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14TH ANNUAL BRIP CONFERENCE

16 & 17 October 2024

Scientific Programme & Abstract Book

Advancing Research:
The Power of Young Minds

Contents

Foreword

It is with great excitement that we welcome you to the 14th Annual Biomedical Research and Innovation (BRIP) Conference, themed "Advancing Research: The Power of Young Minds". This year's meeting is dedicated to celebrating the potential of young researchers in addressing global health challenges.

In a world increasingly facing complex health challenges, the contributions of young scientists are vital. Their unique perspectives and innovative approaches could not only redefine research in non-communicable diseases (NCDs) but also inspire future generations of scientists. As supervisors and mentors, we need to nurture the exploration of young minds, fostering an environment of curiosity and bold ideas.

Over the years, the BRIP Symposium has served as a dynamic platform for postgraduate students to share their research and build collaborations. This year, we will cover a range of topics related to NCDs, exploring cutting-edge research and groundbreaking strategies that can lead to significant advancements in prevention and treatment.

We are honoured to host six esteemed guest speakers who will provoke thoughtful discussions and inspire us with their expertise. These interactions will not only deepen our understanding but also spark new ideas and collaborations that will last beyond this conference.

We extend our heartfelt gratitude to all participants, speakers, and organizers whose dedication has made this conference possible. Your commitment to empowering young minds is a powerful testament to our shared vision for a healthier future.

As we embark on this year's conference, let us embrace the boundless possibilities that arise when young minds are empowered to lead. Together, we can drive impactful research and foster a brighter future.

With warm regards,
Rabia Johnson / Carmen Pheiffer
Co-Deputy Directors
Biomedical Research and Innovation Platform

THE 2024 ORGANISING COMMITTEE

Prof Julia Goedecke

Dr Sylvia Riedel

Prof Carmen Pheiffer

Prof Rabia Johnson

Dr Rianita van Onselen

Dr Stephanie Dias

Dr Jyoti Sharma

Dr Hygon Mutavhatsindi

Dr Nasiema Allie

Dr Zainonesa Abrahams

Dr Nonhlakanipho Sangweni

Dr Kholofelo Malemela

Dr Keren de Buys

Dr Sello Mikasi

DAY 1 WEDNESDAY 16 OCTOBER

Venue – Auditorium (SAMRC Conference Centre, Cape Town) and MS Teams

8h00 – 8h30	Registration	
8h30 – 9h00	Welcome and Opening Address by SAMRC President, Prof Ntobeko Ntusi	
SESSION 1		
Session Chairs: Prof Rabia Johnson & Dr Nonhlakanipho Sangweni		
9:00 – 9:30	**Keynote speaker: Prof Olov Rolandsson, Department of Public Health and Clinical Medicine, Umeå University, Sweden, "*Autoimmunity and different sub-groups of diabetes in Africa: lessons from Ghana*"**	
9:30 – 9:42	Establishing the suitability of the ex-vivo rat retinal model to define the early pathogenic mechanisms underlying diabetic retinopathy	Petra Makua (MSc)
9:42 – 9:54	Glucocorticoids improved inflammation but did not improve inflammation-induced cardiac dysfunction in collagen-induced arthritis rats	Madikadike Moshape (MSc)
9:54 – 10:06	The transcription factor p53 regulates adipose tissue macrophages' phenotype and their capacity to handle lipids	Inès Mucel (PhD)
10:06 – 10:18	Anti-metaflammatory effects of *Momordica balsamina* leaf water extract on 3T3-L1 adipocytes and RAW 264.7 macrophages	Tshedimosho Kgoadi (MSc)
10h18 – 10h50	Tea/coffee	
SESSION 2		
Session Chairs: Dr Rianita van Onselen & Dr Kholofelo Malemela		
10:50 – 11:20	**Keynote speaker: Prof Landon Myer, Department of Public Health, University of Cape Town, "*Intersection of communicable and non-communicable diseases*"**	
11:20 – 11:32	Investigating molecular interactions of hyperglycaemia and SARS-CoV-2 spike protein variants in a model of pancreatic beta cells	Tara Michaels (PhD)
11:32 – 11:44	Investigating mitochondrial function in HIV-associated cardiometabolic disease: preliminary findings from a South African population	Kheya Mokoena (MSc)
11:44 – 11:56	Cytotoxicity and computational approach to unveil the potential benefits of flavonoids in COVID-19 disease and diabetes by targeting AMPK	Fave Yohanna Tata (PhD)
11:56 – 12:08	Genomic variants and associated drug resistance profiles revealed by whole genome sequencing in drug resistant *M. tuberculosis* clinical isolates from Limpopo province	Kabelo Kaapu (PhD)
12:08 – 12:20	Assessing the toxicity of 2-imino-7-nitro-4-(4-chlorophenyl)-2H-1,3- thiazino[3,2-A] benzimidazole (FDM31)-capped gold nanoparticles in zebrafish for potential use in treating microbial infections	Molatelo Rapholo (MSc)
12:20 – 12:40	Pre-lunch walk around campus	
12h40 – 13h40	Lunch	
SESSION 3		
Session Chairs: Prof Carmen Pheiffer & Dr Stephanie Dias		
13:40 – 13:52	Umbilical cord blood metabolomic profiling to reveal potential biomarkers of adverse pregnancy and perinatal outcomes in the Vhembe district: a cross-sectional study	Innocent Moagi (MSc)
13:52 – 14:04	Exploring the potential of DNA methylation as biomarkers for gestational diabetes mellitus	Matladi Masete (PhD)
14:04 – 14:16	Predictors of quality of life among patients with end-stage renal disease in Kano Metropolis, Nigeria	Hussaini Aikawa (PhD)
14:16 – 14:28	Therapeutic strategies for pancreatic cancer: targeting the oncogenic transcription factor TBX2 with chromomycin A5	Jinming Bai (MSc)
14:28 – 14:40	TBX2 as a therapeutic target for the treatment of HPV-negative cervical cancer	Anjani Rama (MSc)
14:40 – 16:10	**Interactive Poster Session 1**	

DAY 2 THURSDAY 17 OCTOBER

Venue – Auditorium (SAMRC Conference Centre, Cape Town) and MS Teams

SESSION 4		
Session Chairs: Dr Hygon Mutavhatsindi & Dr Nasiema Allie		
8:45 – 09:15	**Keynote speaker: Prof Alvaro Viljoen, Department of Pharmaceutical Sciences, Tshwane University of Technology, "*Current status and future of phytomedicine and ethnopharmacology in South Africa*"**	
09:15 – 09:27	Evaluation of *Lessertia frutescens* and *Echinacea purpurea* hepatotoxic effects using HepG2/C3A spheroids and Wistar rats	Sthembile Sithole (MSc)
9:27 – 9:39	Investigating the effects of *Dicerovaryum senecioides* and *Flaveria trinervia* chloroform and methanol extracts on triple negative metastatic breast cancer cells	Tubake Sebei (MSc)
9:39 – 9:51	The *Momordica balsamina* methanol extract mitigates interleukin-6-induced metastatic effects of MDA-MB-231 breast cancer cells through the inhibition of the IL-6/JAK2/STAT3 pathway	Tshwarelo Mohale (PhD)
9:51 – 10:03	Targeting KEAP1-Nrf2-ARE signalling pathway with *Momordica balsamina* aqueous extract to mitigate cisplatin-mediated renal damage.	Mante Dolly Kgakishe (PhD)
10:03 – 10:15	Mitigating hyperglycemic oxidative stress in HepG2 cells: the role of *Carica papaya* leaf and root extracts in promoting glucose uptake and antioxidant defense	Mthokozisi Nxumalo (PhD)
10:15 – 10:27	In vitro and in silico antihyperglycemic potential of *Cyclopia genistoides* crude extracts	Nompilo Cele (MSc)
10h27 – 11h00	Tea/coffee	

SESSION 5		
Session Chairs: Prof Julia Goedecke & Dr Sylvia Riedel		
11:00 – 11:30	**Keynote speaker: Prof Lara Dugas, Loyola University Chicago, USA/University of Cape Town, "*Associations between gut microbiota and cardiometabolic risk in African origin populations: The METS Microbiome study*"**	
11:30 – 11:42	The effect of maternal methyl donor nutrient supplementation on the intestinal barrier in offspring in a model of metabolic disease in rats	Mpho Mokoape (MSc)
11:42 – 11:54	Comparing gut permeability and endothelial function in hypertensive and normotensive pregnant women from Mthatha	Ebenezer Ackah (MSc)
11:54 – 12:06	Postprandial glucose variability and clusters of sex hormones, liver enzymes, and cardiometabolic factors in a South African cohort of African ancestry	Bontle Masango (PhD)
12:06 – 12:18	Characteristics of hypertensive heart failure with a preserved ejection fraction patients in a Black community sample in South Africa	Atlegang Tlhale (PhD)
12:18 – 12:30	Adding insult to injury: a sex-specific investigation of chronic stress on heart function after regional ischemia	Megan Cairns (PhD)
12h30 – 13h25	Lunch	
13:25 – 14:55	**Interactive Poster Session 2**	

SESSION 6	
Session Chairs: Dr Jyoti Sharma & Dr Sello Mikasi	
14:55 – 15:20	**Keynote speaker: Dr Mathilda Mostert, Owner and MD, Precision Oil Laboratories, Tzaneen, "*From research to industry*"**
15:20 – 15:45	**Keynote speaker: Prof Monique Zaal, Gene diagnostics, Cape Town, SA, "*The role of pharmacogenetics for a tailored personalize treatment response*"**
15:45 – 16:30	Prize Giving Prizes presented by Professor Johan Louw, Senior Director of Platforms, SAMRC

POSTER PRESENTERS

Biomedical Research & Innovation Platform Conference 2024
16 & 17 October 2024

Poster number	Name	Title	Degree	Institution
1	Kagiso Makwaana	Evaluation of cytotoxicity of *Euryops floribundus* acetone leaf extract in cervical cancer cells	MSc	University of Limpopo
2	Sesethu Ketse	Hypermethylation of the T-Box transcription factor 3 (TBX3) promoter in breast cancer: a pilot study in African women	MSc	South African Medical Research Council
3	Casandra Mbazima	Evaluation of the effect of *Senecio serratuloides* and *Strychnos madagascariensis* extracts on the absorption and hepatic metabolism of metformin, rosiglitazone, glyburide, atorvastatin.	MSc	University of Zululand
4	Maureen Ramadimetsa Nkwana	The effects of curcumin derivatives on SARS-CoV-2 spike S1 protein induced oxidative stress on macrophage cells	MSc	University of Limpopo
5	Stephen Southway	Evaluating the biphasic effect of metformin on a 3D cardiomyocyte spheroid model rendered insulin resistance	MSc	Stellenbosch University
6	Koketso Maenetja	Investigating the expression patterns of the novel TSPO splice variant, PBR-s, in cervical cancer cells	MSc	University of Limpopo
7	Siphelele Thandekile Thethwayo	The effect of *Bauhinia bowkeri* extracts on anti-hypercholesteremia: insights from in vitro and in silico investigations	MSc	University of Zululand
8	Zuqaqambe Mihlali Mampofu	The relationship between blood pressure and blood glucose level in Walter Sisulu University community	MSc	Walter Sisulu University
9	Hellen Laura Mnisi	Assessing the impact of *Commelina benghalensis* extracts on breast cancer cell	MSc	University of Limpopo
10	Chuma Mabuto	Assessing cardiovascular effects of HIV/AIDS and preeclampsia in pregnant women of African Ancestry in Mthatha, South Africa	MSc	Walter Sisulu University

POSTER PRESENTERS

Poster number	Name	Title	Degree	Institution
11	Nicky-Louise Byrne	Sensitive amplification methods to detect and sequence human parechoviruses, enteroviruses and adenoviruses in cerebrospinal fluid	MSc	Stellenbosch University
12	ZB Mathenjwa	Phytochemical screening, in vitro antibacterial and in silico antidiabetic potential of *Agathosma betulina* extracts	MSc	University of Zululand
13	Kaone Sephiphi	Antipyretic effects of *Schinus molle* in yeast-induced pyrexic Wistar rats.	MSc	Sefako Makgatho Health Science University
14	Aphang Polette	Investigating the cytotoxic effects of *Ozoroa paniculosa* in diet-induced obese C57BL/6 mice	PhD	University of Limpopo
15	Thato Kgatla	The effects of *Aspalathus linearis* (rooibos) against angiotensin II-induced hypertrophy and apoptosis	PhD	Stellenbosch University
16	Cayleigh de Sousa	Targeting CD44 to overcome chemoresistance and metastasis in cervical cancer: insights from ex vivo and in vitro models	PhD	Stellenbosch University
17	Madre Meyer	Utilising personalised medicine to investigate the effects of senescence-induced treatment resistance in cervical cancer patients	PhD	Stellenbosch University
18	Vusi Mbazima	Exploring the anticancer potential of *Momordica balsamina* methanol extract on HT-29 colon cancer cells	Established Researcher	University of Limpopo
19	Zainonesa Abrahams	Development of a bioinformatics pipeline for analyzing gene expression patterns in hypertensive patients	Postdoc	South African Medical Research Council
20	Abegail Mukhetwa Tshivhase	The effect of resveratrol on hyperglycemia-related microRNAs in HepG2 cells	Postdoc	South African Medical Research Council

KEYNOTE SPEAKERS

Prof Olov Rolandsson

Senior Professor of Family Medicine at the Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

Professor Olov Rolandsson (MD, PhD) is a Senior Professor of Family Medicine at the Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden, and a clinical specialist in Family Medicine. He defended his thesis in 2002 with the title: "Islet Beta Cell Autoimmunity – An Epidemiological and Experimental Study". He has been a member of the Immunology of Diabetes Association (IDF) and is presently a member of the steering committee of the European Diabetes Epidemiology Group (EDEG). Professor Rolandsson is presently Principal Investigator (PI) of a regional diabetes register, DiabNorth, that includes about 9500 people with diabetes, a PI for the Metformin and microbiota study (MEMO), and he has just started a re-investigation of a cohort of people with and without diabetes to assess the temporal trend of diabetes-related neuropathy. He also has a close collaboration with Professor Ina Danquah, Bonn University, who is involved in the "Research on Diabetes and Obesity among African Migrants - the RODAM Study" where diabetes autoimmunity has been assessed.

Prof Landon Myer

Division of Epidemiology & Biostatistics and Head of the School of Public Health, University of Cape Town

With a background in epidemiology and medicine, Prof Myer is a researcher who has worked in maternal and child health and HIV treatment and prevention research in South Africa for the past 20 years. He currently is Professor in the Division of Epidemiology & Biostatistics and Head of the School of Public Health at the University of Cape Town (UCT). As an epidemiologist Prof Myer has experience in HIV treatment research across a range of designs with a focus on observational methods in clinical epidemiology. His research emphasizes multidisciplinary collaborations, bringing together teams of basic scientists, clinicians, and population health scientists to address major public health questions. Recent projects include the implementation and optimization of strategies to effectively deliver HIV pre-exposure prophylaxis to pregnant and breastfeeding women in high-burden settings. Related to this, he has provided senior methodological and conceptual oversight to several recent and ongoing major cohort studies, including perinatal epidemiologic studies and prospective birth cohorts.

KEYNOTE SPEAKERS

Prof Alvaro Viljoen

Research fellow Department of Pharmaceutical Sciences, Tshwane University of Technology (Pretoria)

Alvaro completed a BSc, BSc Hons. (cum laude), and MSc (cum laude) in Botany at Stellenbosch University (SA). In 1994, he commenced with a PhD at the University of Johannesburg on the chemotaxonomy of the genus *Aloe*. In 1999, he was appointed as lecturer in the School of Pharmacy at WITS Medical School where he was promoted to Associate Professor in 2004. In July 2005, Prof Viljoen was offered a research fellow position in the Department of Pharmaceutical Sciences, Tshwane University of Technology (Pretoria). More than 100 postgraduate students have graduated under his supervision since 2002. He has authored and co-authored more than 300 peer-reviewed papers (Scopus h index of 55), 2 books, and several book chapters, mostly on the phytochemical exploration and pharmacological activity of indigenous medicinal and aromatic plants. He has been elected to serve on the editorial board of Phytochemistry (Elsevier), the Journal of Applied Research on Medicinal and Aromatic Plants (Elsevier), and is currently the Editor-in-Chief of the Journal of Ethnopharmacology (Elsevier, IF 4.8) since 2017. In October 2013, he was awarded the National Research Chair in Phytomedicine, a position which he holds concurrently as the Director of the SAMRC Herbal Drugs Research Unit in South Africa.

Prof Lara Dugas

AXA Chair in Non-Communicable Disease Epidemiology, University of Cape Town

Prof Dugas is chair in Non-Communicable Disease Epidemiology, hosted at the University of Cape Town (2021-2026), and a Professor of Epidemiology in the Department of Public Health Sciences, Parkinson School of Health Sciences and Public Health, Loyola University Chicago (LUC). She completed her PhD and postdoctoral training at UCT in the Health through Physical Activity, Lifestyle and Sport Research Centre, focusing on the role of energy balance in the development of obesity. In 2007, she joined LUC where she managed a large international study that explored the effects of diet and physical activity on cardiometabolic health in 5 African-origin populations from Ghana, South Africa, Jamaica, Seychelles, and the US. In 2014, she expanded this work to explore the role of the gut microbiota and intermediary metabolites on obesity and diabetes risk. In 2019, she further expanded this work to include the role of the sleep behaviour, and circadian rhythm. In 2021 she was awarded the AXA Chair in Non-communicable Disease Epidemiology, hosted in the Division of Epidemiology & Biostatistics, School of Public Health, UCT. Initially, her programme focused on the intersection of non-communicable diseases, including obesity and type 2 diabetes in populations with a high HIV burden, but has since expanded this to include the impact of a heating climate and non-communicable disease risk in vulnerable populations in Sub-Saharan Africa, leveraging her work in South Africa and Ghana.

KEYNOTE SPEAKERS

Dr Mathilda Mostert

Founder of Precision Oil Laboratories and UPENYA Cosmetics

Dr Mathilda Mostert is the founder of Precision Oil Laboratories and UPENYA Cosmetics and is an expert in the Oil Chemistry field. After completion of her PhD and postdoctoral studies in 2008, she has become a leading figure in the oil industry, spearheading research projects and at the same time establishing and expanding Precision Oil Laboratories. Her experience also led to the creation of UPENYA Cosmetics, a skincare line focused on youth skin. Dr Mostert is an active contributor to international standards as a member of expert committees for Codex and SABS. Additionally, she serves as a consultant within the food and cosmetic oil industry. Her motto is "If you can't measure it, don't mention it," and she is committed to using premium-quality inputs to achieve exceptional results. As one of South Africa's foremost authorities in the fats and oils sector, Dr Mostert's influence extends across the continent. She is married and has three boys; she jokingly credits her multitasking skills to running an all-male household. She enjoys the African Bush and spending time with her family.

Prof Monique Zaal

Executive Director, GENEdiagnostics

Prof Zaahl completed her PhD in Human Genetics in 2003. As a Commonwealth Split-site scholar, she completed most of her study at Oxford University. She was appointed Head of the Genetics Department at Stellenbosch University in 2011. Strategic positioning of the department within the national context was key to her role. She has published 26 research articles in international peer-reviewed journals (8 first author publications and 18 co-author publications), one book chapter, a review article in the field of human genetics, and has trained numerous postgraduate students. Prof Zaahl was also the recipient of the 2006 South African National Research Foundation "Women in Science" award, in the category "Best emerging young scientist", the South African representative at the International Council of Science (ICSU) meeting in April 2007, has been awarded the National Science and Technology Forum (NSTF) award, category: Young Black Researcher, in 2009, was a recipient of the National Order of Mapungubwe in Bronze (awarded by President Jacob Zuma) in 2010, was listed as Mail and Guardian Top 100 women in South Africa (1 of 10 women in the health sector) in 2011 and several others awards. Following her successful professional career as a scientist, she attained her MBA in 2012. These studies developed her competence in strategic planning and enhanced her skills as innovator and entrepreneur. Her entrepreneurial skills were evident with the establishment of GENEdiagnostics (Pty) Ltd in 2010, a genetic testing company. GENEdiagnostics was awarded the SMME Award for most innovative company (awarded by AfricaGrowth) in 2013, was selected to form part of a Bridge International Bootcamp (sponsored by ABSA, Barclays, CEDAR and Stellenbosch University) in 2014, obtained an award at the SA Innovation Summit (category: company with most growth potential) in 2017 and has been selected in 2018 as a Shanduka Black Umbrella company (previous Cyril Rhamaphosa foundation), finalist of the ESKOM Entrepreneur competition

KEYNOTE SPEAKERS

in 2021, finalist of the Cyril Rhamaphosa Black Umbrellas people's choice, selected as a LEAP/ Metropolitan EDP company in 2022 and various others. Furthermore, in 2012, she was appointed as Professor and Executive in the office of the Rector and Vice-Chancellor at Stellenbosch University. The focus of her appointment was to increase the capacity of the Rector and Vice-Chancellor's office and to actively support initiatives that would progress transformation at Stellenbosch University. Prof Zaahl has been appointed on the Boards of Directors as a non-executive director at People Living with Cancer (PLWC), a non-executive director at Terresan Pelagic Fisheries and a non-executive director and Chair at Blue Ocean Mussels and an executive director of GENEdiagnostics (Pty) Ltd. She is also affiliated with the South African National Accreditation System (SANAS) and Health Professions Council of South Africa (HPCSA) as an assessor.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Establishing the suitability of the ex-vivo rat retinal model to define the early pathogenic mechanisms underlying diabetic retinopathy

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BACKGROUND

Diabetic retinopathy is the leading cause of blindness caused by uncontrolled hyperglycaemia in diabetes mellitus. Hyperglycaemic conditions target neuromicrovascular components of the blood-retinal barrier (BRB), including endothelial cells, glycocalyx (particularly syndecan-1), pericytes, and astrocytes, resulting in retinal vascular leakage. However, the early mechanisms in the pathogenesis of retinopathy remain unclear.

OBJECTIVES

To establish and validate an ex-vivo culture rat retinal model that would be suitable to study the pathogenesis of diabetic retinopathy.

METHODOLOGY

Rat eyes were freshly enucleated, the retina dissected from the eye globes and incubated in either 5.5 mM (normoglycaemic) or 25 mM (hyperglycaemic) glucose media for 3 and 24 hours. Multi-immunostaining and confocal microscopy were used to detect astrocytes, pericytes, blood vessels, and syndecan-1. Western blotting was used to quantify syndecan-1. Retinal changes were analysed morphologically and quantified with ImageJ software.

RESULTS

Minimal morphological changes were noted in astrocytes and pericytes under hyperglycaemic conditions by 3 hours. Although structural changes to the BRB were noted in both normoglycaemia and hyperglycaemia by 24 hours, moderate/severe levels and the extent of astrocyte degradation increased in hyperglycaemia by ~41%, and moderate/severe levels with reduced pericyte coverage on blood vessels increased by ~ 28%. Syndecan-1 intensity in retinal vessels was ~47 and ~37% higher in hyperglycaemic retinas at 3 and 24 hours respectively. Western blots showed a 91 and 150% increase in syndecan-1 protein levels in hyperglycaemic retinas at 3 and 24 hours respectively.

CONCLUSION

Although morphological deterioration was also noted at 24 hrs under normoglycaemia, this study demonstrated that hyperglycaemia produced more marked neuro-microvascular morphological changes. This suggests that this model is suitable for studying the early pathogenesis of diabetic retinopathy. Studies are currently underway to determine the best culture medium that will morphologically preserve the retina in normoglycemic conditions for extended tissue culture periods.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Glucocorticoids improved inflammation but did not improve inflammation-induced cardiac dysfunction in collagen-induced arthritis rats

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BACKGROUND

Systemic inflammation in rheumatoid arthritis (RA) plays a crucial role in cardiac impairments, contributing to left ventricular hypertrophy and diastolic dysfunction. While glucocorticoids (GCs) are used to manage inflammation in RA, their long-term use may have adverse effects on the heart. It remains unclear whether GC treatment mitigates or exacerbates inflammation-induced cardiac impairments.

OBJECTIVES

This experimental study investigated the effects of GC treatment on cardiac morphology and function in the collagen-induced arthritis (CIA) rat model.

METHODS

Sprague Dawley rats were divided into control, CIA, GC, and CIAGC groups (n=9 each). The CIA group received 0.2 mL bovine type-II collagen in incomplete Freund's adjuvant, and the CIAGC and GC groups received 10 mg/kg prednisolone daily for six weeks. Body mass, blood pressure, and arthritis scores were measured. Echocardiography assessed cardiac function, and enzyme-linked immunosorbent assays determined circulating concentrations of high sensitivity–C-reactive protein (hs-CRP). LV collagen accumulation was assessed histologically using the picrosirius red stain. Differences were determined by a one-way ANOVA followed by Tukey post hoc tests.

RESULTS

The CIA group had higher hs-CRP levels and heavier LV mass indexed to body mass compared to the controls ($P<0.0001$, and $P=0.01$ respectively) and GC group ($P<0.0001$, and $P=0.02$ respectively). CIA+GC had lower hs-CRP than CIA group ($P=0.02$). Compared to controls, all groups had reduced lateral e' and e'/a' ratios ($P<0.01$), higher relative wall thickness ($P<0.05$), E/e' ratios ($P<0.01$), and collagen area fraction ($P<0.05$). The global longitudinal strain (GLS) was reduced in the CIA and CIA+GC groups compared to controls ($P=0.01$ and $P=0.02$ respectively). The global longitudinal strain rate (GLSR) was reduced in the CIA and CIA+GC groups compared to the controls ($P=0.02$ and $P=0.0009$, respectively).

CONCLUSION

Systemic inflammation induced concentric hypertrophy, diastolic dysfunction, and myocardial deformation. Glucocorticoid treatment in CIA improved inflammation, however, did not worsen inflammation-induced cardiac dysfunction.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

The transcription factor p53 regulates adipose tissue macrophages' phenotype and their capacity to handle lipids

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BACKGROUND

Obesity is a risk factor for metabolic diseases, including insulin resistance (IR) and type 2 diabetes. Excessive expansion of adipose tissue (AT) during obesity is accompanied by macrophage accumulation and the development of metabolic stresses that alter the function and fate of AT macrophages (ATM), resulting in low-grade local and systemic inflammation contributing to the development of IR. However, the molecular mechanisms underlying this metabolic reprogramming of ATMs remain unknown. Transcription factors are crucial regulators of transcriptional programs involved in the polarization and adaptation of macrophages to their environment.

OBJECTIVES

Our preliminary data have shown an upregulation of the transcription factor p53 in obese ATM. Our aim is to investigate the role of p53 in macrophage polarization and its impact on adipocyte function.

METHODOLOGY

We have characterized metabolically activated macrophages (MMe) that phenocopy obese ATM in which p53 has been invalidated (KO) or not. In addition, we used particles to deliver siRNA against p53 specifically to ATMs in obese mice and characterized their metabolic phenotype.

RESULTS

We show that p53 invalidation potentiates polarization into MMe, with an upregulation of genes involved in lipid metabolism such as Ppar1, Cd36 and Abca1. Cellular respiration is increased in KO-MMe, suggesting improved oxidative capacity. KO-MMe accumulate more lipids, and their mitochondrial respiration is more dependent on lipid oxidation. Treatment of adipocytes with conditioned medium from KO-MMe has less deleterious effects on insulin signaling than conditioned medium from control MMe. Finally, we show that p53 invalidation in ATM improves the glucose intolerance in obese mice and favors the expression of lipid handling genes at the expense of inflammatory genes in ATM.

CONCLUSION

Our data suggest that during obesity, p53 upregulation in ATM inhibits their ability to manage lipid, their oxidative capacity, and contributes to the secretion of factors impairing insulin signalling in adipocytes.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Anti-metaflammatory effects of *Momordica balsamina* leaf water extract on 3T3-L1 adipocytes and RAW 264.7 macrophages

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BACKGROUND

Type 2 diabetes mellitus (T2DM) is a metabolic disease that occurs as a result of chronic low-grade inflammation often referred to as metaflammation, triggered by the accumulation of inflammatory molecules. The use of synthetic anti-diabetic drugs has gained momentum worldwide although their health and economic impact cannot be overlooked. Medicinal plants such as *Momordica balsamina* have been explored for their healing properties in the treatment of T2DM.

OBJECTIVES

This study was aimed at investigating the anti-metaflammatory activity of *M. balsamina* water extract on RAW 264.7 macrophages and 3T3-L1 adipocytes and its ability to reduce crosstalk between the two cell lines.

METHODS

M. balsamina plant leaves were collected from Mankweng, in the Limpopo Province, South Africa. Ground leaves were exhaustively extracted with water. Secondary metabolites were quantified using Folin-Ciocalteu method. Ferric reducing antioxidant power assay was used to evaluate the antioxidant capacity of *M. balsamina*. The cytotoxicity of the water extract on RAW 264.7 and 3T3-L1 cells was evaluated using 3-(4,5-dimethylthiazol-2-ly)-2,5-diphenyltetrazolium bromide (MTT) assay. RAW-CM was generated by growing RAW 264.7 macrophages in 1% FBS supplemented media. To mimic the environment of adipocytes near macrophages, 3T3-L1 cells were cultured in RAW-CM. The secreted adipokines were assessed using an MCP-1 and TNF-alpha ELISA assays.

RESULTS

Total phenolic, tannin conten,t and free radical scavenging potential decreased with a decrease in extract concentration. *M. balsamina* displayed significant cytotoxicity on 3T3-L1 macrophages at 1000 µg/mL. The extract inhibited the expression of MCP-1 and TNF-alpha at concentrations of between 62.5 and 250 µg/mL.

CONCLUSION

M. balsamina has potential anti-metaflammatory activity. It inhibited the MCP-1 and TNF-alpha cytokines and could potentially lead to a reduced susceptibility of developing T2DM in obesity-induced metaflammation.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Investigating molecular interactions of hyperglycaemia and SARS-CoV-2 spike protein variants in a model of pancreatic beta cells

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BACKGROUND

Hyperglycaemia is an independent risk factor for severe COVID-19, while the direct SARS-CoV-2 infection of pancreatic ß-cells may drive the emergence of new-onset diabetes post-COVID-19. Moreover, hyperglycaemia upregulates glucose metabolic pathways, including the hexosamine biosynthetic pathway (HBP) and advanced glycation end-product (AGE) formation, mediating various glycosylation and glycation reactions, respectively. The glycosylation and/or glycation of entry proteins may enhance their susceptibility to SARS-CoV-2 spike (S)-protein binding and viral infectivity. However, the interplay between hyperglycaemia and SARS-CoV-2 infection remains to be fully elucidated. We hypothesise that higher HBP and AGE activity modulates S-protein binding and entry pathways in ß-cells.

OBJECTIVES

We aimed to investigate the effect(s) of AGE production and HBP-mediated O-GlcNAcylation on SARS-CoV-2 entry and accessory proteins and downstream molecular outcomes in cultured INS-1 ß-cells under hyperglycaemic conditions.

METHODS

Rat insulinoma INS-1 cells were exposed to high glucose, glucosamine (increases HBP), methylglyoxal (AGE precursor), and recombinant S-protein (WT, ß, δ) variants in separate experiments. Metabolic activity was assessed (WST-1 assays). Western blot analyses were performed to evaluate markers of the HBP (OGT, O-GlcNAc), AGE (RAGE), and SARS-CoV-2 cell surface entry (ACE2, DPP4, APN, TMPRSS2, ADAM10/17) and endosomal pathway (Cathepsin B, Basigin, EEA1, VCP). Glucose-stimulated insulin response was determined using an insulin ELISA.

RESULTS

S-protein variants increased metabolic activity in a time, concentration, and variant-dependent manner ($P<0.01$ versus controls). AGE modulation showed the ß-variant increased total RAGE while WT- and ß-variants increased DPP4 and glycosylated ACE2 ($P<0.05$ versus controls). The δ-variant augmented APN, whereas the WT-variant reduced Basigin ($P<0.05$ versus controls). Cathepsin B was increased in response to all three variants ($P<0.05$ versus controls). Insulin secretion was elevated by the ß-variant and attenuated by the δ-variant under control and hyperglycaemic conditions ($P<0.01$ versus control).

CONCLUSION

AGE induction may prime endosomal entry mechanisms for SARS-CoV-2 S-proteins whilst variants significantly stimulate metabolic activity, acutely modulating ß-cell function.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Investigating mitochondrial function in HIV-associated cardiometabolic disease: Preliminary findings from a South African population

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BACKGROUND

A significant proportion of people living with HIV (PLWH) present with mitochondrial impairment and cardiometabolic disease (CMD). However, the role of altered mitochondrial function in HIV-associated CMD remains unclear.

OBJECTIVES

To explore whether a link exists between HIV-status, CMD and mitochondrial function in a study population from Worcester.

METHODS

Participants were divided into HIV- with (n=23) and without CMD (n=29), and HIV+ with (n=24) and without CMD (n=28). Clinical and demographic data, and blood and urine samples were collected. CMD was defined as presenting with ≥3 cardiovascular risk factors. Mitochondrial function was assessed in isolated peripheral blood mononuclear cells by high-resolution respirometry.

RESULTS

The cohort was relatively young (<40 years) and predominantly female (~70%). Markers of liver fibrosis (fibrosis-4 index; *P*=0.008) and renal impairment (urine albumin-creatinine ratio (ACR); *P*=0.003) were elevated in HIV+ vs HIV-. Routine respiration (O_2 flux: pmol/min/10^6 cells/mL) was lower in HIV+ vs HIV- [0.00 (0.00 to 5.77) vs 2.66 (0.00 to 8.05), *P*<0.001], and inversely associated with HIV-status [Standardised ß (95% CI): -0.724 (-0.891 to -0.557, *P*<0.001]. Leak respiration was inversely associated with hypertension [ß: -0.278 (-0.531 to -0.025), *P*=0.032)] and ACR [ß: -0.244 (-0.484 to -0.005), *P*=0.046]. The F-pathway (O_2 flux) was lower in CMD+ vs CMD- in both HIV- [0.183 (0.00 to 1.904) vs 0.666 (0.00 to 5.077), *P*=0.046] and HIV+ [0.153 (0,00 to 2,240) vs 0.551 (0.00 to 2.480), *P*=0.028]. Complex I-linked respiration was positively associated with HIV-duration [ß: 0.581 (0.016 to 1.146), *P*=0.044].

CONCLUSION

Preliminary findings demonstrate that routine respiration is impaired in the PLWH, and that the F-pathway is reduced in participants with CMD, regardless of HIV-status. Mitochondrial respiratory parameters were associated with HIV-status and duration, and CMD (including hypertension and impaired renal function). Our results suggest that mitochondrial function may be altered in PLWH and CMD, but further research is warranted.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Cytotoxicity and computational approach to unveil the potential benefits of flavonoids in COVID-19 disease and diabetes by targeting AMPK

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BACKGROUND

Hyperglycemia induces damage and escalates complications in several tissues and organs involved in COVID-19. Flavonoids, widely found in natural products, have demonstrated diverse therapeutic activities on metabolic and infectious diseases by activating the 5' adenosine monophosphate-activated protein kinase (AMPK). The molecular mechanisms of these pharmacological activities remain very unclear. Therefore, the study evaluated the molecular mechanisms involved in the flavonoid activation of AMPK.

METHODS

Molecular docking and molecular dynamics simulation using Maestro Schrodinger were used for in silico screening, selecting, and analyzing the flavonoids in *Artemisia afra* and *Catharanthus roseus*. The in vitro cytotoxicity screening of the aqueous leaf extracts of *Artemisia afra* and *Catharanthus roseus* in HepG2, Hek293, and CaCo-2 cells was carried out at the cell densities of 2×10^4 cells/mL in the MTT assay. IC_{20}, which corresponds to 80% cell viability, was used for the cytotoxicity on ATP, MMP, and LDH assays.

RESULTS

An observed decline in ATP, MMP, and increased LDH concentrations of HepG2 cells by *Catharanthus roseus* suggest compromised cellular energy status and potential cell death. The computational analysis unveiled the binding preferences and interactions of the flavonoids with the AMPK compared to metformin and the co-crystallized ligand. Metformin maintained an interesting correlation and consistent pattern when observing the RMSD, MMGBSA, and H–bond occupancy, indicating a high degree of stability and favourable binding interaction despite its relatively low van der Waals contribution (ΔGvdw).

CONCLUSION

These findings unveiled the higher binding energy demonstrated by rutin which suggests superior activity and biological effects. The cytotoxicity assays present *Artemisia afra* and *Catharanthus roseus* as relatively safe and have potential anticancer effects on colorectal.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Genomic variants and associated drug resistance profiles revealed by whole genome sequencing in drug resistant *M. tuberculosis* clinical isolates from Limpopo province

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BACKGROUND

The emergence and spread of drug-resistant tuberculosis (DR-TB) pose a threat to its treatment and management. Thus, this study aimed to investigate the genetic variants and associated drug resistant mutations in DR-TB isolates from Limpopo province.

OBJECTIVES

To investigate *Mycobacterium tuberculosis* (MTB) genetic diversity, drug resistance mutations, and ongoing transmission chains within the Limpopo province.

METHODS

This quantitative study employed the use of whole-genome sequencing (WGS) to characterise 44 drug resistant MTB clinical isolates selected from the Limpopo tuberculosis repository (2021-2023). Isolates were previously characterised by MTBDRplus line probe assay as drug resistant. The isolates were subcultured and further incubated for 2-weeks after initial positivity. Illumina protocol was used for sequencing at 50x depth. Lineages, mutations, drug resistance profiles, and potential clusters were identified using relevant bioinformatics tools.

RESULTS

WGS characterised resistance to all currently available antituberculosis drugs. The WGS characterised most of the MTB isolates as extensively drug-resistant tuberculosis (XDR-TB) (n=14/44; 32%), followed by pre-extensively drug-resistant tuberculosis (Pre-XDR-TB) (n=10/44; 23%). The Euro-American lineage 4.1.1 dominated most drug resistance profiles with 70% (7/10) in rifampicin resistant tuberculosis (RR-TB) and 54% (7/13) in XDR-TB. The Beijing lineage 2.2.1 (n=6/10; 60%) was the dominant lineage in pre-XDR-TB, while other strains belonged to Indo Oceanic lineage 1 and 1 mixed lineage 2 & 4. Cluster analysis showed a 17.5% clustering rate mainly in the Waterberg district and Mopani districts.

CONCLUSION

This study highlights lineage 4 & 2 as major drivers of infection with drug resistant tuberculosis especially in Pre-XDR-TB and XDR-TB in Limpopo province. Therefore, high-quality data linking quantitative phenotypic drug susceptibility testing (DST) and genomic data is needed in Limpopo.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Assessing the toxicity of 2-Imino-7-nitro-4-(4-chlorophenyl)-2H-1,3-thiazino[3,2-A] benzimidazole(FDM31)-capped gold nanoparticles in zebrafish for potential use in treating microbial infections

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BACKGROUND

The spread of infectious diseases caused by microorganisms, including pneumonia and cholera, has been an emerging global issue. Nanotechnology, particularly gold nanoparticles (AuNPs), can reduce antimicrobial-resistant bacteria because they are multivalent, allowing them to bind many types of ligands with high affinity and eradicate bacterial cells. However, chemical methods have raised concerns about toxicity. Green synthesis methods are being considered for a safer alternative, reducing the use of toxic chemicals including sodium borohydride and trisodium citrate.

OBJECTIVES

In this study, the antibacterial activity and toxicity of AuNPs synthesized by incorporating a heterocyclic compound 2-Imino-7-nitro-4-(4-chlorophenyl)-2H-1,3-thiazino[3,2-A] benzimidazole (FDM31) and a *Cola lateritia* stem bark extract was evaluated.

METHODS

The Turkevich and green synthesis methods were applied where *Cola lateritia* plant extracts (CLS) and FDM31 were used. The NPs were characterized by ultraviolet-visible spectroscopy (UV-Vis), dynamic light scattering (DLS), Fourier-transform infrared spectroscopy (FTIR), and X-ray diffraction (XRD) to determine optical characteristics, size and zeta potential, functional groups, and crystalline structure respectively.

RESULTS

The results confirmed the fabrication of all AuNPs since the UV-Vis absorption was detected at 550 nm, while the size, zeta potential, and functional groups ranged from 12 to 30.45 nm and -5 to -33.9 mV, respectively. The antibacterial activity demonstrated that only the gram-positive bacterium, *Mycobacterium smegmutis*, was the most resistant to AuNP-FDM31 due to the decreased response to exposure. The morphology of AuNPs was deduced from analysis by scanning and transmission electron microscopy. The toxicity of the synthesized AuNPs was assessed using the zebrafish development test (ZFET), where the CLS-AuNPs were found to be non-toxic.

CONCLUSION

Based on results, it was concluded that CLS-AuNPs could be used to combat antibiotic drug resistance. According to the In vivo toxicity studies the CLS-AuNPs were non-toxic making them suitable antibacterial agents.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Umbilical cord blood metabolomic profiling to reveal potential biomarkers of adverse pregnancy and perinatal outcomes in the Vhembe district: a cross-sectional study

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BACKGROUND

Adverse pregnancy and perinatal outcomes (APPOs) represent a significant challenge in obstetrics, often leading to maternal and neonatal deaths. Unfortunately, the biological causes and predictive biomarkers for these remain poorly understood. Hence, metabolomic profiling has emerged as a powerful tool for elucidating the underlying biochemical pathways in these complications.

OBJECTIVES

In this cross-sectional study, we investigated the metabolic signatures of APPOs through comprehensive metabolomic analysis.

METHOD

Our cross-section study coupled with purposive sampling enrolled pregnant individuals with and without APPOs. Following consent, sociodemographic information, medical characteristic, and umbilical cord blood samples were collected. Through untargeted metabolomic profiling approach using ultra high performance liquid chromatography-quadrupole-time-of-flight mass spectrometry (UHPLC-q-TOF-MS), we analyzed umbilical cord serum to identify differential metabolites patterns between cases and controls. Multivariate analysis approaches were employed to identify signals that differed between APPOs and uncomplicated pregnancies. Metabolic pathway analysis of perturbed metabolites was conducted using MetaboAnalyst 6.0

RESULTS

Among 129 participants, 25.58% were cases. The majority of participants (42.4%) fell within the age range of 20 to 29 years, while a significant portion, comprising 83.7%, were unemployed. Factors such as maternal age, birth weight, maternal blood pressure, anesthesia use, and delivery mode were significantly associated the risk of APPOs, with corresponding *P* values of 0.032, 0.027, 0.041, <0.001, and <0.001, respectively. Untargeted metabolomic profiling and multivariate analysis using the orthogonal partial least squares discriminant analysis (OPLS-DA) model identified 107 perturbed metabolites in APPOs and uncomplicated pregnancies. Among them, 50 metabolites were upregulated, while 57 were downregulated in perinatal complications at $P<0.05$. Following adjustment for false discovery rate (FDR) $q<0.05$, seven metabolites emerged as significant in APPOs. Furthermore, the affected metabolic pathways, including ethyl lipid metabolism, sphingolipid metabolism, and glycerophospholipid metabolism, were identified as statistically significant.

CONCLUSION

Metabolomic profiling identified specific umbilical cord blood processes closely associated with APPOs, indicating their potential as biomarkers for assessment, prediction, and early intervention strategies.

Exploring the potential of DNA methylation as biomarkers for screening gestational diabetes mellitus

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BACKGROUND

Gestational diabetes mellitus (GDM) is associated with an increased risk of maternal and neonatal adverse outcomes. DNA methylation is increasingly being recognized as a potential biomarker for the early detection of GDM. The aim of this study was to (1) characterise DNA methylation differences in whole blood and examine associations with metabolic risk in women with/without GDM, (2) investigate the association between single nucleotide polymorphisms (SNPs) and DNA methylation in these women, and (3) to elucidate the biological effects of differentially methylated genes in a cell model of GDM.

METHODS

Three CpG sites corresponding to differentially methylated genes, peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC1A), protein tyrosine phosphatase receptor type N2 (PTPRN2) and Insulin gene enhancer protein (ISL1), selected from our previous genome-wide study were validated in women with (n=63) and without GDM (n=118) using bisulfite pyrosequencing. Spearman's correlation coefficient was used to assess the associations between DNA methylation and metabolic risk factors. In silico analysis was conducted to identify transcription factors that bind to the differentially methylated CpG sites of genes of interest. Optimization of HUVECs to establish a GDM cell model to further explore the role of differentially methylated genes.

RESULTS

Accumulative methylation of ISL1 was higher in women with GDM compared to women without GDM (0.9-fold; P=0.03), while no significant differences were observed for PGC1A and PTPRN2. None of the differentially methylated genes were associated with metabolic risks. In silico analysis identified E2F transcription factor 1 (E2F-1), known to play a role in insulin signalling pathways, binding sites on ISL1 gene spanning CpG -3456 region. Cell culture showed increase in cellular metabolic activity with higher glucose concentration and extended period of exposure.

CONCLUSION

This study did not confirm our previous genome-wide findings possibly due to participant heterogeneity between samples. Further in vitro analyses are being conducted to determine the biological significance of the differentially methylated gene, ISL1, in GDM pathophysiology.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Predictors of quality of life among patients with end-stage renal disease in Kano Metropolis – Nigeria

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BACKGROUND

Chronic Renal Failure is a progressive irreversible deterioration in renal function in which the body's power to maintain metabolic, fluid, and electrolyte balance fails, resulting in uremia which causes the patient to depend on hemodialysis to maintain the internal milieu and avoid uremia. In the early stage of renal damage, symptoms may be reduced through hemodialysis, control of fluid intake and regulation of diet, and use of medication, as renal function worsens, these treatments become insufficient. The weight of the disease is felt more in rising countries like Nigeria where there is no health indemnity to meet the massive economic stress faced by the sufferers and their families.

OBJECTIVE

To assess the predictors of quality of life among patients with end stage renal disease in Kano Metropolis, Nigeria.

METHODS

This study utilized a descriptive survey design to assess the predictors of quality of life among patients with end stage renal disease in Kano metropolis. SF -36 questionnaire was adopted for assessing the quality of life.

RESULTS

The study revealed that among the predictors tested using multiple regression at 5% age (t=199; $P \leq 0.005$), marital Status (t= 34.9; $P \leq 0.005$), occupation (26.1; $P=0.005$), educational level (t=22.7; $P \leq 0.005$), and distance from the health facility (t=22.3; $P \leq 0.005$) were found to be significant predictors of health-related quality of life among the patient who participated in the study.

CONCLUSION

In Nigeria, where this current study was conducted, the majority of secondary and tertiary institutions where dialysis care is provided are located in cities and urban areas. Patients in need of these services far from the cities, need to prepare and plan for transport fares and accommodation within or outside the health facility where the services are provided.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Therapeutic strategies for pancreatic cancer: targeting the oncogenic transcription factor TBX2 with chromomycin A5

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BACKGROUND

Pancreatic cancer is a highly metastatic malignancy with a poor prognosis. TBX2, a transcription factor associated with tumorigenesis, is overexpressed in pancreatic cancer and is associated with cell migration. Chromomycin A5 (CA5) is a potential antibiotic-like anticancer agent.

OBJECTIVES

This study investigated the anticancer potential of CA5 and its ability to target TBX2 in a pancreatic cancer model.

METHODS

MTT assay was used to assess the short-term cytotoxicity of CA5, while clone formation assay evaluated its long-term cellular effects. Sphere formation assay was employed to assess the cytotoxicity of CA5 at the 3D level. Wound healing assay was conducted to study the effect of TBX2 on cell migration by knocking down TBX2 using siRNA transfection. Western blotting was utilized to analyze TBX2 knockdown and changes in the expression of TBX2, apoptosis markers, and DNA damage markers after CA5 treatment.

RESULTS

CA5 demonstrated superior short- and long-term cytotoxicity, selectivity for cancer cells, and cytotoxicity at the 3D level compared to the clinical standard Gemcitabine. CA5 treatment led to an increase in H2AX levels, cleavage of caspase family proteins, and PARP cleavage, indicating DNA damage and apoptosis induction. Knockdown of TBX2 in PDAC cells inhibited cell migration, and treatment with CA5 similarly down-regulated TBX2 and inhibited cell migration.

CONCLUSIONS

CA5 exhibited strong cytotoxicity and selectivity against PDAC cells. It exerted multi-target anti-PDAC effects by targeting TBX2, inducing DNA damage, and triggering apoptosis. These findings highlight the potential of CA5 as a promising therapeutic agent for the treatment of pancreatic cancer.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

TBX2 as a therapeutic target for the treatment of HPV-negative cervical cancer

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BACKGROUND

Cervical cancer (CC) poses a significant health burden especially in low- and middle-income countries. While 95% of CC cases are driven by human papillomavirus (HPV) infection (HPV+), the rarer HPV negative (HPV-) type is more aggressive with a poorer prognosis. The mechanisms driving early transformation and progression of HPV- CC remain unclear. Preliminary data reveal that the oncogenic T-box transcription factor, TBX2, is upregulated in HPV- CC cells and that it is repressed by the HPV oncoproteins E6/E7 in HPV+ CC. We hypothesize that TBX2 is important for the HPV- CC phenotype and that it is a novel therapeutic target to treat this neoplasm.

OBJECTIVES

To investigate the role and therapeutic potential of targeting TBX2 in HPV- CC.

METHODOLOGY

TBX2 status was determined in HPV- CC cell lines using the human protein atlas database and western blotting. To determine if TBX2 contributes to HPV- CC, it was depleted by siRNA in C33A HPV- CC cells and the impact on cell proliferation (trypan blue exclusion assay) and migration (2D scratch motility assay) was assessed. The effects of treating C33A cells with the TBX2 targeting commercial drugs (niclosamide and pyrvinium pamoate) were assessed on TBX2 levels (western blotting), cell viability (MTT assays), 3D spheroid growth (Calcein AM staining), long-term cell survival (clonogenic assay), and migration (2D scratch motility assay).

RESULTS

This study reveals that HPV- CC cells (1) express higher levels of TBX2 than HPV+ CC cells; (2) require TBX2 for their proliferation and migration; (3) treated with niclosamide and pyrvinium pamoate have reduced TBX2 levels, long-term cell survival, migration, and 3D spheroid growth.

CONCLUSION

Results from this study reveal that TBX2 promotes HPV- cell proliferation and migration, making it a key factor in this aggressive malignancy. Additionally, we show that two TBX2-targeting drugs could be repurposed to treat this disease.

Evaluation of *Lessertia frutescens* and *Echinacea purpurea* hepatotoxic effects using HepG2/C3A spheroids and Wistar rats

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BACKGROUND

The global use of herbal medicines and supplements is rising, yet many remain untested and poorly regulated, posing risks such as hepatotoxicity. This study examines the potential liver toxicity of two widely used herbal immune boosters, *Lessertia frutescens* (LF) and *Echinacea purpurea* (EP), using HepG2-derived C3A liver spheroids and Wistar rats.

METHODS

Female Wistar rats were divided into control, EP (130 mg/kg BW), and LF (12 mg/kg BW) groups (n=6 each), treated for 21 days. In vitro, HepG2-C3A liver spheroids were treated with EP (100 µg/mL) and LF (130 µg/mL) for 14 days. Liver function was assessed through serum and media analysis for enzymes associated with hepatotoxicity, and gene expression was evaluated using hepatotoxicity PCR arrays and TaqMan probes.

RESULTS

In vivo, LF and EP increased serum ALT, AST, adenylate kinase, and cholesterol levels in Wistar rats. In vitro, EP significantly reduced AST activity (P=0.0093), while both EP (P=0.0325) and LF (P=0.0001) decreased ALT activity. EP also significantly lowered cholesterol levels (P=0.0427). PCR arrays showed decreased expression of efflux transporters (ABCC2, ABCC3) and CYP1A2, with upregulation of SLC2A3 and casp3.

CONCLUSION

EP and LF exhibited potential hepatotoxic effects in vitro, impairing metabolic functions in treated spheroids. Interestingly, these effects were not evident in rats within the treatment period. However, altered gene expression of major efflux and transporter proteins was demonstrated in both models. Therefore, the HepG2/C3A liver spheroid model may be more sensitive for early hepatotoxicity detection, but further long-term in vivo studies and molecular analyses are needed to confirm these findings.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Investigating the effects of chloroform and methanol extract of *Dicerocaryum senecioides* and *Flaveria trinervia* on metastatic breast cancer cells

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BACKGROUND

Plants have been used for centuries in various traditional healing practices worldwide. Research has revealed that some of these plants contain bioactive compounds with potential anticancer properties, not only inhibiting the growth of tumours but also mitigating metastasis. *Dicerocaryum senecioides* and *Flaveria trinervia* have both been reported to have anti-inflammatory and antioxidative effects, which can contribute to inhibiting metastatic processes such as migration of metastatic cells from their primary site and subsequent adhesion at a secondary organ.

OBJECTIVE

Investigating the potential anti-metastatic effects of *D. senecioides* and *F. trinervia* chloroform and methanol extracts on MDA-MB-231 breast cancer cells.

METHOD

The effect of the extracts on the viability of MDA-MB-231 and HEK 293 human embryonic kidney cells was assessed using the cell counting kit-8. To determine the mode of cell death induced by the extracts, annexin-V and dead cell assay was employed. The effect of the extracts on reactive oxygen species formation was assessed with the Muse® Oxidative Stress Kit. A transwell and cell adhesion assay was used to microscopically assess the anti-migratory and adhesive effects of the extracts on MDA-MB-231 cells, respectively. The effects of the extracts on the enzymatic activity of the matrix metalloproteinases (MMPs) were assessed using gelatin-zymography.

RESULTS

The findings revealed that there was no significant effect on cell viability at concentrations below 200 µg/mL ($P<0.05$). The extracts induced apoptotic cell death in a concentration dependent manner. Reactive oxygen species formation was suppressed in the MDA-MB-231 cells treated with the extracts. Moreover, the extracts suppressed cell invasion by inhibiting the activity of MMP-9 & -2, migration, and adhesion. The *D. senecioides* chloroform extract inhibited up to 75% adhesion of the cells while its methanol extract inhibited 60%. The *F. trinervia* chloroform extract mitigated cell adhesion up to 60% and methanol inhibited 65%. Furthermore, the extracts inhibited MMP-2 and -9 activity in MDA-MB-231 by up to 40%.

CONCLUSION

D. senecioides and *F. trinervia* chloroform extracts showed potential as sources of compounds with anti-metastatic activity. Further studies should focus on isolating and characterising these active compounds, followed by in vivo and clinical trials for efficacy evaluation.

The *Momordica balsamina* methanol extract mitigates interleukin-6-induced metastatic effects of MDA-MB-231 breast cancer cells through the inhibition of the IL-6/JAK2/STAT3 pathway

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BACKGROUND

Preclinical and clinical studies have provided evidence of the integral role of the IL-6/JAK2/STAT3 pathway in promoting the initiation, progression, and metastasis of triple-negative breast cancer. However, TNBC treatment remains a challenge.

OBJECTIVES

This study investigated the potential anti-metastatic effects of *Momordica balsamina* methanol extract (MBME) in IL-6-activated MDA-MB-231 breast cancer cell line.

METHODS

The triple-negative breast cancer cells MDA-MB-231 and kidney HEK-293 cells were exogenously activated with IL-6 (50 ng/mL) during treatment to mimic the overexpressed IL-6 in the tumour microenvironment. The MTT and annexin-V assays were used to determine the cytotoxicity of the MBME in MDA-MB-231 and HEK-293 cells. The transwell cell invasion, wound healing, gelatin-zymography, cell adhesion and extracellular matrix (ECM)-protein adhesion assays were performed to assess the potential anti-metastatic potential of the MBME. Real-time qPCR and western blotting were used to investigate the mechanism of action of the MBME in IL-6-activated MDA-MB-231 cells.

RESULTS

The MBME (≤100 µg/mL) exhibited minimal toxicity on the viability of IL-6-activated MDA-MB-231 and HEK-293 cells. Annexin-V assay further confirmed the lack of significant toxicity of MBME (≤100 µg/mL) in IL-6-activated MDA-MB-231 and HEK-293, showing non-significant induction of apoptotic cell death. An increase in *Bax* and decrease in *Bcl-2*, *JAK2*, *STAT3*, *MMP-2*, and *MMP-9* mRNA expression, was observed in extract-treated IL-6-activated MDA-MB-231 cells. Western blot analysis showed that the extract decreased MMP-2, MMP-9, vimentin, pJAK2, and pSTAT3, with increased TIMP-3 protein expression in IL-6-activated MDA-MB-231 cells. Furthermore, a decrease in the activity of MMP-2 and MMP-9 in extract-treated IL-6-activated MDA-MB-231 cells was observed. Moreover, the MBME treatment significantly inhibited the invasive, migratory, adhesive, and attachment to ECM-proteins potential of IL-6-activated MDA-MB-231 cells.

CONCLUSION

The MBME exhibits the potential to inhibit the IL-6-induced metastatic effects of MDA-MB-231 cells by downregulating the IL-6/JAK2/STAT3 pathway.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Targeting KEAP1-Nrf2-ARE signaling pathway with *Momordica balsamina* aqueous extract to mitigate cisplatin-mediated renal damage

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BACKGROUND

Cisplatin's accumulation in kidney cells is a factor that limits its clinical use. The KEAP1-Nrf2-ARE signalling pathway regulates ROS overproduction, which may otherwise induce oxidative stress and inflammation. *Momordica balsamina* is a great source of bioactive compounds with an untapped potential as an adjuvant to cisplatin.

OBJECTIVES

This study investigated the effects of *Momordica balsamina* aqueous extract supplementation on cisplatin-induced oxidative stress and inflammation in HEK-293 cells.

METHODS

In vitro analysis of cisplatin and *M. balsamina* combinatorial treatments on HEK-293 viability and determination of the mode of cell death was done using cell counting kit-8 (CCK-8) and annexin v and dead cell assays. The effects on cisplatin-induced DNA damage and ROS production were assessed by flow cytometry using the Muse Multicolor DNA damage and Oxidative stress assays. Superoxide dismutase (SOD), catalase (CAT), malonaldehyde (MDA) enzyme activities and the glutathione/oxidized glutathione (GSH/GSSG) ratio were evaluated using the SOD, CAT, MDA, GSH colorimetric assays, respectively. Additionally, effects of the combinatorial treatments on cyclooxygenase-2 (COX-2) expression levels were assessed using the Human COX-2 ELISA kit. The expression profiles of KEAP1-Nrf2-ARE signalling pathway proteins and inflammatory proteins were evaluated using western blot analysis.

RESULTS

Momordica balsamina aqueous extract offered significant renoprotection evidenced by reduced BAX/Bcl2 ratio and decreased DNA damage. Extract supplementation mitigated oxidative stress by inhibiting ROS production and enhancing the enzymatic antioxidant system (i.e. SOD, CAT and GSH enzyme activities) in a time- and concentration-dependent manner. Comparative to cisplatin treatment, extract supplementation upregulated nuclear factor-erythroid-2-related factor-2 (Nrf2), heme oxygenase-1 (HO-1), and SOD1 protein expression and downregulated Kelch-like ECH-associated protein 1 (Keap1), tumor necrosis factor-alpha (TNF-), and inducible nitric oxide synthase (iNOS) protein expression.

CONCLUSION

Momordica balsamina aqueous extract has great potential as a reno-protective agent in cisplatin therapy. Accordingly, it's probable effects on cisplatin's anticancer activity should be thoroughly investigated.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Mitigating hyperglycaemic oxidative stress in HepG2 Cells: the role of *Carica papaya* leaf and root extracts in promoting glucose uptake and antioxidant defense

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BACKGROUND

Diabetes often goes undiagnosed, with 60% of people in Africa unaware of their condition. Type 2 diabetes mellitus is associated with insulin resistance and is treated with metformin, despite the undesirable side effects. Medicinal plants with therapeutic potential, such as *Carica papaya*, have shown promising anti-diabetic properties.

OBJECTIVES

This study explored the role of *C. papaya* leaf and root extracts compared to metformin in reducing hyperglycaemia-induced oxidative stress and their impact on liver function using HepG2 as a reference.

METHODS

The cytotoxicity was assessed through the MTT assay, while glucose uptake and metabolism (ATP and ΔΨm) in HepG2 cells treated with *C. papaya* aqueous leaf and root extract were evaluated using a luminometry assay. Additionally, antioxidant properties (SOD2, GPx1, GSH, catalase, and Nrf2) were measured using qPCR and western blot following the detection of MDA, NO, and iNOS, which are indicators of free radicals.

RESULTS

The MTT assay showed that *C. papaya* extracts did not exhibit toxicity in HepG2 cells and enhanced glucose uptake compared to the hyperglycaemic control (HGC) and metformin. The glucose levels in *C. papaya*-treated cells increased ATP production ($P<0.05$) while the ΔΨm was significantly increased in HGR1000-treated cells ($P>0.05$). Furthermore, *C. papaya* leaf extract upregulated GPx1 ($P<0.05$), GSH, catalase ($P<0.05$), and Nrf2 ($P<0.05$), while SOD2 was reduced ($P>0.05$), ultimately lowering ROS ($P>0.05$). Contrarily, the root extract stimulated SOD2 ($P>0.05$), GPx1 ($P<0.05$), and GSH levels ($P<0.05$), reducing catalase ($P<0.05$) and Nrf2 gene expression ($P<0.05$), and resulting in high MDA levels ($P<0.05$). Additionally, the extracts elevated NO levels and iNOS expression ($P<0.05$), suggesting potential RNS activation.

CONCLUSION

The leaf extract stimulated glucose metabolism and triggered ROS production, producing a strong antioxidant response that was more effective than the root extract and metformin. The root extract, especially at high concentrations, was less effective in detoxifying free radicals but maintained elevated SOD2, GSH, and GPx1 levels.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

In-vitro and in-silico antihyperglycemic potential of *Cyclopia genistoides* crude extracts

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BACKGROUND

Diabetes mellitus is a worldwide concern. Side effects and adverse reactions have been reported from the contemporary antidiabetic drugs. This demand to search for less toxic and effective treatments for diabetes from medicinal plants. *C. genistoides* antidiabetic potential is understudied. Therefore, in this study, the in-vitro antioxidants, enzyme inhibition, glucose uptake and in silico molecular docking, and ADMET (absorption, distribution, metabolism, excretion, and toxicity) properties were analysed.

METHODS

The antioxidant activity of *C. genistoides* extracts was assessed using DPPH, ABTS, hydroxyl radical, nitric oxide, metal ion chelating, reducing power and total antioxidant capacity assays whereas the inhibitory potential was tested against DPP4, disaccharidases, pancreatic lipase, α-amylase, α-glucosidase including estimating the uptake of glucose on the C2C12 and 3T3-L1 cell lines and the stimulatory effect of the extracts using the hexokinase and glucokinase enzyme assay. The in-silico assessment was conducted using GCMS, PubChem, Protein Data Bank, discovery studio, pyrx, pkCSM, and ProTox ii webservers.

RESULTS

The extracts were able to scavenge free radicals. In addition, the extracts revealed no significant inhibition of α-glucosidase, poor inhibition of α-amylase, appreciable DPP4 inhibition and significant pancreatic lipase and disaccharidases inhibitory capability. Furthermore, the extracts demonstrated good stimulatory activity on hexokinase and glucokinase which was supported by their capabilities to promote glucose uptake in both the C2C12 and the 3T3-L1 cell lines. The key phytochemicals were then docked with target proteins and the results revealed phytol and 9,12,15-octadecatrien-1-ol to exhibit the strongest binding energies on selected enzymes.

CONCLUSION

The plant possesses an antihyperglycemic potential with the in-silico molecular docking analysis revealing how the best binding compounds may behave inside the body and based on ADMET analysis, the phytochemicals exhibited a wide range of physicochemical, pharmacokinetic, and drug-like qualities and had no major side effects, making them prospective drug candidates for type 2 diabetes.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

The effect of maternal methyl donor nutrient supplementation on the intestinal barrier in offspring in a model of metabolic disease in rats

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BACKGROUND

A maternal diet rich in methyl donor nutrients (MDN), such as choline, folic acid, and vitamins B12 and B6, may provide a preventive strategy against metabolic disease in offspring. Diets high in fat and sugar are known to contribute to metabolic diseases such as obesity and diabetes through impairing the intestinal mucosal lining.

OBJECTIVES

To assess the effect of a maternal MDN-enriched diet on the histological structure of the intestinal barrier and mucin cell distribution in offspring fed a high-fat diet (HFD).

METHODS

Pregnant Sprague Dawley rats (n=7/group) received either a control or MDN-enriched diet containing L-methionine, choline, folic acid, and vitamins B6 and B12. Male offspring, (8 weeks old, n=10/group) were fed a control or HFD diet, while offspring from MDN-fed females were fed an HFD diet (MDN+HFD) for 20 weeks. Subsequently, small intestinal villus length (VL) and crypt depth (CD) were determined in offspring as indicators for nutrient absorption and cell turnover. Goblet and mucin-2 (Muc2+) cell distributions were quantified as markers of mucosal barrier integrity.

RESULTS

A significant increase in body weight was observed in HFD-fed offspring compared to the control group (P=0.0193) as well as the MDN+HFD group compared to the control group (P<0.0001). Jejunal VL was significantly increased in MDN+HFD group compared to controls (P=0.0006). Ileal CD increased significantly in the HFD group (P=0.0058) compared to controls. Ileal goblet cell area increased in the MDN+HFD group (P=0.0428) compared to the HFD group, while Muc2+ cells decreased in the MDN+HFD group (P=0.0209) when compared to controls.

CONCLUSIONS

Feeding offspring with HFD seemingly increased intestinal surface area through increased VL and CD, which may affect intestinal function and nutrient absorption. However, more data is needed to determine whether MDN supplementation can modulate the intestinal mucus layer to protect against diet-induced intestinal dysfunction.

ABSTRACTS: PRESENTATIONS MSc CATEGORY

Comparing gut permeability and endothelial function in hypertensive and normotensive pregnant women from Mthatha

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BACKGROUND

Preeclampsia is the onset of hypertension (blood pressure ≥140/90) at or after 20 weeks of pregnancy with the presence of proteinuria. In South Africa, 18% of the maternal deaths occur due to pregnancy-induced hypertension. Poor placentation is the primary cause of hypertension in pregnancy through an imbalance in circulating pro- and anti-angiogenic factors resulting in endothelial dysfunction. Gut permeability has also been associated with endothelial dysfunction. However, there is still ongoing research into the interaction of these factors in the development of preeclampsia.

OBJECTIVES

This study aimed to compare markers of gut permeability and endothelial function in hypertensive and normotensive pregnant women from Mthatha.

METHODS

This cross-sectional study enrolled 228 pregnant women as participants. Blood pressure was used to group participants as normotensive (BP<140/90 mmHg; n=75); preeclampsia (BP=140/90 to 159/109 mmHg; n= 65) and severe preeclampsia (BP≥160/110 mmHg; n=84). Markers of placental function (placental growth factor, PlGF), gut permeability (zonulin), and endothelial function (asymmetric dimethylarginine [ADMA] and nitric oxide [NO] and their ratio) were measured.

RESULTS

Hypertensive pregnant women (preeclampsia and severe preeclampsia) had a lower gestational age (P<0.05) with 50% early-onset preeclampsia and compromised placental function (lower PlGF; P<0.05). Serum zonulin concentration was similar between all groups. Hypertensive pregnant women also showed features of endothelial dysfunction with higher serum ADMA (P<0.05), lower serum NO (P<0.05), and a higher ADMA/NO ratio (P<0.05). We observed a strong positive correlation between endothelial dysfunction and blood pressure and a positive but weak relationship between gut permeability and endothelial dysfunction.

CONCLUSION

Endothelial dysfunction and poor placental function seem to be the main factors contributing to the development of preeclampsia in pregnant women in Mthatha, South Africa. In addition to that, gut permeability has a minor or no role.

Postprandial glucose variability and clusters of sex hormones, liver enzymes, and cardiometabolic factors in a South African cohort of African ancestry

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BACKGROUND

This study aimed to, first, determine the clusters of sex hormones, liver enzymes, and cardiometabolic factors associated with postprandial glucose (PPG) and, second, to evaluate the variation these clusters account for jointly and independently with polygenic risk scores (PRSs) in South Africans of African ancestry men and women.

METHODS

PPG was calculated as the integrated area under the curve for glucose during the oral glucose tolerance test (OGTT) using the trapezoidal rule in 794 participants from the Middle-aged Soweto Cohort. Principal component analysis was used to cluster sex hormones, liver enzymes, and cardiometabolic factors, stratified by sex. Multivariable linear regression was used to assess the proportion of variance in PPG accounted for by principal components (PCs) and type 2 diabetes (T2D) PRS while adjusting for selected covariates in men and women.

RESULTS

The T2D PRS did not contribute to the PPG variability in both men and women. In men, the PCs' cluster of sex hormones, liver enzymes, and cardiometabolic explained 10.6% of the variance in PPG, with PC1 (peripheral fat), PC2 (liver enzymes and steroid hormones), and PC3 (lipids and peripheral fat) contributing significantly to PPG. In women, PC factors of sex hormones, cardiometabolic factors, and liver enzymes explained a similar amount of the variance in PPG (10.8%), with PC1 (central fat) and PC2 (lipids and liver enzymes) contributing significantly to PPG.

CONCLUSION

We demonstrated that inter-individual differences in PPG responses to an OGTT may be differentially explained by body fat distribution, serum lipids, liver enzymes, and steroid hormones in men and women.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Characteristics of hypertensive heart failure with a preserved ejection fraction patients in a Black community sample in South Africa

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BACKGROUND

In Africa, the prevalence of hypertension (HT) is estimated at 30% and is expected to rise. HT is a risk factor of heart failure with a preserved ejection fraction (HFpEF) and mostly seen in the elderly. Recent studies showed HFpEF being diagnosed in Black young to middle-aged individuals in South Africa (SA). Black, older, and obese patients with HT also present with left ventricular hypertrophy (LVH). The question therefore arises as to whether the characteristics of hypertensive HFpEF differs from those of HT but without HFpEF.

OBJECTIVES

The aim of this study was to explore the characteristics of hypertensive HFpEF patients in a black community sample in SA.

METHODS

This was a case-control study with a total of 125 HFpEF cases and 510 controls enrolled into the study. Participants from African descent, above 18 years, clinically stable and with informed consent underwent echocardiographic, anthropometric, peripheral, and central haemodynamic and pulse wave velocity (PWV) measurements. A HT cohort of 95 HFpEF cases and 256 controls were identified for further analysis.

RESULTS

The mean age of HFpEF patients was 58.85±11.86 years. Obesity was seen in 49% of HFpEF patients and 57% in the control group. No statistically significant differences were observed in central systolic blood pressure between the groups, however, central diastolic blood pressure (P=0.0295) and pulse pressure (P=0.0352) was significantly decreased in HFpEF patients. PWV was significantly increased in those with HFpEF (10.90±4.80 m/s) when compared to the control group (6.93±3.91 m/s), P<0.0001. Lastly, relative wall thickness (P=0.0295) and left ventricular mass indexed to height$^{2.7}$ (P=0.0352) were significantly increased in HFpEF when compared to those without.

CONCLUSION

HT with and without HFpEF is more prevalent in a middle-aged, obese, Black SA sample, however, HFpEF patients also presented with increased arterial stiffness. Concentric LVH is seen in HFpEF compared to eccentric LVH in those with only HT.

ABSTRACTS: PRESENTATIONS PhD CATEGORY

Adding insult to injury: a sex-specific investigation of chronic stress on heart function after regional ischemia

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BACKGROUND

Chronic stress is an important risk factor for cardiometabolic diseases, but the underlying mechanisms responsible for sex-based differences in stress-related cardiometabolic complications remain poorly understood. This study investigated whether chronic stress triggers sex-dependent cardiac dysfunction in isolated rat hearts exposed to regional ischemia.

OBJECTIVES

To identify potential sex-based mechanisms of chronic stress on heart function pre- and post-simulated ischemia.

METHODS

10-week-old male and female Wistar rats underwent chronic restraint stress (CRS) for four weeks (1 hour daily) versus matched controls. Blood samples were collected post-CRS protocol cessation for the analysis of various circulating biomarkers. Ex vivo isolated hearts were then subjected to regional ischemia (25 minutes), and functional parameters were assessed.

RESULTS

Compared to controls, CRS males displayed decreased plasma brain-derived neurotrophic factor (BDNF) levels ($P<0.05$), while CRS females exhibited elevated plasma adrenocorticotropic hormone (ACTH) ($P<0.01$) and reduced corticosterone ($P<0.001$) alongside lower serum estradiol ($P<0.001$) and estradiol/progesterone ratio ($P<0.01$). Of note, CRS females showed increased serum cardiac troponin T ($P<0.05$) and tumor necrosis factor-alpha (TNF-α) ($P<0.01$) with suppressed interleukin (IL)-1α, IL-1ß, IL-6, and IL-10 levels ($P<0.05$) when compared to controls. Ex vivo perfusions revealed that CRS female hearts displayed impaired post-ischemic functional recovery for baseline stroke volume ($P<0.01$), work performance ($P<0.05$), and overall cardiac output ($P<0.01$) when compared to matched controls and CRS males ($P<0.05$). Downstream proteomics analysis of the female hearts revealed distinct proteome profiles between non-ischemic and ischemic zones, and between control and CRS groups.

CONCLUSION

Our findings reveal intriguing sex-specific responses at both the systemic and functional levels in stressed hearts. Here, the dysregulation of stress hormones, pro-inflammatory state, and potential underlying cardiomyopathy in CRS females renders them more prone to damage following myocardial ischemia. Moreover, unique proteomic profiles of reperfused samples highlight potential preclinical mechanisms for the increased risk for adverse cardiac events in chronically stressed individuals.

ABSTRACTS: POSTERS MSc CATEGORY

Evaluation of cytotoxicity of *Euryops floribundus* acetone leaf extract in cervical cancer cells

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BACKGROUND

Cancer remains a significant public health concern, with cervical cancer ranking as the fourth most prevalent cancer in women, worldwide. These soaring numbers can be accredited to inadequacies of the currently used treatment strategies, which are associated with adverse side effects; thus, novel anticancer drugs are required, with medicinal plants attracting a lot of interest. Numerous *Euryops* species have been utilized for medicinal purposes; however, studies have only reported a few species with anticancer activities.

AIM

This study aimed to investigate the potential anticancer activity of *Euryops floribundus* acetone leaf extract against cervical cancer cells.

METHODS

Qualitative phytochemical screening was conducted to determine the presence of bioactive compounds in the acetone extract. The effect of *Euryops floribundus* acetone leaf extract on the viability of HeLa cells was evaluated using the MTT assay, and further confirmed with the Muse® Count and Viability assay. Apoptosis induction in HeLa cells by the extract was assessed using Muse® Annexin V and Dead Cell assay.

RESULTS

Screening of phytochemicals revealed the presence of coumarins, carbohydrates, phenolic compounds, flavonoids and tannins in the extract. Secondly, the extract significantly (***$P<0.001$) reduced the viability of the HeLa cells (with an IC_{50} value of 250 µg/mL), which was confirmed using the Muse® Count and Viability assay. Furthermore, the extract also significantly (**$P<0.01$) induced apoptosis in the same cells.

CONCLUSION

This study demonstrated that *Euryops floribundus* acetone leaf extract exhibits cytotoxic activity against cervical cancer HeLa cells. However, with an IC_{50} value of 250 µg/mL, the potency of the crude extract may be considered moderate. Therefore, further investigation is required for the identification and isolation of bioactive compounds responsible for the observed anticancer activity.

ABSTRACTS: POSTERS MSc CATEGORY

Hypermethylation of the T-Box transcription factor 3 (TBX3) promoter in breast cancer: a pilot study in African women

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BACKGROUND

Breast cancer is the most common cancer among women in South Africa, with more than 50% of women presenting with locally progressed or metastatic breast cancer. Hence, there is an urgent need to develop early diagnosis strategies that will enable more equitable care. Dysregulated expression of the T-Box transcription factor 3 (*TBX3*) may have crucial diagnostic and prognostic implications in breast cancer, yet the precise mechanism(s) controlling its expression remain elusive. The present study aimed to interrogate the possible epigenetic mechanisms responsible for *TBX3* expression in breast cancer.

OBJECTIVES

The aims of this study were to determine (1) the DNA methylation profile of *TBX3* in breast cancer and normal adjacent tissues from South African women, and (2) the relationship between *TBX3* methylation and patient clinicopathological characteristics.

METHODS

DNA was extracted from paired tumour and healthy adjacent tissues obtained from Black South African patients (n=27) diagnosed with operable primary or invasive breast cancer at the Inkosi Albert Luthuli Central Hospital in KwaZulu-Natal, South Africa. DNA methylation across 31 CpG sites within the *TBX3* proximal promoter and first exon were statistically compared between breast cancer tumours and adjacent normal tissues, correlated with gene expression levels, and interrogated with clinicopathological variables.

RESULTS

Despite a large degree of CpG methylation variation between participants, *TBX3* methylation was elevated in tumour samples compared to adjacent normal tissue, with 22 CpG sites reaching statistical significance. An analysis of cumulative *TBX3* methylation across the 31 analysed CpG sites revealed significantly elevated DNA methylation levels in tumours compared to healthy tissue.

CONCLUSION

These findings shed light on the epigenetic mechanisms linking altered *TBX3* expression to the molecular pathogenesis of breast cancer. However, additional studies are required to assess the longitudinal association of *TBX3* with breast cancer in large population-based samples.

ABSTRACTS: POSTERS MSc CATEGORY

Evaluation of the effect of *Senecio serratuloides* and *Strychnos madagascariensis* extracts on the absorption and hepatic metabolism of metformin, rosiglitazone, glyburide, atorvastatin.

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BACKGROUND

Diabetes mellitus, a persistent metabolic condition, poses a significant threat to global human health. Current diabetes and hyperlipidmeia treatments come with notable limitations and adverse effects, underscoring the urgency for cost-effective and safe management strategies. Several studies have demonstrated the ability of *Senecio serratuloides* and *Strychnos madagascariensis* to regulate blood glucose levels, improve insulin sensitivity, and protect insulin-secreting pancreatic beta cells. Therefore, this evaluation aims to assess the potential herb-drug interactions between *Senecio serratuloides* and *Strychnos madagascariensis* and its bioactive compounds with commonly used anti-diabetic and hyperlipidemia drugs to ensure their safe and effective use.

OBJECTIVES

(1) To determine the phytonutrient composition of the herbal extracts; (2) LC/ MS characterization; and (3) to identify potential risk of herb-drug interactions by monitoring induction of CYP3A4 enzymes responsible for the metabolism of metformin, rosiglitazone, glyburide, and atorvastatin using Vivid assay.

METHODS

Extracts were harvested in Northern Kwa-Zulu Natal and processed in the department of Botany. Subsequently, the extracts underwent characterization through LC-MS analysis. The inhibitory effects of the herbal extracts and compounds on the CYP3A4 enzymes were evaluated using the VividTM assay.

RESULT

The LC-MS analysis was conducted to establish the fundamental fingerprint of *Senecio serratuloides* and *Strychnos madagascariensis* extracts. The results indicated that the *Senecio serratuloides* extract exhibited weak inhibition of CYP3A4, whereas the extract *Strychnos madagascariensis* demonstrated strong induction at a concentration of 0.1 µg/ mL The glyburide and rosiglitazone strongly inhibited CYP3A4 at 10 µM, while atorvastatin strongly inducted CYP3A4 across all concentrations. However, metformin demonstrated moderate inhibition at 10 µM.

CONCLUSION

In vitro, the combination of atorvastatin with metformin interfered with the hepatic metabolism of atorvastatin, revealing strong inhibition of CYP3A4, the key enzyme responsible for atorvastatin's hepatic metabolism. To fully elucidate the effect of metformin on the pharmacokinetic profile of atorvastatin, further experiments are required.

ABSTRACTS: POSTERS MSc CATEGORY

The effects of curcumin derivatives on SARS-CoV-2 spike S1 protein induced oxidative stress on macrophage cells

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BACKGROUND

The corona virus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as a global health crisis. Currently, there is no specific treatment for COVID-19 patients. Infection of host cells via interaction with SARS-CoV-2 spike proteins is characterised by hyper-inflammation of the innate immune response leading to overproduction of reactive oxygen species by macrophage. Curcumin has shown potent antioxidant and anti-inflammatory properties in various pathological conditions.

OBJECTIVE

Investigating the potential of curcumin derivatives in ameliorating COVID-19 induced oxidative stress in macrophage cells.

METHODS

The effect of the curcumin derivatives on the viability of RAW 264.7 macrophage cells were assessed by using two assays, absorbance-based (MTT) and fluorescence-based (PI). To determine the mode of cell death induced by the curcumin derivatives, Annexin V/PI assay was employed. An ELISA assay was used to determine the stimulatory effects of curcumin derivatives on IL-6 expression in this cell line. Oxidative stress muse kit and DAF-2 DA were used to determine the levels of reactive oxygen species (ROS), and nitric oxide (NO) produced by Raw 264.7 cells post SARS-CoV-2 spike S1 stimulation and curcumin derivative treatment.

RESULTS

These curcumin derivatives at low doses (1.25 mM-0.625 mM), showed no cytotoxic effect on Raw 264.7 macrophage cells. A significant ($P \leq 0.05$) decrease in Raw 264.7 total apoptotic cells was observed following treatment with 2.5 mM-0.625 mM of curcumin derivatives. The expression levels of IL-6 significantly ($P \leq 0.05$) decreased after treatment with curcumin derivatives in SARS-CoV-2 spike S1 stimulated Raw 264.7 cells compared to untreated SARS-CoV-2 spike S1 stimulated control cells. Treatment with 1 mM curcumin derivatives reduced the production of ROS and NO.

CONCLUSION

This study suggests that curcumin derivatives possess remarkable anti-inflammatory and antioxidant properties, making them potential therapeutic treatment option to explore for the management of hyper-inflammation associated with COVID-19 infection.

ABSTRACTS: POSTERS MSc CATEGORY

Evaluating the biphasic effect of metformin on a 3D cardiomyocyte spheroid model rendered insulin resistance

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BACKGROUND

Non-communicable diseases, such as type-2 diabetes (T2D) and cardiovascular disease (CVD) are rising globally and more so in developing countries. Three-dimensional cell culture allows researchers to mimic in vivo conditions in vitro, providing a valuable drug-screening tool. However, this has not been tested in a cardiovascular spheroid model.

AIM

This study investigated the effect of low and high metformin concentrations on viability, oxidative stress and gene expression in a rat cardiomyoblast 3D spheroid model.

METHOD

Spheroids were cultured in complete (DMEM, 10% FBS and 1% Pen/strep) or metabolic media (MM; complete media + 100 nM insulin with 75 µM palmitic acid and 50 µM oleic acid added 48 hours after seeding) and harvested at 96 hours. Control and MM spheroids were treated with metformin (0.1, 0.5, 2.5 and 5 mM) for 24 hours prior to harvest. The spheroids were imaged and sized every 24 hours, and metformin uptake was determined with LCMS. The effect of metformin on mitochondrial complex II metabolism was determined with a 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) viability assay. Mitochondrial antioxidant levels were assessed with MitoSox red, and mRNA expression of G6PD, Cpt1 and PFK2, normalised to GAPDH, was measured with RT-qPCR.

RESULTS

Metformin uptake in the spheroids were proportional to the treatment concentrations and did not affect size or viability. Metabolic media significantly increased the mitochondrial metabolism compared to controls (P<0.0001), and significantly increased PFK2 levels (P=0.0374) overall (2-Way ANOVA). High concentrations of metformin significantly decreased antioxidant levels (P<0.0001), irrespective of metabolic manipulation.

CONCLUSION

This study shows that this spheroid model takes up metformin without any cytotoxic effects, whilst decreasing mitochondrial ROS production. Metabolic manipulation significantly increased Complex II activity, as well as PFK2 expression, indicating increased glycolysis. This metabolic responsive confirms that this model can be used for drug screening.

Investigating the expression patterns of the novel TSPO splice variant, PBR-s, in cervical cancer cells

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BACKGROUND

Cervical cancer remains one of the major contributors of cancer-related fatalities in women globally, despite advancements in diagnostic tools and treatment modalities. The incidence of cervical cancer continues to rise, underscoring the urgency to identify new biomarkers and therapeutic targets. One promising biomarker is the TSPO (translocator protein) gene, involved in cancer development and progression, exhibiting altered expression and alternative splicing across various cancers.

OBJECTIVES

This study focused on investigating the expression pattern of the novel TSPO spliced variant PBR-s in cervical cancer CaSki cells under the influence of various anticancer agents.

METHODS

The impact of various anticancer agents ($CoCl_2$, Curcumin, A_2O_3, and NaBu) on the survival of CaSki cells was evaluated through the MTT assay and count and viability assay. Cell death in CaSki cells was further evaluated using the Muse® Annexin V and Dead Cell Assay, along with the Muse® MitoPotential Assay. Additionally, the expression of the PBR-s gene was assessed using conventional polymerase chain reaction.

RESULTS

The results showed a notable decrease in the viability of CaSki cells, along with increased late apoptotic cells and disruption of mitochondrial membrane potential under the effect of curcumin, A_2O_3, and NaBu with minimal effect observed on cells subjected to $CoCl_2$. Additionally, the expression of PBR-s varied under the influence of different anticancer agents, showing both increasing and decreasing activity.

CONCLUSION

The anticancer agents could be potential drug targets for regulation of TSPO splice variants on cervical cancer treatment. Also, the PBR-s variant could be potential biomarker for cervical cancer diagnosis and treatment. Furthermore, studies are to be conducted to investigate the mechanism of regulation by the variants as well as protein-protein interactions.

ABSTRACTS: POSTERS MSc CATEGORY

The effect of *Bauhinia bowkeri* extracts on anti-hypercholesteremia: insights from in vitro and in silico investigations

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BACKGROUND

Among the current cholesterol-lowering drugs present, the persistent surge of hypercholesterolemia-related complications ignites a fascinating search for the discovery of novel therapeutics.

OBJECTIVES

This study aimed to investigate the anti-hypercholesterolemic effect of *Bauhinia bowkeri* extracts

METHODS

The plant material was sequentially extracted with n-hexane, DCM and 70% ethanol. The extracts were screened through GC-MS analysis and tested against a wide range of free radicals (ABTS, DPPH, metal iron chelating, hydroxyl radical, nitric oxide and reducing power). Thereafter, the enzyme inhibitory activity of the extracts on pancreatic lipase, cholesterol esterase, and HMG-CoA reductase, as well as bile binding capacity, were evaluated. Molecular docking on HMG-CoA reductase, cyclooxygenase, and hormone-sensitive lipase was also investigated.

RESULTS

A total of number of 122 compounds were detected in all three extracts, only seven common compounds (E-15-Heptadecenal, Diethyl Phthalate, 9,12,15-Octadecatrienoic acid ethyl ester, (Z,Z) Tetradecane 5-methyl-, Octadecane 5-methyl) were found to be common in all extracts. The extract displayed a varying degree of efficiency on free radicals with IC_{50} values ranging from 0.07 mg/mL to 0.41 mg/mL. It is worth noting a concentration-dependent inhibition of pancreatic lipase and cholesterol esterase, along with a reduction in bile binding capacity exhibited by the extracts. In silico investigations revealed significant inhibition of HMG-CoA reductase, cyclooxygenase, and hormone-sensitive lipase with binding affinity ranged between -5.2 to -6.0 kcal/mol.

CONCLUSION

These findings suggest that *Bauhinia bowkeri* extracts possesses potent antioxidant and anti-hypercholesterolemic properties.

ABSTRACTS: POSTERS MSc CATEGORY

The relationship between blood pressure and blood glucose level in Walter Sisulu University community

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BACKGROUND

Hypertension and diabetes are a public health problem in South Africa. An increase blood pressure (BP) which can be characterized by vascular dysfunction is a significant risk factor for diabetes-related vascular problems such as insulin resistance which leads to increase in blood glucose (BG). However, to date, there has been no study done to investigate the relationship between BG and blood pressure (BP) among historically disadvantaged university communities.

OBJECTIVES

The aim of the study was to investigate the relationship between BG and BP among the Walter Sisulu University students and staff members.

METHODS

This cross-sectional study was conducted in Walter Sisulu University. All 230 participants aged 18 years and above, underwent BG and clinic BP measurements using standard procedures.

RESULTS

In a descriptive analysis, the prevalence of diabetes and hypertension were 4.8% and 15.7%, respectively. In a Pearson correlation analysis, BG positively correlated with both systolic blood pressure (SBP) [r=0.36; *P*<0.001] and diastolic blood pressure (DBP) [r=0.28; *P*<0.001]. Furthermore, in a multivariable-adjusted regression analysis, BG positively associated with SBP [adjusted R2=0.29, ß=0.26 (95% CI =0.02;0.05), *P*<0.001], while showing no association with DBP [adjusted R2=0.24, ß=0.10 (95% CI = -0.01; 0.04), P=0.139] adjusted for age, gender, body fat, alcohol, and smoking.

CONCLUSION

BG is associated with BP among historically disadvantaged university students and staff members, implying that BG can be used as a predictor of elevated BP, aiding in the early diagnosis and prevention of cardiovascular diseases (CVDs).

ABSTRACTS: POSTERS MSc CATEGORY

Assessing the impact of *Commelina benghalensis* extracts on breast cancer cell

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BACKGROUND

Female breast cancer is the leading cause of global cancer incidence, with an estimated 2.3 million new cases. Treatments such as radiotherapy, chemotherapy and surgery are used to counteract the impact of this disease; however, conventional treatment approaches may, in some cases, be ineffective; thus the use of medicinal plants is enticing.

OBJECTIVES

The aim of the study was to investigate the antioxidant, cytotoxicity and potential anticancer properties of *Commelina benghalensis* aqueous (aq) extract in breast cancer cells.

METHODS

C. benghalensis (roots, stems and leaves) were collected, dried and extracted using only water. The MDA-MB 231 and MCF-7 breast cells were used in this study. Quantitative 2,2-diphenyl-1-picrylhydrazyl (DPPH) and free radical antioxidant power (FRAP) were used to investigate the antioxidant activities of *C. benghalensis*. The cytotoxicity of the *C. benghalensis* aq-extract was determined using MTT assay and the Muse® cell count and viability assays. Annexin V assay was used to detect and quantify programmed cell death.

RESULTS

The *C. benghalensis* leaf aq-extract exhibited the lowest half-maximum effective concentration (EC_{50}) value of 250 µg/mL for DPPH (55.873 ± 15.39 µg/mL) and (EC_{50}) value of 150 µg/mL FRAP (1.159 ± 0.40 µg/mL). The *C. benghalensis* leaf aq-extract significantly (**P>0.01 and ****P>0.00001) reduced cell viability of MDA MB 231 cells (IC_{50} = 750 µg/mL) after 48 hours, however, MCF-7 the results were non-significant. Additionally, apoptosis was induced in *C. benghalensis* aq treated-MDA-MB 231 cells.

CONCLUSION

C. benghalensis leaf aq-extract possesses antioxidant and anticancer properties, as shown by reduction of cell viability and induction of apoptosis, however the changes were observed in higher concentration which may raise concerns on whether *C. benghalensis* may be considered for anticancer activities. However, the compound will be tested in other breast cancer cell lines and other assays such as dose-response curve will be conducted for further optimization.

ABSTRACTS: POSTERS MSc CATEGORY

Assessing cardiovascular effects of HIV/AIDS and preeclampsia in pregnant women of African Ancestry in Mthatha, South Africa

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BACKGROUND

The risk for cardiovascular diseases is becoming more prevalent in pregnant women of African descent, although not much data are available for women with preeclampsia (PE) as well as women living with the human immunodeficiency virus (HIV). Foetoplacental endothelial dysfunction resulting from these diseases is thought to predispose these women to developing cardiometabolic diseases such as obesity and diabetes mellitus later in life.

OBJECTIVES

This pilot study aimed to investigate cardiovascular vulnerabilities in preeclamptic and HIV- positive women of African ancestry in Mthatha.

METHODS

This cross-sectional study included a total of 18 pregnant women, from which, six were HIV- positive, six were HIV-negative and preeclamptic and six were normotensive and HIV negative with no cardiovascular disease comorbidities. Anthropometry, blood pressure as well as arterial stiffness measurements (Pulse wave velocity and Ankle-Brachial Index) were recorded from this population.

RESULTS

Preeclamptic women were more likely to be overweight and obese (BMI±SD of 30.93±11.40) compared to the normotensive controls (26.33±3.18) and the HIV- positive group (30.69±3.33). Additionally, women with preeclampsia were more frequent in the older age group. The prevalence for hypertension was 45% and was mostly attributed to the preeclamptic group. In a Pearson correlation analysis for the preeclamptic group, PWV positively correlated with all blood pressure parameters, systolic blood pressure (SBP) [r=0.898; *P*<0.001], diastolic blood pressure (DBP) [r=0.905; *P*<0.001] and Heart Rate (HR) [r=0.825; *P*<0.001]. There was no significant correlation for both the HIV-positive and the normotensive control groups.

CONCLUSION

The results obtained in the current study showed that arterial stiffness is indeed associated with blood pressure in preeclamptic women.

ABSTRACTS: POSTERS MSc CATEGORY

Sensitive amplification methods to detect and sequence human-parechoviruses, adenoviruses, and enteroviruses in cerebrospinal fluid

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BACKGROUND

Sudden unexpected death in infancy (SUDI) includes all unexplained deaths in infants aged 7 days to one year. Routine diagnostic tests are utilised to assign a final cause of death in these cases. South Africa has a high infant mortality rate (IMR) ranging from 23.13 to 23.57 per 100 000 live births and is among the top 10 countries for infant mortality globally. The Triple Risk Hypothesis suggests SUDI is more likely to occur during critical developmental stages of the infant. In South Africa, central nervous system (CNS) infections are not well-explored in SUDI cases. Historically, diagnostic panels have focused on herpesviruses, neglecting other viruses like human parechoviruses (HPeVs), human adenoviruses (HAdVs), and human enteroviruses (HeVs), leading to potential under-reporting.

OBJECTIVES

The study aimed to (1) identify previously undiagnosed viral infections in routine and SUDI cerebrospinal fluid (CSF) samples using a targeted approach and (2) analyse the molecular epidemiology of these infections, detailing viral genotypes by age group, season, and sampling year.

METHODS

Viral nucleic acids were extracted from CSF samples on an automated Hamilton extraction platform. Viral RNA was reverse transcribed, and DNA was amplified using nested touch-down PCR. Positive results were confirmed by gel electrophoresis.

RESULTS

Thus far, 61 CSF samples collected from SUDI cases between 1 April 2021 and 31 March 2022 were tested for the presence of HPeV, HAdV and HeV. Of these, 41% (25/61) tested positive for the presence of HeV.

CONCLUSION

The presence of HPeV, HAdV and HeV in CSF from SUDI cases is underexplored and underreported, despite recent research linking these viruses to CNS infections. This method will enable the detection of these viruses where routine methods are not sensitive enough. It will furthermore contribute to the process of assigning a final cause of death in SUDI cases.

Phytochemical screening, in vitro antibacterial and in silico antidiabetic potential of *Agathosma betulina* extracts

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BACKGROUND

Diabetic foot ulcers (DFUs), a chronic diabetes complication, are threatened by antimicrobial resistance, leading to the exploration of medicinal plants such as *Agathosma betulina* for its potential antibacterial and antidiabetic properties.

OBJECTIVES

This study evaluated the in vitro antibacterial and in silico antidiabetic potential of *A. betulina* extracts.

METHODS

The bioactive compounds of *A. betulina* were sequentially extracted using n-hexane and dichloromethane (DCM) solvents. Phytochemical characterization was performed using Fourier Transform infrared spectroscopy (FTIR) and gas chromatography-mass spectrometry (GC-MS) analyses. The antibacterial activity of the extracts was evaluated against *Pseudomonas aeruginosa* (CP083366.1) and *Staphylococcus aureus* (AP025177.1), isolated from DFUs, using minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) assays. In silico studies were conducted to investigate the inhibitory potential of *A. betulina* compounds against key diabetic enzymes, including dipeptidyl peptidase 4 (DPP-4), sodium-glucose co-transporter-2 (SGLT2), and alpha-glucosidase. Molecular docking studies were performed using AutoDock Vina through PyRx to determine binding scores.

RESULTS

GC-MS analysis revealed 2-ethyl-2-hexen-1-al (14.93%) and 2,4-imidazolidinedione- 5,5-dimethyl-3-(2-propenyl) (39.74%) as major phytochemicals in the n-hexane and DCM extracts, respectively. Both extracts showed significant inhibitory effects against *S. aureus* and *P. aeruginosa*, with MICs ranging from 1.25 and 2.5 mg/mL; hence, the MBC values ranged between 2.5 and 5 mg/mL. The computational simulation studies of the compounds derived from *A. betulina* demonstrated substantial activity in inhibiting diabetic enzymes, with 2,4-imidazolidinedione- 5,5-dimethyl-3-(2-propenyl) exhibiting maxima binding affinities ranging from -6.1 to -5.6 kcal/mol in comparison to metformin (-5.6 to -4.9 kcal/mol) with hydrogen bonds and Van der Waals as most dominant interactions.

CONCLUSION

This study suggests that *A. betulina* compounds show potential to inhibit DFU bacteria and exhibit promising antidiabetic properties for novel drug discovery.

ABSTRACTS: POSTERS MSc CATEGORY

Antipyretic effects of *Schinus molle* in yeast-induced pyrexic Wistar rats

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BACKGROUND

Synthetic medications, such as paracetamol and aspirin, are used to treat pyrexia, also known as fever. Traditional medicine remains an alternative therapy as it is widely accessible and presumed to have fewer negative effects. *Schinus molle* has been used traditionally to treat pyrexia related conditions such as pain and inflammation. However, its antipyretic ability has not been scientifically validated.

OBJECTIVES

The study aimed to investigate the effectiveness of *Schinus molle* leaves in fever reduction using male Wistar rats.

METHODS

Twenty-four male Wistar rats were divided into 4 groups [normal control, experimental control, *Schinus molle* treated group and paracetamol treated group (n=6/group)]. A 15% w/v suspension of brewer's yeast was suspended in 0.5% w/v methylcellulose solution and injected subcutaneously into the experimental rats to induce fever. The *Schinus molle* treated group was exposed to plant treatment. Rectal temperatures, body weights and water intake were recorded at regular intervals. Differences within groups were determined using a repeated measure two-way ANOVA followed by a post-hoc test.

RESULTS

There were no differences in body weight among the groups ($P>0.05$). Paracetamol treated group showed a significant reduction in fever ($P<0.01$) when compared to experimental control. Although body temperature decreased in the *Schinus molle* treated group, the reduction was not statistically significant compared to experimental control ($P>0.05$).

CONCLUSION

Paracetamol has more pronounced antipyretic ability than *Schinus molle*. Future studies should explore the traditional use of *Schinus molle* to treat pyrexia over an extended period to determine its efficacy and the optimal rate of usage.

ABSTRACTS: POSTERS PhD CATEGORY

Investigating the cytotoxic effects of *Ozoroa paniculosa* in diet-induced obese C57BL/6 mice

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BACKGROUND

Obesity is associated with low-grade inflammation, leading to complications like insulin resistance and type 2 diabetes. South Africa has one of the highest obesity rates globally, with 42% of women and 13.5% of men being obese, and these numbers are expected to rise by 2025. Current obesity management appears ineffective, prompting interest in natural products like medicinal plants for their potential anti-obesity effects due to their bioactivity, affordability, and lack of side effects. This study focuses on exploring the anti-inflammatory properties of *O. paniculosa* in obese mice and examining the phytochemicals' mechanisms using in silico techniques

METHODS

The study involves collecting the medicinal plant *O. paniculosa* from Limpopo, South Africa, and preparing extracts using acetone and water. These extracts were tested for cytotoxicity on various cell types and their anti-inflammatory effects on RAW 264.7 macrophages and 3T3-L1 adipocytes. The most bioactive extract was used to treat diet-induced obese mice, with further analysis of tissue histology, triglyceride levels, and inflammatory markers using techniques like ELISA and qRT-PCR. The study also included in silico analysis to predict the anti-inflammatory targets and binding conformations of *O. paniculosa* phytochemicals, assessing their pharmacokinetic and toxicological profiles.

RESULTS

The acetone extract showed significant cytotoxicity against 3T3 -L1 cells and C3A cells at a concentration of 1000 µg/mL. The water extract was significantly cytotoxic against 3T3-L1 cells and RAW 264.7 cells from 500 µg/mL. Additionally, the extract was cytotoxic at 250 µg/mL in C3A cells. The expected results are that the bioactive extract of *O.paniculosa* (water or acetone) will inhibit inflammation and obesity in vivo. The in silico data will also corroborate the effects of the plants observed in vivo.

CONCLUSION

The findings of the study suggest that *O.paniculosa* extract has anti-inflammatory potential and could be considered for treatment of low-grade inflammation during obesity.

ABSTRACTS: POSTERS PhD CATEGORY

The effects of *Aspalathus linearis* (rooibos) against angiotensin II-induced hypertrophy and apoptosis

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BACKGROUND

Cardiovascular diseases are a growing global concern especially in developing countries such as South Africa. Medicinal plants such as *Aspalathus Linearis* (rooibos) are gaining attention as alternative therapeutic agents for chronic diseases of lifestyle in this context. Rooibos is a shrub-like plant that has been associated with several health benefits including cardioprotective effects. In isolated cells, it improves high glucose-induced apoptosis and in isolated perfused hearts it reduces infarct size. However, rooibos has never been tested against cardiomyoblast hypertrophy and apoptosis.

AIM

To investigate the effects of rooibos (RB) against angiotensin-II (ANG-II) induced hypertrophy and apoptosis.

METHODS

Undifferentiated H9C2 cardiomyoblasts were treated with Ang-II (20 μM), RB (100 μM) and ANG-II+RB for 48 hours, (n=3 and n=4). The following experimental procedures were performed: HPLC analysis of the RB extract, IC-50 of the RB extract, cell size, cell viability, superoxide (SOD) activity, catalase (CAT) activity, levels of oxidative stress (TBARS), ATP levels, caspase 3 activity, high-resolution respirometry as well as western blotting for markers of hypertrophy, apoptosis, and mitochondrial energetics and metabolism. One-way Anova and t-tests were used to analyse the results and $P<0.05$ was considered as statistically significant.

RESULTS

RB attenuated the effects of ANG-II by reducing cell size ($P<0.01$), increasing cell viability ($P<0.01$), ATP levels ($P<0.05$) and SOD activity ($P<0.05$). RB did not affect CAT activity ($P>0.05$). RB reduced caspase 3 activity ($P<0.05$). RB reduced the expression of Bax ($P<0.05$), a marker of apoptosis and VDAC1 ($P<0.01$), a mitochondrial gatekeeper. RB also restored complex 1-linked leak respiration ($P<0.05$), beta oxidation ($P<0.05$) and glucose oxidation related oxidative phosphorylation ($P<0.05$).

CONCLUSION

Rooibos counteracts Angiotensin II-induced hypertrophy and apoptosis via the improvement of antioxidant and apoptotic pathways and mitochondrial energetics and metabolism.

Investigating the impact of CD44 on chemoresistance and metastasis in cervical cancer: insights from ex vivo and in vitro models

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BACKGROUND

Cervical cancer is a significant global health challenge, mainly due to recurring high-risk human papillomavirus (HPV) infections. Despite treatment advances, chemoresistance and metastasis limit therapeutic effectiveness, resulting in poor outcomes. This study aims to elucidate the molecular mechanisms underlying chemoresistance and metastasis in cervical cancer, focusing on the cluster of differentiation 44 (CD44) as a potential therapeutic target.

OBJECTIVES

By investigating the effects of various chemotherapeutic agents on cervical cancer cells through ex vivo, in vitro 2D, and in vitro 3D spheroid models, this research seeks to uncover insights into the roles of CD44 and epithelial-to-mesenchymal transition (EMT) markers in treatment resistance and metastatic potential.

METHODS

An ex vivo model, as well as 2D and 3D in vitro models, were utilised in this study. Ethical approval (HREC - N22/04/037) and patient consent was obtained for the ex vivo model. Cervical tumour biopsies were treated with doxorubicin, carboplatin, gemcitabine, and paclitaxel. Cell viability was assessed using an MTT assay. CD44 and EMT markers were analysed via western blotting. Wound closure rates were measured using a scratch assay, and circulating tumour cells (CTCs) in patient blood samples were detected using immunofluorescence. Scanning electron microscopy analysed spheroid topography.

RESULTS

Patients exhibited significant chemoresistance to multiple drugs, with elevated EMT markers and CD44 expression. Immunofluorescence confirmed CTC presence, indicating high metastatic potential. Treatment significantly reduced cell viability across all lines, with carboplatin showing effective IC_{50} values. Western blotting revealed altered CD44 expression, EMT markers, and apoptotic pathways. Immunocytochemistry indicated elevated CD44 expression in the spheroid model, suggesting treatment resistance.

CONCLUSION

The findings highlight the challenges posed by chemoresistance and metastasis in cervical cancer. Elevated CD44 and EMT markers were associated with treatment resistance and metastatic potential. These results emphasize the need for further investigation into the molecular mechanisms driving these processes, with CD44 as a promising therapeutic target.

ABSTRACTS: POSTERS PhD CATEGORY

Investigating the effects of senescence-induced treatment resistance in cervical cancer patients

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BACKGROUND

Cervical cancer is a global health concern, and despite several advancements in its prevention, treatment resistance remains a major hurdle in achieving improved patient outcomes. Cellular senescence, specifically the senescence-associated secretory phenotype (SASP), has been implicated in treatment resistance, however, its role in the development of cervical cancer and the associated therapy resistance remains poorly understood.

OBJECTIVE

Therefore, the current study investigates the effects of senescence-induced treatment resistance in cervical cancer patients using a personalised medicine approach.

MATERIALS AND METHODS

Ethical approval for this study was received from Stellenbosch University. Once patients provided consent, a small biopsy of cervical tumour tissue was taken. Biopsies were mechanically dissociated and grown in culture until they reached confluency, whereafter they were seeded into the appropriate culture flasks and treated with low dosage chemotherapies, to allow for appropriate senescence induction. Through a retrospective analysis of patient data, we explored the correlation between cellular senescence markers and treatment response within this cohort. Each patient served as their own control. Patient response to cytotoxic chemotherapy analysis was assessed with an MTT assay, followed by determination of the senescent phenotype using a senescence-associated beta galactosidase (SA-ß-gal) staining kit. Additionally, western blot analysis of specific markers of senescence (p16, p21, p53, Rb, and SASP) and treatment resistance (ABC and MDR1) were performed.

RESULTS

A slight reduction in cell viability was detected when compared to the control groups, due to the administration of low concentrations of chemotherapies. Furthermore, these low dosages of chemotherapies induced senescence in all treatment groups, indicated by increased SA-ß-gal, along with the associated increased expression of treatment resistance markers ABCG2 and MDR1.

CONCLUSION

There is an interaction between senescence-induction and treatment resistance pathways following chemotherapy treatment in cervical cancer patients. This provides insight into the complexity of the mechanisms of cellular senescence and its association with treatment resistance, paving the way for more effective, personalised therapeutic strategies for cervical cancer patients to improve clinical outcomes.

ABSTRACTS: POSTER SCIENTISTS

Exploring the anticancer potential of *Momordica balsamina* methanol extract on HT-29 colon cancer cells

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BACKGROUND

Momordica balsamina, commonly known as balsam apple, is a medicinal plant traditionally used in various cultures for its purported health benefits, including antimicrobial, anti-inflammatory, and anticancer properties. Previous studies have suggested that extracts from this plant exhibit cytotoxic effects on various cancer cell lines, but the specific mechanisms and efficacy against colon cancer cells require further investigation.

OBJECTIVES

This study focused on investigating the anticancer activity of *Momordica balsamina* methanol extract on HT-29 colon cancer cells, aiming to explore its cytotoxic, genotoxic, and apoptotic effects.

METHODS

The cytotoxic effects of the methanol extract on HT-29 cells and C2C12 muscle cells were assessed using the MTT assay. Genotoxicity was evaluated in C2C12 cells with the Muse™ Multi-Colour DNA Damage kit. Mitochondrial potential and cell/nuclear morphology were assessed using the JC-1 assay and acridine orange (AO)/propidium iodide (PI) staining, respectively. Apoptosis was quantified via flow cytometry with annexin V/PI staining, and caspase activation was determined using Caspase-8 and Caspase-9 assays.

RESULTS

The methanol extract demonstrated selective cytotoxicity towards HT-29 colon cancer cells after 24 hours of treatment and induced genotoxicity specifically in these cells. Morphological analysis suggested that the reduction in cell viability was associated with apoptotic cell death, as evidenced by loss of mitochondrial potential, elevated caspase-8 and -9 activities, and annexin V/PI staining.

CONCLUSION

In conclusion, *Momordica balsamina* methanol extract exhibits promising anticancer properties against HT-29 colon cancer cells through the induction of apoptosis and genotoxic effects, highlighting its potential as a therapeutic agent for colon cancer treatment.

ABSTRACTS: POSTER SCIENTISTS

Development of a bioinformatics pipeline for analyzing gene expression patterns in hypertensive patients

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BACKGROUND

Rapid advances in RNA sequencing (RNA-seq) analysis have made it a powerful tool for uncovering genes and pathways linked to disease. South Africa bears the highest burden of hypertension in Africa, with genetic factors contributing 20% to 80% of the variability in individual responses to drug treatment. To better understand the impact of genetic variation in hypertension, transcriptomic investigations are conducted to identify molecular pathways and genes that could be utilized for hypertension management and improved treatment outcomes.

OBJECTIVES

The aim of this study was to develop bioinformatics pipelines for analyzing RNA-seq data, with the goal of uncovering transcriptomic changes associated with the development of hypertension in South African populations.

METHODS

A variety of bioinformatics tools were evaluated for inclusion in the pipeline(s) based on their performance in RNA-seq analysis. To determine the most suitable tools, an extensive literature review and thorough examination of tool documentation were conducted before pipeline design. The selected tools were chosen for their capacity to manage complex transcriptomes and generate accurate gene expression data.

RESULTS

Two RNA-seq pipelines were developed for this investigation both incorporating quality control analysis using the FastQC tool. Pipeline A aligns samples to a reference genome, followed by quantification, differential gene expression analysis (DEGs) and functional analysis. Pipeline B aligns samples to the transcriptome which is followed by DEGs and functional analysis.

CONCLUSION

The bioinformatics pipelines will help with the identification of candidate genes which may potentially be linked to hypertension, which can then be further explored for their clinical relevance. These findings may contribute to developing improved treatment strategies for hypertensive patients.

The effect of resveratrol on hyperglycemia-related microRNAs in HepG2 cells

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BACKGROUND

The disruption in the normal functioning of specific microRNAs (miRNAs), namely miR-30a-5p, miR-126-3p, and miR-182-5p, is strongly linked to the initiation and advancement of type 2 diabetes mellitus. Therapeutic interventions involving endogenous and exogenous substances can restore miRNA regulation.

OBJECTIVE

The current study examines the effect of high glucose (HG) on HepG2 cells and assesses the effects of resveratrol (RES), a polyphenol phytoalexin, on HG-induced miRNA dysregulation.

METHODS

We evaluated the levels of three miRNAs (miR-30a-5p, miR-126-3p, and miR-182-5p) expression and their target genes (Sprouty-related EVH1 domain containing 1 (SPRED1), Forkhead box O1 (FOXO1), Glucose-6-phosphatase (G6P), Neuronal differentiation 1 (Neurod1) in HepG2 cells treated with high glucose (40 mM) and resveratrol (25 and 50 µM). The levels of miRNAs and mRNAs expression were measured using qPCR, after 48 and 72 hours.

RESULTS

Exposure to HG for 48 and 72 hours decreased the expression of miR-126-3p while increasing the expression level of its target gene SPRED1 in HepG2 cells. Conversely, RES treatment increased the expression of levels of miR-126-3p and reduced the expression of SPRED1. The HG treatment decreased miR-182-5p and enhanced the expression of FOXO1 and G6P. RES treatment increased miR-182-5p expression, concomitant with a reduction of FOXO1 and G6P levels. Furthermore, HG decreased miR-30a-5p levels, which subsequently increased Neurod1 expression. Conversely, treatment with RES increased miR-30a-5p while simultaneously reducing Neurod1.

CONCLUSION

Treatment with resveratrol showed a potential therapeutic application by increasing miR-30a-5p, miR-126-3p, and miR-182-5p expression levels. In addition, resveratrol may mitigate the effects exerted by miRNAs on their respective target genes.

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