nations patients to increase the acceptability of both the virtual TOCS service and HMR service was emphasised. It was also suggested that understanding of culturally safe healthcare may be lacking in clinicians that do not identify as First Nations.

Discussion. The study suggests the need for regular cultural safety training in the context of First Nations peoples, approaching the implementation of HMRs for First Nations patients with a holistic understanding of their healthcare needs, and ensuring patient awareness of the services being provided both in and out of hospital.

Australian Commission on Safety and Quality in Health Care, 2017. Safety Issues at Transitions of Care: Consultation report on perceived pain points relating to clinical information systems

Australian Institute of Health and Welfare (AIHW) 2024. Aboriginal and Torres Strait Islander Health Performance Framework: summary report March 2024

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P485

Pharmacists' potential roles within a youth mental health service: a qualitative exploration

Miss Sanam Fathabadi

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Sanam is a graduate pharmacist currently completing her internship at Prince of Wales Hospital in Randwick, Sydney. Her research focuses on potential roles pharmacists can play in supporting mental health care for young people, particularly within youth mental health services. She is interested in improving mental health outcomes and believes pharmacists' skills and expertise can be applied in new areas to help enhance mental health care.

Pharmacists' Potential Roles Within A Youth Mental Health Service: A Qualitative Exploration

Sanam Fathabadi¹, Claire L O'Reilly¹, Jack C Collins¹, Blake Hamilton², Donna Fowler², Connie Janiszewski², Sara McMillan³, Sarira El-Den^{1*}

The University of Sydney School of Pharmacy, The University of Sydney¹, Sydney, NSW, Australia; *headspace* Camperdown², Brain and Mind Centre, The University of Sydney, Sydney, NSW, Australia; School of Pharmacy and Medical Sciences, Griffith University³, Southport, QLD, Australia.

Introduction. The prevalence and burden of mental illness among young people is rising, globally. Youth mental health services, such as *headspace* in Australia, offer young people access to multidisciplinary mental healthcare, specifically designed to address their needs. Pharmacists are medicines experts whose skills are increasingly utilised in expanded areas of practice; however, literature exploring pharmacist-delivered mental healthcare for young people is limited.

Aims. To explore views of *headspace* staff regarding medication use among young people who engage with youth mental health services and potential roles for pharmacists within the *headspace* service model.

Methods. Semi-structured interviews were conducted with staff from an inner-city *headspace* centre in Sydney. An interview guide was developed to capture views on medication use among young people accessing youth mental health services and potential roles for pharmacists within this context. Reflexive thematic analysis was conducted.

Results. Twelve staff members were interviewed in September and October 2023 (mean interview time = 19.65 min). The data captured the views of a range of staff, performing clinical and non-clinical roles at *headspace*, and was analysed to generate four themes: (i) gaps in medication-related care, (ii) potential roles for pharmacists at *headspace*, (iii) pharmacists working with general practitioners, and (iv) a "one-stop shop".

Discussion. There are opportunities for pharmacists to improve young peoples' experiences using psychotropic medications through the provision of medication information to clients and caregivers. Pharmacists could also contribute to multidisciplinary case reviews but clarifying their specific roles when working alongside general practitioners is necessary. Uncertainty regarding the feasibility of pharmacist-led services at *headspace* and a lack of awareness regarding pharmacists' full scope of practice warrant further investigation into how pharmacists' skills and expertise can be utilised to support young people accessing youth mental health services.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P486

Adverse events associated with cannabis-based product use in people living with cancer

Dr Joanna Harnett

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Adverse events associated with the use of cannabis-based products in people living with cancer: a systematic scoping review.

Irene Cheah¹, Jennifer Hunter^{1,2}, Ingrid Gelissen¹, Jocelin Chan¹, Joanna E Harnett¹.

1. School of Pharmacy, Faculty of Medicine and Health, University of Sydney, Australia

2. Health Research Group Sydney, Australia

Introduction Despite increasing prevalence of CBP use in cancer care, information about the safety of CBP remains limited.

Aims. This scoping review aims to characterise adverse events (AEs) associated with the use of cannabis-based products (CBP) in people living with cancer.

Methods. Joanna Briggs Institute methodology for scoping reviews was applied. A search was performed in MEDLINE, Embase, CINAHL, Scopus, Web of Science Core Collections and AMED from their inception to 7 May 2023.

Results. This review included 152 studies. Randomised controlled trials (RCTs) (n=61), non-randomised controlled trials (n=26) and case reports (n=23) were most common. CBP was mainly used in gastrointestinal, liver, or peritoneal cancer (n=98) and haematological or lymphoid cancer (n=92), primarily to manage nausea and vomiting (n=78) and cancer pain (n=37). The most common CBP ingredients were combinations of THC and CBD (n=69), synthetic THC (n=47), single compounds of THC (n=42), and CBD (n=16) with diverse forms, administration routes and doses. The primary methods of administration were oral (n=94) and inhalation (n=54). A broad range of AEs were reported across the studies, mostly commonly nervous system (n=118), psychiatric (n=101) and gastrointestinal system (n=81) AEs. Diverse patient characteristics, CBP ingredients, forms and dosages, and significant under-reporting and low-quality reporting were observed in many studies.

Discussion. The findings from this scoping review emphasise the need for more rigorous research designs that prioritise comprehensive, standardised reporting of AEs and CBP use to elucidate the safety profile of CBP use in cancer care.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P487

Are we ignoring a burden of preventable harm - drug-herb interaction risks?

Dr Jocelin Chan

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Jocelin Chan – PhD, B. Pharm (1st class honours) is a research associate at the University of Sydney School of Pharmacy. She is also a practicing community pharmacist and a pharmacy owner. Jocelin's research interests include drug-herb interactions; the use of *Annona muricata* (Graviola) in people living with cancer; quality use of complementary medicines, and the quality of herbal medicine products. She contributes to the development and review of monographs to resource healthcare professionals with evidence-based knowledge about drug-herb interactions. Her recent research includes evaluating the safety and tolerability of a herbal product (*Annona muricata*) through a clinical study in collaboration with Concord Cancer Centre, Sydney Australia.

Are we ignoring a burden of preventable harm - risk of drug-herb interactions?

Wai-Jo Jocelin Chan, Andrew J McLachlan, Jennifer Hunter, Joanna Harnett^{1,2}. The University of Sydney, Sydney Pharmacy School, Faculty of Medicine and Health Research Group Pty. Limited, Sydney, NSW, Australia

Introduction. Complementary medicine (CMs) containing herbs, are predominantly purchased by the Australian public through pharmacies. Unwanted drug-herb interactions can be avoided through consumers and pharmacy staff being aware of the risks. The true prevalence of adverse events associated with drug-herb interactions in Australia is uncertain due to chronic underreporting.

Aims. To identify the prevalence of specific drug-herb interaction risks using real world sales data.

Methods. Two drug-herb pairs with well-established pharmacokinetic evidence of interactions were used to examine the prevalence of drug-herb interaction risk. Pharmacy transaction data was analysed to identify the number of instances where oral contraceptives (OCP) and St. John's wort (*Hypericum perforatum*) and/or atorvastatin and green tea (*Camellia sinensis*) products were purchased together using a "basket analysis" approach (investigating combinations of health products that occur together frequently in consumer transactions in pharmacy). This analysis was conducted using IQVIA Consumer Health pharmacy sales data from April 2023 to March 2024.

Results. St. John's Wort was purchased with an OCP in 0.03% of transactions and green tea in 0.02% of atorvastatin transactions. These equate to approximately 21,598 females using an OCP and 24,832 adults using atorvastatin who were potentially at risk of a drug-herb interaction.

Discussion. The findings highlight how Australians' access, and possible use of CMs, is placing them at risk of drug-herb interactions. The bio-psycho-social, and economic implications of an interaction occurring between St John's Wort and the OCP that results in an unplanned pregnancy are profound. Likewise, the clinical implications of concurrent use of green tea, which can reduce the systemic exposure to atorvastatin, has important implications for cardiovascular risk. A limitation of this study is that sales data do not confirm that patients were ingesting these products concomitantly. In summary, drug-herb interactions pose a burden of preventable harm. These findings highlight the opportunity for point-of-sale medicines information and advice to reduce the potential health burden of drug-herb interactions.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P488

Co-designing an intervention to optimise medicine information handover after discharge from hospital

Dr Holly Foot

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Co-designing an intervention to optimise medicine information handover after discharge from hospital

Holly Foot¹, Leslie Oldfield¹, Faith Yong², Elizabeth Manias³, Tin Fei Sim⁴, Melissa Baysari⁵, Ian Scott⁶, Gerben Keijzers^{7,8,9}, Claire Jackson², Mark Morgan⁸, Barbara Mullen¹⁰, Richard Norman¹⁰, Laetitia Hattingh.^{1,11} School of Pharmacy, Univ of Queensland¹, Brisbane, QLD, Australia; Faculty of Medicine, Univ of Queensland², Brisbane, QLD, Australia; School of Nursing & Midwifery, Monash Univ³, Clayton, VIC, Australia; Curtin Medical School, Curtin Univ⁴, Bentley, WA, Australia; School of Medical Sciences, Univ of Sydney⁵, Sydney, NSW; Metro South Clinical Digital Health and Informatics, Princess Alexandra Hospital, Woolloongabba, QLD Australia Emergency Department, Gold Coast Hospital⁷, Southport, QLD, Australia; Faculty of Health Sciences & Medicine, Bond Univ⁸, Robina, QLD, Australia; School of Medicine, Griffith University⁹, Southport, QLD, Australia; School of Population Health, Curtin Univ¹⁰, Bentley, WA, Australia; Allied Health Research, Gold Coast Health¹¹, Southport, QLD, Australia.

Introduction. The handover of patient medicine information at discharge from hospitals to primary care clinicians is inconsistent and contributes to fragmented care and medicine safety risks. This study forms the stakeholder engagement phase of a trial to improve medication handover and reduce medication-related hospital readmissions.

Aim. To identify the factors that impact on discharge medicine information handover as perceived by consumers, hospital-based (pharmacists, doctors, nurses) and community-based (pharmacists, general practitioners) clinicians.

Methods. Consented participants attend one face-to-face or online focus group to discuss barriers and solutions to improving medicine information handover at discharge. Interactive and participatory methods were used to engage participants and stimulate robust discussions. NVivo[®] software was used to code and analyse the discussions.

Results. In total, 67 participants, consisting of 19 consumers, 32 hospital-based clinicians from six hospitals and 16 community-based clinicians consented into the study. Eleven focus groups were conducted between March and August 2024, lasting on average 76 minutes per workshop. Consumer-driven solutions to improve medicine handover included: follow-up phone call after discharge, better engagement about medicines and easy access to digital medical records. Hospital and community-based clinicians' solutions included utilising current technologies to full potential (e.g. MyHealthRecord) and designing a digital system that integrates all parties involved in the patient's care.

Discussion. The themes that emerged from consumers and clinicians will be used to co-design a multifaceted intervention to improve medicine information handover between hospital and primary care clinicians.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P489

Getting rid of FRIDs: Addressing the use of fall-risk-increasing drugs in aged-care

Ms Catherine Laird

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Getting rid of FRIDs: Addressing the use of fall-risk-increasing drugs in aged-care

Catherine Laird¹, Kylie A. Williams¹, Helen Benson¹ Graduate School of Health, UTS¹, Sydney, NSW, Australia

Introduction. The use of fall-risk-increasing drugs (FRIDs) are a serious healthcare problem for aged care residents. (Montero-Odasso et al, 2022). One approach to reducing the use of FRIDs is pharmacists completing medication reviews to identify and recommend opportunities to deprescribe them (Montero-Odasso et al, 2022). However, evidence that this results in reduced use of FRIDs in clinical practice is limited (Sluggett et al, 2022).

Aims. To evaluate pharmacist medication review recommendations involving FRIDs.

Methods. A retrospective cross-sectional study of medication review reports was conducted. Pharmacists identified recommendations involving FRIDs were extracted from the reports. Recommendations were assessed for consistency with the guidelines for comprehensive medication management reviews including use of the Situation Background Assessment Recommendation (SBAR) communication tool and application of the principles of patient centred care.

Results. Analysis was completed on 966 medication review reports. Recommendations to deprescribe FRIDs accounted for 19.7% (n=520) of all pharmacist medication review recommendations. Assessment of these recommendations revealed ineffective communication of how recommendations aligned with principles of patient centred care. For instance, 130 (26.2%) recommendations did not include a description of the resident's clinical situation and assessment that led to the recommendation to deprescribe a FRID. Furthermore, there were only three (0.6%) recommendations in which the pharmacist assessment included the resident's (or their representatives) viewpoint on deprescribing.

Discussion. Pharmacists conducting medication reviews for aged care residents frequently made recommendations to deprescribe FRIDs. Effective communication by pharmacists of how deprescribing would benefit the individual resident's clinical situation and align with their goals of care could increase implementation of these recommendations.

Montero-Odasso M, van der Velde N, Martin FC et al. (2022) *Age Ageing*, 51:1-36

Sluggett JK, Caughey GE, Air T et al. (2022) *BMC Geriatr*, 22:493

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P490

Healthcare professional's attitudes towards new virtual transition of care stewardship pharmacist role

Miss Siniti Herath

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Siniti is a fourth-year pharmacy student at the University of Sydney (USYD). She is currently undergoing her Honours research project in the Western NSW Local Health District where she is exploring a virtual medication-centred pharmacy-led intervention that aims to support patients during their transition from hospital to home. Siniti works part-time at a local pharmacy in North Sydney and had the exciting opportunity to learn about toxicovigilance in India. She is interested in exploring the expanding scope of pharmacy within hospitals and the community.

Healthcare professional's attitudes towards new virtual transition of care stewardship pharmacist role

Siniti Q Herath¹, Bushra Haque¹, Kingston Yeung¹, Jonathan Penm^{1,2}. Faculty of Medicine and Health, Univ of Sydney¹, Camperdown, NSW, Australia; Dept of Pharmacy, Prince of Wales Hosp², Randwick, NSW, Australia.

Introduction. Transition of care from the hospital to the home is a period of high risk for medication-related errors. This is particularly true for rural and regional hospitals that face their own unique challenges such as geographical isolation and limited access to supplies and healthcare.

Aims. We aim to explore the perspectives of healthcare professionals' in the acceptability and barriers of the new virtual transition of care stewardship (TOCS) pharmacist in initiating a post-discharge Homes Medicine Review.

Methods. Semi-structured interviews with pharmacists, doctors, nurses and allied health were conducted between August and September 2024 in-person or online. Interview guide was developed using the Consolidated Framework for Implementation Research. Interviews continued until data saturation occurred, and were audio-recorded and transcribed verbatim. Data analysis was conducted using the inductive thematic approach to identify common themes.

Results. In total, 20 interviews were conducted with healthcare professionals in rural and regional New South Wales. Overall, health care professionals were accepting of the virtual TOCS pharmacists role and believed it would reduce medication-related readmissions. However there were concerns regarding resourcing and funding of the service, which could impact the reach of this service. Acceptability from patients varied, with age, health literacy, digital literacy, and attitude towards healthcare all playing a role. Finally, integration into existing workflow was considered with workplace education and support being emphasised.

Discussion. The virtual TOCS pharmacist and their facilitation in post-discharge HMR's was widely supported and accepted. The findings highlight that appropriate funding, patient and staff education, and providing suitable alternatives to cater for the wide range of patients need to be made to ensure an optimal service is provided for rural and regional patients.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P491

Usage trends in Pharmaceutical Benefits Scheme cancer drugs in Australia: an analysis

Miss Jasmine Lee

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Jasmine Lee is a PhD candidate at the University of Sydney's School of Pharmacy and a registered pharmacist. Her research revolves around the economics and usage patterns of anticancer drugs, with a focus on forecasting future trends to inform healthcare budgeting and policy.

Usage trends in Pharmaceutical Benefits Scheme cancer drugs in Australia: an analysis

Jasmine Lee¹, Anastasios Panagiotelis², Rose Cairns^{1,3}, Nial J. Wheate^{1,4} School of Pharmacy, Faculty of Medicine and Health, The University of Sydney¹, Sydney, NSW, Australia; The University of Sydney Business School², Sydney, NSW, Australia; NSW Poisons Information Centre, The Children's Hospital at Westmead³, Sydney, NSW, Australia; Office of the Deputy Vice-Chancellor (Education), Macquarie University⁴, Sydney, NSW, Australia

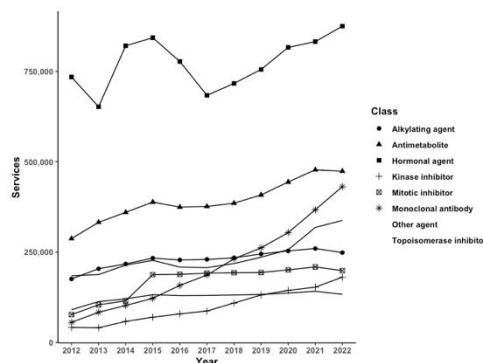
Introduction. Cancer treatment remains a significant and escalating healthcare expense in Australia. While annual reports on total cancer care costs are available, the potential impact of evolving treatment guidelines and the introduction of new drugs on future budgeting remains largely uncertain.

Aims. The aim of this study was to examine the trends in the use of pharmaceutical benefits scheme (PBS)-listed cancer drugs in Australia over the past decade.

Methods. PBS codes for all PBS-listed cancer drugs that were listed in government-endorsed treatment protocols were obtained and used to retrieve usage data. Their patterns of use, represented by the number of prescriptions (services) processed by Services Australia, were analysed for the period between 2012 to 2022.

Results. The overall prescribing of cancer drugs is outpacing Australia's population growth, primarily due to an ageing population and the accelerated rise in cancer diagnoses observed over the past decade. From 846 eviQ protocols, 141 cancer drugs were available on the PBS, of which kinase inhibitor (39 drugs) and monoclonal antibody drugs (24 drugs) had the highest increase in use during the study period; 16% and 23% respectively. Of the 8 drug classes, hormonal agents (20 drugs) were the most prescribed.

Discussion. The utilisation of PBS-listed cancer drugs is increasing faster than population growth, especially for high-cost monoclonal antibody and kinase inhibitor drugs, indicating continued pressure on government spending.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P492

Multidisciplinary perspectives on hospital pharmacist roles in tertiary settings: a qualitative study

Ms Kyung Min Kirsten Lee

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Kirsten is a registered pharmacist with a rich background in research and medication supply. She holds a Master of Research in Pharmacy and has led various projects, including those for the International Pharmaceutical Federation, which resulted in peer-reviewed publications and pharmacy advocacy reports. Her work has been presented at both national and international conferences, where it has influenced global pharmacy decision-makers. As a clinician, Kirsten has specialised expertise in medication supply, ranging from procurement to robotic dispensing and high-risk medication management, across both community and hospital settings. She has a strong interest in implementation and multidisciplinary research and is eager to contribute further in this field.

Multidisciplinary perspectives on hospital pharmacist roles in tertiary settings: a qualitative study

Kyung Min Kirsten Lee¹, Ivanka Koeper², Michaela E Johnson³, Amy Page⁴, Debra Rowett¹, Jacinta Johnson¹. Clinical and Health Sciences, University of South Australia¹, Adelaide, SA, Australia; SA Pharmacy², Central Adelaide Local Health Network, SA Health, Adelaide, SA, Australia; Flinders University³, Bedford Park, SA, Australia; UWA Centre for Health & Ageing⁴, University of Western Australia, Perth, WA, Australia

Introduction. Interprofessional collaboration leads to improved patient and organisational outcomes. Hospital pharmacists play a pivotal role in multidisciplinary teams, and it is imperative to understand multidisciplinary viewpoints on hospital pharmacists' roles to guide role prioritisation and organisational efficiency. However, no study has extensively investigated diverse multidisciplinary views on the value of pharmacist roles in tertiary settings.

Aims. This study aims to explore the perceptions of hospital pharmacist roles and services held by non-pharmacist health professionals using focus groups and semi-structured interviews.

Methods. Multiple focus groups and semi-structured interviews were held via a virtual conferencing platform. Study participants were non-pharmacist health professionals with experience working with pharmacists in hospital settings. Focus group/interview recordings were transcribed and underwent thematic analysis. Overarching themes were categorised and mapped against work system models to conceptualise organisational implications. Participant demographics were summarised using descriptive statistics.

Results. Twenty-seven health professionals participated, including doctors (n=9), nurses (n=9) and allied/other health professionals (n=9). Three major themes were identified: (i) overarching perceptions regarding hospital pharmacists; (ii) professional niches of hospital pharmacists; and (iii) future opportunities to optimise hospital pharmacy services. Hospital pharmacists were perceived as essential members of the healthcare team. Valued professional niches of hospital pharmacists included roles as patient and health professional educators, transition-of-care facilitators, and quality use of medicines analysts. Opportunities for optimisation identified included tailoring roles to specific units and promoting specialisation.

Discussion. This study provides important multidisciplinary insights into hospital pharmacists' roles in Australia, identifying the niche expertise pharmacists bring to healthcare. The study advocates for strategic role optimisation and further research to enhance clinical, economic and organisational outcomes.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P493

Implementation of a proposed algorithm to de-labelling penicillin allergy in community pharmacy

Dr Angelina Lim

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Angelina Lim is a lecturer at Monash University and her key interests are simulation, authentic assessment, generative artificial intelligence, antimicrobial stewardship and paediatric endocrinology. Angelina's main expertise lies in designing and evaluating Objective Structured Clinical Examinations. Angelina has embarked on many pharmacy related career paths, starting with hospital pharmacy, then community pharmacy (still practicing), public health sector and research. She still maintains links with the Murdoch Children's Research Institute (MCRI) working on projects in disability and paediatric endocrinology. Angelina is dedicated to teaching and education research and aims to use evidence based pedagogical approaches to drive her teaching and curriculum design.

Implementation of a proposed algorithm to de-labelling penicillin allergy in community pharmacy

Angelina Lim¹, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University¹, Melbourne, VIC, Australia; Sharmila Khumra², Pharmacy Department, Austin Health², Melbourne, VIC, Australia; Elise Mitri²; Bogil Shin¹; Jenny Quin¹; Katija Juric¹; Limhour Kruoch¹; Lydia Liu¹;

Introduction. A false allergy/type A allergy labelled as a true penicillin allergy can lead to unnecessary avoidance of penicillins, often resulting in using less effective and broader-spectrum antibiotics. Community pharmacists have a pivotal role to play in de-labelling false allergies or preventing false allergy labels from occurring.

Aims. To investigate the number of opportunities to de-label type A allergies in community pharmacies across Victoria via implementation of an algorithm based on a hospital validated beta lactam antibiotic allergy assessment tool^a.

Methods. A quasi-experimental study. Six community pharmacies were included and patients were recruited daily for 7 weeks between April – May 2024. All patients presenting to the community pharmacy dispensary were asked about allergies and management followed a proposed algorithm for allergy management. De-labelling outcomes were recorded. Facilitators and challenges to implementing the service were also collected through semi-structured interviews.

Results. Over 3500 patients were seen in the 7-week period with 24.3% of patients reported a false type A allergy. All patients presenting with Type A allergies were attempted to be de-labelled. Of those who were attempted to be de-labelled, 81.8% reported acknowledgement of the non-true allergy. Those who were not receptive mainly claimed using the label to protect them using a penicillin that cause them side effects. Older patient groups and patients who have been discharged recently from hospital were hardest to de-label. There is still a public misconception that there is an endless supply of different types of antibiotics, and the public is largely unaware of how allergy labels impact antimicrobial resistance.

Discussion. The proposed algorithm for management of penicillin allergies was easily implemented across community pharmacies to guide de-labelling and allergy education and can be a useful tool for future practice. Upskilling pharmacists to manage penicillin allergy can help improve the public misconceptions and reduce risk of antimicrobial resistance.

^aDevchand M et al (2019) J Allerg Clin Immunol 74(6), 1725-1730.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P494

Evaluating psychometric properties of medication-related quality indicators in RACHs: A systematic review

Mrs Lakeesha Sandamali Liyanage

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Lakeesha Sandamali Liyanage is currently pursuing a PhD at the University of Canberra. She earned her Bachelor of Pharmacy degree from the University of Ruhuna, Sri Lanka, in 2016. With a diverse career as a hospital pharmacist, community pharmacist, and academic, she has demonstrated a strong commitment to advancing the field of pharmacy. Her research interests focus on pharmacy practice, the quality use of medicines, and pharmacy education. Lakeesha has actively contributed to her field by presenting her research at multiple conferences and is passionate about fostering collaboration and innovation in pharmacy to improve patient outcomes.

Evaluating psychometric properties of medication-related quality indicators in RACHs: A systematic review

Lakeesha Liyanage¹, Thilini Sudeshika¹, Louise Cox¹, Mark Naunton¹, Sam Kosari¹. Faculty of Health, University of Canberra¹, Bruce, ACT, Australia.

Introduction. Quality indicators (QIs) are important for tracking and enhancing healthcare quality. In residential aged care homes (RACHs), medication-related QIs are essential for ensuring the quality of medication usage. Given that residents often take multiple medications, these QIs play a crucial role in monitoring and improving medication management and providing up-to-date information on medication usage. These QIs need to satisfy certain psychometric properties. However, the literature presents a variety of properties and testing methods for these QIs.

Aims. This systematic review aims to examine and synthesise the methodologies employed to assess psychometric properties of medication related QIs in RACHs including validity, reliability, feasibility, applicability, sensitivity, measurability, appropriateness and usefulness.

Methods. A systematic search was conducted in CINAHL, MEDLINE, PsycINFO, Scopus, and Web of Science Core Collection, covering articles published since inception until May 2024. Covidence software was used for title and abstract screening, and full text reviewing. Quality of the selected articles was evaluated using MMAT.

Results. The search yielded a total of 14,430 articles. Following the elimination of duplicates (n=6681) and the evaluation of articles against the inclusion and exclusion criteria, 124 articles were selected for full text review. Among them 20 full-text articles were deemed suitable for inclusion in the review. In the included studies, polypharmacy and the antipsychotic medication usage were the commonly tested medication related QIs. The most commonly reported psychometric properties were validity (n=11, 55%), reliability (n=8, 40%) and feasibility (n=8, 40%), with one study reported other properties including applicability, sensitivity, measurability, appropriateness and usefulness. The Delphi method was the most frequently used method for validity and feasibility tests.

Discussion. There is a need for improved assessment and reporting practices to ensure the validity, reliability, feasibility, and other psychometric properties of QIs in residential aged care settings. Inconsistencies among the methods used for testing these psychometric properties have been observed. This inconsistency underscores the necessity for standardised protocols for testing medication-related QIs, including the required psychometric properties and the standard methodologies to evaluate them.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P495

Effectiveness of interventions to increase safe and appropriate medicine disposal: systematic review

Miss Amy Ma

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Amy is a recent graduate of the Bachelor of Pharmacy (Honours) program at the University of Sydney, with a keen interest in medication safety and public health. For her Honours research project, Amy focused on safe medicine disposal practices, specifically exploring ways to enhance community pharmacists' role in educating the public about proper disposal methods.

In 2025, Amy is set to commence her role as a hospital intern pharmacist, where she aims to apply her research experience in clinical settings and further develop her professional skills.

Effectiveness of interventions to increase safe and appropriate medicine disposal: systematic review.

Amy S Ma¹, Andrew J McLachlan¹, Christina Abdel Shaheed^{2,3}, Danijela Gnjidic¹, Jonathan Penm^{1,4}, Toni Riley⁵, Stephanie Mathieson^{1,3}. Sydney Pharmacy School, The University of Sydney¹, Sydney, NSW, Australia; Institute for Musculoskeletal Health, Sydney Local Health District², Sydney, NSW, Australia; Sydney Musculoskeletal Health, The University of Sydney³, Sydney, NSW, Australia, Department of Pharmacy, Prince of Wales Hospital⁴, Randwick, NSW, Australia; Return Unwanted Medicines⁵, Cheltenham, VIC, Australia.

Introduction. Reducing the availability of unused medicines is a component of ensuring medication safety. However, current literature on how best to increase medicine disposal is unclear.

Aims. To investigate the effectiveness of interventions designed to increase safe and appropriate medicine disposal.

Methods. Electronic databases and trial registries were searched from inception to 16th February 2024 for randomised trials of interventions aiming to increase medicine disposal (of any drug class) compared to any control. The primary outcome was the change in the proportion of participants that disposed their unused medicines. Secondary outcomes were changes in patient (e.g. knowledge of disposal strategies), population (e.g. poisonings), environmental and economic outcomes. The original Cochrane tool was used to assess risk of bias. Random-effects meta-analysis was conducted. Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the quality of evidence. PROSPERO registration: CRD42023491797.

Results. Twenty-three studies were included (18 studies published from 2016 to 2023 plus 5 ongoing trials). The mean age of the 5,347 participants was 43.2 years (SD 13.6). All studies were conducted in North America and targeted opioid analgesic disposal. Interventional strategies of providing disposal kits (Risk Ratio [RR] 1.42, 95% Confidence Interval [CI] 1.13 to 1.79, moderate evidence), education alone (RR 1.47, 95%CI 1.03 to 2.09, low evidence), education plus reminder prompts (RR 2.51, 95%CI 1.30 to 4.83, moderate evidence), and education plus disposal kits (RR 2.00, 95%CI 1.03 to 3.87, moderate evidence) increased disposal compared to routine practice. Secondary outcomes were infrequently reported.

Discussion. There is low to moderate quality of evidence supporting the use of interventions to increase the disposal of unused medicines compared to routine practice. Secondary outcomes were recorded infrequently and may be a pathway for future research.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P496

Medicine prices availability and affordability in 57 developing and middle-income countries

Mr Lachlan Oldfield

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Medicine prices availability and affordability in 57 developing and middle-income countries: a secondary analysis update Lachlan Oldfield¹, Jonathan Penm², Ardan Mirzaei¹, Rebekah Moles¹. Sydney Pharmacy School, The University of Sydney¹, Sydney, NSW, Australia; Department of Pharmacy, Prince of Wales Hospital², Sydney, NSW, Australia. Introduction. Medication shortages are a global concern. The WHO and HAI have developed a methodology to survey medicine prices, availability, and affordability in low- and middle-income countries. This paper updates the analysis for 57 countries using this methodology. Aims. To update the analysis of medicine affordability, availability, and pricing across 57 countries using the WHO/HAI methodology, and highlight disparities between public and private sectors. Methods. We used the HAI Essential Medicines Access Database and four electronic databases to locate studies using the WHO/HAI methodology. 74 surveys from 57 countries were included. Data on availability, affordability, and pricing were extracted and synthesised for 15 commonly surveyed medicines. Results. Public sector availability of generic medicines ranged from 38.6% to 68.3% across WHO regions. Medicine prices were high, with patients paying 3.2 to 12.4 times international reference prices for generics and over 25 times for originator products. Treatment costs often required multiple days' wages. Discussion. The results highlight significant disparities in access to essential medicines. Despite some progress, global accessibility remains a concern. Targeted strategies from governments and healthcare organisations are needed to address economic and logistical barriers.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P497

Pharmacists are responsible for patient outcomes when dispensing opioids.

Mr William Olsen

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Will is a PhD candidate entering the final year of his project. Having completed a Bachelor of Pharmacy with honours in 2018, Will is a practicing pharmacist with clinical experience in a range of community settings. His PhD project is in pharmacy ethics, exploring the responsibilities of pharmacists in the context of the opioid crisis. Will is also passionate about education, with a particular interest in teaching ethical decision-making.

Pharmacists are responsible for patient outcomes when dispensing opioids.

William Olsen¹, Chris Freeman^{1,2,3}, & Adeleke Adewumi¹, Adam La Caze¹

School of Pharmacy, The University of Queensland¹, Brisbane, QLD, Australia; Faculty of Medicine, The University of Queensland², Brisbane, QLD, Australia; Metro North Hospital and Health Service³, Brisbane, QLD, Australia

Introduction: Prescription opioids cause significant harm globally. In many countries, the prevalence of this harm is increasing. Around the world, policy and regulation have been utilised to promote safety in response to opioid-related harm. Pharmacists play an important role in the supply of prescription opioids; this role has been expanded with the introduction of measures such as Prescription Drug Monitoring Programs and subsidised naloxone supply programs.

Aim: This paper provides an ethical argument to establish and describe the responsibilities that pharmacists have when dispensing prescription opioids.

Methods: Four premises are provided in relation to pharmacist responsibilities and opioid harm. Each premise, we argue, is well accepted. Together they provide a basis for pharmacist responsibilities when dispensing opioids: (1) opioid related harm is common and associated with prescribed opioids, (2) pharmacists are able to act to reduce opioid-related harm, (3) pharmacists are responsible for patient outcomes within their scope of practice, and (4) pharmacists are independently responsible for their professional decisions. The basis for each premise and possible counterarguments are considered in turn.

Results: Given the principles set out in this argument, pharmacists have a responsibility to reduce the risk of opioid-related harm. This includes specific responsibilities when dispensing opioids to assess the risk of opioid-related harm and to implement risk mitigation strategies. Pharmacists are accountable for the harms that occur due to a failure to meet these responsibilities.

Discussion: While there are substantial challenges that pharmacists may face in fulfilling their responsibilities when dispensing opioids, improved clarity regarding these responsibilities provides a basis for navigating these challenges.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P498

Needs assessment of self-care facilitation by Indonesian community pharmacies to international travellers

Mr Antonius Pratama

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Antonius Nugraha Widhi Pratama is a third-year PhD candidate and casual academic staff at Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, Australia. He is also a lecturer at the Faculty of Pharmacy, Universitas Jember, Indonesia. Throughout his academic journey, Antonius received several scholarships and grants from Indonesia and Australia. His research interests are in social and administrative pharmacy and public health pharmacy. His current PhD project is about self-care needs assessment among international travellers in Indonesia and the readiness of Indonesian community pharmacies to facilitate self-care for the travellers. Antonius can be contacted at a.pratama@sydney.edu.au or anton.farmasi@unej.ac.id.

Needs assessment of self-care facilitation by Indonesian community pharmacies to international travellers

Antonius NW Pratama¹, Brahmaputra Marjadi², Rebekah J Moles¹, Carl R Schneider¹. Sydney Pharmacy School, The University of Sydney¹, Sydney, NSW, Australia; School of Medicine, Western Sydney University², Sydney, NSW, Australia.

Introduction. International travellers visiting Indonesia may experience self-treatable illnesses requiring assistance from local community pharmacies. Aside from the limited knowledge of self-care facilitation for international travellers in the Indonesian context from the literature, studying factors related to self-care facilitation for international customers will help identify the need for improving this service.

Aims. This study aimed to assess the needs of community pharmacy staff providing self-care facilitation to international tourists in Indonesia.

Methods. Qualitative semi-structured interviews were conducted online with community pharmacists and pharmacy technicians from Magelang (near Borobudur) and Badung (in Bali), Indonesia. Participants were recruited using snowball sampling after an initial purposive sampling. Deductive content analysis using Brata's Self-Medication Provision Model was conducted.

Results. Twelve participants (five from Magelang and seven from Badung) were interviewed. At the pharmacy staff-patient interaction level, most participants felt they had sufficient knowledge to facilitate self-care. However, participants' confidence varied and was influenced by self-motivation, longer work experience, frequent interactions, better foreign language skills and the presence of a translator. At the organisational level, most participants agreed that self-care facilitation service for international travellers is essential, with some citing that it could maintain the travellers' confidence to visit Indonesia. Support from the pharmacy manager or owner varied from in-house product knowledge training to English communication skill courses. However, some pharmacy staff admitted to not receiving that support. At the external pharmacy environment level, some pharmacy staff cited challenges in finding substitutes for requested medicines or pharmacy supplies that are not commonly available in Indonesia. Another factor cited as hindering self-care facilitation was the regulation of antibiotic dispensing with a prescription.

Discussion. This study highlights the need among pharmacy staff for continuing professional development on this topic to help improve their confidence using various media. Another highlight is the need to revisit the regulations of pharmacy supply and dispensing in Indonesia to support self-care facilitation.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P499

Impact of futile medications on performance capacity in palliative care: Systematic review

Miss Jana Powell

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Impact of futile medications on performance capacity in palliative care: Systematic review

Jenna Powell¹, Jennifer Ong¹, Sydney Pharm School, Faculty of Med and Health, The Univ of Sydney ¹, Sydney, NSW, Australia.

Introduction. The prevalence of potentially inappropriate medications and futile medications in patients with life-limiting illnesses is high and is associated with poor patient outcomes by increasing the risk of polypharmacy (Graca et al, 2020). As it in turn is associated with increased medication side effects, adverse drug reactions, falls, fractures, and physical and functional impairments, polypharmacy can impact quality of life and performance capacity (Fried et al, 2014).

Aim. The aim of this systematic review was to synthesise the evidence in relation to the effect of polypharmacy and futile medications on performance status, activities of daily living, dignity and quality of life in palliative care patients.

Methods. Embase, MEDLINE, PsycINFO, Web of Science and Google Scholar were searched extensively using keywords from inception to the 1st of April 2024 to identify relevant studies. Studies were included if patients received palliative care or had a life-limiting illness. Comparator groups included patients experiencing polypharmacy or who were taking at least 1 'potentially inappropriate' or 'futile' medication and at least one outcome of interest was reported.

Results. A total of ten clinical studies met the eligibility criteria. Two studies measured performance status (2/10, 20%), three studies measured activities of daily living (3/10, 30%), and seven studies measured quality of life (7/10, 70%) with some studies measuring multiple outcomes. While most studies showed patients who experienced polypharmacy or continued 'futile' medications had poorer item scores statistically, only three studies (3/10, 30%) found these changes to be clinically significant.

Discussion. Numerous studies highlighted the interaction between polypharmacy and futile medications on the listed outcomes in terms of item scores, though certain issues such as multiple morbidities and different life expectancies warrant careful consideration. Though some studies showed polypharmacy contributed to worsening clinical outcomes for patients, a strong conclusion could not be made based on the results about the clinical significance.

Fried TR et al (2014) J Am Geriatr Soc 62:2261-2272.

Graca JA et al (2020) Ann. Oncol 31: S937

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P500

Implementation of specialist-initiated Home Medicines Reviews for osteoporosis: patients' experiences of intervention

Ms Fatima Rezae

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Implementation of specialist-initiated Home Medicines Reviews for osteoporosis: patients' experiences of intervention

Fatima Rezae¹, Rebekah Moles¹, Stephen Carter¹. School of Pharmacy, Univ of Sydney¹, Sydney, NSW, Australia

Introduction. The Safer medicines To reduce falls and refracture for Osteoporosis (#STOP) clinical trial evaluates the effectiveness of specialist-initiated Home medicines Reviews (HMRs) to patients living with osteoporosis after being treated in fracture liaison services. Patients' experiences provide insights into the quality and delivery of HMRs informing future implementation ensures sustainability and transferability.

Aim. We aimed to explore the experiences of patients in the intervention arm of the trial.

Methods. Semi-structured telephone interviews were conducted with patients after experiencing HMR. Interviews were recorded and transcribed. The first author developed the preliminary themes and subthemes using inductive thematic analysis and discussed the findings among the authors.

Results. Eleven interviews were conducted with nine patients. There were four main themes identified: 1. Intervention is insightful (enhanced understanding of osteoporosis and medications, gained awareness of falls risk increasing drugs (FRIDs)); 2. Appreciated and inspired by intervention delivery (valued personalised advice and holistic care, empowered to take responsibility for bone health); 3. Welcomed falls and refracture prevention (aimed to minimise medication-related falls, adhering to osteoporosis treatment); 4. Expressed the importance of pharmacists understanding complete fracture history.

Discussion. To ensure best outcomes, pharmacists need to maintain a personable approach to care. Pharmacists are advised to demonstrate to the patient that they have taken a wholistic approach to bone health, have taken the patient's life history of fractures into account and can provide flexible approaches to initiating and maintain the deprescribing of FRIDs in partnership with their general practitioner.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P501

Influence of beliefs and health literacy on medication-related outcomes in older adults

Miss Eman Rafhi

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Eman Rafhi is a third-year PhD candidate completing her Doctor of Philosophy at RMIT University in Melbourne, Australia. She holds a Bachelor's degree in Pharmacy with Honours from RMIT University and works as a pharmacist alongside her research. Her research investigates the influence of beliefs and health literacy on medication-related outcomes in older adults. Eman's dual role as a researcher and practicing pharmacist allows her to bridge theory and practice, aiming to improve healthcare quality and medication safety for older adults.

The influence of beliefs and health literacy on medication-related outcomes in older adults.

Eman Rafhi^{1,2}, Julie Stevens¹, Ieva Stupans¹, Joon Soo Park², Kate Wang^{1,2}. Pharmacy Dept, RMIT Univ¹, Bundoora, VIC, Australia; School of Allied Health, The Univ of WA², Crawley, WA, Australia

Introduction. Older adults often contend with multiple chronic diseases which necessitates the use of multiple medicines, however they also face an elevated risk of harm when medicines are used inappropriately. Research suggests that socioeconomic disadvantage, beliefs, and health literacy may all correlate with non-adherence and inappropriate medicine use (Andersson Sundell & Jönsson, 2016; Wamala et al., 2007; Zheng et al., 2019).

Aims. To investigate the influence of beliefs and health literacy on medication-related outcomes in older adults.

Methods. Participants ≥ 65 years living in the community were invited to complete a survey. Participants were asked to report demographics, medicines and complete three questionnaires: Self-Efficacy for Appropriate Medication use Scale (SEAMS), Beliefs about Medicines Questionnaire (BMQ) and Health Literacy Questionnaire (HLQ). Descriptive statistics, regressions and correlations were calculated using the Statistical Package for Social Sciences software.

Results. Two hundred participants were recruited, with 154 included for analysis (63.6% female, age range 65-110 y). Participants had a mean BMQ necessity score of 17.5 (SD=5.1) and concern score of 11.9 (SD=4.2), indicating strong beliefs in the necessity of medicines and few concerns. Mean health literacy scores were high across all four scales (scale 1, 5, 6 and 9). Regarding polypharmacy, 61 participants (39.6%) were using \geq five medicines. Mean SEAMS score was 33.2 out of 39 (SD=8.0), indicating high self-efficacy for adherence. Lastly, 18 participants reported use of a potentially inappropriate medicine. Regression analysis revealed statistical significance between participants' BMQ necessity scores and polypharmacy. Additionally, positive correlation were identified between necessity beliefs and both polypharmacy and adherence, respectively.

Discussion. Older adults with a stronger belief in the necessity of their medicines are more likely to engage in polypharmacy and exhibit higher self-efficacy for adherence.

Andersson Sundell, K., & Jönsson, A. K. (2016) *Int J Clin Pract*, 70:277-285

Wamala et al. (2007) *Int J Qual Health Care*, 19:134-140

Zheng et al. (2019). *Front Pharmacol*, 10:1537

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P502

Adverse drug event-related hospital admissions among Australian aged care residents

Dr Mohammed Salahudeen

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Adverse drug event-related hospital admissions among Australian aged care residents

Sheraz Ali¹, Gregory M Peterson¹, Colin M Curtain¹, Andrea Wilson², Mohammed S Salahudeen¹. School of Pharmacy and Pharmacology, University of Tasmania¹, Hobart, TAS, Australia; Department of Geriatric Medicine, Royal Hobart Hospital², Hobart, TAS, Australia.

Introduction. Approximately one in five hospital admissions among Australians aged 65 years are medication-related. Identifying factors contributing to adverse drug event (ADE)-related hospitalisations is crucial for developing improvement strategies.

Aims. To investigate the determine, characteristics, causality, severity, preventability, and independently associated factors for ADE-related admissions in aged care residents admitted to the major public hospitals in Tasmania.

Methods. We reviewed medical records of residential aged care facility (RACF) patients. ADEs were identified via chart review and a trigger tool, with hospitalisations due to ADEs confirmed by expert consensus. The causality, preventability, and severity of each ADE were assessed using standard criteria.

Results. Among 500 randomly selected residents, 91 (18%) experienced potential ADE-related hospitalisations. ADEs were categorised as possible (n=58, 64%) or definite/probable (n=33, 36%). The ADE-related hospitalisation group had significantly more diagnoses, potentially inappropriate medications, prior adverse drug reactions (ADR), and higher anticholinergic burden and GerontoNet risk scores. Common ADEs included falls (n=19, 21%), hypotension (n=16, 18%), and confusion/delirium (n=10, 11%). Frequently implicated drugs were renin-angiotensin system inhibitors (n=43, 47.3%), opioids (n=43, 47.3%), and diuretics (n=40, 44%). Most ADEs were moderately severe (n=90, 99%) and not preventable (n=60, 66%). Rheumatologic disease (OR 1.89, 95% CI 1.09-3.30, p=0.024) and previous ADR (OR 12.91, 95% CI 6.84-24.37, p<0.001) were associated with ADE hospitalisations.

Discussion. This study highlights that hospitalisations for moderately severe ADEs are common among RACF residents, with opioids and antihypertensives frequently implicated. Rheumatologic disease and previous ADR were identified as independent risk factors, suggesting the need for tailored interventions.

Ali S, et al. (2024) J Am Med Dir Assoc. 22:105041.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P503

Ward pharmacists' awareness, perceptions and experiences of PPMC provided in the ED

Dr Mohammed Salahudeen

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Ward pharmacists' awareness, perceptions and experiences of PPMC provided in the ED

Tesfay M Atey¹, Barbara C Wimmer¹, Gregory M Peterson¹, Mohammed S Salahudeen¹. School of Pharmacy and Pharmacology, University of Tasmania¹, Hobart, TAS, Australia.

Introduction. A patient's medication chart is a crucial tool for hospital clinicians to communicate and access important information. To enhance medication chart accuracy, a partnered pharmacist medication charting (PPMC) was trialled in a tertiary hospital's emergency department (ED) at the Royal Hobart Hospital, Tasmania.

Aims. To explore ward pharmacists' awareness, perceptions, and experiences of PPMC.

Methods. A cross-sectional study was conducted using a self-administered online questionnaire, reviewed for content and validity by two senior clinical pharmacists. All eligible ward clinical pharmacists at the hospital were invited to participate. Eligibility criteria included at least three months of ward experience, familiarity with both PPMC and traditional medication charting approaches, and implied consent for participation. The PPMC approach involved a pharmacist-documented best-possible medication history (BPMH) followed by a clinical discussion between a pharmacist and a medical officer to co-develop a treatment plan and chart medications in the ED. The traditional approach involved medical officer-led medication charting without a pharmacist-collected BPMH in the ED. In both approaches, a ward pharmacist provided full clinical pharmacy service on the ward.

Results. Seventeen participants were included in the analysis. Ward pharmacists reported positive experiences with PPMC, noting it helped reduce their workload by improving medication chart accuracy. On average, a ward pharmacist saved approximately 41 minutes per patient with PPMC activities in the ED. Short staffing was identified as the main barrier to effective PPMC implementation. Suggestions for improvement included workforce retention, upskilling, and education.

Discussion. Most ward pharmacists had positive experiences with PPMC, which generally improved their workload and inpatient care. Short staffing was identified as a key area for service improvement.

Atey TM, et al. (2023) *Int J Environ Res Public Health*. 13;20(2):1452.

Atey TM, et al. (2023) *Front Pharmacol*. 8;14:1273657.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P504

Paediatric off-label and unlicensed prescribing patterns in primary care: a systematic review

Dr Julie Stevens

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Dr Julie Stevens is a Senior Lecturer and Program Manager at RMIT University. She is a registered pharmacist with experience across hospital and community pharmacy settings. Her research focus is on clinical research within areas of diabetes, gastrointestinal function, and aged care, and pharmacy practice research focused on digital health technologies, health literacy and clinical interventions.

Paediatric off-label and unlicensed prescribing patterns in primary care: a systematic review

Julie E Stevens¹, Meaghan E Coyle¹, Tracey David¹, Jemma Erwin¹, Wageha Taleb¹.

¹School of Health and Biomed Sci, RMIT Univ¹, Bundoora, VIC, Australia.

Introduction. The magnitude of 'off-label' (OL) (outside the product license terms) and unlicensed (UL) prescribing for children has raised concerns. OL and UL prescribing is commonly extrapolated from adult data without paediatric PK/PD or clinical trial data, and may lead to paediatric adverse effects or toxicities not seen in adults. The prevalence of OL and UL prescribing is as high as 36% in paediatric hospital wards (Turner et al, 1998), and 90% in neonatal intensive care (Conroy et al, 1999); however, the extent of OL and UL prescribing in primary care is less well studied.

Aims. To evaluate the use and prescribing patterns of OL and UL medicines in children in primary health care.

Methods. A literature search was conducted using PubMed, MEDLINE, Embase and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) from inception to August 2023 to identify studies evaluating OL and UL prescribing patterns in paediatric primary health care. Two independent investigators completed study selection, data extraction and quality assessment. Outcomes included prevalence and incidence of OL, UL and 'on-label' prescribing.

Results. Seventeen studies, involving ~900,000 children, were included. Twelve of the 17 studies were retrospective observational studies, eleven involved general practices (GP), two used insurance data, two involved primary health care units, one was set in a community pharmacy, and one surveyed GPs and paediatricians at a conference. Study duration ranged from five days to 11 years. Seven studies examined OL and UL use for all medication types, while others focused on specific medications or medication classes. While most studies reported OL use, few reported UL use. OL use in included studies ranged from 6.6% to 94.4%, and the age group with the highest rate of OL use was conflicting. Using a dose higher, lower or different to the recommended dose was the most frequent type of OL use; age, formulation and route of administration were less common; however, the type of OL use varied according to whether studies examined OL use among all medications or specific medicines. UL use ranged from 0.3% to 16.8%.

Discussion. OL and UL prescribing of medicines for paediatric patients in primary healthcare is relatively common.

Conroy S, et al. (1999) Arch Dis Child Fetal Neonatal Ed 80:F142-F144.

Turner S, et al. (1998) BMJ 316:343-345.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P505

Exploring Sick Day Medication Guidance via Medication Management Reviews

Ms Mimi Truong

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Mimi Truong is a clinical pharmacist and PhD candidate at the University of Sydney. She combines her experience in community and hospital pharmacy with a passion for patient care to research ways to improve medication safety in people with kidney disease.

Exploring Sick Day Medication Guidance via Medication Management Reviews

Mimi Truong¹, Connie Van¹, Wubshet Tesfaye², Kamal Sud³, Ronald L Castolino^{1,4}.

School of Pharmacy, Faculty of Medicine and Health, The University of Sydney¹, Sydney, NSW, Australia;

School of Pharmacy, Faculty of Health and Behavioural Sciences², The University of Queensland³, Brisbane, QLD, Australia;

Nepean Kidney Research Centre, Department of Renal Medicine, Nepean Hospital³, NBMLHD, Kingswood, NSW Australia;

Pharmacy Department, Blacktown Hospital⁴, WSLHD, Blacktown NSW, Australia.

Introduction. The use of medications such as sulfonylureas, ACE inhibitors, diuretics, metformin, ARBs, NSAIDs and SGLT2 inhibitors (SADMANS) during acute dehydrating illnesses can increase the risk of acute kidney injury (AKI) in people with chronic kidney disease (CKD). It is recommended to provide patients with sick day medication guidance (SDMG) to withhold SADMANS medications during acute illness, especially for patients with existing CKD since AKIs can further worsen kidney function. Overseas, implementation of these SDMG is poor and it is not known if Australian healthcare services adequately facilitate SDMG to prevent such DRP.

Aims. We aimed to explore if current pharmacy services facilitate SDMG by identifying DRP found with SADMANS group of medications and identifying if any SDMG recommendations were made.

Methods. A retrospective analysis was done on 201 home medicines reviews and 408 residential medication management reviews. Types of DRP and sick day recommendations were recorded using a modified version of DOCUMENT.

Results. Overall, 32% and 71% of participants used SADMANS medications in aged care facilities and community settings, with the incidence of DRP ranging from 9-71%. DRP specific to SADMANS included issues with “toxicity or adverse drug reaction”, “monitoring”, “contraindications” and “drug selection”. The two most problematic medications were diuretics and metformin. No sick day medication recommendations were provided to participants despite a high proportion of users.

Discussion. Lack of SDMG may be due to lack of pharmacist awareness or knowledge. More research is warranted to improve awareness of SDMG and gather evidence on clinical outcomes of providing SDMG.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P506

Asthma Control and Management among Arabic-Speaking immigrants in Australia

Dr Thilini Thrimawithana

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Thilini is a dedicated academic with a multifaceted career as a pharmacist, teacher, and researcher. Her research activities focus on improving chronic disease management among culturally and linguistically diverse (CALD) populations and optimising the quality use of complementary medicines. Her research aims to identify strategies to prevent and manage cardiometabolic diseases. Thilini employs a variety of methodologies, including qualitative interviews and intervention trials, to develop and implement strategies that enhance the quality of care provided to people from CALD backgrounds. Thilini is also interested in exploring innovative approaches to improving the quality use of complementary medicines, striving to bridge the gap between traditional and modern medicine. Her research endeavours focus on enhancing the understanding and application of complementary medicines through dosage form design, aiming to ensure their safe and effective integration into healthcare practices.

Asthma Control and Management among Arabic-Speaking immigrants in Australia

Malath Al-Juhaishi, Chiao Xin Lim, Vincent Chan, Ieva Stupans, Thilini R. Thrimawithana. Pharmacy, School of Health and Biomedical Sciences, RMIT University, Melbourne, VIC 3083, Australia.

Introduction. Asthma prevalence is notable among Australians, including minority populations such as Arabic speaking Middle Eastern migrants and refugees (1). Effective asthma self-management requires appropriate knowledge and skills.

Aim. This study aimed to assess asthma control, perceptions, and inhaler technique among Arabic-speaking immigrants in Australia.

Methods. A cross-sectional study design was employed, and Arabic-speaking adults diagnosed with asthma were invited to complete an anonymous self-administered questionnaire. Participants were recruited through a multi-faceted approach from February to June 2024. The questionnaire comprised of six key sections: demographics, asthma control, illness perception, asthma knowledge, information resources, and inhaler use. The questionnaire was available in Arabic, in both soft and hard copy formats. Data were analysed using IBM Statistical Package for the Social Sciences Software (SPSS).

Results. Most participants indicated that asthma had a low to moderate negative impact on their lives. Weather, humidity, and family history were identified as the main causes of asthma. The majority (n=30) of participants reported having uncontrolled asthma. The study results also highlighted that none of the participants used their metered-dose inhaler correctly, with majority of the participants missing 3 or more steps from the checklist.

Discussion. The study highlights significant challenges in asthma control and management among Arabic-speaking migrants and refugees in Australia. The findings suggest the need for targeted educational interventions to improve asthma control and asthma self-management among Arabic speaking immigrants in Australia.

1. Australian Bureau of Statistics. *Asthma* [Internet]. Canberra: ABS; 2022 [cited 2024 May 31]. Available from: <https://www.abs.gov.au/statistics/health/health-conditions-and-risks/asthma/latest-release>.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P507

Effect of thiamine supplementation on hepatic GIP modification in obese diabetic rats

Dr Yuka Kohda

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Yuka Kohda started as a renal pharmacologist and toxicologist. She obtained her PhD at the division of pharmacology, Osaka University of Pharmaceutical Sciences. Since then, she has been fascinated by a new research discovery—“Neues.” She is a focused and diligent researcher and has collaborated with various colleges, hospitals, and companies to conduct research that has the potential to contribute to the advancement of healthcare. She currently studies oxidative stress at the Department of Pharmacotherapeutics and Toxicology, Faculty of Pharmacy, Osaka Medical and Pharmaceutical University. Oxidative stress plays an important role in the onset and progression of various diseases. Although we the COVID-19 pandemic has ended, the obesity and diabetes pandemic have shown no signs of subsiding. Dr. Yuka Kohda believes that prevention of obesity-induced diabetes secondary is critical in many countries. We can learn about “Neues” at the ASCEPT, APFP, and APSA Joint Congress 2024, Melbourne.

Effect of thiamine supplementation on hepatic GIP modification in obese diabetic rats

Yuka kohda¹, Hitoshi Matsumura¹, Nobuyuki Fukuishi², Saori Tanaka¹, Ryuji Kato¹. Department of Pharmacotherapeutics and Toxicology, Faculty of Pharmacy, Osaka Medical and Pharmaceutical University¹, Osaka, Japan; Department of Pharmacology, College of Pharmacy, Kinjo Gakuin University², Aichi, Japan.

Obesity is linked with type 2 diabetes in terms of increasing the risk of developing type 2 diabetes and that of its associated morbidity. We previously reported that thiamine supplementation decreases body weight and visceral fat mass in rats with obesity-related diabetes. Glucose-dependent insulintropic polypeptide (GIP) acts on pancreatic β cells to promote insulin secretion. According to established theory, GIP is derived from the gastrointestinal tract. We previously discovered increased expression of the incretin GIP gene (*Gip*) in the livers of obese rats with diabetes receiving high-dose thiamine. We focused on liver-derived GIP to demonstrate GIP protein expression in the liver and visually present localization of GIP in the liver.

Four-week-old male Otsuka Long-Evans Tokushima Fatty (OLETF) rats that exhibit progressive obesity and metabolic disorders, were randomly divided into two groups: an unsupplemented control group and a thiamine-supplemented group receiving 2 g of thiamine/L in drinking water for 51 weeks. Microarray analysis of *Gip* expression was performed in the livers of OLETF rats at 55 weeks of age. GIP protein expression in the liver was determined by western blotting analysis. Furthermore, GIP was immunohistochemically stained to visualize its localization in the liver.

Gip expression was higher in the livers of high-dose thiamine-supplemented OLETF rats compared with control OLETF rats. At the age of 55 weeks, high-dose thiamine supplemented OLETF rats had increased GIP protein expression compared with control OLETF rats. GIP protein expression was increased in thiamine-supplemented rats despite the suppression of obesity and diabetic complications.

Our previous study demonstrated the increased expression of the *Gip* in the livers of thiamine-supplemented rats. In addition, we previously reported that the streptozotocin-induced diabetic state triggered GIP expression in rat livers. In the

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



present study, GIP protein expression in the liver was increased in thiamine-supplemented rats compared with that in controls, suggesting that it is involved in preventing and controlling obesity-related diabetic complications. The novel findings of this study that GIP is expressed in the liver, is likely to be added to the story regarding GIP modification of the obese diabetic state.

P508

Air pollution effects on genome stability: human biomonitoring and *in vitro* approach

Dr Goran Gajski

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

*Goran Gajski, PhD is a Senior Scientific Associate at the Institute for Medical Research and Occupational Health in Zagreb, Croatia with a scientific background in biochemistry and molecular biology. In genetic toxicology, he uses various methodological approaches, both *in vitro* and *in vivo*, on different cell and animal models to investigate the effects of various physical and chemical agents on organisms, tissues, cells, and cell structures with special emphasis on the DNA molecule. Moreover, the scope of his work also comprises human biomonitoring studies in different environmental and occupational settings. He was involved in several national and international projects as principal investigator and team member and has published more than 130 papers and book chapters that have been cited more than 5000 times with an h-index of 38 (by Google Scholar). For his work he received several national and international scientific awards, among other the Danubius Young Scientist Award issued by the Austrian Federal Ministry of Science and the National Award for Science in the Field of Natural Sciences issued by the Croatian Parliament. Currently, he is a chair of the International Comet Assay Group an affiliated group of the European Environmental Mutagenesis and Genomics Society. He is a European Registered Toxicologist (ERT) and Editorial Board member of the journal *Medicine*®.*

Air pollution effects on genome stability: human biomonitoring and *in vitro* approach

Goran Gajski¹, for HUMNap/EDIAQI projects, Institute for Medical Research and Occupational Health¹, Zagreb, Croatia.

Introduction. Both indoor and outdoor air pollution can have adverse effects on human health and the environment, but outdoor pollution often receives more attention due to its visibility and widespread impact. However, indoor air pollution can be equally harmful, especially since people spend a significant amount of time indoors.

Aims. We aimed to investigate how air pollution can affect genomic stability and our health by determining possible associations between air pollutants and biomarkers of exposure and effects.

Methods. This was done by human biomonitoring as well as by translating real-scenario exposure to *in vitro* (human lung carcinoma A549 cells and human peripheral blood cells) using the comet and micronucleus assays.

Results. Retrospectively we evaluated genomic instability in blood cells of Zagreb (Croatia) residents ($N=130$) and associated those biomarkers with air pollution levels during the years 2011-2015. There was no observed significant positive association between assayed parameters showing also that the measured air pollution parameters were mainly below regulatory limits, except for B[a]P. Prospectively, we investigated the effects of air pollution and BTEX (benzene, toluene, ethylbenzene, and xylene) exposure on genomic instability in blood and buccal cells of the same population ($N=60$) during the years 2021-2022, and revealed that all measured outdoor air pollutants agreed with previously reported values and

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



were below the regulatory limits, except for PM₁₀ particles and B[a]P bound to PM₁₀. Here, we also did not observe a notable impact of air pollutants on tested parameters. *In vitro* evaluation of different polycyclic aromatic hydrocarbons, present in indoor and outdoor air, as single compounds, binary, and complex mixtures indicated their cell- and concentration-dependent cyto/genotoxicity.

Discussion. Since air pollution is considered a significant health issue, and is often site-specific, more studies using biomarkers of exposure and effect could be expected. This will also lead to the development of appropriate models for the prediction of air pollution-induced effects on humans and the environment.

Supported by the Croatian Science Foundation (#1192 HUMNap) and Horizon Europe (#101057497 EDIAQI)

Gajski et al (2022) IJMS 23(17):10083

Geric et al (2024) JoX 14(1): 368–379

P509

UVA induces glycolytic reprogramming by regulating acid extruders in A375 melanoma cells

Miss Pin-Chen Lin

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

UVA induces glycolytic reprogramming by regulating acid extruders in A375 melanoma cells

Pin-Chen Lin¹, Eagle Yi-Kung, Huang¹. Department of Pharmacology, National Defense Medical Center¹, Taipei, Taiwan.

Introduction. Melanoma is the deadliest form of skin cancer, with the highest mortality rates. Ultraviolet (UV) radiation, specifically UVA (315–400 nm) and UVB (280–315 nm), is the greatest risk factor for melanoma. One of the hallmarks of cancer cells is altered metabolism, particularly increased glycolysis regardless of oxygen levels, known as the Warburg effect. This effect causes cancer cells to produce large amounts of lactate and protons, thus upregulating acid extruder proteins such as Na⁺/H⁺ exchanger (NHE), Na⁺/HCO₃⁻ cotransporter (NBC) and monocarboxylate transporters (MCT) to further extrude excess acid, creating an acidic tumor microenvironment in favor of tumor progression. Previous studies have reported that UVA enhances the Warburg effect and promotes tumor progression. However, the effects of UVA on pH homeostasis and the microenvironment of melanoma cells have not been examined.

Aims. In light of the importance of pH homeostasis in cancer progression, the present study aims to investigate the long-term effects of UVA on metabolic status and pH regulation in melanoma cells (A375).

Methods. A375 cells were exposed to UVA (6 J/cm²) once daily for 3 consecutive days. Seahorse XFp Analyzer was used to measure the changes in metabolic status. Intracellular pH was measured by microspectrofluorimetry with a pH-sensitive fluorescent dye, BCECF. NH₄Cl pre-pulse and lactate techniques were used to determine NHE and MCT activity. Western blot analysis and flow cytometry were performed to examine the total and cell membrane protein expression of acid-extruders, respectively. Transwell insert assay was used to measure the microenvironmental effects.

Results. Our preliminary data shows that UVA (6 J/cm²) once daily for 3 consecutive days enhances the glycolysis capacity of A375 cells and upregulates the activity and expression of acid extruder proteins to maintain pH homeostasis in melanoma cells. Besides, the UVA-exposed cell created a more acidic microenvironment, which favored the surrounding cells to migrate.

Discussion. Our data suggests that UVA induces the tumor-associated Warburg effect by regulating acid extruder activity to maintain pH homeostasis and further create a microenvironment conducive to cancer growth. It is also interesting to note that MCT seems to play a significant role in terms of extruding acid in UVA-exposed melanoma cells.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P510

Understanding the pharmacokinetics of enteric coated sodium valproate in overdose

Prof Andrew Rowland

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Andrew Rowland is a Professor of Clinical Pharmacology at Flinders University. He leads a highly productive team of researchers at the forefront of advancing extracellular vesicle isolation and analysis for use with human biospecimens. Andrew's team are world leaders in the isolation and characterisation of tissue specific extracellular vesicles from blood and work closely with industry and clinicians to apply this technology to improve patient outcomes by enhancing drug efficacy and minimising harms. Andrew's 143 peer-reviewed manuscripts have been cited more than 6,500 times, reflecting the high impact of his research, Andrew's five-year field-weighted citation index of 7.74. Andrew holds leadership roles across multiple professional societies, including ASCEPT, where he serves on the society's Board of Directors and is actively involved in philanthropic initiatives, through organisations including Flinders Foundation, Starlight and Tour de Cure.

Understanding the pharmacokinetics of enteric coated sodium valproate in overdose

Angela Rowland¹, Sam Alfred¹, Andrew Rowland². Toxicology Service, Royal Adelaide Hospital¹, Adelaide, SA, Australia; College of Medicines and Public Health, Flinders University², Adelaide, SA, Australia.

Introduction: A challenge to establishing best practice in response to overdose involving sodium valproate (VPA) is the limited pharmacokinetic data at doses well above the therapeutic range. This impacts the ability to accurately predict clinical course, initiate early interventions to prevent neurological sequelae before reaching toxic concentrations, and to measure the effectiveness of new interventions. One such treatment of interest is administration of meropenem, which has the potential to rapidly increase VPA elimination and attenuate toxicity in overdose. The parameters of clinical relevance are maximum plasma concentration (C_{max}), time to peak plasma concentration (t_{max}) and half-life ($t_{1/2}$).

Aims: To build and verify a physiologically based pharmacokinetic model describing the kinetics of exposure to enteric coated (EC) sodium valproate (EC-VPA) in overdose, and the effect of administering meropenem.

Methods: A minimal PBPK model for EC-VPA was built and verified using the Simcyp Simulator (version 19.1). The model incorporated an advanced dissolution, absorption and metabolism (ADAM) absorption model with a monolithic system solid modified release formulation and concentration dependent plasma protein binding profile. EC-VPA elimination was defined based on enzyme kinetics as the K_m and V_{max} for individual metabolic pathways to enable assessment of saturable clearance pathways. The performance of the model was verified by comparison to published plasma concentration time profiles for EC-VPA. The impact of meropenem administration on EC-VPA exposure was simulated by adjusting the percentage of EC-VPA available for reabsorption and scaling V_{max} for UGT mediated elimination pathways. Virtual clinical trials were performed in $n=120$ healthy subjects aged 18 to 50 years (50% female).

Results: At a 500 mg dose the kinetics of simulated EC-VPA exposure reflected the concentration time profile observed in clinical trials; t_{max} , C_{max} , AUC and $t_{1/2}$ were 4.5 hrs, 45.2 mg/L, 1,115 mg/L.hr, and 16.1 hrs, respectively. Prolonged t_{max} and $t_{1/2}$, and non-dose proportional increase in C_{max} were observed in overdose. Co-administration of meropenem resulted in only minor attenuation of C_{max} , but a 2-fold reduction in $t_{1/2}$, consistent with increased clearance.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



Discussion: A PBPK model describing the kinetics of EC-VPA exposure at doses up to 110 g was built and verified. This model may be applied to interrogate the effectiveness of various interventions to minimise VPA exposure in overdose including administration of activated charcoal and administration of meropenem.

P511

Cytotoxicity assessment employing environmentally relevant micro- and nanoplastics libraries.

Dr Yuya Haga

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Cytotoxicity assessment employing environmentally relevant micro- and nanoplastics libraries.

Yuya Haga¹, Sota Manabe^{1,2}, Hirofumi Tsujino^{1,2,3}, Haruyasu Asahara^{1,2,4}, Ryotaro Tsutsumi⁵, Kazuya Nagano⁵, Kazuma Higashisaka^{1,2,6}, Yasuo Tsutsumi^{1,2,4,7}, Grad. Sch. Pharm. Sci., Osaka Univ.¹, Osaka, Japan; Sch. Pharm. Sci., Osaka Univ.², Osaka, Japan; Museum Links, Osaka Univ.³, Osaka, Japan; Inst. for Open and Transdisciplinary Res. Initiatives, Osaka Univ.⁴, Osaka, Japan; Sch. Pharm. Sci., Wakayama Med. Univ.⁵, Wakayama, Japan; Inst. for Advanced Co-Creation Studies, Osaka Univ.⁶, Osaka, Japan; Global Ctr. for Med. Eng. and Informatics, Osaka Univ.⁷, Osaka, Japan.

Introduction. The prevalence of microplastics (MPs; particles smaller than 5 mm) and nanoplastics (NPs; smaller than 1 µm) in the environment has raised concerns regarding potential biological effects, highlighting the need for further investigation. However, environmental MNPs vary widely in properties like size, shape, and surface modifications, often overlooked in lab studies using uniform particles.

Aims. This study aims to address the critical gap in understanding the environmental impact of MNPs by developing libraries that accurately reflect their complex physicochemical properties, enabling comprehensive safety evaluations.

Methods. Polyethylene (PE) and Polyvinyl chloride (PVC) were chosen as representative polymers due to their widespread use. Sphere, fragmented and surface-oxidized MNPs were generated to mimic environmental conditions. ATR-IR analysis and scanning electron microscopy were employed to confirm their properties. Cytotoxicity was evaluated by MTT assay.

Results. Surface-oxidized MNPs were created through exposure to vacuum UV light at 172 nm in air, mimicking environmental conditions. ATR-IR analysis detected hydroxy and carbonyl groups on the surface. NPs were produced using a precipitation-based method outlined in previous literature. Using these MNPs libraries, cytotoxicity assessments were performed. Surface-oxidized MNPs demonstrated elevated cytotoxicity compared to their non-oxidized MNPs, as indicated by cytotoxicity assays. These results emphasize the necessity of incorporating environmental factors into MNPs safety evaluations.

Discussion. The development of these libraries provides a valuable tool for conducting comprehensive safety evaluations, including oral and inhalation exposure tests, and various hazard analyses. These resources are accessible for distribution upon request through future collaborations. For inquiries concerning these libraries, please contact Yuya Haga at haga-y@phs.osaka-u.ac.jp.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P512

Molecular mechanism of malignant change by Benzopyrene-induced cellular senescence

Ms Natsuko Kitamoto

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Molecular mechanism of malignant change by Benzopyrene-induced cellular senescence

Natsuko KITAMOTO¹, Yuya HAGA^{1,2}, Kazuma HIGASHISAKA^{1,2,3}, Yasuo TSUTSUMI^{1,2,4,5}. Grad. Sch. Pharm. Sci., Osaka Univ.¹, Osaka, Japan; Sch. Pharm. Sci., Osaka Univ.², Osaka, Japan; IACS, Osaka Univ.³, Osaka, Japan; MEI Ctr., Osaka Univ.⁴, Osaka, Japan; OTRI, Osaka Univ.⁵, Osaka, Japan.

Introduction. The association between chemical substances like benzopyrene (BP) and cancer has been extensively studied for years. However, the majority of research has centered on the initial stages of carcinogenesis, which occur early in cancer development. Understanding the malignant change process that leads to cancer recurrence and metastasis still lacks comprehensive insight. In this point, recent discoveries have revealed that BP induces cellular senescence, a state of growth arrest triggered by cellular stressors such as DNA damage, which has been implicated in malignant change.

Aims. Our study seeks to uncover how BP contributes to malignant change by inducing cellular senescence.

Methods. Exposure of estrogen receptor (ER)-positive breast cancer cells MCF7 to BP or benzopyrene diol epoxide (BPDE) (0, 0.1, 1 μ M) for 3 days induced cellular senescence. Additionally, RNA-seq analysis was conducted on MCF7 cells induced with cellular senescence by BP and BPDE, aiming to identify potential candidate genes contributing to malignant change.

Results. Cellular senescence was induced in MCF7 cells following a 3 days exposure to BP and BPDE. Following BP exposure, MCF7 cells initially displayed reduced cell proliferation akin to typical cellular senescence. However, continued cultivation in BP-free medium led to the restoration of proliferation capacity, ultimately indicating the potential for acquiring even greater proliferation ability than prior to BP exposure. Mechanistically, exposure to BP resulted in the nuclear translocation of Aryl hydrocarbon receptor (AhR) and ER α prior to changes in cellular senescence markers being observed. Furthermore, RNA-seq analysis revealed a downregulation of several genes commonly associated with the suppression of cancer malignant transformation in both BP and BPDE exposure groups.

Discussion. BP was suggested to induce cellular senescence. Furthermore, the senescence induced by BP indicated the potential for reversible recovery of cell proliferation ability. Our future efforts will focus on elucidating the mechanistic link between AhR and the candidate genes identified through RNA-seq analysis.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P513

Effects of heavy metals on interleukin-8 release from prostate stromal WPMY-1 cells

Mr Chadchan Supsamarnwong

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Chadchan Supsamarnwong graduated from Mahidol Wittayanusorn School and is now studying at the Faculty of Medicine, Ramathibodi Hospital.

Effects of heavy metals on interleukin-8 release from prostate stromal WPMY-1 cells

Supsamarnwong C¹, Woonfak P², Settacomkul R², Vivithanaporn P². Faculty of Medicine Ramathibodi Hospital, Mahidol University¹, Bangkok, TH.; Chakri Naruebodindra Medical Institute, Faculty of Medicine Ramathibodi Hospital, Mahidol University², Samut Prakan, TH.

Introduction. Benign prostatic hyperplasia (BPH) is a common cause of prostatic enlargement, causing urinary obstruction, in elderly male and prostate cancer (PCa). WPMY-1 cell line is a human prostatic stromal myofibroblast cell used as a model to study stromal-epithelial interaction in BPH and PCa (Webber et al., 1999). Heavy metals are major environmental pollutants that are related to several health disorders, including prostate disorders. Heavy metals cause excessively increasing reactive oxygen species (ROS) generation, abnormal homeostasis, disrupting normal hormonal regulation, which can promote further inflammation in the prostate (Silva et al, 2023). Chronic and recurrent prostate inflammation plays a role in BPH and PCa pathogenesis (Nunzio et al., 2011). Levels of lead and cadmium are higher among BPH and PCa patients (Singh et al, 2023).

Aims. To investigate and compare the effects of various concentrations of heavy metals, including cadmium (CdCl₂), zinc (ZnCl₂), nickel (NiCl₂), lead (PbCl₂) and manganese (MnCl₂) on IL-8 production in WPMY-1 cells.

Methods. WPMY-1 cells were treated with heavy metals at different concentrations for 24 hours. Cell viability was measured by MTT and IL-8 levels in supernatant were measured by ELISAs.

Results. From MTT results, the maximum non-toxic concentrations of CdCl₂, ZnCl₂, NiCl₂, PbCl₂, and MnCl₂ were 50, 1000, 1000, 250, and 500 μM, respectively. From ELISAs results, PbCl₂ at 100, 250 μM and MnCl₂ at 250, 500 μM significantly increased the level of IL-8 compared to untreated cells. However, CdCl₂, ZnCl₂, and NiCl₂ did not increase IL-8 production in WPMY-1 cells.

Discussion. In our study, lead and manganese induced IL-8 secretion in human prostate stromal WPMY-1 cells; therefore, exposure to these two heavy metals could lead to prostate disorders such as BPH and PCa.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P514

CASK mediates docetaxel- and oxidative stress-induced prostate cancer cell death

Prof Wan-wan Lin

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

CASK mediates docetaxel- and oxidative stress-induced prostate cancer cell death

Wan-Wan Lin¹, Varsha Rathore^{2,3}, Duen Yi Huang¹. Department of Pharmacology, College of Medicine, National Taiwan University¹, Taipei 100233, Taiwan; Chemical Biology and Molecular Biophysics, Taiwan International Graduate Program, Academia Sinica², Taipei 115201, Taiwan; Institute of Biotechnology, College of Life Sciences and Medicine, National Tsing Hua University³, Hsinchu 300044, Taiwan.

Introduction. Calcium/calmodulin-dependent serine protein kinase (CASK) is a scaffold protein and its major identified function is most in the brain. To date, the role of CASK in cancer biology remains elusive.

Aims. To determine the role of CASK in docetaxel- and H₂O₂-induced prostate cancer cell death.

Methods. We generated the stable CASK knockdown PC3 cells by lentivirus.

Results. CASK silencing can reduce anti-microtubule agents including docetaxel, epothilone B and vincristine induced cell apoptosis and G2/M cell arrest. CASK silencing also upregulates Mcl-1 but downregulates Bax and Bak at resting state of PC3 cells. Moreover, CASK silencing activates AKT/mTOR and AMPK, but inhibits GSK3 β . We found selective inhibitors of AKT, mTOR, and AMPK can reduce cell viability, while inhibitor of GSK3 β can enhance cell survival under docetaxel treatment in control and/or CASK silencing cells. We further found the contributions of AKT/mTOR/GSK3 β and AMPK in regulation of Mcl-1 expression. Of note, PARP-1 activity confers a cell protective role in docetaxel-treated CASK silencing cells by reducing γ H2AX expression, while PARP-1 inhibitor olaparib reduces the cell protective effect of CASK silencing. Moreover, CASK silencing also protects PC3 cells from H₂O₂-induced PARP-1 activation, mitochondrial dysfunction and cell parthanatos.

Discussion. CASK is a novel regulator of cancer cell death and might involve in therapeutic effectiveness in prostate cancer.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P515

Oxyresveratrol and resveratrol reduce lead-induced IL-6 and IL-8 secretion from human astrocytes

Mr Putin Nudaeng

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Putin Nudaeng, a Medical student I graduated high school from Suankularb Wittayalai Thonburi school, Bangkok, Thailand. I'm currently a third-year medical student from the Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

Oxyresveratrol and resveratrol reduce lead-induced IL-6 and IL-8 secretion from human astrocytes.

Nudaeng P¹, Woonfak P², Jutabla P², Vivithanaporn P² Faculty of Medicine Ramathibodi Hospital, Mahidol University¹, Bangkok, TH.; Chakri Naruebodindra Medical Institute, Faculty of Medicine Ramathibodi Hospital, Mahidol University², Samut Prakan, TH.

Introduction. Lead (Pb) accumulation in the nervous system potentiates the risk of many neurological defects. Pb induces the activation of astrocytes and the release of pro-inflammatory mediators from astrocytes. Resveratrol and its hydroxylated derivative, oxyresveratrol, can decrease the expression of pro-inflammatory cytokines. The present study hypothesized that oxyresveratrol and resveratrol can reduce Pb-induced pro-inflammatory cytokines secretion from U-87 MG human astrocytoma cells.

Aims. Our first objective is to determine the effect of Pb on cytokine secretion in U-87 MG cells. Next, we aim to determine the effects of oxyresveratrol and resveratrol on Pb-induced cytokine levels in U-87 MG cells and their underlying mechanisms.

Methods. Cell viability and cytokine production were measured at 24 hours by MTT and ELISA, respectively. The signaling protein responsible for cytokine production was detected at 30 minutes by Western blot.

Results. Pb up to 500 μ M and co-treatment of Pb with oxyresveratrol and resveratrol at 25 and 50 μ M did not decrease cell viability. Pb at 50 and 500 μ M increased secretion of IL-6 and IL-8. Oxyresveratrol and resveratrol at 25 and 50 μ M reduced Pb-induced secretion of IL-6 and IL-8. Oxyresveratrol and resveratrol inhibited the phosphorylation of ERK1/2 and JNK proteins.

Discussion. Our results show that both oxyresveratrol and resveratrol could reduce Pb-induced inflammation from human astrocytes. Thus, both compounds could potentially be developed for Pb-related inflammation in the central nervous system.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P516

CXCL5 inhibition improved renal tubular epithelial cells injury of diabetic kidney disease

Miss Ching Chen

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

I am Ching Chen, a pharmacology Ph.D. candidate at National Yang-Ming Chiao Tung University. My research focuses on vascular medicine, molecular biology, diabetes mellitus, and kidney disease, with expertise in experimental animal model design and drug development. My research is dedicated to understanding the role of the chemokine CXCL5 in diabetes and its complications. I have extensively explored the bidirectional interactions of CXCL5 in diabetic nephropathy and its potential therapeutic mechanisms. Through both in vitro and in vivo experiments, I have demonstrated the significant impact of CXCL5 on diabetic nephropathy. These findings highlight my deep understanding and innovative contributions to the field.

CXCL5 inhibition improved renal tubular epithelial cells injury of diabetic kidney disease

Ching Chen^{1,2}, Jaw-Wen Chen^{1,2,3,4,5,6} and Ting-Ting Chang^{1,2,5,7}. Dept of Pharmacol, National Yang Ming Chiao Tung Univ¹, Taipei, Taiwan. Sch of Med, National Yang Ming Chiao Tung Univ², Taipei, Taiwan. Fac of Med, Coll of Med, Taipei Medical Univ³, Taipei, Taiwan. Div of Cardiology, Taipei Medical Univ Hosp⁴, Taipei, Taiwan. Cardiovascular Research Center, Taipei Medical Univ Hosp⁵, Taipei, Taiwan. Cardiovascular Research Center, National Yang Ming Chiao Tung Univ⁶, Taipei, Taiwan. Biomed Ind Ph.D. Program, National Yang Ming Chiao Tung Univ⁷, Taipei, Taiwan.

Introduction. Diabetic kidney disease (DKD) is a major cause of chronic kidney disease (Umanath K, et al, 2018). Hyperglycemia induces the release of inflammatory chemokines and cytokines, activating inflammatory pathways that exacerbate the progression of DKD. Increased levels of CXC motif chemokine ligand 5 (CXCL5) have been observed in both clinical and experimental studies of diabetes (Ruster C et al, 2008).

Aims. This study aimed to explore the direct effects and underlying mechanisms of CXCL5 on DKD in renal tubular epithelial cells.

Methods. Human renal proximal tubular epithelial cells were stimulated with high glucose in the in vitro experiments. Cell reactive oxygen species (ROS) production was measured using the Amplex Red Hydrogen Peroxide/Peroxidase assay. Cell apoptosis was measured using the TUNEL assay. Inflammatory, fibrotic and apoptotic proteins expression was measured using western blotting.

Results. The expression of CXCL5 was increased in high glucose-stimulated renal tubular epithelial cells. Inhibition of CXCL5 by neutralizing antibodies reduced ROS production. Inhibition of CXCL5 through the administration of CXCL5-neutralizing antibodies downregulated p-JNK and reduced expression of downstream inflammatory and fibrotic proteins including interleukin (IL)-1 β , IL-6, tumor necrosis factor- α , collagen-1, transforming growth factor- β and p-smad2/3. Inhibition of CXCL5 also decreased the number of apoptotic cells and protein expression including cleaved caspase-3 and poly ADP-ribose polymerase.

Discussion. These findings suggest that CXCL5 inhibition may protect renal tubular epithelial cells from high glucose-stimulated injury. Further studies are needed to verify whether this effect is consistent in the in vivo studies.

Ruster C et al, (2008) Front Biosci 13:944-55

Umanath K et al, (2018) Am J Kidney Dis 71(6):884-95

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P517

Diosgenin attenuated ischemia-reperfusion injury-induced AKI and AKI-to-CKD transition

Miss Tien Yun Lan

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

My name is Tien-Yun Lan, and I am currently a Ph.D. student at the Institute of Pharmacology, National Yang Ming Chiao Tung University, Taiwan. My research primarily focuses on pharmacology related to kidney diseases, with a particular emphasis on acute kidney injury (AKI). In July 2024, I published a study exploring a novel potential therapeutic agent for ischemia-reperfusion-induced acute kidney injury.

As I move forward in my research career, I am expanding my focus to the discovery of potential therapeutic agents for diabetes and cardiovascular diseases—two major global health concerns.

Diosgenin attenuated ischemia-reperfusion injury-induced AKI and AKI-to-CKD transition

Tien-Yun Lan^{1,2} and Ting-Ting Chang^{1,2,3,4}. Dept of Pharmacol, National Yang Ming Chiao Tung Univ¹, Taipei, Taiwan. Sch of Med, National Yang Ming Chiao Tung Univ², Taipei, Taiwan. Taipei, Taiwan. Cardiovascular Research Center, Taipei Medical Univ Hosp³, Taipei, Taiwan. Biomed Ind Ph.D. Program, National Yang Ming Chiao Tung Univ⁴, Taipei, Taiwan.

Introduction. Acute kidney injury (AKI), a global medical concern lacking effective pharmacological treatment, has been closely linked to the development of chronic kidney disease (CKD) (Zhu et al., 2022). Ischemia-reperfusion (I/R) is the primary cause of AKI, which can elevate oxidative stress in the kidney and trigger the underlying mechanisms of inflammation and fibrogenesis, resulting in kidney dysfunction (Sun et al., 2022). Diosgenin, a natural compound, was reported to have anti-inflammatory and antioxidative properties (Mohamadi et al., 2021).

Aims. This study aimed to investigate the effects of diosgenin on I/R-induced AKI and AKI-to-CKD transition.

Methods. In the in vitro experiment, human renal proximal tubular epithelial cells were exposed to I/R conditions to evaluate the antioxidative properties of diosgenin. AKI animal model was established in mice through the induction of I/R in the left kidney and excising the right kidney. Diosgenin was administered after AKI induction, renal function and histological analysis of kidney tissues were conducted. The protein expression was analyzed by using Western blotting.

Results. Diosgenin reduced the generation of reactive oxidative species in I/R-stimulated human proximal tubular cells. Treatment with diosgenin reduced serum levels of creatinine and blood urea nitrogen in animals with I/R-induced AKI. Diosgenin administration also improved the kidney histological changes such as tubular epithelial cell injury and collagen deposition after the I/R injury. Treating AKI mice with diosgenin downregulated the inflammatory, fibrotic, and epithelial-mesenchymal transition-related proteins in kidney tissue.

Discussion. Diosgenin exhibited renoprotective effect in I/R-induced AKI and in the transition from AKI to CKD. The protective effect of diosgenin on the kidneys may be mediated through its antioxidant and anti-inflammatory mechanisms. However, further research is necessary to verify the specific mechanism by which diosgenin confers its protective effects in cases of I/R-induced AKI.

ZHU, Zijing, et al. (2022) *Metabolism*, 131: 155194.

SUN, Wenjuan, et al. (2022) *Frontiers in Pharmacology*, 13: 807452.

Mohamadi, N., et al. (2021) *J Asian Nat Prod Res*, 23(5): 466-477.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P518

Considerations of the expanded guanylate cyclase family in gastrointestinal health

Dr Helen Irving

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Considerations of the expanded guanylate cyclase family in gastrointestinal health

Helen Irving^{1,2}, Ilona Turek^{1,2,3}, Cassandra Cianciarulo^{1,2}, Trang Nguyen^{1,2}, Chris Gehring⁴. ¹La Trobe Institute for Molecular Science, La Trobe University¹; Department of Rural Clinical Sciences, La Trobe University², Bendigo, VIC, Australia; Australian Centre for Disease Preparedness, CSIRO³, Geelong, VIC, Australia; Department of Chemistry, Biochemistry and Biotechnology, University of Perugia⁴, Perugia, Italy.

Introduction. Guanylate cyclases (GCs) catalyze the formation of guanosine 3',5'-cyclic monophosphate (cGMP) from guanosine-5'-triphosphate (GTP) and include the soluble GCs and membrane-bound GCs like GC-C receptors or heat stable enterotoxin receptor. Functional GC catalytic centres with low activity within kinase domains exist in plants. These crypto GCs generate cGMP essential for both intramolecular and downstream signalling.

Aims. Search and identify and begin characterisation of crypto GCs in the human proteome.

Methods. Pattern matching searches in the human annotated proteome were made using ScanProsite (Expasy). Vector constructs were prepared using Gateway cloning and site directed mutagenesis. Recombinant proteins were generated and cGMP production was assessed. THP-1 wildtype and CRISPR/Cas 9 generated IRAK3^{-/-} knockout cells were used along with cells containing NFκB reporter systems. cGMP, IL6 and TNFα were measured using ELISA kits.

Results. 18 candidates, including the neurotropic receptor tyrosine kinase 1 (NTRK1) and interleukin 1 receptor associated kinase 5 (IRAK3) that negatively regulates immune response in macrophages. NTRK1 has a functional GC embedded within the intracellular kinase domain similar to crypto GC plant receptor kinases. *In vitro* characterization shows that the embedded NTRK1 GC is functional. IRAK3 is a cytosolic protein containing a functional GC embedded in the pseudokinase domain. A selected alanine screen revealed amino acids essential for catalytic activity. Using genetic and pharmacological approaches we show that IRAK3 depends on self-generated cGMP for effective downstream signalling in immune cells to limit cytokine production.

Discussion. These findings point to hitherto unsuspected roles of localised cGMP enriched nanodomains essential for intramolecular and downstream signalling in mediating innate immune responses and inflammation and NTRK1-dependent growth and neoplasia. The impacts different levels of intracellular cGMP in immune cells in the intestine will be discussed in relation to GC-C and human diseases like inflammatory bowel disease.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P519

Pharmacological investigation of 5-HT effects on the isolated porcine urethra

Dr Iris Lim

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr. Iris Lim is an Assistant Professor in Biomedical Sciences at Bond University. Her main research interests focus on investigating the physiology and pharmacology of the lower urinary tract to discover treatments for lower urinary tract disorders. Dr. Lim is also a passionate educator and is particularly dedicated to utilising innovative tools and methods, such as gamification and game-based learning, to enhance student learning experiences and engagement.

Pharmacological investigation of 5-HT effects on the isolated porcine urethra

Eriq Burovski¹, Donna Sellers¹, Russ Chess-Williams¹, Iris Lim¹. Centre for Urology Research, Faculty of Health Sciences and Medicine, Bond University¹, Gold Coast, QLD, Australia.

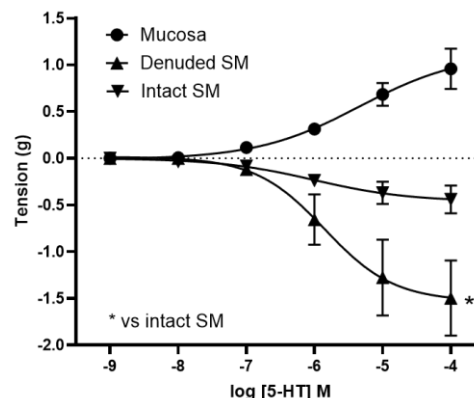
Introduction. Clinical pharmacological treatments available for stress urinary incontinence are limited (Harland et al., 2023).

Aims. The present study aimed to investigate the effects of 5-HT in the porcine urethra, to explore potential new treatment targets.

Methods. Using an organ bath setup, contractile responses of isolated porcine proximal urethral strips (denuded smooth muscle, mucosa-intact smooth muscle, and mucosa) to increasing concentrations (10 nmol/L – 100 µmol/L) of 5-HT were examined. In another set of experiments, concentration responses to 5-HT were repeated in the absence and presence of ketanserin (30 nmol/L) in paired tissue strips. Paired Student's *t*-tests were performed to identify statistically significant differences where a *p*-value of < 0.05 was considered statistically significant.

Results. When subjected to 5-HT, the urethral mucosal strips generated a concentration-dependent increase in tone, while the smooth muscle strips concentration-dependently relaxed. Urethral smooth muscle strips with intact mucosa relaxed significantly lesser than strips denuded of mucosa. At higher concentrations of 5-HT (10 µmol/L and above), the spontaneous contraction rate exhibited by the mucosa was significantly enhanced (*p*=0.0013). Ketanserin (30 nmol/L) significantly attenuated the 5-HT-induced tonic contractions in the mucosal strips (*p*=0.0026), but did not affect the 5-HT-induced relaxatory responses in urethral smooth muscle strips or the 5-HT-induced increase in spontaneous contraction rate in mucosal strips (*p*>0.05).

Discussion. The present findings suggest that 5-HT-induced tonic contractile responses in the urethral mucosa is mediated by the 5-HT_{2A} receptor subtype.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P520

Cytotoxicity of Doxazosin in Bladder Cancer Cells and Effects on Bladder Function

Mr Liam O'Callaghan

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Liam O'Callaghan is a PhD student and Assistant Teaching Fellow at Bond University. After completing an accelerated Bachelor of Biomedical Science degree in 2020, Liam developed a keen interest in research and laboratory techniques. This led him to complete a First-Class Honours project on repurposing α -1 antagonists to treat prostate cancer, which yielded promising results. Liam's PhD project, which is on track for completion in mid-2025, is now assessing the efficacy of the same drug class in treating bladder cancer. Liam is also passionate about shaping the future of researchers and clinical practitioners alike, enjoying a busy schedule of teaching alongside his own academic pursuits.

Cytotoxicity of doxazosin in bladder cancer *in vitro* and impact on bladder function

Liam A O'Callaghan¹, Russ Chess-Williams¹, Katie Powell¹, Catherine McDermott¹. Centre for Urology Research, Faculty of Health Sciences and Medicine, Bond University¹, Gold Coast, QLD, Australia.

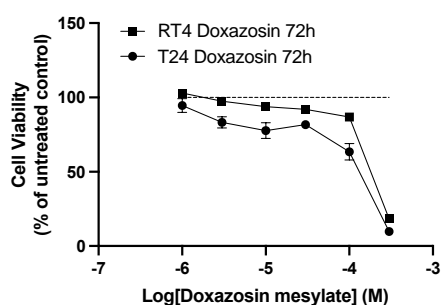
Introduction. Bladder cancer is a prevalent, complex, and costly disease. Current treatments often involve the use of intravesical agents; however, these treatments are frequently limited by high recurrence rates and side effects that adversely affect the quality of life.

Aims. This study aimed to evaluate the cytotoxicity of the α 1-adrenoceptor antagonist doxazosin on high-grade (T24) and low-grade (RT4) human bladder cancer cells. Additionally, the effects of luminal doxazosin treatment on normal bladder function were investigated using a porcine model.

Methods. T24 and RT4 cells were incubated for 2 hours with doxazosin (1-300 μ M) or vehicle (DMSO), mimicking intravesical treatment. Cell viability was assessed at 24, 48, and 72 hours using the resazurin reduction assay. The luminal surface of female porcine bladders was treated with doxazosin (300 μ M) or vehicle in modified Ussing chambers for 2 hours, followed by organ bath studies to assess functional responses.

Results. T24 and RT4 cells pre-treated with doxazosin showed a statistically significant, concentration-dependent decrease in cell viability after 24, 48, and 72 hours. There was no significant change in bladder responses to carbachol, ATP, electric field stimulation, or KCl after doxazosin treatment. However, there was a significant increase in the maximum contractile response to carbachol in the full-thickness bladder tissue (39.48 mN/mg [Control] vs. 50.74 mN/mg [Doxazosin]; $p < 0.001$), with no significant change in potency detected (pEC_{50} 5.53 \pm 0.14 [Control] vs. 5.77 \pm 0.12 [Doxazosin]).

Discussion. The study demonstrates that doxazosin induces concentration-dependent cytotoxicity in high-grade (T24) and low-grade (RT4) bladder cancer cells while having little effect on normal bladder function. This suggests its potential for targeted therapeutic interventions in bladder cancer.



ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P521

Uropathogenic *Escherichia coli* causes significant urothelial damage in ex vivo porcine bladders

A/Prof Lu Liu

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Uropathogenic *Escherichia coli* causes significant urothelial damage in an *ex vivo* porcine bladder model, with no protective effect observed from cranberry or D-mannose

Jenane Konesan¹, Kylie J Mansfield², Lu Liu¹, School of Biomedical Sciences, UNSW Sydney¹, Sydney, NSW, Australia; Graduate School of Medicine, University of Wollongong², Wollongong, NSW, Australia

Introduction. Urinary tract infections (UTIs) are common infections primarily caused uropathogenic *Escherichia coli* (UPEC). To date, there is limited understanding of how UPEC affects the physiology of the bladder mucosal layer. UTIs are typically treated with antibiotics. However, due to the rise in antimicrobial resistance, there is a demand to identify other nonantibiotic alternatives.

Aims. This study aimed to investigate the impact of UPEC on the urothelium and lamina propria in an *ex vivo* porcine bladder model. Isolated bladder mucosal strips were also studied for their contractility in response to acetylcholine, serotonin, and neurokinin A. The effects of cranberry and D-mannose against UPEC infection were also determined.

Methods. Sheets of full-thickness bladder specimens from fresh female porcine bladders were placed in chambers with media separately bathing the luminal side and serosal surface. The luminal side was treated with antibody-free media (control), cranberry (3 mg/mL) or D-mannose (10 mM), with or without UPEC (UTI89, OD600:0.4) for 4 hours at 37°C, followed by processing for organ bath, H&E staining, and immunohistochemistry experiments.

Results. UPEC demonstrated significant damage to the urothelial integrity (urothelial cell loss), barrier function, and permeability (loss of uroplakins and tight junction protein ZO-1 expression). Remarkably, bladders infected with UPEC demonstrated a significantly higher contractility response to serotonin compared to the control. However, neither cranberry nor D-mannose provided a protective effect against urothelium damage caused by UPEC challenge. Additionally, the UPEC-induced increase in contractile response to serotonin was not reversed by cranberry.

Discussion. UPEC caused significant damage to the urothelium and uroplakin layer, and neither cranberry nor D-mannose demonstrated a reduction in this damage. Although some oedema was observed within the submucosal layer, where the contractile mechanisms involve myofibroblasts and thin smooth muscle bundles, the majority of the UPEC-induced damage was confined to the urothelial layer and did not result in noticeable changes in contractility. Overall, this study provided valuable insight into how UPEC causes significant damage to urothelial cell biology. Additionally, it highlighted the potential role of serotonin in bladder infections.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P522

Could darifenacin side effects include non-muscarinic interactions in the bladder?

Miss Vineesha Veer

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Vineesha Veer, BBiomedSci (Hon.), is a doctoral student researching the physiology and pharmacology of the lower urinary tract at the Centre for Urology Research, Faculty of Health Sciences and Medicine, Bond University. Vineesha's research aims is to identify any alternative mechanisms of antimuscarinics for patients with overactive bladder, to potentially better patient's compliance and outcomes when prescribed this drug class. Vineesha also has a passion for medical education and teaches a variety of physiology and pharmacology based subjects at Bond University.

Could darifenacin side effects include non-muscarinic interactions in the bladder?

Vineesha Veer¹, Russ Chess Williams¹ and Christian Moro¹.

Faculty Health Sciences and Medicine, Bond University¹, Robina, QLD, Australia

Introduction. Though antimuscarinics are the first-line pharmaceutical treatments for overactive bladder (OAB), 70% of newly diagnosed OAB patients cease antimuscarinics within one year. Previous literature suggests that darifenacin, a commonly prescribed OAB antimuscarinic, may influence non-muscarinic bladder contractions, potentially explaining reported side effects and reduced effectiveness (Veer, 2023).

Aims. To identify any non-muscarinic influences on contraction from darifenacin on detrusor or urothelium with lamina propria (U&LP) tissues.

Methods. Strips of porcine detrusor or U&LP were mounted into isolated tissue baths. Carbachol concentration-response curves were performed on paired tissues in the absence or presence of darifenacin (100 nM). Maximum contraction values from control and intervention curves were compared. Single-dose response experiments were also conducted in the presence of darifenacin (100 nM) with serotonin (100 µM), prostaglandin E₂ (10 µM), histamine (100 µM), αβ-methylene-ATP (10 µM), angiotensin II (100 nM), neurokinin A (300 nM) and carbachol (10 µM).

Results. For concentration-response experiments, darifenacin significantly reduced maximum contraction force to carbachol in both adult detrusor (n = 8) and U&LP (n = 9) tissues ($p < 0.05$). In single dose experiments, darifenacin significantly reduced maximum contraction in U&LP tissue preparations to carbachol by 49% (n = 10) and αβ-methylene ATP by 42% (n = 11). The reduction in maximum contraction by darifenacin was observed in detrusor tissue preparations to carbachol by 43% (n = 11), αβ-methylene ATP by 57% (n = 12), prostaglandin E₂ by 73% (n = 10), histamine by 75% (n = 12), and serotonin by 56% (n = 12).

Discussion. Darifenacin presents as an antimuscarinic medication that influences non-muscarinic pathways in urinary bladder tissue. This suggests darifenacin has the potential to either assist OAB patients with non-muscarinic pathophysiology or otherwise cause alternative side effects. Future directions include a systematic review to identify how darifenacin's secondary mechanisms may impact patient compliance and adverse effects.

Veer V, Chess-Williams R, Moro C (2023) *Neurourol. Urodyn.* 42(5):1080-1087.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P523

Depressed porcine ureter contractility with acute hypoxia is not alleviated by pre-conditioning

Prof Donna Sellers

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

Biography:

Dr Sellers has forged a distinguished academic career combining research and teaching at leading universities and hospitals in the United Kingdom. Focussing her research interests on the physiological and pharmacological function of smooth muscle, she has collaborated with fellow research scientists to relate her findings to medical disorders such as overactive bladder function and the complications of diabetes. Complementing her research portfolio, Dr Sellers has taught undergraduate and postgraduate subjects at Sheffield Hallam University, the University of Sheffield and the University of Manchester prior to joining Bond University's Faculty of Health Sciences and Medicine in 2009.

Depressed porcine ureter contractility with acute hypoxia is not alleviated by pre-conditioning

Emma Falk², Iris Lim¹, Elouise Tye¹, Thomas Carlsson², Russ Chess-Williams¹, Catherine McDermott¹, Donna J Sellers¹.
¹Centre for Urology Research, Bond University, Gold Coast, QLD, Australia; ²The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden.

Introduction. The damaging effects of hypoxia and the protective effects of hypoxic pre-conditioning using brief, intermittent hypoxic episodes or pharmacological agents such as adenosine have been described in the urinary bladder (Yu et al., 2004). The effects of hypoxia in other lower urinary tract (LUT) tissues, such as the ureter, which also experience hypoxia and ischaemia due to infection and obstruction with stones, are not yet known.

Aims. The aim was to examine the acute effects of hypoxia on contractility of the isolated porcine ureter and any potential protective effects of pre-conditioning.

Methods. Strips of ureter from female pigs from a local abattoir were mounted in Krebs bicarbonate buffer (37°C) under normoxia (95%O₂, 5%CO₂), mild hypoxia (95%air(21%O₂, 79%N₂), 5%CO₂) or severe hypoxia/glucose-free conditions (95%N₂, 5%CO₂). The effects of cumulative concentrations of phenylephrine and 5-HT on ureteral phasic contractions were recorded. Pre-conditioned tissues were exposed to mild or severe hypoxia followed by a period of normoxia (10 min. each), before switching to continued hypoxia. Statistical analysis was via two-way ANOVA.

Results. Under normoxic conditions phenylephrine and 5-HT increased the frequency and amplitude of phasic contractions in ureteral strips. Mild hypoxia significantly reduced the maximum frequency of phenylephrine-induced responses (by 71%, p<0.05, n=8), but did not affect amplitude, and similarly reduced the frequency of 5-HT-induced contractions (by 64%, p<0.05, n=8), but not the amplitude. Phasic and agonist-induced contractions completely ceased under severe hypoxic conditions. Preconditioning did not prevent the effects of mild or severe hypoxia.

Discussion. Ureteral smooth muscle is very sensitive to changes in oxygen levels *in vitro*. This may contribute to the symptoms experienced by patients with hypoxia due to ureteral stones or infections. Pre-conditioning using brief, intermittent hypoxic episodes did not prevent the depression, which is different to the bladder, and may suggest a difference in the mechanisms of oxygen sensing/signalling in the ureteral smooth muscle.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P524

Polymerization level of dietary fructans differentially affect the intestinal microbiota interactions

Miss Qin Yuan

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

P525

Targeting pain: A novel adjunct treatment to relieve BCG-immunotherapy induced side effects

Ms Georgia Bourlotos

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Georgia Bourlotos is currently in her second year of her PhD at Flinders University in the Neurourology Research Group. She graduated with a Bachelor of Medical Science and Honours in Medical Science from Flinders University. Her research focuses on bladder cancer and improving patient outcomes and their wellbeing. Georgia has previously published a review titled "BCG induced lower urinary tract symptoms during treatment for NMIBC - Mechanisms and management strategies" (DOI: 10.3389/fnins.2023.1327053) in Frontiers in Neuroscience. She was awarded the Flinders Health and Medical Research Institute PhD Scholarship and the Australian Governement Research Training Program Scholarship. Georgia is passionate in exploring potential pathways to reduce pain in patients suffering from superficial bladder cancer.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P526

Effects of acute hypoxia and pre-conditioning on contractility of isolated porcine urethra

Prof Donna Sellers

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Dr Sellers has forged a distinguished academic career combining research and teaching at leading universities and hospitals in the United Kingdom. Focussing her research interests on the physiological and pharmacological function of smooth muscle, she has collaborated with fellow research scientists to relate her findings to medical disorders such as overactive bladder function and the complications of diabetes. Complementing her research portfolio, Dr Sellers has taught undergraduate and postgraduate subjects at Sheffield Hallam University, the University of Sheffield and the University of Manchester prior to joining Bond University's Faculty of Health Sciences and Medicine in 2009.

Effects of acute hypoxia and pre-conditioning on contractility of isolated porcine urethra

Samantha Padeloup², Iris Lim¹, Elouise Tye¹, Thomas Carlsson², Russ Chess-Williams¹, Catherine McDermott¹, Donna J Sellers¹. ¹Centre for Urology Research, Bond University, Gold Coast, QLD, Australia, ²The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Introduction. Chronic ischaemia and hypoxia have been linked to bladder dysfunction, with evidence for protective effects of hypoxic pre-conditioning in the bladder, using brief hypoxic episodes or pharmacological agents such as adenosine (Hisadome *et al.*, 2007). However, little is known about the effects in related lower urinary tract tissues, such as the urethra, which can experience hypoxia and ischaemia due to atherosclerosis or bladder outlet obstruction.

Aims. To investigate the acute effects of hypoxia on contractility of the isolated porcine urethra and the potential protective effects of pre-conditioning.

Methods. Female porcine urethra strips from a local abattoir were mounted in Krebs bicarbonate buffer (37°C) under normoxia (95%O₂, 5%CO₂), mild hypoxia (95%air (21%O₂, 79%N₂), 5%CO₂) or severe hypoxia/glucose-free conditions (95%N₂, 5%CO₂). Responses to phenylephrine and carbachol were recorded. Separate tissues were pre-conditioned using mild or severe hypoxia followed by normoxia (10 minutes each), before switching to hypoxic conditions. Statistical analysis was via two-way ANOVA, with P<0.05 considered significant.

Results. Mild and severe hypoxia depressed maximal responses to both agonists. Phenylephrine responses were depressed by 62% (mild hypoxia, n=8) and by 84% (severe hypoxia, n=10) (p<0.05 and p<0.01 vs normoxia). Carbachol responses were depressed by 60% (mild hypoxia, p<0.05) and by 90% (severe hypoxia, p<0.01). Preconditioning did not alleviate the depression of carbachol responses, although preconditioning under mild, but not severe, hypoxic conditions partially prevented depressed phenylephrine responses.

Discussion. Acute hypoxia depresses contractility of the urethra. Depression of α_1 -adrenoceptor-mediated responses, the main regulator of urethral tone, under mild hypoxia was partially prevented by a short period of pre-conditioning. Whilst the depressed contractility may contribute to symptoms associated with ischaemia in patients, including incontinence, pre-conditioning as a potential future therapeutic avenue requires further investigation.

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P527

Impact of structural difference in fructans from polygonatum cyrtoneuma on anti-inflammatory activity

Miss Qin Yuan

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

P528

The effect of chemical hypoxia on urothelial mediator release

Miss Elouise Tye

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 10:30 AM - 11:10 AM

The effect of chemical hypoxia on urothelial mediator release

Elouise S Tye¹, Catherine McDermott¹, Russ Chess-Williams¹ & Donna J Sellers.¹ Centre for Urology Research, Faculty of Health Sciences and Medicine, Bond University, Gold Coast, QLD, Australia¹.

Introduction. Poor bladder blood flow can lead to hypoxia and resultant bladder dysfunction (Andersson et al, 2017). The urothelium is known to play a role in maintaining normal bladder function (Birder et al, 2013), however, there is limited research on the impact of hypoxia on urothelial function and mediator release.

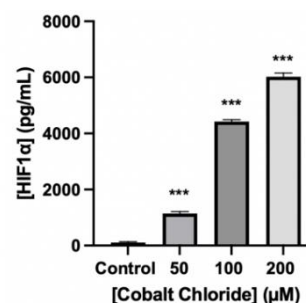
Aims. This study aimed to investigate the effect of chemical hypoxia on urothelial mediator release *in vitro*.

Methods. Chemical hypoxia was induced using the method of Teti et al (2018) in RT4 urothelial cells. The cells were treated with cobalt chloride (50-200 μ M) for 24 hours.

To confirm if hypoxia was induced, HIF1- α activity was assessed in control and cobalt chloride treated cell lysate. Cell viability was assessed using the methylene blue assay. Basal and hypotonic stretch induced release of urothelial ATP, ACh and PGE₂ were assessed using commercially available kits.

Results. Cobalt chloride treatment had no effect on cell viability. There was a significant concentration-dependent increase in HIF-1 α levels ($P < 0.001$), confirming HIF-1 α was induced following 24-hours cobalt chloride treatment. No difference in basal or stretch induced ATP, or PGE₂ release was observed, however there was a significant decrease in basal ACh ($P < 0.05$) following exposure to 200 μ M cobalt chloride.

Discussion. Chemically induced hypoxia was confirmed by increased HIF-1 α levels in cobalt chloride treated cells, which was associated with a decline in basal ACh release corresponding to the highest level for HIF-1 α expression. This may be a useful model to investigate longer term changes in urothelial function with hypoxia.



Andersson KE et al (2017) Therapeutic Advances in Urology 9:11-27.

Birder L and Andersson KE (2013) Physiological Reviews 93:653-680.

Teti G et al (2018) Stem Cells International 2018:3237253-3237259

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



P529

Metformin-Mediated Improvement in Solubility, Stability, and Permeability of Nonsteroidal Anti-Inflammatory Drugs

Prof Yong Lyu

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Yang Lyu, Researcher of the Drug Crystal Research Center in Institute of Materia Medica, the director of the National Center for Drug and Metabolites Analysis and Research, and the director of the Drug Crystal Research Center in the Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College.

Her research directions include: drug quality analysis research, research on polymorphic forms of innovative and generic drugs, research on drug standards and reference materials, research on new technologies and methods for drug analysis, and research on three-dimensional structures of drugs and organisms.

As the project leader, she presided over and undertaken nearly 20 national and provincial-level scientific research projects, including key projects for scientific and technological basic work, major new drug creation, scientific and technological major projects, comprehensive platform for major new drug creation, subsidy projects for major new drug creation by the Ministry of Science and Technology, and national key research and development plans. In the past 5 years, 85 research papers have been published. As the pharmaceutical leader, completed 8 national Class 1 new drug research and development projects. The chief editor has published two monographs. Received 90 Chinese invention patents and 2 PCT patents. Received 2 national second prizes for scientific and technological progress and 19 provincial and ministerial level awards. Led the formulation of 7 national technical standards and obtained 216 national level standard substances for measurement of drugs and active ingredients.

Metformin-Mediated Improvement in Solubility, Stability, and Permeability of Nonsteroidal Anti-Inflammatory Drugs

Yang Lu*, Qi An, Dezhi Yang, Li Zhang. Beijing Key Laboratory of Polymorphic Drugs, Center of Pharmaceutical Polymorphs, Institute of Materia Medica, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China.

Introduction. Nonsteroidal anti-inflammatory drugs (NSAIDs) are class II biopharmaceutics classification system drugs. The poor aqueous solubility of NSAIDs can lead to limited bioavailability after oral administration.

Aims. Metformin (MET) is a small molecule compound, which can be used in crystal engineering to adjust the physical and chemical properties of drugs and improve the bioavailability of ketoprofen and phenylbutazone.

Methods. According to the literature research and preliminary studies. We synthesized two drug-drug molecular salts (ketoprofen-metformin and phenylbutazone-metformin) with NSAIDs and thoroughly characterized them using SCXRD, PXRD, DSC, and IR analysis to improve the poor solubility of NSAIDs. Two new drug-drug molecular salts were evaluated by in vitro and in vivo experiments combined with theoretical calculation.

Results. In vitro evaluation studies revealed that the thermal stability and solubility of NSAIDs-MET were substantially enhanced compared with those of NSAIDs alone. Unexpectedly, an additional increase in permeability was observed. Since

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



the structure determines the properties, the structure was analyzed using theoretical calculations to reveal the intermolecular interactions and to explain the reason for the change in properties.

Discussion. The salt formation of NSAIDs with MET could substantially increase the bio-absorption rate of NSAIDs, according to the in vivo pharmacokinetic findings, which provides an experimental basis for developing new antipyretic and analgesic drugs with rapid onset of action.

Yu MC et al (2023) *Pharmaceutics* 15: 1196.

Yang DZ et al (2022) *Chin. Chem. Lett.* 34: 107964.

P530

Improving the hygroscopicity and bioavailability of ligustrazine using cocrystallization technology

Dr Yifei Xie

Poster presentations 4: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Biography:

Yifei Xie, Ph D., Assistant researcher of the National Center for Pharmaceutical Screening in Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College.

Her research direction is new technologies and methods for drug analysis for the prevention and treatment of cardiovascular and cerebrovascular diseases and metabolic diseases.

She mainly participated in research tasks such as Technology Major Special Projects and National Key R&D Plan, National Natural Science Foundation and Beijing Natural Science Foundation. In 2016, as the second person, she won the third prize of Liaoning Provincial Natural Science Award. In recent five years, 18 research papers have been published, including 6 SCI papers and 6 first and co-author papers. 16 national invention patents have been applied, including 3 invention patent authorizations.

Improving the hygroscopicity and bioavailability of ligustrazine using cocrystallization technology

Yifei Xie^{1,2}, Li Zhang¹, Yang Lu^{1*}. Beijing Key Laboratory of Polymorphic Drugs, Center of Pharmaceutical Polymorphs, Institute of Materia Medica, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China; Beijing Key Laboratory of Drug Target and Screening Research, National Center for Pharmaceutical Screening, Institute of Materia Medica, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China.

Introduction. Ligustrazine (TMP) has been widely used in pharmacological research, especially in the treatment of ischemic vascular diseases. However, the low oral bioavailability and hygroscopicity of ligustrazine limit its potential in preparation, storage, and biological properties.

Aims. Improve the hygroscopicity of TMP by cocrystallization technology and improve the bioavailability in vivo.

Methods. In this experiment, three salicylic acid compounds including 5-nitrosalicylic acid (NSA), 5-sulfosalicylic acid (SSA), and 4-aminosalicylic acid (ASA) were chosen as cofomers, three kinds of cocrystals/salt of TMP were obtained and characterized by SCXRD, PXRD, FT-IR, and DSC. The hygroscopicity was investigated by the DVS method. The absorption of cocrystal/salt in male SD rats was investigated by pharmacokinetic experiment.

Results. Compared with TMP, the equilibrium solubility of TMP-NSA, TMP-SSA and TMP-ASA. The solubility was improved in the media with pH of 7, 6.8, and 4.5. Especially, the equilibrium solubility of TMP-SSA in medium solutions with pH 4.5, 6.8, and 7.0, increased by 7.49 times, 8.27 times, and 6.15 times respectively. In the hygroscopic experiment, the weight of

ASCEPT, APFP & APSA Joint Congress

1–4 Dec 2024

Melbourne Convention &
Exhibition Centre, Australia



TMP increased to 27.03% at 90% humidity. The weight increase of TMP-SSA is 5.61% less than that of TMP, while the weight changes of TMP-NSA and TMP-ASA are less than 0.5%. Pharmacokinetic experiments showed that the C_{max} of TMP-NSA and TMP-ASA increased by 2.23 times and 4.14 times respectively, and the area under the drug curve increased by 1.13 times and 1.55 times respectively.

Discussion. The cocrystal/salt formed by the combination of TMP and three salicylic acids improves the hygroscopicity and solubility of TMP and improves the oral bioavailability of TMP to some extent. These cocrystals/salt can provide a reference for the drug development of TMP.

Xie YF et al (2024) *Molecules* 29:2208.

Zhang L et al (2021) *Molecules* 26:2677.

P532

Exploring the role of cancer-associated fibroblasts on breast cancer cell death

Dr Alice Hui Li Bong

Poster presentations 3: Drug Discovery, Drug Disposition and Response, Innovation and Industry, Neuropharmacology, Pharmacogenomics, Pharmacy Practice, Toxicology, Urogenital and Gastrointestinal, Goldfields Event Space, December 3, 2024, 1:15 PM - 2:10 PM

Exploring the role of cancer-associated fibroblasts on breast cancer cell death.

Alice HL Bong¹, Farzaneh Forouz¹, Gregory R Monteith¹.

School of Pharmacy, The University of Queensland¹, Brisbane, QLD, Australia.

Introduction. Breast cancer remains a leading cause of cancer-related deaths in women worldwide. To develop more effective breast cancer treatments, a better understanding of tumour-promoting signals not only within cancer cells, but also the tumour microenvironment is required. Cancer-associated fibroblasts (CAFs) constitute the main cell type within the tumour stroma providing proliferation and metastasis-promoting signals to cancer cells. In contrast, there are limited studies assessing the role of CAFs on breast cancer cell death in the context of calcium signalling.

Aims. To develop a method to assess the role of CAFs on breast cancer cell death and define changes in calcium signalling in co-cultures of breast cancer cells and fibroblasts treated with cell death inducers.

Methods. Breast cancer cell lines expressing a H2B-GFP green nuclear marker were co-cultured with HMF3S fibroblasts and stained with propidium iodide to assess breast cancer cell death. Breast cancer cell death was defined based on the percentage of propidium iodide positive cells. Breast cancer co-cultures were treated with cell death inducers (staurosporine, paclitaxel, hydrogen peroxide) for 24 h prior to imaging. To assess calcium signalling changes in breast cancer co-cultures during cell death, live cell imaging of HMF3S cells expressing a red calcium sensor (jRCaMP1b) co-cultured with breast cancer cell lines expressing a green calcium sensor (GCaMP6m) were incubated with the aforementioned cell death inducers and imaged using an automated epifluorescence microscope.

Results. H2B-GFP, jRCaMP1b, GCaMP6m and propidium iodide enabled the differential resolution of calcium signalling in breast cancer cells and fibroblasts in co-culture. It also facilitated the assessment of potential differences in cell death sensitivity in breast cancer cells in co-culture.

Discussion. Methodologies involving genetically-engineered cell models described in this study are suitable for co-culture studies designed to simultaneously assess calcium signalling and cell death.

Monteith, G R et al (2017) *Nat Rev Cancer*, 17(6): 373-380

Rizzolio S et al (2022) *J Exp Clin Cancer Res*, 41:319