16TH FRANK WARREN CONFERENCE

POLOKWANE | 3 - 7 DECEMBER 2023

Conference Book

CONTENTS

Welcome statement from the Chairperson of SACI-OCD

Dear Delegates

On behalf of SACI and the Organic Chemistry Division, I would like to welcome you all to the 2023 Frank Warren National Organic Chemistry Conference. While the northern regions of South Africa are no strangers to hosting the Frank Warren, this is the first edition to be hosted in Limpopo and it is a wonderful opportunity for delegates to experience this beautiful part of the country.

The Frank Warren is a key date in the South African chemistry calendar, where the ethos of collaboration and community is perpetuated in all facets of these meetings. This is evidenced by the traditionally large cohort of student delegates who attend the Frank Warren. It is no secret that the current funding landscape in South Africa is challenging, which in turn makes finding conference funds a significant obstacle. I would therefore like to thank all the delegates who have made the necessary sacrifices to attend. This support is essential for the ongoing sustainability of SACI, which we gratefully acknowledge. To that end, I would also like to extend a special thanks to the numerous generous sponsors and donors, without whom this conference would not be possible.

To our international guests, welcome to South Africa. Your intellectual contributions and personal perspectives of the field are a critical element of a successful Frank Warren. I hope that in addition to engaging with the local organic chemistry landscape, you take this opportunity to enjoy some of what this uniquely beautiful country has to offer.

Well done to all the speakers, many of whom are Frank Warren veterans, and many others who will be presenting their first poster or oral at a conference. Good luck to you all! I would like to offer a special congratulations to Wilfred on delivering this year's Frank Warren Lecture. A well-earned accolade.

Finally, to Comfort and the rest of the LOC, congratulations on pulling off another successful Frank Warren Conference and putting together a superb line-up. This takes a huge amount of effort and time, which the SACI organic chemistry division greatly appreciates.

I hope everyone engages, enjoys, and builds life-long relationships in chemistry.

Best wishes,
Clint Veale

SACI-OCD Chairperson

16th Frank Warren Conference Local Organizing Committee

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Conference Organizer	Ms Laila Smith (South African Chemical Institute)

Message from the LOC Chairperson

Dear Delegates

The day has finally arrived, and we have reached the final stop on "The Road to Polokwane", our motto for this year's Organic Chemistry PhD Seminars!

It is my pleasure and privilege to welcome you to the wonderful Limpopo Province, the northernmost province in South Africa. The province is home to many important landmarks including the mighty Limpopo river, the breath-taking Magoebaskloof Valley, the unforgettable Kruger National Park, and the legendary Mapungubwe Cultural Landscape (a UNESCO heritage site). After this week the province will also be known for the most informative and enjoyable Frank Warren Conference!

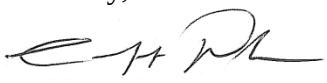
The Frank Warren National Organic Conference (FWC) is the flagship organic chemistry conference organized by the Organic Chemistry Division of the South African Chemical Institute (SACI-OCD). A specialist organic chemistry meeting has been hosted bi-annually in South Africa since 1961 until 2016 when the calendar of SACI events was revised such that the conference is now held every three years. This conference was due to be held in 2022, but was postponed due to the upheavals unleashed by the COVID-19 outbreak in 2020 which pushed many meetings to online/remote gatherings. Thus, we are thrilled to host you in-person to the magnificent Protea Hotel Ranch Resort in Polokwane!

The Limpopo Province's motto is "Peace, Unity and Prosperity" which complements our conference theme of "**Securing Africa's Future Through Organic Chemistry Research**". This is the first time that the FWC is held in Limpopo, so let this be the week where organic chemists meet peacefully with the united objective to share, discuss, and be motivated to pursue research that contributes to the security and prosperity of Africa and her people.

The planning and organization for such a conference can only be successful with the generous support of partners and sponsors. First and foremost, amongst these is the guidance and seed-funding support from the SACI EXCO and the SACI-OCD who fully supported our intention to bring this prestigious conference to Limpopo. We are also extremely grateful to the financial and logistical support from the member institutions of the SACI North Section (SACI-NS): Sefako Makgatho Health Sciences University (**SMU**), Tshwane University of Technology (**TUT**), University of Limpopo (**UL**), University of Mpumalanga (**UMP**), University of Pretoria (**UP**), University of Venda (**Univen**), Council for Scientific and Industrial Research (**CSIR**), and the South African Nuclear Energy Corporation Limited (**NECSA**). We also acknowledge the support of the Department of Science and Innovation (DSI) and MINTEK for their support to subsidize the participation of postgraduate students in this conference. Finally, we appreciate the support from the sponsors and exhibitors at this conference; these are South African companies involved in the promotion of science and chemistry, particularly organic chemistry, so please take some time to visit their exhibitions and engage them in how they may contribute to boosting your research.

The scientific committee have excelled in assembling an exciting list of invited speakers and presentations from the abstract submissions, including poster flash presentations and the actual poster presentations. I wish you all a successful and informative conference, and trust that you will take the advantage of this opportunity to share ideas, to establish new friendships, networks and future collaborations.

Sincerely,



COMFORT NKAMBULE
CHAIRPERSON

(*On behalf of the 2023 FWC LOC*)

CONFERENCE INVITED SPEAKERS

Invited Plenary Lecturers

- Prof Wilfred Mabusela (University of Western Cape, South Africa)

- Dr BG Hlangothi (Nelson Mandela University, South Africa)
- Prof Neil Koorbanally (University of KwaZulu-Natal, South Arica)
- Prof Moses Langat (Royal Botanic Gardens Kew, UK)
- Prof Tobias Ritter (Max-Planck-Institut fuer Kohlenforschung, Germany)
- Prof Dr Colleen Scott (Mississippi State University, USA)
- Prof Willem van Otterlo (Stellenbosch University, South Africa)

Invited Keynote Lecturers

- Dr Njabulo Gumede (Walter Sisulu University)
- Prof David Khanye (Rhodes University)
- Dr Paseka Moshapo (University of Johannesburg)
- Dr Jenny-Lee Panayides (CSIR)
- Prof Amanda Rousseau (University of the Witwatersrand)
- Prof Clinton Veale (University of Cape Town)

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About the H3D Foundation

H3D Foundation is a nonprofit organization that was established in 2019 to build on the success of the University of Cape Town Holistic Drug Discovery and Development (H3D) Centre's capacity development programs. H3D Foundation aims to position Africa as a global player in innovative pharmaceutical R&D by building infrastructure as well as the skills of scientists and researchers based in Africa. Moreover, one of the key elements in the mission of the H3D Foundation is to advocate for the use of science in job creation and to create an absorptive capacity to identify, attract, develop, nurture and retain talent in drug discovery related sciences across the African continent.

Learn more at www.h3dfoundation.org.

"Bringing data science and AI/ML tools to infectious disease research" Workshop 2022 – photo credit Tamara Krige

CONFERENCE PROGRAM

03 December 2023

Time	Activity	
13h00 - 17h00	Registration	All delegates
18h00 – 22h00	**Welcome Remarks & Reception**	

Day 1

4 December 2023

*Opening Session: **Prof CM Nkambule***		
Time	**Lecture**	**Speaker**
8h30 - 8h50	Welcome and conference opening by the Vice-Chancellor & Principal of the University of Limpopo	Prof NM Mokgalong
8h50 - 9h40	**PL-1**: Playing Lego with aldehydes, acetophenones, acids and amines to design and synthesise bioactive conjugate quinolines, quinoxalines and benzimidazoles	Prof N Koorbanally
9h40 - 10h10	**KN-1**: Heterocyclic inhibitors of Plasmodium falciparum	Prof AL Rousseau
10h10 - 10h30	**Coffee &Tea**	
*Teuns Van Ree (**UNIVEN**) Session: **Dr VJ Tembu***		
Time	**Lecture**	**Speaker**
10h30 -10h50	Repurposing of the organic compounds as potential corrosion inhibitors	Dr T Leboho
10h50 - 11h10	Flow chemistry and reaction engineering tools for the competitive manufacture of pharmaceuticals in South Africa	Prof D Riley

11h10 - 11h30	Energy Harvesting Potential of Azobenzene and Perylene Tetracarboxylic Bisimide Derivatives: Synthesis, Phase Transition, and Computational Study	Dr N Molefe
11h30 - 11h50	Synthesis of peptide nucleic acids (PNAs) using a safety-catch protecting group strategy - Compatible with Boc-Chemistry	Dr E Macedo Brasil
11h50 - 12h10	High Performance GC- & GCÃ—GC-TOFMS metabolomics-Based approach for discovery of potential diabetes II biomarkers in human plasma	Dr C Kannigadu
12h10 - 12h30	Quinolone analogues of benzothiazinone: Synthesis, antitubercular structure-activity relationship and ADME profiling	Ms PS Dube
12h30 - 12h50	Biocatalytic and enantioselective synthesis of chiral oxygenated heterocycles	Ms MV Ndlovu
13h00 – 14h00	**Lunch**	
*Robert Vleggaar (**UP**) Session: **Prof S Mnyakeni-Moleele***		
Time	**Lecture**	**Speaker**
14h00 - 15h00	**PL-2**: Organic Chemistry in Materials Science	**Prof C Scott**
15h00 - 15h30	**KN-2**: Molecular Hybridization Approach in the Design of Biologically Active Compounds	**Prof S Khanye**
15h30 – 15h45	**Coffee &Tea**	
*Joseph Michael (**WITS**) Session: **Dr R Mohlala***		
15h45 - 16h05	New pentacyclic triterpenes from Strychnos henningsii and their Antidiabetic Activity	Dr N Latolla
16h05 - 16h25	LC-MS profiling of an extract of Euphorbia grandicornis with anti-HIV activity	Dr S Hlengwa
16h30 - 17h30	Flash Poster Presentations (6 minutes each)	
18h00 – 22h00	**Bush Braai Dinner**	

Day 2

5 December 2023

*Cedric W Holzapfel (**UJ**) Session: **Dr M Selepe***		
Time	**Lecture**	**Speaker**
8h30 - 9h30	**PL-3**: Late-Stage Functionalizations	**Prof Tobias Ritter**
9h30 - 10h00	**KN-3**: Sustainability and the pharmaceutical industry: The rise of the machines	**Dr J-L Panayides**
10h00 – 10h30	**Coffee &Tea**	
*Siegfried E Drewes (**UKZN**) Session*: ***Dr N Khanyile***		
Time	**Lecture**	**Speaker**
10h30 - .10h50	Finding the ajoene sweet-spot: structure-activity relations that govern bioavailability and cancer cell cytotoxicity	Dr C Kaschula
10h50 - 11h10	Structural characterization, and quantum chemical study of the 7-acetyl-5-nitrobenzofurans as anticancer agents with antioxidant properties	Dr MM Maluleka
11h10 - 11h30	Design, synthesis, structure-activity relationship/structure-property relationship analyses toward the identification of preclinical anti-infective agents	Prof R Beteck
11h30 - 11h50	Teaching systems thinking in and for Organic Chemistry	Prof L Pilcher
12h10 - 12h30	Quinoline-1,2,3-triazole molecular hybrids: Synthesis, antimicrobial evaluation and molecular docking studies	Mr P Seboletswe
12h30 - 12h50	Forgotten Gems: Exploring triazenes' untapped potential as antimalarials and antimicrobials	Dr FJ Smit
12h50 – 14h00	**Lunch**	
*Dawie Roux (**UFS**) Session**: Prof W Nxumalo***		
Time	**Lecture**	**Speaker**
14h00 - 15h00	**PL-4**: Novel bioactive products from African Croton genus	**Prof M Langat**

15h00 - 15h30	**KN-4**: Modern approaches in the design of synthetically aware new chemical entities in drug discovery	**Dr N Gumede**
15h30 – 15h45	**Coffee &Tea**	
*Douglas Rivett (**RU**) Session: **Mr N Makhubele***		
15h45 - 16h05	Adventures in the synthesis of imidazo[1,2-a]pyridin-3-amines as possible HIV-1 NNRTIs	Prof M Bode
17h30 – 21h30	**Poster Presentations with Wine & Cheese**	

Day 3

6 December 2023

*Hebert EM Magojo (**UFH**) Session: **Prof RM Mampa***		
Time	**Lecture**	**Speaker**
8h30 - 9h30	**PL-5**: Plant Extracts as Sustainable Alternatives for Tyre Waste Management	Dr BG Hlangothi
9h30 - 10h00	**KN-5**: Native Mass Spectrometry as a Tool for Rapid Elucidation and Modulation of Difficult to Access Transient Protein-Protein Interactions	**Prof C Veale**
10h00 – 10h30	**Coffee &Tea**	
*Piet Steyn (**SU**) Session: **Dr MM Maluleka***		
Time	**Lecture**	**Speaker**
10h30 - 10h50	A fractionated marine extract library to enrich marine biodiscovery efforts in South Africa	Prof DR Beukes
10h50 - 11h10	Phytochemical screening of commercial pine bark extracts for adherence to US pharmacopeia requirements	Mr L Samuwi
11h10 - 11h30	Stereoselective synthesis of functionalized pyrrolidines as potential anti-tubercular compounds	Mr ND Thobejane
11h30 - 11h50	Fmoc Removal in Solid-Phase Peptide Synthesis using Morpholine: Good Performance and Suppression of Side-Reactions	Ms SN Mthembu
Excursions, free afternoon & evening		

Day 4

7 December 2023

*Ivan R Green (**UWC**) Session: **DR TC Leboho***		
Time	**Lecture**	**Speaker**
8h30 - 9h30	**PL-6**: Synthesizing complex bioactive structures through convergent coupling reactions	Prof W van Otterlo
9h30 - 10h00	**KN-6**: Exploring alternative amidation reactions and new phosphine ligands for palladium cross-coupling applications	**Dr P Moshapo**
10h00 – 10h30	**Coffee &Tea**	
*James R Bull (**UCT**)Session: **Dr ST Mthembu***		
Time	**Lecture**	**Speaker**
10h30 -10h50	In silico discovery of new analogues of 1-Heteroaryl-2-Alkoxyphenyl as potential inhibitors of SARS-CoV-2	Dr OE Oyeneyin
10h50 - 11h10	The design, synthesis and anti-tubercular properties of the sulfonated tri-substituted benzofuran derivatives.	Mr K Mojapelo,
11h10 - 11h30	I love chemistry! What now?	Dr J van Tonder
11h30 - 11h50	How NMR can help you to better understand the aggregation behaviour of amino acid surfactants	Mr E Wiese
11h50 - 12h10	Halogenated ortho-Hydroxybenzenecarbonyl derivatives as precursors to biologically relevant organic Motifs	Prof MJ Mphahlele
12h10 - 12h30	Palladium-catalyzed regiodivergent C-H olefination of imidazo[1,2a] pyridine carboxamide and unactivated Alkenes	Prof R Karpoormath
12h30 - 12h50	Organically shaking things up - Foray into mechanochemistry	Prof RWM Krause
13h00 – 14h00	**Lunch**	

*Frank Warren Lecture**: Prof C Veale***		
14h00 - 15h00	**PL-7**: Exploring the natural product chemistry of South African medicinal plants	Prof WT Mabusela
15h00 – 15h30	**Coffee &Tea**	
18h00 – 22h00	**Conference Gala Dinner & Awards**	

Key: **PL** (Plenary Lecture), **KN** (Keynote Lecture)

PLENARY LECTURE ABSTRACTS

Frank Warren Lecture

Exploring the natural product chemistry of South African medicinal plants

Wilfred T Mabusela

Department of Chemistry, University of the Western Cape, Bellville, South Africa

E-mail: wmabusela@uwc.ac.za

Keywords: medicinal plants, natural products, phytochemistry

The chemistry of natural products derived from plants has grown significantly since the discovery of salicylic acid derivatives from the willow tree, for their antipyretic properties which in turn led to development of aspirin. Subsequently a number of other bioactive compounds have been discovered, some of which have made it to the pharmaceutical industry.

On the other hand, there has been global growth in the commercialization of herbal products, both in the formal and informal sectors. The complexity of the natural product composition of plants in general is such that not all such constituents may be described fully for any single plant. However, efforts to probe deeper have been sustained through the advancement of analytical technologies which facilitate such investigations. Pursuance of such studies will also be invaluable in the future when quality control of herbal products becomes a necessity.

This lecture will describe a personal journey of my laboratory's contributions towards a better understanding of some medicinal plants that are used in the South African context.

Plant Extracts as Sustainable Alternatives for Tyre Waste Management

J Mnyango[a], S Hlangothi[a], C Woolard[b] and B Hlangothi*[a]

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[b]*Faculty of Engineering, Stellenbosch University, Private Bag X1, Matieland, Stellenbosch, 7602, South Africa*

Keywords: *Tulbaghia* species, sulphur compounds, devulcanization, rubber recycling.

The increasing accumulation of car tyre waste poses a significant environmental challenge, necessitating sustainable solutions for effective management and recycling. Devulcanization, a method used for reclaiming rubber from waste tyres, involves breaking down the crosslinked molecular structure of vulcanized rubber to restore its processability and functionality. This process is preferred over other recycling processes such as crumbing and pyrolysis because the recovery of raw materials for re-use ranks higher in the South African waste management hierarchy. However, the commercial devulcanization agents are uneconomical and environmentally unfriendly, hence the necessity to search for cost-effective and eco-friendly alternatives. Plant extracts of the widely researched *Thulbaghia* species are known to be rich with organo-sulphur compounds, which are chemical compounds observed in the well-known commercial devulcanization agents, were explored in this study as alternative devulcanizing agents due to their sustainability and the results obtained are positive. Another important feature of this research is the use of a reactor under supercritical CO_2 instead of common solvents. This was intentionally chosen to better the eco-friendliness of the process.

This presentation will include experimental methodologies typically associated with plant extraction and compound identification, and processes employed first to vulcanize and then devulcanize the rubber compounds. Characterization of samples included the use of common techniques such as FTIR, GPC, NMR, TGA and rubber swelling tests. Findings proved that the *Tulbaghia* plant extracts, leaves and bulbs, can produce improved-quality recovered rubber when reacted under supercritical CO_2 conditions.

Playing Lego with aldehydes, acetophenones, acids and amines to design and synthesise bioactive conjugate quinolines, quinoxalines and benzimidazoles

Neil A. Koorbanally

School of Chemistry and Physics, University of KwaZulu-Natal

Cancer, diabetes and bacterial infections are three diseases that plague all nations, whether developed or not. While the first two are non-communicable diseases, bacterial infections can spread rapidly, and becomes life threatening when the microbes mutate and become resistant to known drugs. Infant mortality has increased dramatically over the past decade, especially in hospitals, due to antimicrobial resistance, which has been cited as a real threat to neonatal survival. In 2023 alone 569,000 deaths were linked to antimicrobial resistance in 35 North and South American countries and an estimated 700,000 deaths occur annually in Africa. The figures for cancer are markedly higher with 10,000,000 deaths occurring globally in 2022, with the top 10 countries being in Europe and North America. Amongst the three, the statistics for diabetes is the highest, with over half a billion people living with diabetes globally and approximately 7 million deaths occurring annually due to diabetes. Although drugs are available for all three diseases, there is still an urgent need for new alternates to known drugs, to combat bacterial resistance, and to find alternatives with lower side-effects than current drugs, especially anticancer and antidiabetic therapies.

Our work focuses on the synthesis of hybrid molecules of quinolines, quinoxalines and benzimidazoles as potential therapeutics for the treatment of bacterial infections, cancer and diabetes. We use basic aldehyde, acetophenone, acid and amine organic precursors amongst others to synthesise small libraries of conjugate molecules and test them for their pharmaceutical activity. Variation in the libraries are brought about by using various substituted precursors in the synthesis. Several molecules and libraries have been found to be active in anticancer, antidiabetic and antibacterial assays, which have the potential to be hit compounds for the treatment of these diseases.

This presentation will outline some of the strategies used to design these molecules and highlight some of our most active compounds.

Novel Bioactive Products from African *Croton* genus

Moses Langat[a]

[a] *Science Department, Royal Botanic Gardens Kew, E-mail: m.langat@kew.org*

Keywords: 16th Frank Warren, Abstract, Conference.

For the past 15 years we have been studying the chemistry of African *Croton* genus. This paper present novel bioactive constituents of *Croton* genus, mainly, with potential anti-HIV, anti-cancer and anti-plasmodial activities. Kenyan *Croton megalocarpus* and *C. dichogamus*, have exhibited crotofolane diterpenoids and sesquiterpene lactones with modest anti-HIV effects, inhibiting HIV-1 protease. Previously, *C. megalobotrys* was shown to have anti-HIV phorbol esters, in a Botswanan regimen used for HIV/AIDS management, and recently, we demonstrated using chemical analysis, in silico and in vitro reverse transcriptase, protease and integrase inhibitory experiments that patented Kenyan, anti-HIV tea, Carevid made of various parts of 14 Kenyan plants, including *C. macrostachys*, has potential against HIV virus. Congolese, *C. mubango* exhibited an isopimarane diterpenoid and *C. haumanianus* exhibited a kaurane diterpenoid, with significant activities and selectivity, each, against three of the NCI's 60 cancer cell lines at the single dose concentration of 10−5 M. The isopimarane from *C. mubango* was active against the melanoma (MALME-3M), the ovarian (IGROV1) and renal (UO-31) cancer cell lines, whereas an esterified kaurane from *C. haumanianus* was active against the colon (HCT-116), the melanoma (M14) and the renal (786-0) cancer cell lines. South African *C. gratissimus* exhibited a rare example, 2,12-cyclocembrane diterpenoid, with moderate activities against the PEO1 and PEO1TaxR ovarian cancer cell lines. We have observed that chemical constituents from the *Croton* species have potential anti-HIV and anti-cancer activities.

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Late-Stage Functionalizations

Prof. Tobias Ritter, PhD

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Keywords: 16th Frank Warren, Abstract, Conference, Late-Stage Functionalizations.

Late-stage functionalization reactions reliably functionalize already complex molecules to quickly access value-added molecular diversity. Late-stage functionalization is desirable in many areas of discovery such as in drug or agrochemical development, and a requirement in other areas such as the synthesis of positron-emission tomography (PET) tracers. I will describe the development of novel, modern highly selective reactions in late-stage functionalization, as well as their application in transition-metal-catalyzed and photoredox reactions, with a focus on the synthesis of 18F and 19F containing complex small molecules. In particular, I will describe the development of a broadly useful new C-H functionalization reaction to form arylsulfonium salts that can engage in a multitude of follow-up reactions to create molecular complexity for applications in catalysis, drug discovery, and medicine.

Organic Chemistry in Materials Science

Colleen Scott[1]*, Chathuranga S L. Rathnamalala[1], Ishanka Rajapaksha[1], Nicholas W. Pino[2], Selena Hernandez[2], Melissa Y. Lucero[2], Chelsea B. Swartchick[2], Abdul Kalam Shaik[3], Nathan I. Hammer[3], Amanda K. East[2], Steven R. Gwaltney[1], Jefferson Chan[2],Mohammed Almtiri[1], Hari Giri[1], Ranganath Wahalathantrige Don,[1] and Daijun Feng[1].

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Keywords: 16th Frank Warren, NIR dyes, Conference, Conducting polymers, Polyaniline.

Grand challenges continue for the efficient synthesis of known compounds and the development of new and interesting compounds using C-H functionalization reactions; specifically, when the compounds to be synthesized are material based. However, due to the highly active research in this area, C-H functionalization has been demonstrated to be a very useful technique for the synthesis of materials for organic devices such as Organic Light-Emitting Diodes (OLEDs), Organic Field Effect Transistors (OFETs), and Organic Photovoltaic (OPVs) devices. Still, very few studies have been done to investigate the use of C-H activation reaction to prepare fluorescent dyes. Consequently, our group has been investigating the use of C-H activation reaction to prepare NIR fluorescent dyes for application as biosensors, and deep tissue imaging. In this presentation, we describe our design rationale for a series of new NIR I & II dyes that are readily accessible by the C-H activation reaction. These dyes have absorption and emission wavelengths between 700 nm – 1200 nm.

Conjugated polymers (CPs) play a leading role in the field of organic semiconducting materials. These polymers have great electronic, thermal, and optical properties. Besides, they have better solubility, low temperature processability, and mechanical properties when compared to conventional semiconductors. These characteristics are very attractive for applications such as OFETs, OLEDs, OPVs, power storing devices, and sensors. In this presentation, we will discuss our design strategy, synthesis, and characterization of two kinds of CPs; polyphenoxazine, which is a polyaniline mimic, and a new n-type DPP polymer developed from a new DPP scaffold.

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2. Chathuranga S L. Rathnamalala, Selena Hernandez, Melissa Y. Lucero, Chelsea B. Swartchick, Abdul Kalam Shaik, Nathan I. Hammer, Amanda K. East, Steven R. Gwaltney, Jefferson Chan,* and Colleen N. Scott,* *Angew. Chem. Int. Ed.* ***2023****, e202214855.*
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5. Ranganath Wahalathantrige Don, Timothy J. Dowell, Briana L. Simms, Davita L. Watkins, David O. Wipf, and Colleen N. Scott,* *Polym. Chem.*, 2022, **13**, 759-767. Selected by Editors as a HOT Polymer Chemistry article
6. Chathuranga S. L. Rathnamalala, Nicholas W. Pino, Bailey S. Herring, Mattea Hooper, Steven R. Gwaltney, Jefferson Chan,* and Colleen N. Scott* *Org. Lett*. 2021, **23**, 7640−7644.
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Synthesizing complex bioactive structures through convergent coupling reactions

Willem A. L. van Otterlo[a]

[a] *Department of Chemistry and Polymer Science, Stellenbosch University, Stellenbosch, E-mail: wvo@sun.ac.za*

Keywords: Convergent syntheses, bioactive molecules, click reactions, asymmetric biaryl couplings.

So-called "coupling reactions" allow for the synthesis of significantly more complex products by the controlled chemical joining of suitably substituted building blocks, an overall approach that has been described as synthetically "convergent". Amongst the important coupling reactions in modern organic synthesis are "click" chemistry and biaryl coupling reactions. Examples of both these valuable strategies will be highlighted during this talk.

In the medicinal chemistry portion of this presentation, recent collaborative work from our group involving the synthesis of bi-domain irreversible inhibitors of the important kinase Akt using copper-mediated click chemistry will be described.[1] The Akt kinase has been identified as a verified anti-cancer target and selective inhibitors of this enzyme are thus of significant interest.

In addition, in terms of our interest in natural product synthesis, the first direct asymmetric total syntheses of a family of 5,8'-naphthylisoquinoline alkaloids from their fully substituted precursors will be discussed. The syntheses of these naphthylisoquinoline alkaloids are of specific interest due to their underutilised anti-cancer potential against hard-to-kill pancreatic cancer cell lines which thrive under "austere" low nutrient conditions. The synthesis of the naphthylisoquinoline alkaloids employed a novel nickel-catalysed atroposelective cross-coupling reaction[2] which has recently been further developed through collaborative research eforts.[3]

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KEYNOTE LECTURE ABSTRACTS

Modern approaches in the design of synthetically aware new chemical entities in drug discovery

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The advent of computers to model the effects of small organic molecules and macromolecules and simulate their behaviour/interactions has been a game changer in medicinal chemistry. Modern medicinal chemistry approaches are helping synthetic organic chemists to synthesize compounds that are designed and evaluated for their protein-ligand interactions at molecular level prior to synthesis.

Furthermore, the advancement in High Performance Computing (HPC) technology has also enabled medicinal and computational chemists to use alchemical techniques such as Free Energy Perturbation and Thermodynamic Integration techniques, which are computationally intensive to correctly predict the binding affinities of protein-ligand interactions. In my talk I will further dwell into the outcomes of my research such as the granting of patents in different due restrictions. I will also talk about what aspects of IP protection do organic chemist and/or computational chemists need to account for when collaborating with other scientists.

Lastly, I will show case research outputs of students that I have co-supervised for their master's and PhD studies in this research area.

Molecular Hybridization Approach in the Design of Biologically Active Compounds

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Keywords: Molecular hybridization, Quinoline, Breast cancer, *Mycobacterium tuberculosis*.

The incidence and prevalence of infectious diseases continue to undermine the global efforts to control and manage these diseases. In drug design, and among different reported approaches, molecular hybridization is an important medicinal chemistry tool to design and chemically modify a diverse range of molecules to develop biologically active compounds. The hybridization strategy involves an amalgamation of pharmacophoric moieties of different bioactive compounds to yield a single hybrid compound with improved affinity and efficacy compared to the parent compounds. This strategy has led to diverse compounds with desirable selectivity, dual or different modes of action, and reduced side effects.[1]

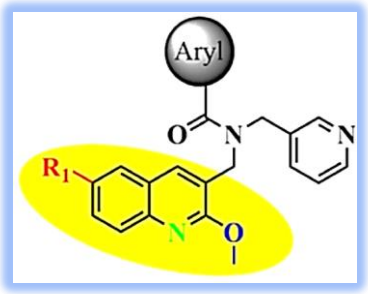

Figure 1: Bedaquiline derived arylquinolicarboxamides assembled by molecular hybridization approach.

This presentation will focus on our recent efforts in designing biologically active hybrid compounds, which were achieved using molecular hybridization techniques.[2,3] Some of the resultant compounds have demonstrated remarkable activity against protozoan parasites, *Mycobacterium tuberculosis*, and breast cancer.[4]

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Exploring alternative amidation reactions and new phosphine ligands for palladium cross-coupling applications

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Keywords: Amides, Nitroarenes, Palladium, Catalysis.

Amides are ubiquitous in a variety of beneficial natural and synthetic molecules.[1] Thus, their efficient synthesis with minimal waste generation is desirable. Traditionally, reactions between carboxylic acids or equivalent derivatives and amines are used to form amides. However, these reactions tend to produce large quantities of undesirable by-products due to the use of stoichiometric requirements of activating agents. The direct use of nitro compounds as coupling partners has become attractive as these provide a step-economic approach to amide synthesis.[2] This lecture will reflect on new methodologies that we have established for the synthesis of amides and the use of nitro compounds as coupling partners in amidation reactions. In addition, phosphine ligands are known to be influential on the outcomes of palladium-catalyzed reactions. Parameters such as electron density and steric effects around the phosphorus atom often determine the reaction rate, catalyst stability, and reaction yields.[3] This lecture will also highlight new electron-deficient phosphine ligands and their applications in palladium-catalyzed cross-coupling reactions.

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Sustainability and the pharmaceutical industry: The rise of the machines

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Keywords: API process development, continuous flow, automation dashboard, sustainable manufacturing

One of the most profound lessons from the Covid-19 pandemic has been the intricacy of the intertwined global pharmaceutical network and how disruptions in one country can contribute to dangerous supply shortages across all regions. Reliance on the importation of finished drugs, or the active pharmaceutical ingredient (API) itself, is a security of supply risk for the country and the self-sufficiency of a local manufacturing capability has become a key focus for future pandemic preparedness.

Within this context, South Africa has the added challenge of operating a two-tier health system where the majority of the population are supported through a resource-stressed public sector and there exists a persistent disparity in the procurement and use of orphan drug treatments, while also suffering from a range of critical drug shortages in recent years. In addition, the rise of counterfeit, substandard and falsified medicines are a growing concern, which is highlighted by the shocking number of childhood deaths on the African continent in 2022 from contaminated cough and pain syrups alone.

The industry lacks data-driven and evidence-based prioritization of drugs for local manufacture that consider our diverse population, and there is a need for the inclusion of modern API manufacturing technologies that provide competitive advantage. By linking to Industry 4.0 concepts, the CSIR is responding to this challenge by scaling cutting edge integrated continuous flow chemical production, emerging biocatalytic conversions, and integrating smart technology for online process monitoring and intelligent process optimization, to leverage the fast flow of information and manufacture in new ways[1]. Through this integrated approach and a strong focus on green strategies for process improvement, waste reduction and energy efficiency, FuturePHARMA is supporting the development of *"a dynamic African pharmaceuticals manufacturing industry with access to critical and modern drugs through innovative and world class processing technology"*.

Case studies will highlight the development of a flow-based route to a non-steroidal anti-inflammatory drug[2] and discuss recent efforts to develop an economical platform for controlling and automating flow equipment[3], with a discussion on the opportunities for sustainable manufacturing in an African context (conveniently set against the backdrop of the first UN Climate Change Conference to host a Health Day, COP28, being held in the same week).

Heterocyclic inhibitors of *Plasmodium falciparum*

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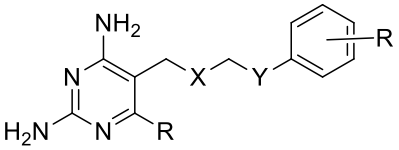
Keywords: 2,4-diaminopyrimidine, indolin-2-ol, *Plasmodium falciparum*.

According to the most recent World Malaria Report, the malaria epidemic resulted in 619 000 deaths globally in 2021.[1] The majority (95%) of these deaths, and the 245 million malaria cases reported that year, occurred in the WHO African region due to *Plasmodium falciparum* infection. Of great concern is that these statistics show a marked increase from 2015, in which 230 million malaria cases and 429 000 malaria deaths were reported. Drug and insecticide resistance, and malaria service disruptions during the COVID-19 pandemic are considered the major contributing factors. Although there are promising malaria vaccines under development, these remain less than 100 % effective, and as such there remains a need for the development of novel antimalarial agents.

Our research has focused on the design and synthesis of heterocyclic inhibitors of *P. falciparum*. The synthetic approaches to two series of compounds and their *in vitro* antiplasmodial activity will be described in this presentation. The first series of compounds contain a 2,4-diaminopyrimidine core (**1**) and are designed to act as inhibitors of *P. falciparum* dihydrofolate reductase (*Pf*DHFR), a key enzyme in the folate metabolic pathway.[2,3] The second series of compounds contain an indolin-2-ol core (**2**), and were synthesised by an unusual Grignard addition reaction to isatin-derived ketimines. These compounds show promising antiplasmodial activity *in vitro*, although the target is unknown.



1 X = NH, CH_2
Y = O, CH_2

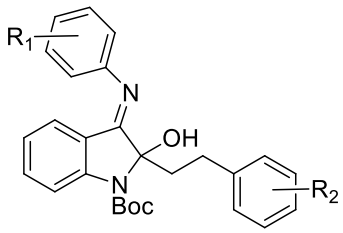


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Figure 1: Heterocyclic scaffolds displaying promising antiplasmodial activity *in vitro*.

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Native Mass Spectrometry as a Tool for Rapid Elucidation and Modulation of Difficult to Access Transient Protein-Protein Interactions

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Keywords: 16th Frank Warren, Abstract, Conference.

Transient Protein-Protein Interactions (PPIs) are central mediators of protein activity and signaling networks. Accordingly, their modulation has significant impact on cell metabolism and regulation and as such are considered promising albeit challenging opportunities to expand druggable chemical space. However, the transient nature of these interactions, which requires weak short-lived associations between partner proteins also makes the interfaces of transient PPIs particularly challenging to characterize and drug. In addition to significant challenges with valid bioassay results, in the context of drug discovery, the lack of structural information hampers the rational design of PPI modulators. Here we describe the development of a new native mass spectrometry (MS) approach to directly detect and elucidate the minimal protein-peptide association of transient PPI interfaces.

Furthermore, we demonstrate how a native MS model of the pro-oncogenic HSP90 – HOP PPI could discern competitive inhibitors of the target PPI, which though medicinal chemistry and chemical biology workflows, have translated into promising probe compounds for studying Kaposi's sarcoma herpes associated virus (KSHV), the causative agent of the HIV related Kaposi's sarcoma.

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ORAL PRESENTATION ABSTRACTS

L1: REPURPOSING OF THE ORGANIC COMPOUNDS AS POTENTIAL CORROSION INHIBITORS

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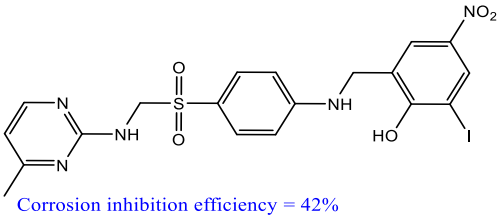
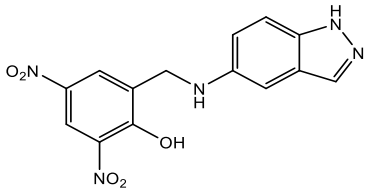
Keywords: 5-Aminoindazole, Sulfamethazine, Sulfamezarine, Corrosion inhibition

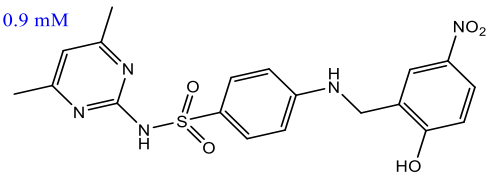
Corrosion is the deterioration of materials and is common in metals. With metals used in many commercial applications, it cannot be ruled out that they are prone to various modes of corrosion which changes its properties. Thus, the impact of corrosion usually leads to economic losses due to the ever increasing cost of metal structure rehabilitation [1]. Thus, use of corrosion inhibitors is often a good solution to prevent corrosion phenomena and to provide a more acceptable life time of metallic structures. Therefore, organic compounds are used as corrosion inhibitors because they contain atoms (nitrogen, oxygen, sulfur and phosphorous), aromatic ring or triple bonds that reduce corrosion attack in aqueous solutions [2]. In this research project, we report on 5-aminoindazole derivatives, sulfamethazine derivatives, and sulfamezarine derivatives as potential corrosion mitigating compounds.



Corrosion inhibition efficiency = 42%
Medium: 1 M H_2SO_4
Temperature: 50 °C
Concentration: 0.9 mM



Corrosion inhibition efficiency = 52%
Medium: 0.5 M H_2SO_4
Temperature: 50 °C
Concentration: 0.15 mM



Corrosion inhibition efficiency = 74%
Medium: 1 M HCl
Temperature: 50 °C
Concentration: 4.5 mM

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L2: Flow chemistry and reaction engineering tools for the competitive manufacture of pharmaceuticals in South Africa

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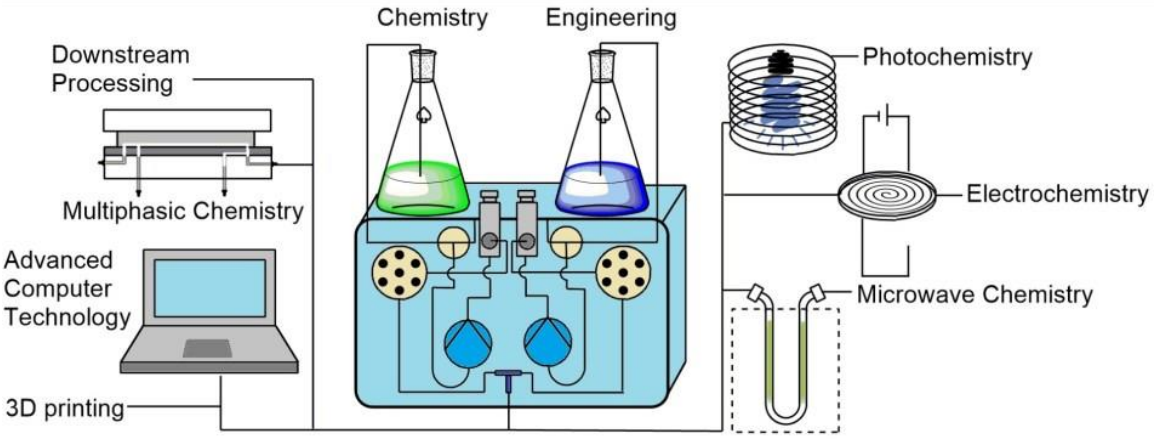
Keywords: Flow Chemistry, Pharmaceuticals, Reaction Engineering.

The procurement of pharmaceuticals represents the fifth largest contributor to South Africa's trade deficit, and a high local reliance on foreign imports has left South Africa exposed to risk associated with supply and demand and fluctuations in FOREX rates.[1] As a result, there have been a growing incidence of drug stockouts which in addition to negatively impacting end users afflicted by disease/s there has been a sharp increase in drug piracy and counterfeiting as a direct result.[1] In response to these issues there has been a drive by both the public and private sectors to localize (and regionalize within the SADC region) an African pharmaceutical manufacturing sector.[1] The realization of this goal is slowly beginning to materialize, however, there are still several challenges to be overcome including a lack of relevant infrastructure, a lack skilled human capital and issues associated with competitiveness against foreign importers.

The use of advanced manufacturing technologies in the form of flow chemistry have been identified to allow us to leapfrog existing technologies (batch-based manufacturing) and afford a competitive advantage over established foreign manufacturers who have been slow to adopt as a result of being hamstrung by sunk capital in the form of existing batch-based manufacturing infrastructure.[2]

Highlighted in this presentation is how we are addressing these issues through the development of new flow-based reactor technologies and methodologies, and the development of integrated continuous flow based-process routes to pharmaceuticals of relevance to the African sector.



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L3: Energy Harvesting Potential of Azobenzene and Perylene Tetracarboxylic Bisimide Derivatives: Synthesis, Phase Transition, and Computational Study

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Keywords: Azobenzene, Perylene tetracarboxylic bisimide (PTCBI) derivatives, Energy harvesting.

Energy harvesting has emerged as a crucial area of research in recent years due to its potential to provide sustainable and renewable power sources.[1] In this study, we explore the energy harvesting potential of a novel class of materials based on azobenzene and perylene tetracarboxylic bisimide (PTCBI) derivatives respectively through a comprehensive investigation that integrates synthesis, phase transition analysis, and computational modelling. The synthesis of azobenzene and perylene tetracarboxylic bisimide derivatives was carried out using a multi-step organic synthesis approach. Our findings suggest that some of these materials exhibit promising energy harvesting capabilities, with reversible phase transitions that can be triggered by external stimuli, such as light or temperature changes. The synergy between experimental synthesis, phase transition analysis, and computational modelling presents a comprehensive approach to understanding and enhancing the energy harvesting capabilities of azobenzene and PTCBI derivatives. This research contributes to the ongoing efforts to develop innovative materials for renewable energy generation and underscores the importance of a multidisciplinary approach in addressing the energy challenges of our time.

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L4: Synthesis of Peptide Nucleic Acids (PNAs) using a Safety-Catch Protecting Group Strategy - Compatible with Boc-Chemistry

Edikarlos Brasil[2], K. P. Nandhini[1,2], Sikabwe Noki[1,2], Fernando Albericio[2,3,*] and Beatriz G. de la Torre[1,*]

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2 Peptide Science Laboratory, School of Chemistry and Physics, University of KwaZulu-Natal, Westville, Durban 4000, South Africa.
3 CIBER-BBN, Networking Centre on Bioengineering, Biomaterials and Nanomedicine, and Department of Organic Chemistry, University of Barcelona, Martí i Franqués 1-11, 08028 Barcelona, Spain.
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Keywords: Boc, Fmoc, HO-Mmsb-linker, ketopiperazine, side-reaction, solid-phase, sulfide, sulfinyl, sulfoxide

Peptide Nucleic Acids (PNAs) are an intriguing class of synthetic biomolecules with great potential in medicine. Regarded as short DNA mimics, in which the ionic sugar-phosphate backbone is modified by repeating N-(2-aminoethyl) glycine units gripped by amide bonds, PNAs are synthetically developed in a similar fashion to peptides. Moreover, the nonionic peptide-like backbone of PNAs adds important structural properties as compared to that of oligodeoxynucleotides, such as elasticity and chemical adaptability. Further advantages include high thermal stability, remarkable binding to complementary sequences by standard Watson-Crick base pairing, and resistance to degradation by proteases or nucleases. Herein, a successful PNA solid-phase synthesis approach has been employed using a safety-catch protecting group scheme. First, two novel PNA monomers, [Boc-PNA-A(Msz)-OH (1) and Boc-PNA-C(Msz)-OH (2)], were synthetized following four consecutive reaction steps, the second of which relates to the 4-(methylthio)-benzyloxycarbonyl (Mtz) protection of the exocyclic amino group of the nucleobases adenine and cytosine in the form of a carbamate group, then oxidation to 4-(methylsulfinyl)-benzyloxycarbonyl (Msz). The sulfinyl-based Msz is fully stable to TFA conditions and therefore orthogonal to Boc and Fmoc groups but labile upon reduction to thio-based Mtz. The use of [Boc-PNA-A(Msz)-OH (1) and Boc-PNA-C(Msz)-OH (2)] provided key insight into the advantage over Fmoc chemistry as well as the synthetic efficiency of the PNA pentamer [PNA(TATCT)-βAla-OH][1] (Figure 1).

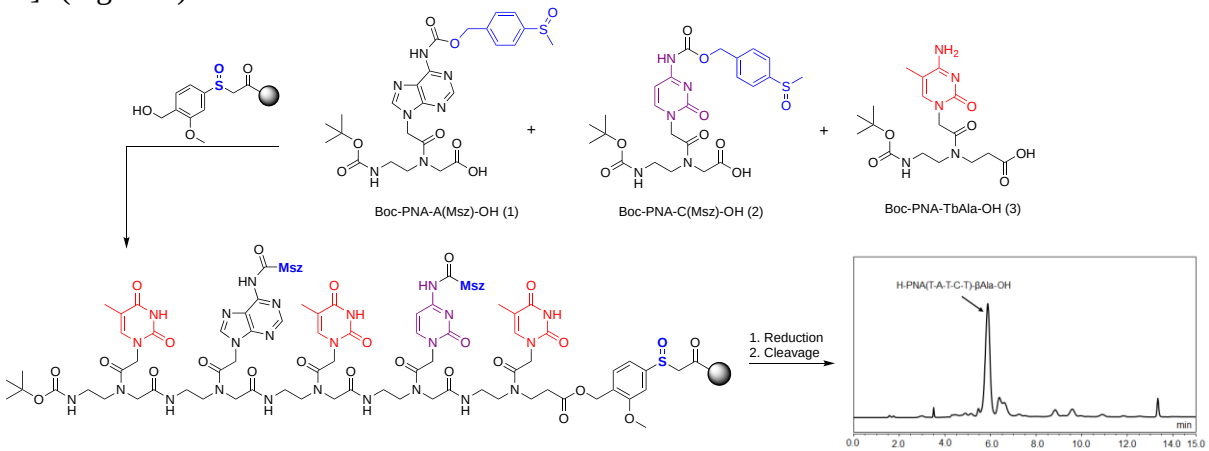

Figure 1. Synthetic strategy for the PNA pentamer [PNA(TATCT)-βAla-OH].

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L5: High Performance GC- & GC×GC-TOFMS Metabolomics-Based Approach for Discovery of Potential Diabetes II Biomarkers in Human Plasma

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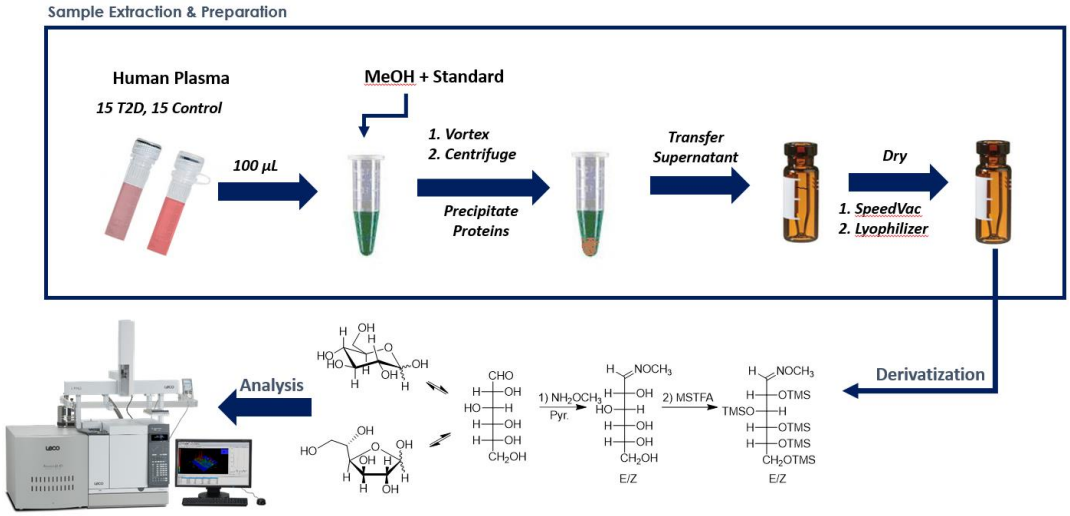
Keywords: Diabetes, Time-of-Flight Mass Spectroscopy, ChromaTOF Tile

Diabetes mellitus is a complex, chronic illness that is characterized by elevated blood glucose levels that occurs when there is either cellular resistance to insulin action, and/or pancreatic β-cells that do not produce sufficient insulin.[1] The most common form of this disease is type 2 diabetes (T2D), which represents approximately 90% of all cases worldwide.[1] Diabetes is a major cause of blindness, kidney failure, heart attacks, strokes, and lower limb amputations[1]. Thus, there is a critical need for cost-effective strategies for systematic screening of T2D to identify new biomarkers for early disease detection.[1]

The objective of our study was to develop an untargeted metabolite profiling methodology for the analysis of human plasma samples. Control and diseased samples were prepared, derivatized and then analysed using GC and GC×GC-TOFMS. ChromaTOF software was then used to process and deconvolute the collected data to find all the compounds of interest, mainly acids, amino acids, diacids, fatty acids, monosaccharides and reduced sugars. It was found that GC×GC-TOFMS was able to separate coeluting analytes and give 2x more data than GC-TOFMS. ChromaTOF Tile, a statistical processing software was then used to identify and compare trends, patterns, and significant differences between features of potential T2D biomarkers across the analyzed samples.



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L6: L11: Quinolone analogues of benzothiazinone: Synthesis, antitubercular structure-activity relationship and ADME profiling

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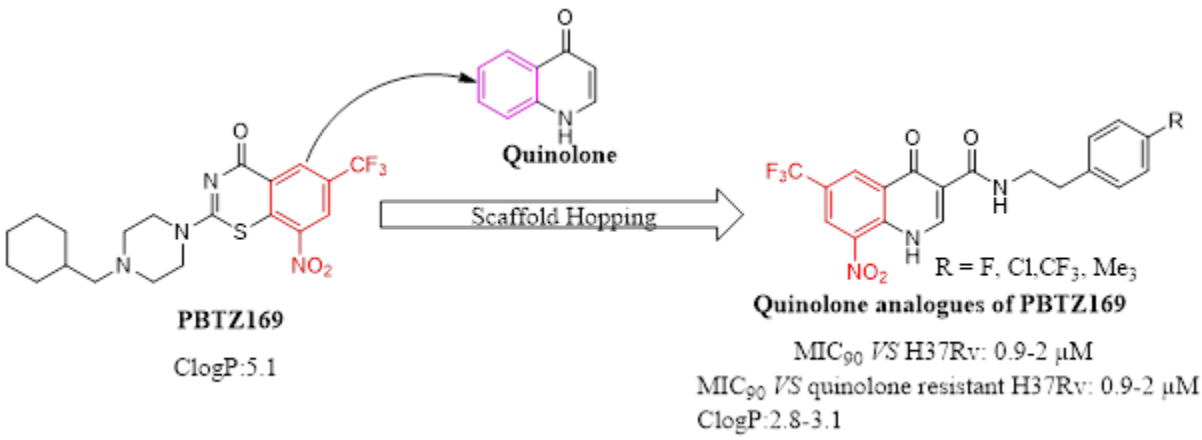
[a] *Centre of excellence for pharmaceutical sciences (Pharmacen), North-West University, Potchefstroom Campus, South Africa.*

Keywords: DprE1, quinolone, nitro compounds, *Mycobacterium tuberculosis*, benzothiazinone

*Mycobacterium tuberculos*is (Mtb) has an impermeable cell wall which gives it an inherent ability to resist many antibiotics. DprE1, an essential enzyme in Mtb cell wall synthesis, has been validated as a target for several TB drug candidates. The most potent and developmentally advanced DprE1 inhibitor, PBTZ169, is still undergoing clinical development. With high attrition rate, there is need to populate the development pipeline. Using a scaffold hopping strategy, we imprinted the benzenoid ring of PBTZ169 onto a quinolone nucleus. Twenty-two compounds were synthesised and screened for activity against Mtb, with six compounds exhibiting sub micromolar activity of MIC_{90} <0.244 µM. Compound **25** further demonstrated sub-micromolar activity when evaluated against wild-type and fluoroquinolone-resistant Mtb strains. This compound maintained its sub-micromolar activity against a DprE1 P116S mutant strain but showed a significant reduction in activity when tested against the DprE1 C387S mutant.



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L7: Biocatalytic and enantioselective synthesis of chiral oxygenated heterocycles

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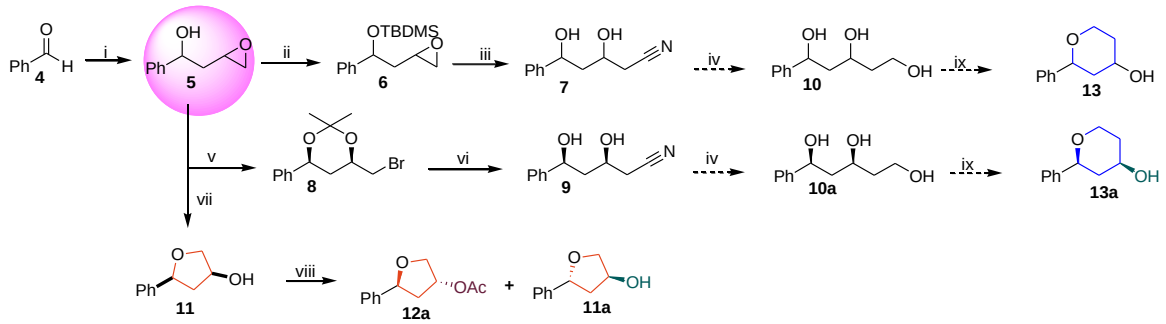
Keywords: Heterocyclic compounds, Stereoselectivity, Biocatalysis.

The Flavours and Fragrances industry is a rapidly growing multi-billion dollar global industry, mainly driven by expanding markets in middle-to-low income countries, including South Africa[1]. Heterocyclic compounds are among the key targets in this industry. This includes the commercially available fragrances like clarycet (**1**), rhubafuran (**2**) and florol (**3**), all these have heterocyclic moieties tetrahydrofuran (THF) and tetrahydropyran (THP) with several chiral centres[2]. We envisaged that chiral THFs and THPs could be synthesized from 1,2,4-triols or 1,3,5-triols via a mild stereoselective cyclodehydration which our research group has already demonstrated does not lead to loss of stereochemistry[3]. The β-hydroxy epoxide **5** was identified as the key intermediate (Scheme 1)



(i) (a)Zn, All-Br, NH_4Cl THF; ((b) *m*-CPBA CH_2Cl_2; (ii) TBDMSCl, imidazole,DMF; (iii)(a) KCN, TBAI, H_2O, DMF (b) TBAF, THF; (iv)(a) DIBAIL-H, $PhCH_3$ (b) $NaBH_4$; (v) (a) vinylMgBr, THF (b) DMP, p-TsOH, Acetone; (vi) (a) KCN, TBAI, H_2O, DMF (b) 80% AcOH; (vii) a)$HClO_4$ -H_2O, 20°C(b)$HClO_4$ -H_2O, 100°C; (viii) PPL, Vinyl acetate, CCl_3; (ix) Bu_2SnO, p-TsCl, Et_3N.

Scheme 1. Synthesis of THF and THP heterocyclic compounds

The allylation and epoxidation of **4** resulted in good yields (78%) of **5**. Diol protection at **8** favouvered the formation of *syn*-diol **9.** Compound **13** was accessed from **5** by either opening the epoxide ring or displacing bromine with cyanide, and cyclisation of the resulting triol. cyclisation of **5** resulted in formation of **11**, and the racemate mixtures of **11** were resolved using lipase.

1. Flavors and Fragrances Market Size, Share & Industry Analysis, by type (flavors and fragrance) by application (Food & Beverage, Cosmetic & Personal Care, Pharmaceutical, Home & Floor Care, Fine Fragrances). https://www.fortunebusinessinsights.com/flavors-and-fragrances-maket-102329 (accessed Sep 14, 2023)
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L8: New Pentacyclic Triterpenes from *Strychnos henningsii* and their Antidiabetic Activity

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Keywords: Pentacyclic triterpenes, *Strychnos henningsii*, Antidiabetic activity.

Diabetes mellitus (DM) has a growing prevalence globally. Complications as a result of type 2 DM (T2DM) have been recorded as the second largest cause of death in South Africa[1] where health care inadequacies, cultural – and traditional beliefs, and socioeconomic issues, lead to the use of various medicinal plants to manage DM.[2,3] *Strychnos henningsii* Gilg is known for its rich indole alkaloids and is utilised by locals to manage DM.[4,5] Thus, this study focused on the phytochemical investigation and antidiabetic activity of *S. henningsii*, from the Eastern Cape, in the pursuit of novel compounds for the management of DM. Fractionation and purification of a MeOH:$CHCl_3$ (8:2) bark crude extract resulted in the isolation and characterisation of the five pentacyclic triterpenes (PT) (Figure 1), henningsal (**1**), henninglupal (**2**), 19-ethylene henningsyl (**3**), alpha-amyrin acetate (**4**), and 19-ethylene henningsal (**5**).[6,7] All the isolated PTs are novel, except for compound **4**, which is reported for the first time in *S. henningsii*. *In vitro* MTT cytotoxicity, α-amylase – and α-glucosidase inhibition bioactivity assays were used to determine the applicability of the isolated PTs in the management of T2DM. *In vitro* MTT cytotoxicity of the PTs was evaluated on Caco-2 cell lines, where all exhibited low cytotoxic effects up to 125 µM. All the PTs exhibited *in vitro* α-amylase – and α-glucosidase inhibition activity. The highest percentage of enzyme inhibition was observed in the α-glucosidase inhibition for TP **3** (83.93 ± 8.675 at 250 µM). This study contributes new knowledge through the isolation of the novel potential drug lead PTs for the management of T2DM.

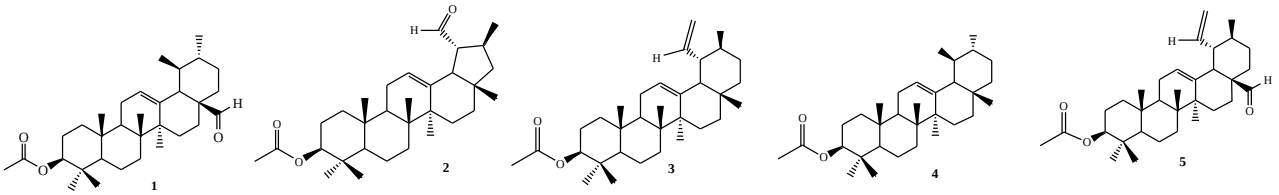

Figure 1: Pentacyclic triterpenes **1-6** isolated from *Strychnos henningsii*

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L9: LC-MS profiling of an extract of *Euphorbia grandicornis* with anti-HIV activity

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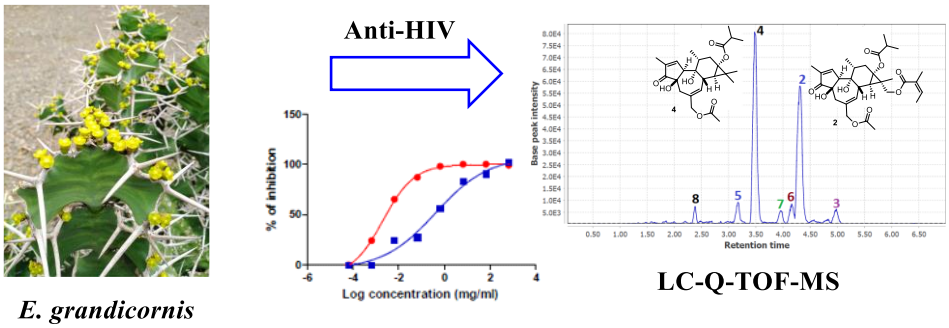
Keywords: Anti-HIV, LC-MS, *Euphorbia grandicornis*, tigliane phorbol esters.

Phorbol esters, plant metabolites present in Euphorbiaceae and Thymelaceae, have attracted attention because of their anti-HIV and HIV-latency reversal activity.[1-3] In a survey to evaluate the anti-HIV activity and phorbol ester content of South African Euphorbiaceae, an extract of *Euphorbia grandicornis* A. Blanc was identified as a species that shows good anti-HIV activity. This study aimed to identify the phorbol esters present in this plant. A detailed LC-MS analysis of the latex and extracts of *E. grandicornis* led to the identification of six known and one new tigliane-type phorbol ester. The structures and molecular formulae of the compounds identified were based on an extensive evaluation of the fragmentation patterns observed in the ESI-Q-MS and ESI-TOF-MS spectra.



Scheme 1: schematic diagram of this study.

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L10: Finding the ajoene sweet-spot: structure-activity relations that govern bioavailability and cancer cell cytotoxicity

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Keywords: garlic, anti-cancer, structure-activity relationship, bioavailability

Garlic is a spice and medicinal plant that has been used since ancient times to promote health and fight disease. There are a number of small bioactive organosulfur compounds in garlic, with different chemotypes containing different sulfur-containing functional groups. These compounds are proposed to act on a molecular level by undergoing thiolysis exchange with a biological thiol such as a cysteine residue on a protein or glutathione. Many of the garlic OSCs, including the small thiophile ajoene, show good anticancer activity; however, there are concerns over their bioavailability. In this study, we synthesised two small libraries of ajoene analogues for probing the significance of the vinyl disulfide/sulfoxide backbone with respect to cancer cell cytotoxicity and in vitro blood stability. We also incorporated polar side groups into the molecule to improve aqueous solubility. It was found that compounds containing a vinyl disulfide functional group displayed a superior cytotoxicity, although they also showed very poor blood stability. These compounds were also the most electrophilic at the allyl-*S* sulfur atom in the disulfide, as modelled by the Fukui function and the HOMO-LUMO gap, indicating that both cytotoxicity and blood stability are interconnected, and relate to their ability to undergo thiolysis. The dihydroajoenes and deoxydihydroajoenes, both lacking the double bond, were less cytotoxic but displayed greatly improved blood stability. Ajoene was found to target Cys-β93 in haemoglobin through *S*-thiolation, which is its proposed target in this location. The dihydroajoenes prepared in this study present themselves as good candidates for future therapeutic development against cancer.

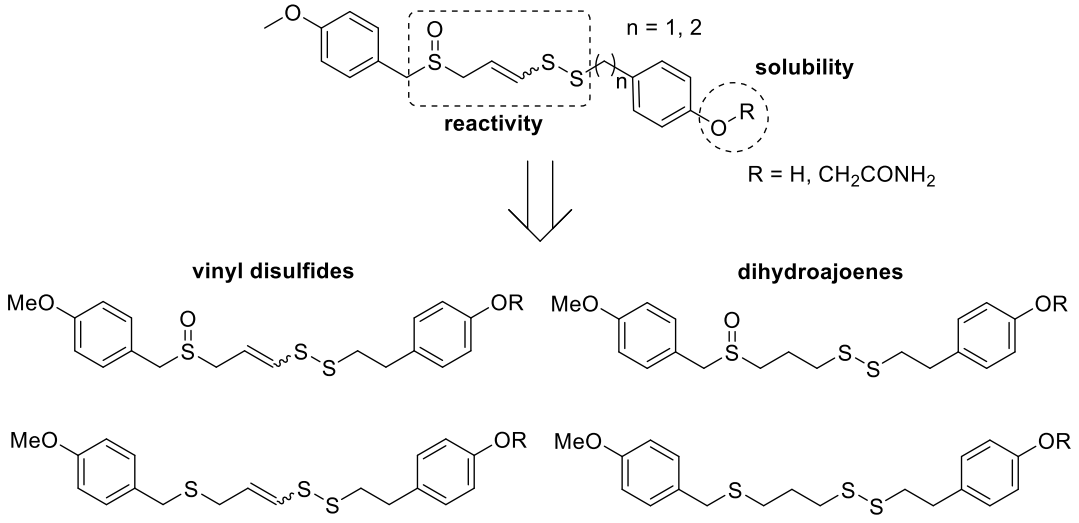

Figure 1. **Design of the ajoene library**. The ajoene library varied the functionalities of the monosulfide (as sulfide or sulfoxide) and the vinyl disufide (as is or saturated) to create ajoene/deoxyajoene and dhydroajoene/deoxydihydroajoene variants, respectively.

L11: Structural Characterization, and Quantum Chemical Study of the 7-Acetyl-5-nitrobenzofurans as Anticancer Agents with Antioxidant Properties

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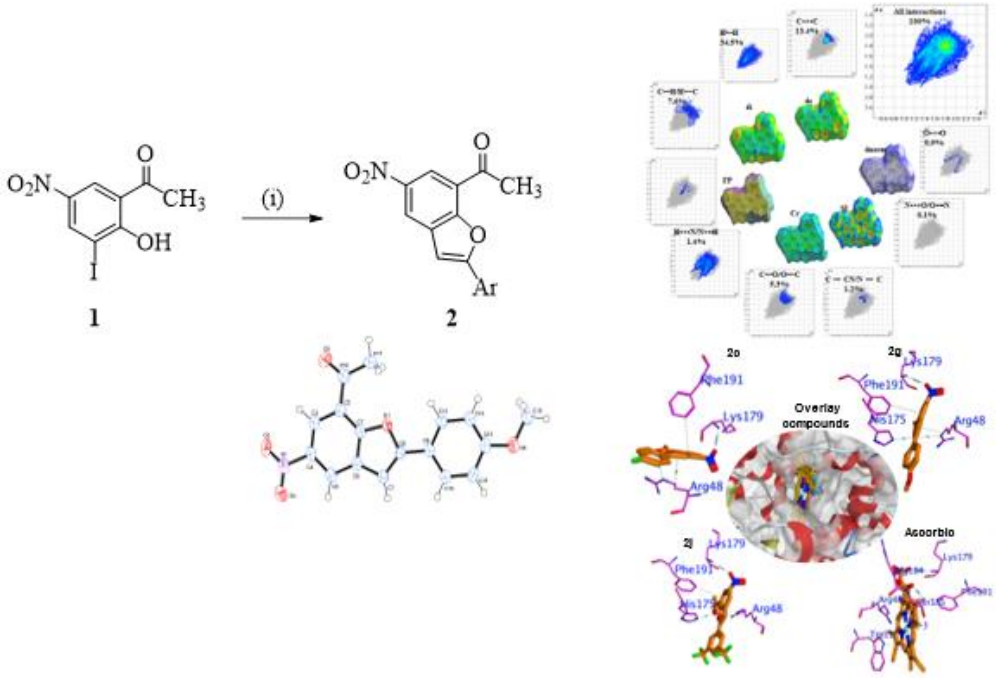
Keywords: benzofurans, noncovalent interactions, crystal structure.

Despite substantial progress in comprehending the molecular pathways underlying the development of cancer, a definitive therapeutic intervention capable of achieving complete eradication of the illness remains elusive.[1,2] A series of 7-acetyl-2-aryl-5-nitrobenzofurans were synthesized via tandem Sonogashira cross-coupling of 2-hydroxy-3-iodo-5-nitroacetophenone with terminal acetylenes and subsequent in situ Cacchi-type cycloisomerization of the 5-alkynylated intermediates. The surface analysis and fingerprint diagrams of Hirshfeld revealed the diverse intermolecular interactions. To determine the optimized structure, frontier molecular orbitals, reactive parameters, and molecular electrostatic potential, DFT calculations were performed. In addition, DFT and QTAIM calculations were used to examine intramolecular interactions. These benzofuran derivatives were examined for their antiproliferative activity in vitro against the human breast cancer (MDA-MB-231) and cervical cancer (Caski) cell lines and their antioxidant activity was determined by their Fe-reducing power in the ferric ion reducing antioxidant power (FRAP) assay .



(i) $HC{\equiv}CC_6H_4R$, $PdCl_2(PPh_3)_2$, CuI, Cs_2CO3, EtOH

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L12: Design, synthesis, structure-activity relationship/structure-property relationship analyses toward the identification of preclinical anti-infective agents.

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Keywords: Synthesis, Quinolone, Antibacterial, Antiparasites, Tuberculosis, Conference.

Herein we describe novel quinolone compounds bearing a hydrophilic amine chain and varied substituted benzyloxy units. These compounds demonstrate broad spectrum activities against acid fast bacterium, Gram-positive and -negative bacteria, fungi, and leishmania parasite. Several compounds maintained antitubercular activity against moxifloxacin, isoniazid, and rifampicin resistant *M. tuberculosis*, while some exhibited low micromolar activities (< 1 µg/mL) against WHO critical pathogens—*C. neoformans, A. baumannii, P. aeruginosa*. Compounds in this study are metabolically robust, demonstrating % remnant of > 98 % after 30 minutes in the presence of human, rat, and mouse liver microsomes. Several compounds thus reported here are promising leads for the treatment of diseases caused by infectious agents.
Our talk will present the synthetic design, and iterative synthesis executed, as well as the structure-activity, and structure-property relationships of the investigated series.

L13: Teaching Systems Thinking in and for Organic Chemistry

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Keywords: Systems Thinking, Abstract, Organic Chemistry

The convergence of the output of the IUPAC 2017 project on Systems Thinking in Chemistry Education and a challenging PhD project in physical-organic chemistry highlighted the deficit of fully reductionist chemistry education and the need to introduce systems thinking in undergraduate teaching. Systems thinking was introduced to first-year chemistry using the topic of the surfactant linear alkyl benzene sulfonate. The chemical system drew on content such as a structural representation of organic compounds, conformation, the role of structure in intermolecular forces, the role of intermolecular forces in the emergent properties of surfactants, e.g. micelle formation, foaming with the resultant cleaning effects of detergents, and chemical reaction types. The topic was useful for highlighting the idea that chemicals have benefits for humanity, but have hazards that must be managed.

It was clear from the gains from the first-year project that students would benefit from multiple opportunities to continue to develop systems thinking skills and a capacity to cope with complexity. We therefore used an S_N2 organic reaction as a vehicle to further develop system thinking skills for chemistry in the second year (Figure 1). Explicitly developing systems thinking skills has the potential to deliver chemistry graduates who are better able to reason like chemists and can make a difference to global sustainability.

Insert figures and schemes below the abstract text. These are optional and should not be sent separately.

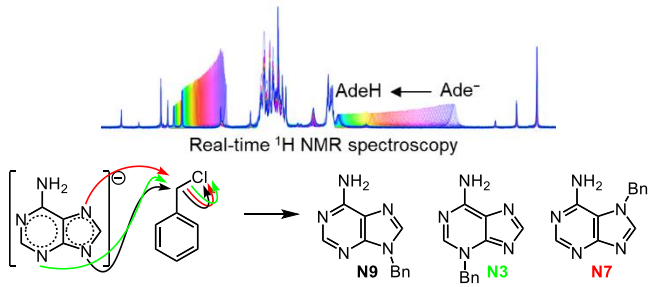

Figure 1: An organic reaction system to teach systems thinking

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L14: Quinoline-1,2,3-triazole molecular hybrids: Synthesis, antimicrobial evaluation and molecular docking studies

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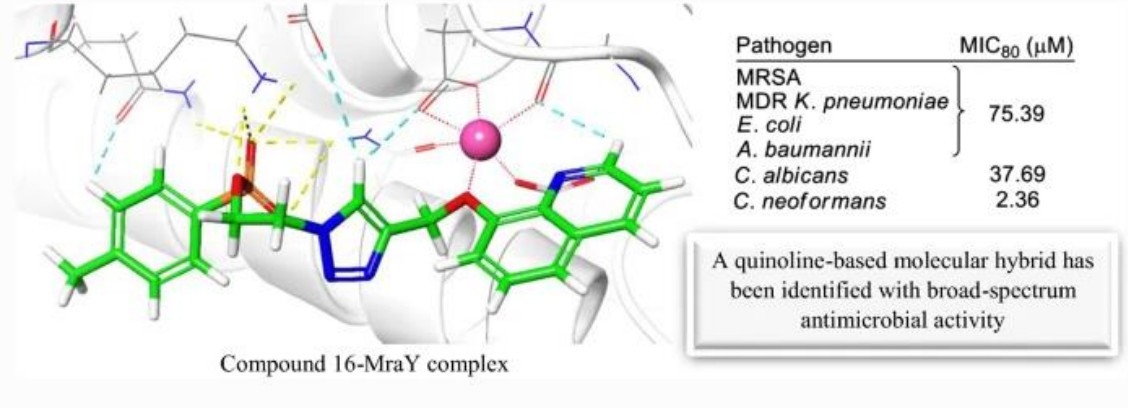
Keywords: Antimicrobial, quinoline, triazole, molecular hybridization, docking

Molecular hybridization technique is considered a worthy approach in drug design as the incorporation of two or more scaffolds into one entity displays multiple-receptor recognition and an improved therapeutic effect. [1] In this regard, we synthesized quinoline-tethered 1*H*-1,2,3-triazole molecular hybrids and structurally characterized them using different spectroscopic techniques and evaluated their activity against different bacterial and fungal strains. The most active compound (**16**) of the series showed an MIC_{80} value of 75.39 μM against methicillin-resistant *S. aureus*, *E. coli*, *A. baumannii*, and multidrug-resistant *K. pneumoniae*. Moreover, it was also most active against *C. albicans* and *C. neoformans* at an MIC_{80} value of 37.69 and 2.36 μM, respectively, more than the standard drug fluconazole. Furthermore, in silico ADME predictions revealed excellent drug-like properties while molecular docking revealed several ligand-protein interactions which could explain the observed experimental potencies.



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L15: Forgotten Gems: Exploring Triazenes' Untapped Potential as Antimalarials and Antimicrobials

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[b]*Institute for Sustainable Malaria Control, University of Pretoria, Lynnwood Road, Pretoria, 0028*
[c]*Rural Health Research Institute, Charles Sturt University, Orange, NSW, Australia*

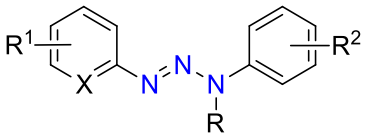
Keywords: malaria, antimicrobial infections, triazenes, antimalarial evaluation, drug development

Malaria and antimicrobial infections remain significant global health concerns, necessitating the continuous search for novel therapeutic approaches. Triazenes are a class underutilized group of compounds characterized by a linear arrangement of three nitrogen atoms, rendering them structurally distinct from their cyclic counterparts. This study investigates the efficacy of triazenes against malaria and explores their antimicrobial activity.

Antimalarial evaluation revealed low µM activity against NF54 strain of *P. falciparum*, the causative agent of malaria. The antimicrobial activity of the triazenes against bacteria and fungi was investigated through disc diffusion screening. The antimicrobial efficacy of triazenes has been observed against both Gram-positive and Gram-negative bacteria, as well as multidrug-resistant strains, making them potential candidates for combating drug-resistant infections.

Furthermore, triazenes possess favourable physicochemical properties, such as good stability, solubility, and low toxicity, which are essential for drug development. The structural versatility of triazenes allows for the modification of their chemical composition to enhance their potency, selectivity, and pharmacokinetic properties. These modifications can be tailored to target specific pathogens, increasing the potential for personalized treatment strategies.

In conclusion, this study highlights the potential of triazenes as promising candidates for the development of novel antimalarial and antimicrobial therapeutics. Further investigations are necessary to determine the structure-activity relationships and optimize the pharmacological properties of these compounds. The results warrant additional research, including MIC studies, to further explore the antimicrobial activity of the triazenes. Ultimately, these findings contribute to the development of more effective strategies for combating malaria and microbial infections.



X = N, CH; R = OH, H

L16: Adventures in the synthesis of imidazo[1,2-a]pyridin-3-amines as possible HIV-1 NNRTIs

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Keywords: imidazo[1,2-*a*]pyridines, NNRTIs, reductive amination, oxidative ring-opening

From the perspective of medicinal chemistry, imidazo[1,2-*a*]pyridines are privileged scaffolds, demonstrating a wide range of biological activities.[1] Our previous work has demonstrated that imidazo[1,2-*a*]pyridin-3-amines such as **1** (Figure 1) possess excellent antiviral activity against wild-type HIV-1[2] but lose activity against mutant viral strains. Thus, synthesis was undertaken of a range of more flexible compounds, such as **2** (Figure 1), that could possibly possess enhanced activity against mutant strains. The synthesis of these compounds, although ultimately achieved, gave rise to some unexpected results along the way and the overall synthetic journey towards these compounds will be discussed. Key steps in the synthesis included use of the Groebke-Blackburn-Bienaymé reaction, the Kornblum oxidation and reductive amination, while decarboxylation and oxidative ring-opening were some of the unanticipated outcomes.

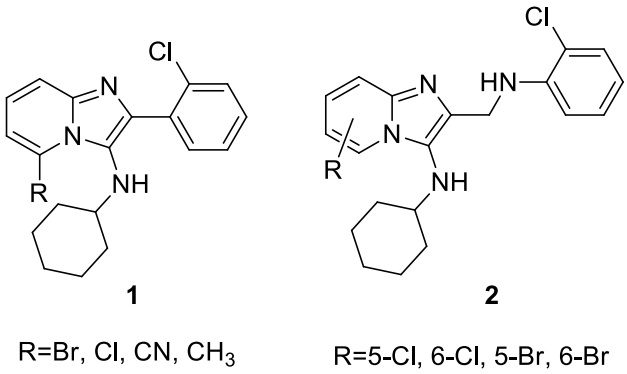

Figure 1

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L17: A fractionated marine extract library to enrich marine biodiscovery efforts in South Africa

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Keywords: Marine biodiscovery, fractionated library, marine natural products

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South Africa's extensive coastline boasts a wealth of marine biodiversity that remain underexplored in the context of natural product discovery. As the field of marine biodiscovery continues to gain momentum worldwide, efforts to harness the therapeutic potential of marine organisms have become increasingly important. This presentation highlights our efforts in building and exploiting a library of fractionated marine extracts to enhance biodiscovery efforts in South Africa.

Over the past 10 years, our research team has collected a diverse array of marine invertebrates, algae and microorganisms from various coastal and deep-sea habitats along the South African coastline. These organisms were carefully processed to generate a library of crude extracts, followed by fractionation into bioactive subfractions using chromatographic techniques. This process effectively concentrates minor compounds in selected fractions and improve bioactivity detection and identification if individual components. This presentation will present details of our ongoing efforts and the future prospects of marine biodiscovery in South Africa.

Insert figures and schemes below the abstract text. These are optional and should not be sent separately.

L18: Phytochemical screening of commercial pine bark extracts for adherence to US pharmacopeia requirements

Samuwi L, Stark A

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Keywords: Pycnogenol, pine bark, extraction.

Maritime pine (*P. pinaster*) bark extract is described in the US pharmacopeia 35,[1] and is sold as Pycnogenol®, a registered trademark of Horphag Research (Geneva, Switzerland) by various companies both in South Africa and abroad. Pycnogenol® has been studied for potential health benefits, including protection against cardiovascular, kidney, hepatic, cancer, digestive, and retinal issues.[2] A paper by Chen et al.[3] indicated that certain commercial products sold may actually be adulterated. The project aimed to extend on the data of Chen et al. by adding six commercial Pycnogenol® samples to their data set. For that purpose, their High-Performance Liquid Chromatography (HPLC) method was validated and further improved. This allowed for the quantification of the main components of this pine extract, namely catechin, caffeic acid, ferulic acid and taxifolin. The data was subjected to Principal Component Analysis (PCA), allowing for the identification of non-compliant samples. Furthermore, the commercial samples were subjected to the tests of the USP35 monograph to assess whether they comply with its stipulations. Finally, one commercial sample was fractionated using preparative column chromatography, and various separated compounds identified using two-dimensional Nuclear Magnetic Resonance techniques.

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L19: Stereoselective synthesis of functionalized pyrrolidines as potential anti-tubercular compounds

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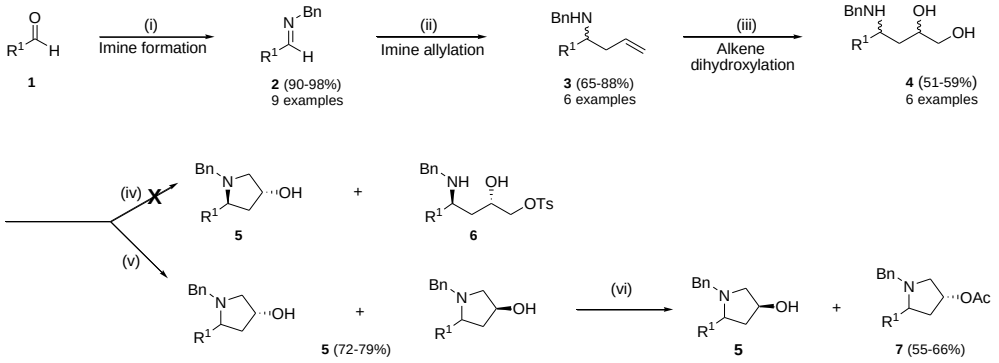
Keywords: Pyrrolidine, Drug discovery, TB drugs.

Small-ring heterocycles play an important role in drug discovery and appear frequently in drugs or prodrugs. According to Alien and co-workers, drugs containing pyrrolidines with a hydroxyl moiety have the potential to exhibit inhibitory activity against mycobacterium tuberculosis (M.*tb*).[1] Since South Africa has the third highest toll of global TB incidence, it is incumbent on local scientists to be involved in the search for new anti-TB drugs to fight the epidemic.[2] The facile and environmentally friendly general synthesis of pyrrolidine compounds could be an important asset to generate lead compounds. Thus, the key objective of this project was the application of a generic synthetic approach to produce a diverse library of pyrrolidines as shown in Scheme 1 based on the diastereoselective tin-mediated cyclodehydration/sulfonylation (CDS) reaction.[3]



Conditions: (i) $BnNH_2$ (1.2 eq), *p*-TsOH (10mol%), DCM, reflux, 3 h (ii) AllylMgBr, THF, 3 h (iii) $KMnO_4$ (aq), NaOH, EtOH, 17 h (iv) Bu_2SnO (5 mol%), *p*-TsCl, Et_3N, DCM, reflux, 3.5 h (v) $SOCl_2$, NaOH,3 h, (vi) Lipase-*Aspergillus Oryza,* Isopropyl acetate, CH_3CN, 22 h, rt

Scheme 1. General design for the synthesis of substituted pyrrolidines

Different oxidation/dihydroxylation methods were tried on the homoallylic amines **3** resulting in poor yields and decomposition. Ultimately a cold solution of $KMnO_4$ in basic medium (NaOH) oxidized the majority of **3** to the 4-amino-butanediols **4** in moderate yields (51-59%). The CDS reaction failed to give either **5** or **6** and resulted only in *N*-sulfonylation. Pyrrolidines **5** were eventually obtained via a $SOCl_2$ induced cyclodehydration in good yields (72-79%). Finally, the resolution of racemate pyrrolidine **5** via biocatalysis was employed. The 3-acyloxyl derivatives **7** was obtained from lipase *Aspergillus Oryza* catalyzed transesterification of a racemate 3-hydroxylpyrrolidines **5** in moderate yields (58-65%).

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L20: Fmoc Removal in Solid-Phase Peptide Synthesis using Morpholine: Good Performance and Suppression of Side-Reactions.

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Keywords: Fmoc; aspartimide; diketopiperazine; side reactions; solid-phase peptide synthesis.

Solid Phase Peptide Synthesis (SPPS) is a go-to strategy for peptide manufacturing in industrial and academic sectors. Especially with the increased acceptance and approval of peptidyl drugs by the FDA (Food and Drug Administration) and the pharmaceutical world at large. The SPPS strategy usually consists of attaching the *N*-terminus protected amino acid to the solid support, removing the protection, washing, coupling of the next amino acid, washing, and repeating until the target peptide is achieved. In these reactions, the optimization of specific reagents is often of paramount importance, as failure to do so can compromise the entire synthetic process.

Fmoc-based syntheses are friendlier than Boc-based syntheses but the use of repetitive treatment with base during Fmoc removal steps can lead to the formation of undesirable side reactions imposing a big challenge in downstream processing including a loss in yield of the desired peptide. Those side reactions include but are not limited to diketopiperazine (DKP) formation from acid peptides, aspartimide (Asi) formation when there's aspartic acid or asparagine, and Cys which leads to the formation of piperidinyl adducts and racemization/epimerization. Piperidine (PIP), a most used base is also a restricted and most importantly hazardous chemical with a greenness score of 6.9 on a scale of 0-10 in GSK's reagent selection guide. Modification of bases includes using rectifiers/ modifiers or a combination of different bases of which there have been no reports of any significant improvement concerning the minimization of DKP and/or aspartimide formation. To prevent or minimize side reactions during the synthesis process, meet regulatory standards, and afford high-quality crude peptides, it is necessary to find an alternative to PIP.

Here, we studied the performance of morpholine, a less basic secondary amine and a non-regulated substance, as an alternative to PIP for Fmoc removal in SPPS. We also evaluated its capacity to minimize DKP and Asi formation, epimerization, and adduct formation during the synthesis of C-terminus peptide acids.

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L21: *In Silico* Discovery of new analogues of 1-Heteroaryl-2-Alkoxyphenyl as potential inhibitors of SARS-CoV-2

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Keywords: SARS-CoV-2, Computer-aided drug design, Machine learning, Molecular docking, Molecular dynamics simulation

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The pandemic SARS-CoV-2 caused serious economic devastation. Efforts to combat the disease involved the investigation of herbs and synthetic chemicals. The approved FDA drugs for the treatment of the disease have been implicated in some debilitating side effects. Structural activity relationship (SAR) helps in repurposing drugs and come with derivatives that are more effective, less toxic, and overcome the issue of resistance. Some 1-Heteroaryl-2-Alkoxyphenyl were reported in literature for their anti-COVID activity [1]. Here, their molecular descriptors were used to generate mathematical models to predict their activity via traditional QSAR (genetic function approximation) and machine learning models. Results from the GFA-QSAR model showed that it was reliable and valid as the validation parameters passed the statistical test of significance (Correlation Coefficient (R) = 0.9377, R^2 = 0.898489, R^2 adjusted = 0.873112, R^2 predicted = 0.8792 (all $\geq$ 0.6); R^2 - Q^2 = 0.159 ($\leq$ 0.3), Q^2 cv = 0.89833 ($\geq$ 0.5); LOF = 0.139184 (the closer to 0 better). The Grid-SVR model performed better than the GFA-based QSAR model. The lead molecules were further subjected to SAR investigation to obtain new molecules whose bioactivity are now predicted using the models generated. The new molecules were docked at the active sites of SARS-CoV-2 receptors to unravel the interaction between them and the amino acid residues of the receptors. The stability of the docked molecules and the receptors were ascertained via molecular dynamics simulation. These molecules are currently considered for synthesis and further investigation against SARS-Cov-2 cell lines.

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L22: The design, synthesis and anti-tubercular properties of the sulfonated tri-substituted benzofuran derivatives.

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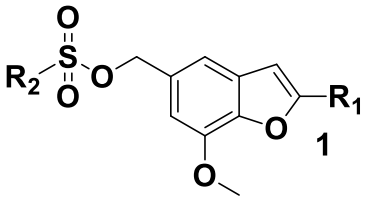
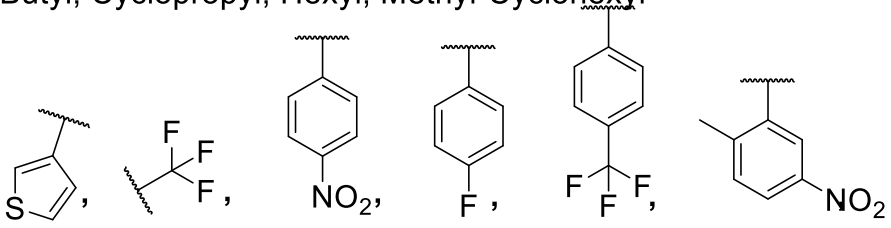
Keywords: Tuberculosis, *Mycobacterium tuberculosis*, benzofuran, Sonogashira cross-coupling.

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis* and it is usually present in the lungs as pulmonary tuberculosis.[1,2] Benzofuran derivatives are versatile biodynamic agents that can be used to design, develop potentially useful therapeutic agents and have drawn a considerable interest as powerful systems displaying a wide range of biological properties including antimicrobial, antiparasitic, anti-tubercular, and antitumor.[3,4] Therefore, four (4) benzofuran derivatives were successfully synthesized using Sonogashira cross-coupling starting from 5-iodovanillin. This was followed by the reduction of alcohol and subsequent sulfonation of the alcohol functional group to yield eight (8) benzofuran derivatives (**1**). Furthermore, biologically evaluation of the synthesised derivatives (**1**) against *Mycobacterium tuberculosis* will be investigated.



R_1 = Butyl, Cyclopropyl, Hexyl, Methyl-Cyclohexyl

R_2 = 

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L23: I love chemistry! What now?

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Keywords: chemical industry, employment scope.

Life happened and chemistry crossed your path somewhere. You absolutely love it and decide to enter a life-long relationship with the subject. Suddenly you find yourself with abundant knowledge very few people seem to be interested in. Were the years of dedication, sweat and tears worth it?

L24: How NMR can help you to better understand the aggregation behaviour of amino acid surfactants

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Keywords: amino acid surfactant, relaxation NMR, amphoteric surfactant.

Amino acid surfactants (AASs) have been gaining interest over the past two decades because of their good biodegradability properties, and the fact that they can be synthesized from renewable sources. AASs consisting of an amino and a carboxylic acid group allows the possibility to synthesise a variety of AASs derivatives. In this study, the concentration-dependant surface tension reduction of a water phase was analysed with a tensiometer. AASs with a critical micelle concentration (CMC) as low as 0.01 mmol/L and a surface tension, γ_{CMC}, of 27.8 mN/m was synthesised. Furthermore, NMR-diffusometry, a bulk flow analysis technique, was applied to gain insight into the characteristic timescale for surface tension relaxation, τ_s. The τ_s of various AASs were determined to establish the rate of surface tension reduction, and its relation to the structure. It was found that the τ_s was inversely proportional to the CMC. The surfactant tail length spanned from 8 to 22 carbons and displayed a τ_s between 1.78 µs and 6000 s. Rapid surface tension reduction is important for aerosol efficiency in, for example, agrochemical droplet spreading and surface wettability. Molecular rigidity was studied by NMR-relaxometry. T_1-inversion recovery and T_2-spin echo experiments were conducted to study different proton environments. The dynamic movement and rigidity of the various proton environments provides valuable insight to the structure and size of the formed aggregates. A database of physicochemical properties of the various surfactants could be used by the surfactant industry to optimise a particular application.

L25: Halogenated *ortho*-Hydroxybenzenecarbonyl Derivatives as Precursors to Biologically Relevant Organic Motifs

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Keywords: *ortho*-hydroxybenzenecarbonyl derivatives; halogenation; transformation; structure

Halogenated *ortho*-hydroxybenzenecarbonyl derivatives continue to assert themselves as versatile templates for the synthesis of novel organic compounds with medicinal properties. Several review papers on the medicinal applications of these structurally simple compounds continue to be published in the literature showing their potential to be considered as the new chemical space in drug discovery. Halogenated *ortho*-hydroxybenzenecarbonyl derivatives are not only of importance in the context of drug development, but their conformations and crystalline structures continue to attract considerable interest to study inter- and/or intramolecular non-covalent interactions such as hydrogen and halogen bonding interactions, aromatic-aromatic stacking interactions as well as the weak van der Waals or dipole-dipole interactions.[1] These non-covalent contacts help to stabilize the interactions of drug molecules with their protein targets and contribute to the affinity of small molecule inhibitors. We study these interactions in solution and in the solid state with the aim of enabling a more rational use of these classes of interactions in drug design.[2-6] Sure-fire methods for the synthesis of the title compounds, their geometry or conformation as well as some of their chemical transformations into derivatives containing these functional heads will be described.

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Funding from the University of South Africa (UNISA) and the National Research Foundation (GUN: SRUG2204203861*) is gratefully acknowledged.*

L26: Palladium-Catalyzed Regiodivergent C-H Olefination of Imidazo[1,2a] pyridine Carboxamide and Unactivated Alkenes.

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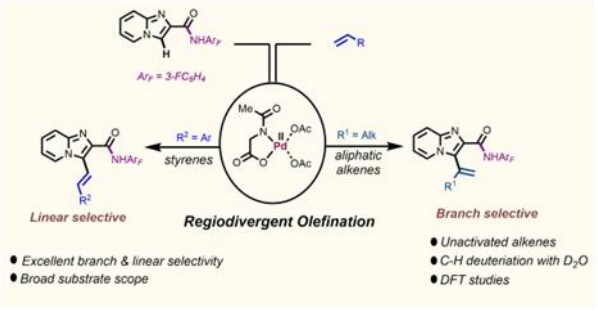
Keywords: 16th Frank Warren, Abstract, Conference.

In the last two decades, transition metal-catalyzed oxidative C-H alkenylation reactions via C-H bond activation have advanced significantly and led to many groundbreaking discoveries[1,2]. However, site selectivity and cleaving strong C-H bonds remain challenges. A ligand and directing group (DG) combination has allowed for site-selective C-H bond cleavage. Regiodivergent C-H olefination with a single catalytic system remains underdeveloped. Recently, a unified protocol was reported for Imidazo[1,2a] pyridine carboxamides, generating branched and linear olefinated products. The protocol can be applied for C-H deuteriation and is compatible with various styrenes and aliphatic alkenes. Preliminary experimental studies and computational investigations suggested that regiodivergent olefination can be controlled by olefin insertion and β-hydride elimination steps.



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L27: Organically shaking things up - Foray into mechanochemistry

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Keywords: Mechanochemistry, Green Chemistry, Multi-component Reactions.

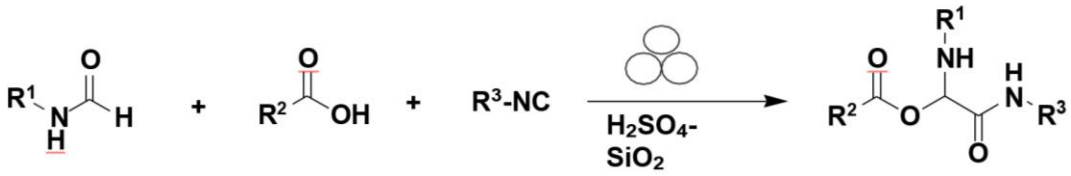
Despite being known through the writings of Theophrastus for over 2300 years, the application of mechanical energy to effect chemical reactions was not explored until recently. This is especially true in the field of organic synthesis, where reactions in aqueous media or in "solvent-free" conditions were often frowned upon.

With the advent of Green Chemistry and a greater focus on sustainability, minimizing the use of hazardous chemicals and solvents has become a priority. As one such technique, "mechanochemistry", as the application of mechanical energy to effect reactions, has emerged as a useful solvent-less technique in synthesis.

In our group we have explored a range of mechanical-energy techniques, from simple "grindstone chemistry" using a pair of mortar and pestle, to more automated ball-milling techniques.

In this presentation, I will describe some of the reactions and applications, from two- component condensation reactions to multicomponent reactions.

The methods are facile and clean, typically displaying many of the Green Chemistry features such as safety, high atom economy, and time-efficiency. They are also showing some unexpected results that may be useful for future developments.



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FLASH POSTER ROSTER

Poster #	Delegate Name	Title
P04	Mashweu, Ms A	Non-canonical amino acids with donors and acceptors for the stabilization of gel-forming peptide nanostructures
P09	Magwaza, Ms NT	Synthesis, and transformation of 5-bromo-3-methyl-7-iodo-1H-indazole into Novel polycarbo-substituted 1H-indazoles derivatives and evaluation for biological activity & radical scavenging profiling.
P19	Mpuputla, Mr M	The phytochemistry and cytotoxic activity of drimia altissima extracts
P21	Leoma, Mr MB	Using computational techniques to uncover new insights into the squalene monooxygenase inhibitors for lowering cholesterol in cardiovascular biology.
P23	Segodi, Mr RS	Synthesis of imidazo [1,2-a]pyridine and pyrazolo [1,5-a]pyridine derivatives as potential kinase inhibitors of Plasmodium falciparum parasite
P33	Ndwandwe, Ms B	Synthesis and Characterization of Perylene Tetracarboxylic Bisimide Derivatives for Advanced Solar Energy Harvesting
P34	Mokoena, Mr FS	Synthesis of ulopterol and meranzin hydrate and their analogues as potential antibacterial agents.
P39	Khuzwayo, Ms S	The synthesis and evaluation of 3-benzoylbenzofurans and their pyrazole derivatives against HIV-1 infections and cancer
P41	Mathebula, Ms N	The selective reduction of a Morita-Baylis-Hillman adduct-derived ketone using various ketoreductase enzyme preparations
P84	Rasalanavho, Dr M	Mycochemical analysis and structural elucidation of compounds from an indigenous mushroom species, Termitomyces sagittiformis
P87	Sibanda, Ms U	Pharmacophore modelling, QSAR study, insilico ADME prediction of N-phenylphenoxyacetamide derivatives, oxadiazole compounds and N-substituted tropinones with the potential of EthR inhibition.

POSTER ABSTRACTS

POSTER ROSTER

Poster #	Delegate Name	Title
P01	Singh, Prof P	Antidiabetic potential of 1,3,4-oxadiazole-1,2,3-triazole conjugates via a-glucosidase and a-amylase inhibition
P02	Tshiluka, Dr NR	Conventional synthesis of Aflatoxin M1 and M2 from B1
P03	Ragedi, Mr MTC	Isocyanide-based Ugi-multi-component (U-MCR) synthesis of 3-indole-tetrazoles and their antimycobacterial evaluation
P04	Mashweu, Ms A	Non-canonical amino acids with donors and acceptors for the stabilization of gel-forming peptide nanostructures
P05	Manhas, Dr N	Antidiabetic studies of new Rhoadnine-pyrazole molecular hybrids
P06	Singh, Dr T	Iridium-Catalyzed Double Convergent 1,3-Rearrangement/
P07	Wright, Ms S	Some anomalous reactions of TMS-containing cyclobutenones
P08	Essop, Ms L	Towards the synthesis of polycyclic N-heterocyclic compounds from malic acid as acyclic biorenewable source
P09	Magwaza, Ms NT	Synthesis, and transformation of 5-bromo-3-methyl-7-iodo-1H-indazole into Novel polycarbo-substituted 1H-indazoles derivatives and evaluation for biological activity & radical scavenging profiling.
P10	Nkoana, Mr J	Synthesis, conformational analysis and biological evaluation of 2,3 dihydrobenzo[b][1,5]thiazepines as potential α-Glucosidase and/or α-Amylase inhibitors
P11	Mhlongo, Ms S	Development of Quinoxaline Based Molecular Hybrids as Potential Antimicrobial Agents
P12	Kumar, Mr G	Ultrasonic energy promoted synthesis of bisthioglycolic acid derivatives in deep eutectic solvents-A greener approach
P13	Ntshele, Ms TA	Synthesis, Characterization and Biological Evaluation of 1-(1H-1,2,3- triazol-4-yl)methyl)-1-pyrazolo[3,4-b]quinoline hybrids
P14	Mbhokazi, Ms TN	Synthesis of sulfonylthioureas containing two carbon linker as potential antidiabetic drugs
P15	Aboo, Ms P	The synthesis and anticancer activity of new quinolone phenylhydrazone hybrids

P16	Uwumubyeyi, Mrs V	The in vitro antioxidant and antidiabetic potential of South African medicinal plant species (Rhoicissus rhomboidea, Rhoicissus capensis and Cyphostemma Auriculatum)
P17	Visagie, Ms S	Extraction and isolation of alkaloids from the plant Cissampelos capensis L. f. with anticancer properties
P18	Ankomah, Mr E	Design and Synthesis of SWIR Probes for Bioimaging
P19	Mpuputla, Mr M	The phytochemistry and cytotoxic activity of drimia altissima extracts
P20	Ngubane, Ms NP	An efficient and facile microwave assisted synthesis of 2-amino-3-carbonitrile 4H-chromene based analogues
P21	Leoma, Mr MB	Using computational techniques to uncover new insights into the squalene monooxygenase inhibitors for lowering cholesterol in cardiovascular biology.
P22	Govender, Dr H	Synthesis and Antibacterial Activity of Quinoline-3-carboxamide derivatives
P23	Segodi, Mr RS	Synthesis of imidazo [1,2-a]pyridine and pyrazolo [1,5-a]pyridine derivatives as potential kinase inhibitors of Plasmodium falciparum parasite
P24	Mokgopa, Mr KP	High throughput virtual screening of aptamers as anticancer therapeutics against oncogenic MiRNAs
P25	Nyoni, Ms NTP	Synthesis and pharmacological evaluation of benzimidazole-1,2,3-triazole-quinoline molecular hybrids as potential antitubercular
P26	Jordaan, Dr MA	Virtual screening, molecular docking studies and DFT calculations of FDA approved compounds similar to the nonnucleoside reverse transcriptase inhibitor (NNRTI) efavirenz
P27	Mashaba, Mr C	The design and synthesis of quinoline-urea-benzothiazole hybrid compounds as antitubercular agents
P28	Tshiwawa, Dr T	Cholesterol Dynamics in Cardiovascular Disease: A Computational Study on Lipid behaviour within Biological Systems
P29	Bokhe, Ms W	Exploring the Impact of Alkyl Chains on the Photochromic Behaviour and Liquid Crystallinity of Azobenzene Compounds

P30	Moodley, Dr T	Method development, validation, and oral acute toxicity of a quinoline-benzothiazole hybrid compound
P31	Malusela, Ms T	Synthesis of novel 6, 8-disubsituted-chromone-3-carboxylic acid derivatives
P32	Xulu, Ms J	Green synthesis of silver nanoparticles mediated dacryodes edulis stem bark for the treatment of the SARS-COV-2.
P33	Ndwandwe, Ms B	Synthesis and Characterization of Perylene Tetracarboxylic Bisimide Derivatives for Advanced Solar Energy Harvesting
P34	Mokoena, Mr FS	Synthesis of ulopterol and meranzin hydrate and their analogues as potential antibacterial agents.
P35	Mokganya, Ms KJ	Design, synthesis, and molecular modelling of aryl substituted 2-(4-(sulfonyl) styryl)quinazolin-4(3H)-ones as potential anticancer agents
P36	Shaik, Mr BB	Design and synthesis of quinoline-pyrimidine inspired hybrids as potential plasmodial inhibitors
P37	Noki, Mr S	Safety-Catch Protecting Group Scheme for Solid-Phase Peptide Synthesis
P38	Amod, Ms L	Identification and SAR evaluation of β-haematin inhibiting coumarins active against chloroquine-resistant Plasmodium falciparum
P39	Khuzwayo, Ms S	The synthesis and evaluation of 3-benzoylbenzofurans and their pyrazole derivatives against HIV-1 infections and cancer
P40	Lategan, Mr H	Extraction and anti-cancer evaluation of metabolites from southern African plants
P41	Mathebula, Ms NP	The selective reduction of a Morita-Baylis-Hillman adduct-derived ketone using various ketoreductase enzyme preparations
P42	Rashamuse, Dr TJ	Design, synthesis and investigation of photophysical and electrochemical properties of precursor materials containing alkylated 1H-benzo[d]imidazol-6-yl) as π-spacer for use in photovoltaic applications
P43	Mhlongo, Ms JT	New analogs of the Cecropin A and Melittin B hybrid CA(1−7) M(2−9) with improved properties
P44	Mabasa, Dr TF	Photolytic of azides and their application using a continuous photochemical reactor

P45	Sosibo, Dr S	Machine learning chemical space exploration of JNK3 inhibitors for Alzheimer's disease drug discovery
P46	Wanyama, Dr WPJ	Reductive biocatalysis of prochiral ketones to alcohols using a variety of yeasts
P47	Mohite, Mr SB	Green and Sustainable approach of palladium-catalyzed C-H olefination of Imidazo[1,2a] pyridine carboxamide
P48	Mathenjwa, Dr GS	Exploring the tumour extracellular environment as a new mode of heat shock protein (HSP) 90 inhibition
P49	Mabatamela, Mr L	Synthesis of imidazopyridazine and pyrazolopyrimidine derivatives as potential inhibitors of Plasmodium kinases PI4K and PKG.
P50	Ralepelle, Ms U	Reduction of α, β-alkynyl carbonyl compounds using SnCl2 and other metal salts.
P51	Musinyali, Ms V	Synthesis of sulfonylureas as potential anti diabetic drugs
P52	Dilebo, Mr KB	Bio-renewable based synthesis of anthraquinone-centered natural products
P53	Johnston, Mr Z	A batch-flow hybrid approach for the synthesis of the Schistosomiasis treatment praziquantel
P54	Maluleke, Mr BK	Synthesis of Quinoxaline Derivatives and Evaluation of their Biological Activity against Tuberculosis
P55	Zimuwandeyi, Dr M	Towards the synthesis of hydroxylated polyamines
P56	Maree, Mr M	Synthesis and evaluation of flexible pyrimethamine analogues as antifolates targeting drug resistant malaria
P57	Mabena, Ms N	Synthesis of Sulfonated (poly ether- ether ketone) membranes for Iron Redox flow battery
P58	Munapo, Ms TD	Design, synthesis and evaluation of anti-HIV and antiplasmodial activities of some hydroxypyridinone-aminoquinoline derivatives
P59	Rambau, Mr J	In Silico study of DNA metabolic enzymes for cancer treatment
P60	Jugmohan, Dr J	Determining the Optimal Reaction Pathway for Methanol Production Prior to Extensive Design Decisions – Application of the ASSF Tool

P61	Mthembu, Dr S	Synthesis of polysubstituted pyrroles via enaminone intermediates
P62	Jaceni, Mr K	Towards a bio-renewable based synthesis of flavonoids and benzofuro[3,2-b]chromenones as potential UV absorbers
P63	Smit, Dr F	Synthetic Possibilities for Hemilabile Ligands: A Case Study of Decacyclo[10.8.15,8.02,11.04,9.013,20.015,18]-heneicosane-3,10,14,19-tetraone
P64	Zulu, Ms D	An investigation of the herbicidal activity of plant Artemisia afra Jacq. ex Willd.
P65	Machakaire, Mr T	Identification of anti-inflammatory compounds from South African plant species
P66	Nkuna, Ms LP	Synthetic review and characterization of new psychoactive compounds (NPC) for potential use by the law enforcement agencies
P67	Mabunda, Mrs K	Phytochemistry and Cytotoxicity Studies from Clerodendrum Glabrum and Combretum Nelsonii Roots against the Breast and Colon Cancer Cell Lines
P68	Mkhize, Mr S	Synthesis of imidazo[1,2-a]pyridin-3-amine derivatives with heteroatom linkers as potential HIV-1 reverse transcriptase inhibitors
P69	Plakas, Ms AM	Synthesis and characterisation of functionalised indolin-2-ols and their application as antimalarial agents
P70	Masemola, Ms L	Phytochemical investigation of secondary metabolites from Pappea capensis for anticancer properties
P71	Butsi, Dr KR	A Green and Efficient Synthesis of Ethambutol
P72	Mabaso, Mr BA	The synthesis of bridged disaccharides
P73	Marondedze, Dr E	Reaction-enhanced solvent extraction of carboxylic acids from aqueous solution using hydroxyl-functionalized ionic liquids
P74	Chavalala, Mr HE	Synthesis of 5-substituted-4,6-diaminopyrimidine derivates as potential inhibitors of PfCDK1 and PfCDK4 for malaria treatment and transmission-blocking
P75	Thukwane, Mr T	Synthesis of fused bicyclic rings via cyclodehydration of triols using catalytic dibutyltin oxide

P76	Vosloo, Prof HCM	The synthesis and characterization of novel Guerbet-type and linear N-alkyl amino acid surfactants
P77	Madzivha, Ms P	Quantitative analysis of wet process phosphoric acid reaction by spectroscopic techniques
P78	Khumalo, Mr MM	Development and application of “tag, capture, and release” derivatizing protocol for alcohols
P79	Makhakhayi, Ms L	Phytochemistry and Cytotoxicity Studies from Clerodendrum Glabrum and Combretum Nelsonii Roots against the Breast and Colon Cancer Cell Lines
P80	Rakodi, Mr GH	Synthesis and characterization of amino ferrocenyl heterocyclic and cyclopentane-dicarboxylate ligands
P81	Madibana, Ms TL	Rapid Method for Iodination of Phloroglucinol Derivatives
P82	Phuthi, Mr M	Phytochemistry, chemical, and biopharmaceutical profiling of halleria lucida for anticancer properties
P83	Bokgobelo, Ms K	Synthesis of sulfamethazine derivatives as inhibitors of corrosion on aluminum metal in HCl medium.
P84	Rasalanavho, Dr M	Mycochemical analysis and structural elucidation of compounds from an indigenous mushroom species, Termitomyces sagittiformis
P85	Oderinlo, Dr O	Antidiabetic Activity of Methyl Gallate from Mezoneuron benthamianum Leaf: Structural modification and in-silico studies
P86	Swana, Ms L	Exploring possible inhibitors targeting the SARS-CoV-2 MPRO enzyme extracted from Dacryodes edulis stem bark
P87	Sibanda, Ms U	Pharmacophore modelling, QSAR study, insilico ADME prediction of N-phenylphenoxyacetamide derivatives, oxadiazole compounds and N-substituted tropinones with the potential of EthR inhibition.
P88	Selowa, Mr K	Synthesis of Sulfamezarine derivatives as potential corrosion inhibitor of zinc metal in 1 M sulphuric acid solution
P89	Ramaite, Prof IDI	Synthetic studies and biological evaluation of chromone-based derivatives

P90	Vangara, Dr S	Easy access to the synthesis of 4,5-dihydrooxazole/5,6-dihydro-4H-1,3-oxazine derivatives via carboxamides
P91	Tchegnitegni, Dr B	Bioactive Arylnaphthalide Lignans from Justicia depauperata
P92	Mugwena, Ms D	
P93	Ngcobo, Mr NK	Identification of alpha-glucosidase inhibitors from indigenous plants
P92	Sikakane, Ms B	Application of Doped Titanium dioxide as Heterogeneous Visible-Light Photocatalyst in Organic Synthesis
P93	Mahlangu, Ms S	The use of blended and single essential oils in management of anxiety and stress.

P01: Antidiabetic potential of 1,3,4-oxadiazole-1,2,3-triazole conjugates via α-glucosidase and α-amylase inhibition

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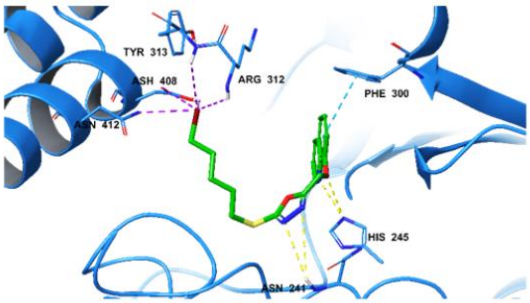
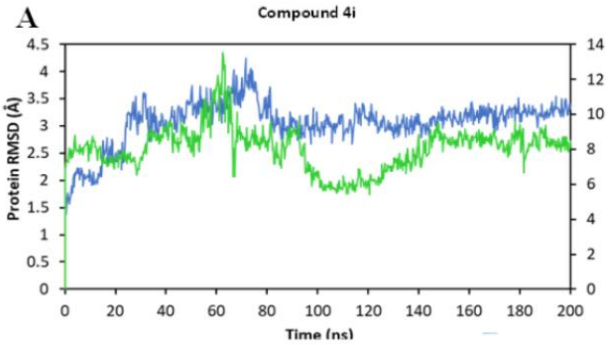
Keywords: Diabetes mellitus, 1,3,4-oxadiazole-1,2,3-triazoles

Diabetes mellitus (DM) is a metabolic disorder that is characterized by elevated levels of glucose in the blood and is one of the major threats to global health security. Approximately, 530 million people are living with this disorder worldwide with nearly 7 million deaths in 2021 due to DM-related complications [1]. Typically, the patients develop type 2 diabetes mellitus (T2DM) primarily due to insulin resistance that leads to multiple problems including cardiovascular disorder, nervous system damage, eye damage, stroke, and kidney disease [2].

In this study, we combined two pharmacologically significant scaffolds, 1,3,4-oxadiazole and 1,2,3-triazole in a single molecular hybrid to develop a new series of molecular conjugates and evaluated their antidiabetic potential via α-glucosidase and α-amylase inhibition which are key enzymes in glucose production in the body. The most active compound (**4i)** of the series bearing a bromopentyl sidechain displayed the stronger α-glucosidase inhibition (IC_{50} = 15.85 µM) relative to reference drug acarbose (IC_{50} = 17.85 µM). Furthermore, the kinetic studies disclosed the mode of α-glucosidase inhibition as non-competitive thus classifying these conjugates as allosteric inhibitors [3]. Finally, the in silico docking and molecular dynamics simulations provided insights into the protein-ligand interaction profile and stable complexation of promising conjugates at the allosteric site of α-glucosidase.





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P02: Conventional synthesis of Aflatoxin M1 and M2 from B1

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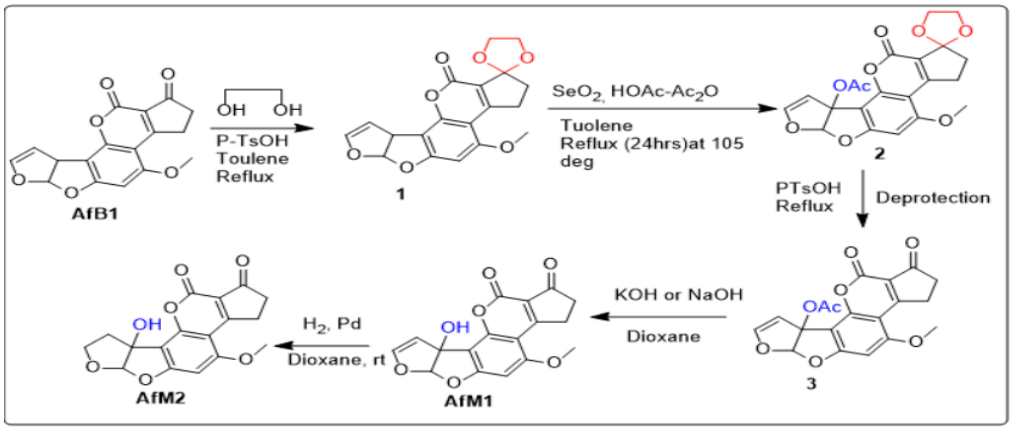
Keywords: Aflatoxin M1 and M2, Synthesis, Conventional methods

Food safety remains one of a serious global challenge especially in the agricultural and food production sector where a large quantity of products is produced to address food insecurity.[1] Aflatoxins (Afs) are a class of highly mycotoxin which are found from several fungal and moulds of aspergillus *parasiticus* and *flavus*. [2] Among from twenty known aflatoxins, there are six main aflatoxins namely: aflatoxin B1 (AfB1), aflatoxin B2 (AfB2), aflatoxin G1 (AfG1), aflatoxin G2 (AfG2), aflatoxin (AfM1) and aflatoxin M2 (AfM2).[3] AfM1 and AfM2 are the hydroxylated AfB1 and AfB2 which are mostly secreted through milk.[4]

Utilising a conversion reported method by Paul et.al.[5], this project will began by protecting the **AfB1** ketone with glycol in the presence of p-toluene sulfonic acid to give **AfB1** ketal **1.** The ketal **1** was subjected into acetylation with selenium dioxide to produce acetate of **AfB1 2**. Deprotection of acetate **2** in the presence of acid afforded compound **3** which was hydroxylated using potassium hydroxide to give desired **AfM1** in good yield **4**. Furthermore, **AfM1** was hydrogenated in the presence of palladium on carbon to afford **AfM2** toxin as depicted in **Scheme 1**. Both purified AfM1 and M2 were characterised using a combination of NMR, HRMS and FTIR spectroscopies.



Scheme 1: Conventional synthesis of Aflatoxin M1 and M2

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P03: Isocyanide-based Ugi-multi-component (U-MCR) synthesis of 3-indole-tetrazoles and their antimycobacterial evaluation

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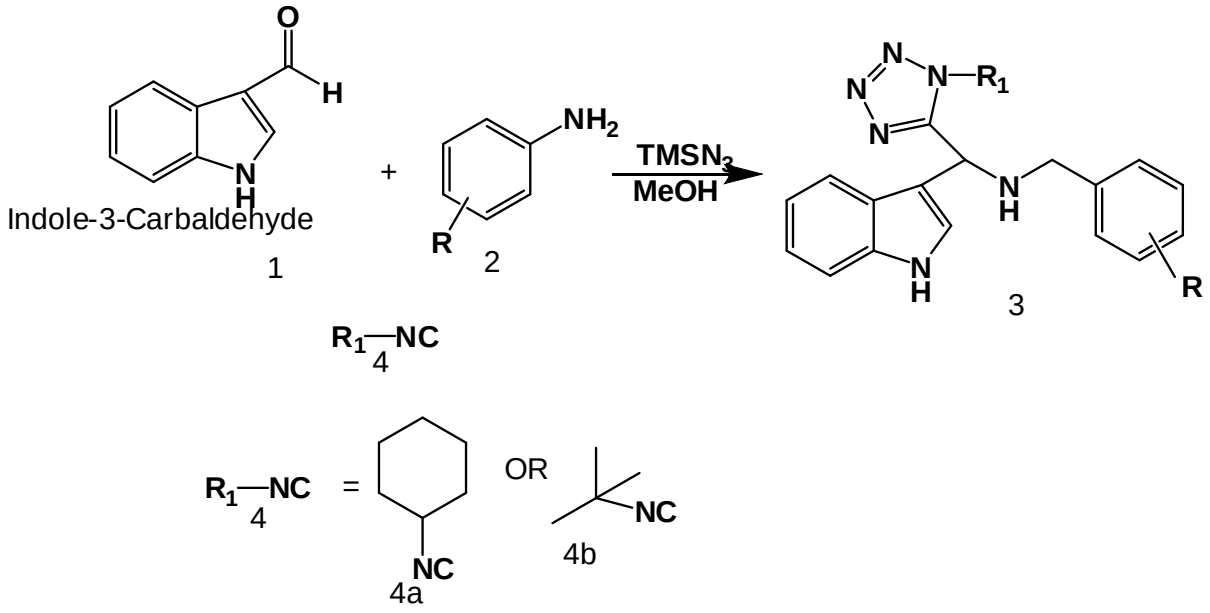
Keywords: U-MCR, Tuberculosis, tetrazole, Indole-3-carbaldehyde.

Tuberculosis (TB) is an ancient and tenacious airborne ailment that has been a life-threatening disease for over a century, which is caused by a bacillus type of bacteria called *Mycobacteria tuberculosis* (*Mtb*) [1]. Although curable, the emergence of -resistant strains of *Mtb* threatens its management, such that it requires the second line drugs which are expensive, toxic, have a more extended treatment duration compared to first-line drugs, and are less effective [2]. Thus, there is an urgent need to find new treatment regimens that will be effective against both resistant and non-resistant strains. To this end, a series of 3-Indole tetrazole derivatives (Scheme 1) were synthesised in a single pot *via* the isocyanide-based Ugi multicomponent procedure in 35 to 96 % yields. The synthesised compounds were fully characterised using 1D and 2D NMR, IR, and their purity was checked by HPLC. Thereafter, their antimycobacterial activities were assessed against the H37Rv *Mtb* strain and found to have moderate activity over a 14-day assay with MIC90 ranging from 67 to 618 mg/mL (or micromolar).

Synthetic procedure



Scheme 1.

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P04: Non-canonical amino acids with donors and acceptors for the stabilization of gel-forming peptide nanostructures

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Keywords: unnatural amino acids, peptides, hydrogels,

Peptides molecule fold and self-assemble by non-covalent forces, forming nanostructures such as nanofibers and nanotubes, which can create different types of soft materials such as gels.[1] Peptide-based hydrogels can function as bio-compatible carriers for therapeutic delivery.[2] Recently, it has been shown that the amphipathic hexapeptide **4** (H-FQFQFK-NH_2, Figure 1) forms stable hydrogels. Interestingly, in vivo studies demonstrated that co-formulating a cargo (small molecule or a protein) within the hydrogel resulted in a sustained release of the cargoes up to 1-2 days.[3]

In order to enhance the release time window, we aim to improve the non-covalent interactions between the peptide hydrogelators by means of additional donor-acceptor interactions. Herein, we report the synthesis of modified unnatural[4] acceptor- and donor-substituted amino acids and their incorporation into various positions of the known gel-forming hexapeptide. The synthesis of the modified acceptor- and donor-substituted amino acids starts from abundant natural L-asparagine **1a** and L-glutamine **1b**. They are firstly degraded by Hoffmann rearrangement to lysine homologues **2a,b**, which are then coupled with donor and acceptor groups to afford the Fmoc-protected amino acids **3**. The target hexapeptides were prepared using the automated solid state peptide synthesis and then tested for their gelation properties.

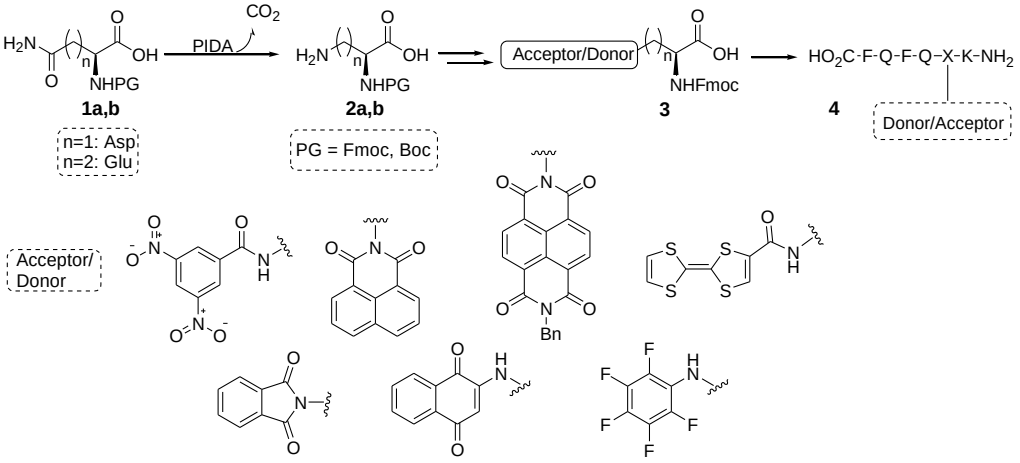

Figure 1. Synthesis and incorporation of modified amino acids into a hexapeptide.

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P05: Antidiabetic studies of new Rhoadnine-pyrazole molecular hybrids

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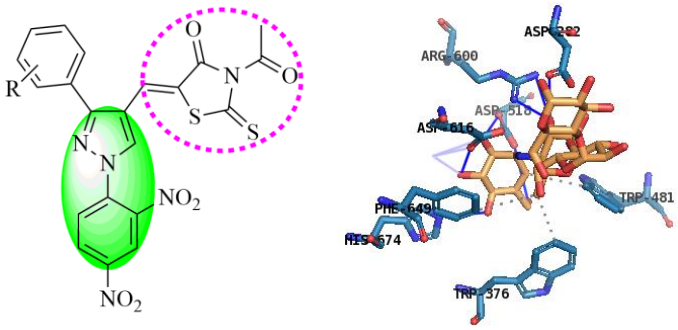
Keywords: Rhoadnine-pyrazole, diabetes

Type II diabetes is a chronic disease that when untreated/mismanaged leads to complicated health problems, including heart disorders, retinopathy, and neuropathy [1] Current therapies in the management of diabetes include oral administration of antidiabetic drugs, intramuscular insulin injection, as well as dietary and lifestyle changes [2]. However, these techniques have limited efficacy and suffer several limitations; hence necessitate further efforts to probe new and innovative antidiabetic therapies.

Two of the most attractive targets of antidiabetic chemotherapeutics in the control of blood glucose levels are α-glucosidase and α-amylase enzymes. These enzymes degrade carbohydrates into sugars. Thus, the inhibition of the α-glucosidase and α-amylase enzymes is essential for delaying carbohydrate degradation and glucose absorption, which decreases the amount of overall glucose in the body, and inevitably reduces the effect of diabetes [3]. In this work, the molecular hybrids of rhodanine with pyrazole were synthesized and tested in vitro against α-glucosidase and α-amylase enzymes. To establish the role of molecular hybridization, the simple rhodanine analogs were also developed, tested against the enzymes, and compared [4]. The rhodanine-pyrazole hybrids as expected exhibited superior activity when compared with their simple phenyl analogs with more selectivity towards alpha amylase. Furthermore, the molecular docking studies of these compounds revealed the critical pharmacophoric features contributing to inhibitory activity.



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P06: Iridium-Catalyzed Double Convergent 1,3-Rearrangement/ Hydrogenation of Allylic Alcohols

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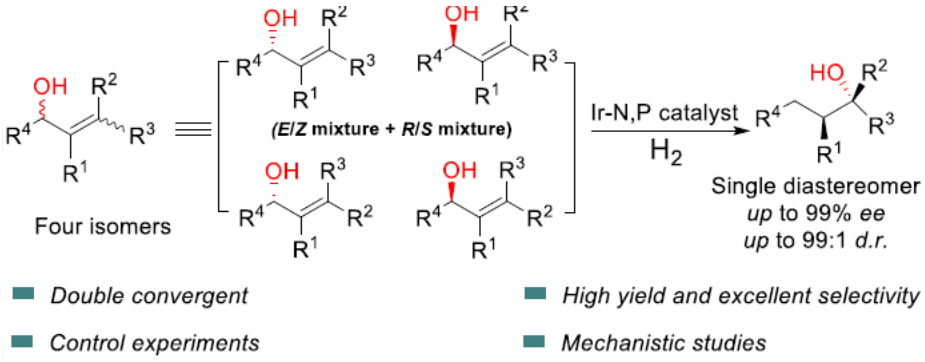
Keywords: Hydrogenation, Allylic alcohols, Convergent, DFT, Iridium catalysis.

Stereoconvergent catalysis is a green and sustainable approach that converts racemic or isomeric mixtures of starting materials to a single enantioenriched product. For DKR processes, racemic starting material can be converted to enantiomerically enriched products with up to 100% yield and has been well investigated in the past half century.[1]

For enantioconvergent hydrogenations, the E and Z olefins, which usually generate opposite enantiomers,[1] are hydrogenated to the same enantiomerically enriched product independent of the double-bond geometry. Thus far, no method exists that can convert multiple isomers (more than two isomers) to a single enantiopure product.

Enantioconvergent catalysis has the potential to convert different isomers of a starting material to a single highly enantioenriched product.[2] A novel enantioselective double convergent 1,3-rearrangement/hydrogenation of allylic alcohols using an Ir-N,P catalyst was developed. A variety of allylic alcohols, each consisting of a 1:1:1:1 mixture of four isomers, were converted to the corresponding tertiary alcohols with two contiguous stereogenic centers, in up to 99% ee and 99:1 d.r.

To further understand the transformation, DFT calculations for an aryl substituted allylic alcohol and an alkyl substituted allylic alcohol were conducted. The minimized conformations of the starting materials and possible rearrangement products were calculated. The DFT calculations, and control experiments suggest that the 1,3-rearrangement is the crucial stereodetermining element of the reaction.



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P07: Some anomalous reactions of TMS-containing cyclobutenones

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Keywords: Cyclobutenone, desilylation.

Cyclobutenones are useful intermediates due to their strained rings and enone moieties[1,2]. They have been shown to have great potential in the direct synthesis of poly-substituted benzene rings[3]. We sought to exploit this reactivity of cyclobutenones in our planned total synthesis of aglycones gilvocarcins, a class of natural products that possess poly-substituted naphthalene framework. During these studies, in an attempted desilylation of cyclobutenone **1** under standard desilylation conditions, resulted in several anomalous reactions. For example, when cyclobutenone **1** was treated with TBAF in acetic acid at room temperature, the desired desilylated cyclobutenone **2** was obtained in 31% yield alongside rearranged cyclobutenone **3** (28%). Alternatively, when cyclobutenone 1 was treated with K_2CO_3 in MeOH as solvent, furnished acrylate **4**, with 78% yield. Further experiments were conducted to probe the mechanism of the reaction. In addition, the scope and limitation of the reaction studies are underway.

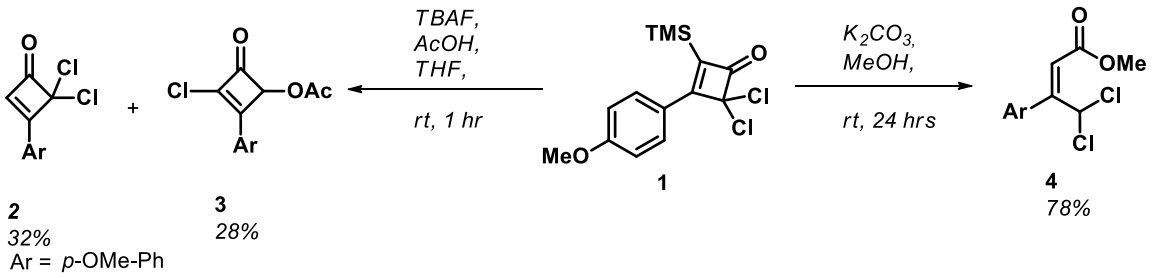

Figure 1. A general scheme of the formation of TMS-cyclobutenone rings and the different products formed, when removing the TMS-group.

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P08: Towards the synthesis of polycyclic *N*-heterocyclic compounds from malic acid as acyclic biorenewable source

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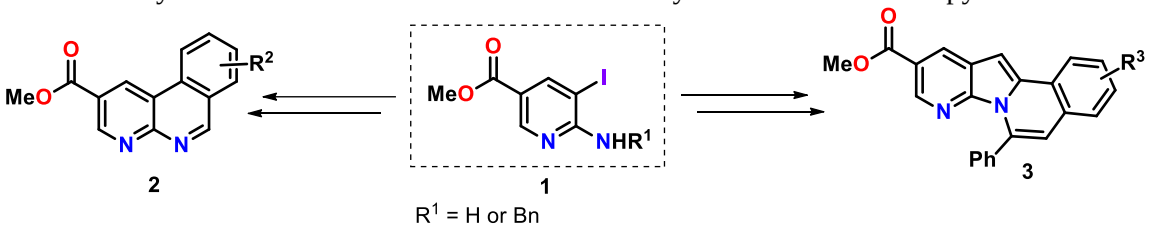
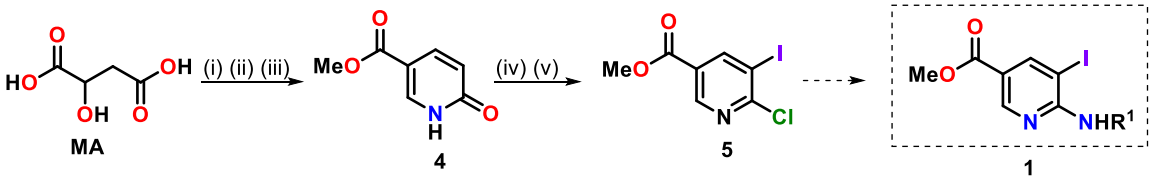
Keywords: 2-Aminopyridine, Biorenewable, *N*-Heterocyclic compounds, Kinase inhibitors, Malic acid.

Biorenewable building blocks have enjoyed increased popularity amongst synthetic chemists, following the proclamations of the twelve principles of Green Chemistry by Anastas and Warner[1,2]. Enormous efforts have been directed towards the synthesis of functional molecules using carbocyclic biorenewable resources[3,4]. The synthesis of the ubiquitous *N*-heterocyclic compounds from biorenewable starting materials remains largely unexplored. To address this, we sought to employ suitably functionalized 2-aminopyridines **1** as a common starting material to synthesize derivatives of benzo[*c*][1,8]naphthyridine **2** and pyrido[3',2':4,5]pyrrolo[2,1-*a*]isoquinoline **3** (Scheme 1), which could be used as kinase inhibitors. The requisite 2-aminopyridine derivative **1**, was in turn synthesized from malic acid (**MA**) in six steps as shown in Scheme 2. In our synthesis, **MA** was converted to 6-hydroxynicotinate **4** in three steps with an overall yield of 49% (Scheme 2). 6-Hydroxynicotinate **4** was then iodinated with NIS and chlorinated with POCl3 to give 6-chloro-5-iodonicotinate **5** in an overall yield of 77 %. Current studies involve optimization of the aminolysis of 6-chloro-5-iodonicotinate **5** to the key intermediate 2-aminopyridine derivative **1**.



Scheme 1. Proposed synthesis of benzo[c][1,8]naphthyridine **2** and pyrido[3',2':4,5]pyrrolo[2,1-a]isoquinoline **3** from the common 2-aminopyridine derivatives **1**.



Reaction conditions: (i) H_2SO_4, 95 °C, 2 h; (ii) MeOH, 100 °C, 2 h, 92%; (iii) HMDS, DBU, MeCN, 25 °C, 48 h, 53%; (iv) NIS, MeOH, 70 °C, 30-45 min, 96%; (v) DIPEA, $POCl_3$, 1,4-dioxane, 100 °C, 2 h, 80%.

Scheme 2. Synthesis of functionalized 2-aminopyridines.

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P09: Synthesis, and transformation of 5-bromo-3-methyl-7-iodo-1*H*-indazole into Novel polycarbo-substituted 1*H*-indazoles derivatives and evaluation for biological activity & radical scavenging profiling.

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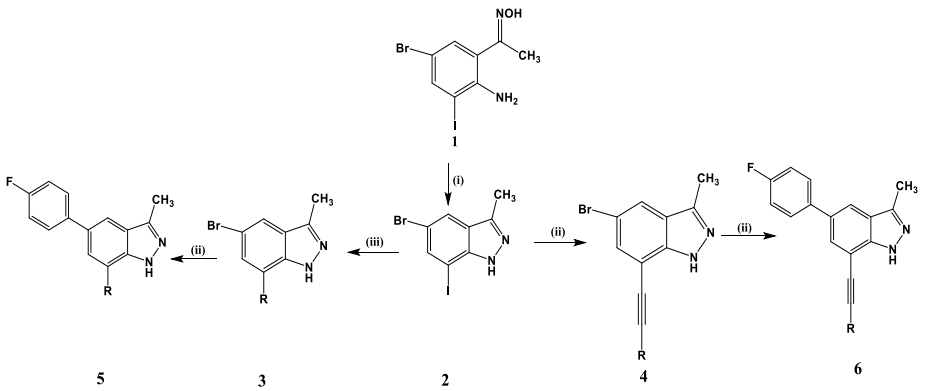
Keywords: 1*H*-indazole, Sonogashira cross-coupling, Suzuki-Miyaura-cross coupling, Enzymatic assay, Antioxidant activity, cytotoxicity, molecular docking

Indazoles that form the basis of this study are the indole bioisosteres consisting of a pyrazole ring fused with the benzene ring. These compounds have attracted much attention in synthesis due to their wide range of biological activities including anti-inflammatory, anti-HIV, anti-diabetic, and anti-tumor activities.[1] 1-(2-Amino-5-bromo-3-iodophenyl)ethanone oxime **1** was reacted with methylenesulfonyl chloride in the presence of Et_3N as a base to afford 5-bromo-3-methyl-7-iodo-1*H*-indazole **2** (Scheme 1). Compound **2** was then subjected to Sonogashira or Suzuki-Miyaura cross-coupling with terminal acetylenes or aryl boronic acids to afford novel 5-bromo-3-methyl-7-substituted-1*H*-indazoles **3** (R = -C≡CAr[1]) and **4** (R = Aryl), respectively. Further functionalization of **3** and **4** *via* Suzuki-Miyaura cross-coupling reaction with 4-fluorophenylboronic acid afforded the corresponding polycarbo-substituted indazoles **5** and **6**, respectively. The prepared compounds were, in turn, evaluated for potential biological activity as anti-diabetic agents through enzymatic assays *in vitro* against α-amylase, α-glucosidase and protein tyrosine phosphatase1 beta (PTP1B) as well as for radical scavenging properties.[2,3.]



Reagents and conditions: (i) $(CH_3)_2SO_2Cl$, Et_3N, DCM, 0 °C to RT, 6 h; (ii) HC≡CAr[1], $PdCl_2(PPh_3)_2$, CuI, K_2CO_3, THF: H_2O, 3 h, RT; (iii) $ArB(OH)_2$, $PdCl_2(PPh_3)_2$, K_2CO_3, toluene:ethanol (4:1, v/v), 12 h
Scheme 1: Synthesis and transformation of 1*H*-indazoles **2** into 7-polycarbosubstituted derivatives.

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P10: Synthesis, conformational analysis and biological evaluation of 2,3 dihydrobenzo[*b*][1,5]thiazepines as potential *α*-Glucosidase and/or *α*-Amylase inhibitors

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Keywords: 2,3-dihydrobenzo[*b*][1,5]thiazepines; X-ray structure, DFT; α-glucosidase; α-amylase

The 2,4-diaryl-2,3-dihydrobenzo[b][1,5]thiazepines were prepared by condensing the binucleophile 2-aminothiophenol and the ambident electrophilic 5-bromo-2-hydroxychalcones[1]. The structures and conformation of the synthesized compounds were determined using spectroscopic methods in combination with single crystal X-ray diffraction (SC-XRD) technique. Both ^{1}H-NMR & IR spectroscopic techniques confirmed participation of the hydroxyl group in intramolecular hydrogen bonding interaction with a nitrogen atom. SC-XRD confirmed the presence of a six-membered intramolecularly hydrogen bonded pseudo-aromatic ring, which was supported by a DFT method on **2b** as a representative example in the gas phase. In comparison to acarbose (IC_{50} = 7.56 0.42 M), compounds **2a** (Ar = -C_6H_5), **2c** (Ar = -C_6H_4(4-Cl)), and **2f** (Ar = -C_6H_4(4-$CH(CH_3)_2$) showed higher inhibitory action against *α*-glucosidase. Their respective IC_{50} values were 6.70 ± 0.15 µM, 2.69 ± 0.27 µM and 6.54 ± 0.11 µM. The compound **2f**, which showed enhanced activity against *α*-glucosidase, also significantly inhibited α-amylase (IC_{50} = 9.71 0.50 M).

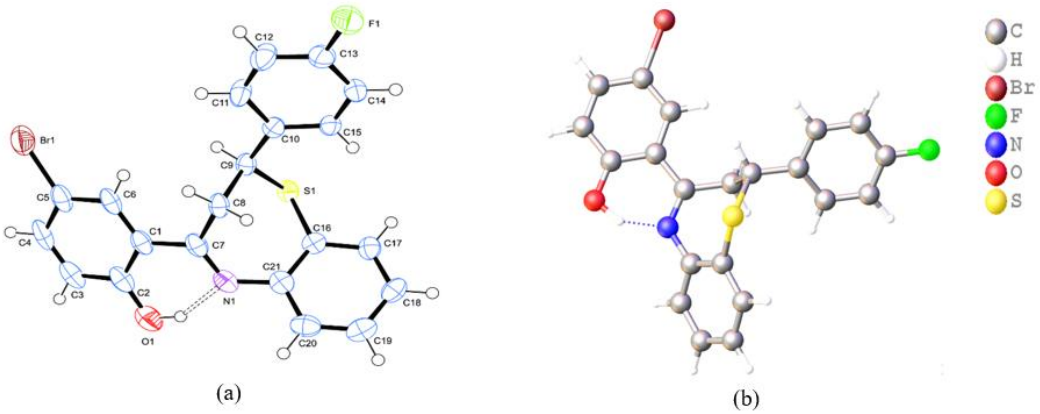

Figure 1: ORTEP diagram of 2b with thermal ellipsoids drawn at 50% probability level (a) and its optimized geometry (b) at the B3LYP/LANL2DZ level. The atom-labelling scheme for this compound is based on the XRD structure and the numbering differs from the systematic one.

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P11: Development of Quinoxaline Based Molecular Hybrids as Potential Antimicrobial Agents

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Keywords: Quinoxaline, Thiazolotriazole, Antimicrobial.

The quinoxaline moiety has a heterocyclic backbone which is formed by the infusion of the benzene and pyrazine ring. Quinoxaline have been previously proven to possess notable pharmacological activities seeing that the moiety can be found in pharmaceutical drugs, some of which have antibacterial, anti-TB and antidiabetic properties [1-3]. The quinoxaline moiety is also found in riboflavin (vitamin B2), echinomycin and triostin A which are naturally occurring hybrid molecules. Echinomycin and triostin A are used as antibiotics [4].

There is a growing trend for the formation of molecular hybrids for the treatment of different ailments, with antibiotic activity being one of the sought-out function for these molecules due to the increasing global concern regarding antibiotic resistance [5]. Antibiotics have greatly improved the life and wellness of humans, animals, and plants on a global scale. It is thus very important that newer antibiotics are developed to combat for the resistance of the already existing molecules.

In this work, the synthetic design and characterisation of a small library of quinoxaline-thiazolotriazole hybrid molecules along with their antibacterial analysis results will be presented.

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P12: Ultrasonic energy promoted synthesis of bisthioglycolic acidderivatives in deep eutectic solvents-A greener approach

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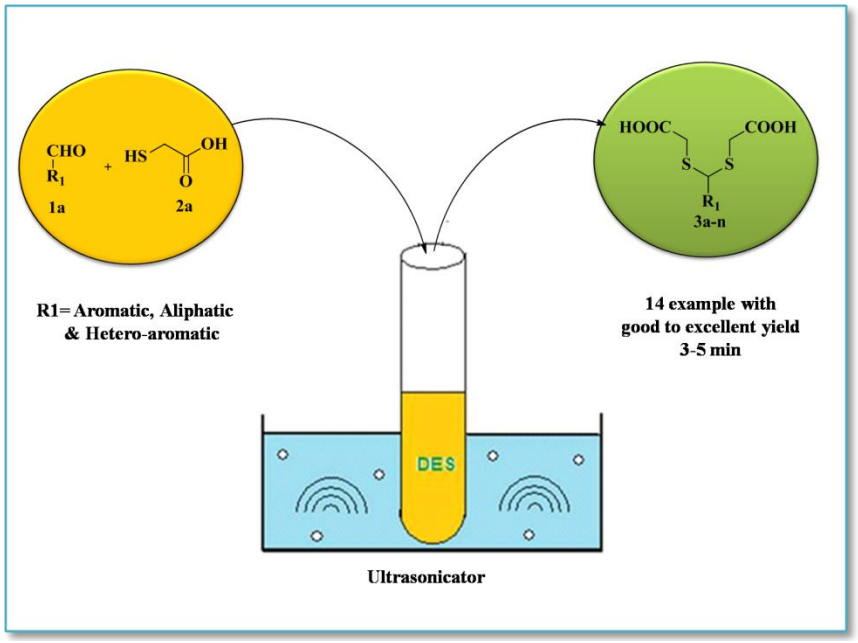
Keywords: ultrasonic energy, green chemistry, bisthioglycolic acid, deep eutectic solvent, Carbon–Sulfur bond formation.

Carbon–Sulfur bond formation strategies are significant due to the importance of linkages in the sulfur-containing scaffolds which are found in biologically active compounds.[1] Sulfones, and sulfonamides are common sulfur-containing scaffolds that are found in medicinal drug. For instance, 1,3-oxathiolan-5-one has shown antiviral activity, and PLA2 inhibitory activity.[2] Moreover, bisthioglycolic acid and its derivatives have been reported to play a significant role as a precursor in the formation of many sulfur-containing heterocyclic compounds.

The present methodology explored the effectiveness and versatility of deep eutecticsolvent with ultrasonic energy as an eco-friendly protocol for the synthesis of bisthioglycolicacid derivatives. Bisthioglycolic moiety holds its role as a potent scaffold in sulfur- containing drugs. The presented strategy offers significant advantages such as green catalystas well as solvent, excellent yield, short reaction time, and simple reaction workup. This methodology shows a wide range of substrate scope that contain both electron-donating as well as electron-withdrawing groups.



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P13: Synthesis, Characterization and Biological Evaluation of 1-(1H-1,2,3-triazol-4-yl)methyl)-1-pyrazolo[3,4-b]quinoline hybrids

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Keywords: Pyrazoloquinoline-1,2,3-triazole, Click-chemistry, Antibacteria, Anticancer, Antidiabetics, Antituberculosis.

The major cases of increasing drug resistance drives the urgency for the drug development sectors to focus research on molecular hybridization aiming to synthesize more potent drugs. Twenty novel 1-(1H-1,2,3- triazol-4-yl)methyl)-1-pyrazolo[3,4-b]quinoline compounds were synthesized via the copper(I) catalyzed [3+2] dipolar cycloaddition (CuAAC) of different organic azides and 1-(prop-2-yn-1-yl)-1H-pyrazolo[3,4-b]quinoline[1,2]. These target compounds were confirmed with NMR (^{1}H, ^{13}C, 2-D), FT-IR and HRMS. The synthesized compounds were investigated for their bioactivities. Antibacterial and antituberculosis showed moderate activity for some of the compounds with no hits as all the active compounds were less potent than the standards ciprofloxacin (antibacterial, MIC = 1.4-11.8 µM) and Erythromycin (antituberculosis, MIC = 40.3 µM). The antidiabetics assay against α-glucosidae and α-amylase enzymes showed promising results for compounds 9a,10a & 11a as the exhibited high % inhibition than the standard acarbose with less potency as their IC_{50} values were 2 folds higher than the standard. The anticancer assay showed impressive results against HepG2 (Liver) cancer cell line as compounds 1a,2a,3a,4b,5d & 1c were more potent than the standard f-fluorouracil (IC_{50} = 1745.1 µM) with IC_{50} values between 813.7-1699.1 µM.

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P14: Synthesis of sulfonylthioureas containing two carbon linker as potential antidiabetic drugs

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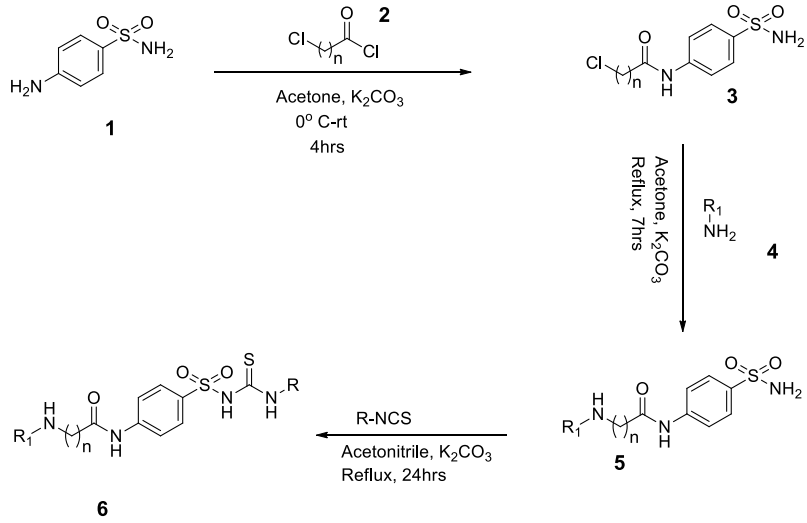
Keywords: Alpha-amylase, Alpha-glucosidase, Antidiabetic drugs, Sulfonylthiourea.

Diabetes is a metabolic disease that occurs when there is a deficiency in insulin production or no insulin in the pancreas.[1] It is estimated that the number of people affected by diabetes will rise to 700 million by 2045, leading the World Health Organization to consider diabetes an epidemic.[2] Diabetes imposes a significant financial burden on the public healthcare in South Africa. The purpose of this project was to synthesize a series of sulfonylthioureas as antidiabetic drugs by converting a urea to thiourea moiety. The novel sulfonylthiourea were designed and synthesized over three reaction steps using different appropriate synthetic methods (**Scheme 1**). The successfully synthesized final compounds will be probed for their activity against alpha-glucosidase and alpha-amylase to analyse if they can work as antidiabetic medications.



where R= phenyl,cyclohexyl,butyl,propyl
R_1= Morpholine, Aniline, N-Methylaniline, 2,6-N-Methylaniline
n = 1 or 2

Scheme 1: Synthetic scheme.

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P15: The synthesis and anticancer activity of new quinolone phenylhydrazone hybrids

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Keywords: quinolone, phenylhydrazone, hybrid, antibacterial, anticancer

Owing to the variety of biological activities exhibited by the quinolone[1,2] and phenylhydrazone[3] moieties, it was hypothesized that the combination of these moieties via hybridization would result in the formation of a hybrid compound with enhanced biological activity[4]. Thus, fourteen quinolone phenylhydrazone hybrid compounds (thirteen new and one known) were synthesized via a four-step synthetic route which involved acetylation of differently substituted anilines, followed by the Vilsmeier-Haack reaction, then *o*-nucleophilic substitution, and finally nucleophilic addition. The structures of the final compounds were then confirmed using NMR, FTIR, UV-Vis, and HRMS spectroscopy as well as CHN elemental analysis. The anticancer activity of the final compounds and the quinolone intermediate compounds was evaluated. Compound 5m was identified as a potential anticancer agent as it was the least active against non-cancerous human embryonic kidney (HEK293) cells (IC_{50} = 64.57 µg/100 µL) and showed good activity against liver cancer (HepG2) cells (36.31 µg/100 µL).

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P16: The *in vitro* antioxidant and antidiabetic potential of South African medicinal plant species *(Rhoicissus rhomboidea, Rhoicissus capensis* and *Cyphostemma Auriculatum*)

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Keywords: Antioxidant activity, antidiabetic activity, *Rhoicissus* species.

Diabetes is currently one of the global epidemics closely associated with oxidative stress. Reports indicate that more than 536 million people are living with diabetes, and this number is expected to exceed 783 million by 2045. The existing medications for this condition are known to cause various adverse effects. As a result, researchers are investigating medicinal plants as potential alternatives for diabetes treatment. This study investigates the antioxidant and antidiabetic potential of both crude extracts and pure compounds isolated from South African medicinal plants belonging to the genera, *Rhoicissus* and *Cyphostemma*. Chromatographic purification of the roots and leaves of *R. rhomboidea*, *R. capensis*, and *C. auriculatum* led to the isolation of several flavonoids, triterpenoids and some pigment compounds. The structures of the compounds were identified using NMR, UV/Vis, IR, and mass spectrometry. To assess antioxidant activity, the crude leaf and root extracts were evaluated against 1,1-diphenyl-2-picrylhydrazyl (DPPH), ferric reducing antioxidant power (FRAP), and 2,2′-Azino-bis(3-ethylbenzthiazoline-6-sulfonate (ABTS). The *in vitro* antidiabetic properties of the extracts were assessed by evaluating the inhibition of alpha-amylase and alpha-glucosidase enzymes. All crude methanol extracts demonstrated notable antioxidant and antidiabetic activity when compared to the positive controls (Acarbose and butylated hydroxytoluene). It is worth mentioning that the isolated flavonoids have been previously reported in literature for their potential antidiabetic effects. The results provide potential validation for the utilization of these plants in traditional medicine for the treatment and management of diabetes.

P17: Extraction and isolation of alkaloids from the plant *Cissampelos capensis* L. f. with anticancer properties

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Keywords: *Cissampelos capensis*, extracts, alkaloids.

Cancer has become a world health crisis, affecting millions of people globally. Particularly, it has become a cause of concern for South Africa. However, various medicinal plants have been used for the management of cancer. *Cissampelos capensis* L. f. is an example of such a plant, which traditional practitioners have used to manage cancer in the Eastern Cape.[1, 2]

C. capensis is attributed to a rich diversity of alkaloids.[3] This has been proven by isolating the active compounds with potential use for medicinal purposes.[2] Traditional healers still make use of *C. capensis* to aid various ailments, as it is readily available and a cheaper alternative compared to over-the-counter anticancer medications.[1]

The study, therefore, focused on the methanol:chloroform, methanol, ethanol, total tertiary alkaloid and the aporphine alkaloid extracts of the *C. capensis* rhizomes for the qualitative and quantitative chemical analysis. LCMS and HPTLC were used for the tentative identification and detection of alkaloids in the crude material. The isolated compounds were purified by preparative thin-layer chromatography and characterised using FTIR, NMR and HRMS, spectroscopic and spectrometry techniques. Lastly, the anticancer activity of *C. capensis* will also be presented at this conference.

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P18: Design and Synthesis of SWIR Probes for Bioimaging

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Presented By: Emmanuel Ankomah
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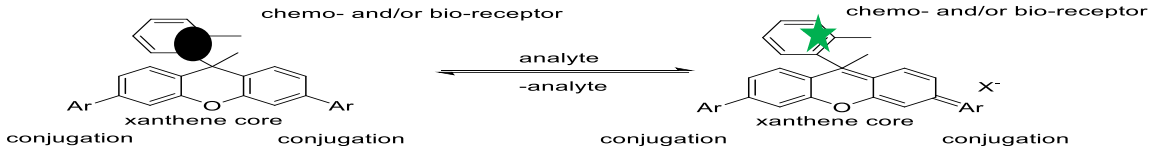
Keywords: SWIR Probes, Bioimaging

The development of shortwave infrared (SWIR) emission probes has been a huge advancement in the field of biological sensing and imaging due to their long absorption and emission wavelengths. These SWIR emission probes offer several advantages; the SWIR light enables deep tissue penetration, reduced background fluorescence, and cause minimal cellular damage. The xanthene-based dyes, fluorescein, and rhodamine, have their own unique structural and photophysical properties that enable them to be used as biosensors, but not in deep tissue. Their absorption and emission wavelengths lie within the range of the background fluorescence of biological samples, resulting in low resolution. It has become essential to develop SWIR emission probes based on xanthene dyes for application in deep tissue.

Research in the Scott group designs and synthesizes novel SWIR xanthene-based dyes for advancement in the field of biological sensing and imaging. The modification of the acceptor xanthene core with various conjugated donor molecules is a key aspect of our approach to lower the bandgap of the dyes. By using triflated or brominated xanthene cores as substrates and reacting them with different conjugated donor molecules, we have developed SWIR probes with molecular switching mechanisms. Interestingly, we have discovered that the direct arylation reaction is essential in the synthesis of our dyes. One notable advantage of these probes is their strong photoacoustic signal, which can be useful in imaging techniques, since they do not have good emission properties. Additionally, their biological compatibility and photostability make them suitable for long-term imaging and sensing applications.

By combining the structural and photophysical properties of xanthene-based dyes with the benefits of SWIR emission, work in our research group contributes to the development of improved analytical techniques for detecting and monitoring important analytes in biological systems. These advancements have the potential to enhance our understanding of metabolic processes and enable more precise and sensitive biological sensing and imaging.



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P19: THE PHYTOCHEMISTRY AND CYTOTOXIC ACTIVITY OF *DRIMIA ALTISSIMA* EXTRACTS

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Lung cancer (LC) and colorectal cancer (CRC) are currently the leading causes of cancer deaths globally.[1] Literature suggests chemotherapy is first line treatment and management LC and CRC.[2 – 5.] This method is associated with many disadvantages including undesirable side effects, limited efficacy, severe toxicity which results in limited survival benefit, and multidrug resistance.[4] On this regard, traditional medicines such as *Drimia species* have been recognized and recommended as an attractive approach for the treatment of cancer,[7,8,9] preventing side effects andimproving the quality of life in cancer patients.[6]

Organic extracts of *D. altissima* were phytochemically studied by chromatographic (TLC, pTLC, HPLC, HPTLC, FTIR) and spectroscopic methods (NMR and FTIR). Chromatographic techniques were also employed for isolation, identification, and purification of active constituents, whereas spectroscopic methods were utilized for identification of present compound functional groups and structural elucidation.

Biological evaluation was performed against human adenocarcinoma cell lines: LC (A549) and CRC (CaCO-2 and HT-29), using melphalan as the positive control. From the results, the test samples exhibited significant cytotoxicity at all tested concentrations in all 3 cell lines. Exhibiting increased cytotoxicity in A459 cells (< 20% cell viability), followed by HT-29 (< 40% cell viability) and Caco-2 cells (< 60% cell viability).

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P20: An efficient and facile microwave assisted synthesis of 2-amino-3-carbonitrile 4*H*-chromene based analogues.

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Keywords: chromenes, microwave assisted synthesis

Compounds comprising of chromene scaffolds has been extensively explored in drug discovery over the past decades[1]. This is due to their display of a broad spectrum of pharmacological and biological activities such as anticancer, antioxidant, anti-microbial and antitubercular amongst others[1,2,3]. Their low toxicity and versatility, combined to the broad pharmacological properties continues to inspire medicinal chemists in the search for new therapeutic agents. In this study, a small library consisting of six 2-amino-4-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**a-f**), six 2-amino-4-aryl-8,8-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile ***(*g-l**) and six 2-amino-4-aryl-7-methyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile ***(*n-r**), was synthesised via a multicomponent microwave radiation. Excellent yields (82-94%) were obtained in 5 min by using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in catalytic amounts.

^{1}H NMR spectroscopy revealed intriguing results in respect to the splitting patterns of methylene signals for (**g-r**) compounds, due to long range coupling effect and possible flipping of the cyclohexane ring. Moreover, FT-IR spectra showed three diagnostic absorption bands resonating at 3400-3100 cm^{-1} region, attributed to the asymmetric, symmetric and bending overtone vibration modes NH_2 functionality. Single crystal structures of **c, e, f**,**g, h, n, o, p,k** and **l** were grown and exhibited a wide spectrum of intermolecular hydrogen bonding motifs. Compounds **c, p, o** crystalized in $P2_1/c$ and **e** in P-1, while (**h, g, n**) and (**f, k, l**) crystalized in $P2_1/n$ and C2/c space groups respectively.

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P21: Using computational techniques to uncover new insights into the squalene monooxygenase inhibitors for lowering cholesterol in cardiovascular biology.

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Keywords: high cholesterol; squalene monooxygenase inhibitors; Terbinafine; high throughput virtual screening: molecular dynamics simulations.

Over the past decades, drugs called statins have been used in lowering high cholesterol, unfortunately, several studies show that people who are taking statins experience the side effects, especially in elderly patients, women of child birthing possibility, and children [1]. For this reason, we conducted *in-silico* investigations into the squalene monooxygenase (SM) inhibitors that can potentially lower cholesterol in cardiovascular biology [2]. In this framework, we have performed molecular docking calculations, Molecular dynamics (MD) simulations, molecular mechanics-generalized born surface area (MM-GBSA), and Quantum mechanics/molecular mechanics calculations (QM/MM). From a theoretical perspective, the results obtained from docking indicate that the antimycotic ligand good binding affinities of -8,4 kcal/mol towards cholesterol target protein PDB ID 2ZCS in comparison to other compounds, MM-GBSA was used to investigate the binding free energies for the protein-ligand complexes . MD results indicate that the stability of the ligand in the binding pocket was achieved during the 100 ns simulations. The HOMO-LUMO energy gaps obtained from DFT calculations provided information about the reactivity of the ligands [3]. Other insights of the protein-ligand complexes were obtained from a hybrid ONIOM QM/MM study. Our discoveries suggest that antimycotic SM inhibitors, Terbinafine and its derivatives, and anticholesterolemic SM inhibitors have the potential to be used as alternative and safer remedies for lowering cholesterol in the future and need to be validated by experimental methods.

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P22: Synthesis and Antibacterial Activity of Quinoline-3-carboxamide derivatives

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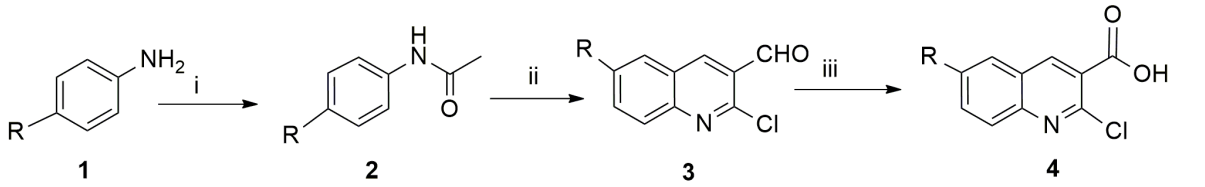
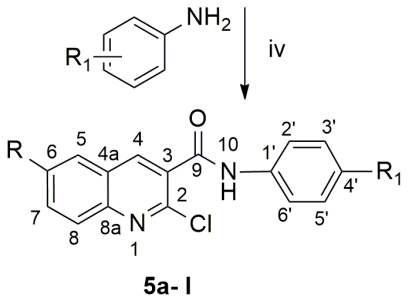
Keywords*:* quinoline-3-carboxamide, Vilsmeier-Haack, antibacterial

Twelve new substituted 2-chloroquinoline-3-carboxamide derivatives were synthesized from acetanilides using the Vilsmeier-Haack reaction, producing 2-chloro-3-carbaldehyde quinolones. This was followed by oxidation of the 3-carbaldehyde to the carboxylic acid and coupling this group with differently substituted anilines. Confirmation of the structures of the final compounds was done by NMR analysis, mass spectrometry and single crystal XRD. The chemical shifts of H-5 and H-8 were affected by the substituent at C-6. This substituent also influenced the chemical shift of C-5, C-7 and C-8, with C-5 and C-7 being more shielded in **5j** (F substituted) in comparison to **5g** (Cl substituted) and **5d** (CH_3 substituted). The compounds showed weak activity in the mM range against Gram +ve and -ve bacteria of which **5b**, **5d** and **5f** showed the best activity with MBC values for **5b** being 3.79 mM against MRSA and **5d** and **5f** having MBC values of 3.77 and 1.79 mM against *S. aureus* ATCC 25923 respectively.



	R	R_1		R	R_1
5a	H	H	**5g**	Cl	H
5b	H	CH_3	**5h**	Cl	CH_3
5c	H	F	**5i**	Cl	F
5d	CH_3	H	**5j**	F	H
5e	CH_3	CH_3	**5k**	F	CH_3
5f	CH_3	F	**5l**	F	F



5a- l

Scheme Error! No text of specified style in document.**.1** Synthetic route to 2-chloroquinoline-3-carboxamides **5a-l**; i acetic anyhdride, acetic acid; 1 h; ii DMF, $POCl_3$, 82°C, reflux 24 h; iii $NaClO_2$, $NaH_2PO_4.2H_2O$, butan-1-ol, r.t., 2 h; iv EDC, Et_3N, HOBt, DMF, r.t., 24 h.

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P23: Synthesis of imidazo [1,2-a]pyridine and pyrazolo [1,5-a]pyridine derivatives as potential kinase inhibitors of *Plasmodium falciparum* parasite.

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Keywords : Malaria, protozoan, *plasmodium falciparum*, kinases, *Pv*PI4k, *Pf*PKG, imidazo [1,2-a]pyridine and pyrazolo [1,5-a]pyridine.

Malaria is a disease that impacts negatively on the global health status and contributes more to mortality rate in the less developed countries [1]. The diseases arise from the protozoan parasite of genus *Plasmodium* [2]. *Plasmodium* kinases have been found to be important in facilitating several critical stages in the parasite lifecycle [2]. Targeting and inhibiting the activities of the enzymes implicated in the pathogenesis and/or progression of malaria such as *Pv*PI4K and *Pf*PKG [3] represent the most effective therapeutic strategy for the treatment of this disease. A series of Imidazopyridines [4] , pyrazole [5] exhibit a wide range of pharmacological properties of antimalarial activities. Considering the therapeutic potential of imidazo [1,2-a]pyridine and pyrazolo [1,5-a]pyridine against malaria, a series of novel imidazo [1,2-a]pyridine and pyrazolo [1,5-a]pyridine derivatives have been synthesised and evaluated for their activity as potential kinase inhibitors (*Pv*PI4K and *Pf*PKG) of *plasmodium falciparum* parasite.

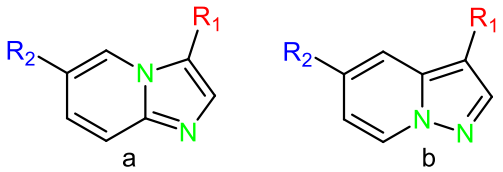

Figure 1**a** and 1**b**: Imidazo [1,2-a]pyridine and Pyrazolo [1,5-a]pyridine scaffolds respectively.

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P24: High throughput virtual screening of aptamers as anticancer therapeutics against oncogenic MiRNAs

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Keywords: microRNA, aptamers, molecular modelling, High throughput virtual screening and SELEX

According to the World Health Organization, cardiovascular complications and cancer are recognized as the highest leading causes of death [1-2]. Cancer is caused by abnormal cells that refuses to through the apoptosis process [3]. MicroRNAs are small, highly conserved non-coding RNAs, involved in gene expression. MicroRNAs have been reported to be involved in the development of cardiovascular complications and cancer [4]. MicroRNAs assembles into RISC (RNA-induced silencing complex), which activates the complex that targets the messenger RNA. miRNAs regulate their targets by translational inhibition and mRNA destabilization [5]. For this reason, miRNA can be classified as oncogenic or tumor suppressor. Oncogenic miRNA have recently been labelled as a target for inhibitors. In this study, we propose rational drug designing of aptamers (synthetic RNAs, synthesized using combinatorial synthetic method), which involve high throughput virtual screening and optimization of aptamers. The tools that can be used to screen such large library of macro-molecules were not available, hence we developed our novel tool called T_SELEX program which is a Theoretical automated **Systematic Evolution of Ligands by EXponential enrichment** (**SELEX**) python package/software. This tool is used to overcome the challenge of modelling of large library of macromolecules which includes prediction of RNA secondary structures, RNA 3D structure predictions, RNA-RNA interactions predictions and molecular docking.

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P25: SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF BENZIMIDAZOLE-1,2,3-TRIAZOLE-QUINOLINE MOLECULAR HYBRIDS AS POTENTIAL ANTITUBERCULAR

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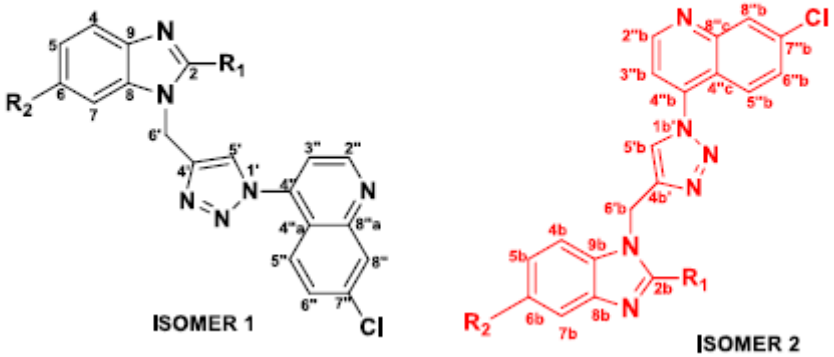
Keywords: 16th Frank Warren, Abstract, Conference.

Tuberculosis (TB) caused by Mycobacterium *Tuberculosis* (*Mtb*) is still a significant threat to human health, with millions infected and hundreds of thousands losing their lives yearly, particularly in developing countries such as South Africa. Compounding this is the issue of drug and multi-drug resistance. For this reason, there is a growing need and urgency to discover new classes of chemical compounds that will exhibit a different mechanism of action (MOA) from those currently used. A quinoline moiety has been considered an excellent pharmacophore for the design of anti-TB drugs based on the outstanding outcomes exhibited by bedaquiline, in the treatment of multidrug-resistant TB. Furthermore, the benzimidazole moiety has also been shown to possess excellent anti-TB activity. This research adopted the molecular hybridization strategy to design new antimycobacterial agents. In a four-step synthetic protocol, a series of eleven (11) new benzimidazole-triazole-chloroquinoline hybrids were successfully synthesized in 55 - 80% yields as mixtures of inseparable isomers. These compounds were fully elucidated by FT-IR and NMR (1D, 2D), and their masses confirmed by HR-MS. As isomeric mixtures, these hybrids were further evaluated for their antimycobacterial activity against the H37Rv strain of *Mycobacterial tuberculosis*, and a selected number of front-runner compounds were further screened for cytotoxicity. All the synthesized hybrid compounds showed excellent activity (MIC90: 1.07 - 8.66 µM), better than the first-line drug, ethambutol (MIC90 = 9.54µM). Compound **7d** with MIC90 value of 2.08 µM , CC50 0.27 µM and 149.50% cell viability was identified as the most promising compound.



P26: Virtual screening, molecular docking studies and DFT calculations of FDA approved compounds similar to the nonnucleoside reverse transcriptase inhibitor (NNRTI) efavirenz

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Nkululeko Damoyi, Michael Shapi

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Keywords: Pharmaceutical chemistry, Theoretical chemistry, COVID-19, NNRTI, Virtual screening Efavirenz, HIV.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was confirmed as the causative virus of COVID-19 disease, which is currently a worldwide pandemic. Efavirenz, a non-nucleoside reverse transcriptase inhibitor (NNRTI), is one of the most potent chemical compounds proposed to treat COVID-19 infection. We, therefore, performed virtual screening on FDA approved drugs that are similar to the efavirenz moiety. Subsequently, the compounds were subjected to screening by analyzing their drug-likeness, such as Lipinski's rule of five and ADMET properties. Molecular docking study revealed that Met165, His41, His163, and Phe140 were important interacting residues for COVID-19 main protease receptor-ligand interaction. Five top-ranked compounds, podophyllotoxin, oxacillin, lovastatin, simvastatin, and gefitinib, were selected by virtual screening and docking studies. The highest occupied molecular (HOMO) orbital, lowest unoccupied molecular orbital (LUMO) and energy gap values was calculated using density functional theory (DFT). The results of the study showed that lovastatin and simvastatin might be considered as lead compounds for further development for COVID-19 main protease inhibitors.[1]

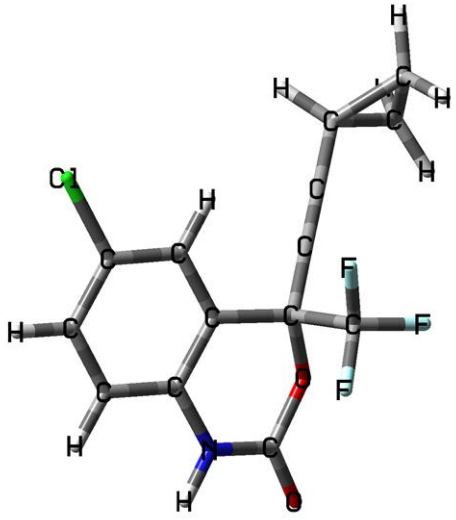

Figure 1: Optimized structure of efavirenz.

Jordaan MA, Ebenezer O, Damoyi N, Shapi M. Virtual screening, molecular docking studies and DFT calculations of FDA approved compounds similar to the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz. Heliyon. 2020 Aug 11;6(8):e04642.

P27: The design and synthesis of quinoline-urea-benzothiazole hybrid compounds as antitubercular agents

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Keywords: benzothiazole, quinoline, urea, hybridization.

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*Mtb*), is an ancient illness that has plagued humanity for over a century[1]. Currently, almost one-third of the world's population is infected with *Mtb*, and 1.5 million people die each year from the disease. *Mtb* drug resistant to currently available drugs surpass research and development of new TB treatments[2]. As a result, there is an urgent need to develop extremely powerful innovative medications with a different mechanism of action compared to the existing drug arsenal, which is becoming less effective.

A small library of Quinolin-urea-benzothiazole hybrids (depicted in figure 1) were designed and tested for their anti-TB activities. These compounds were successfully synthesized in yields ranging from 50-90% using a three-step synthetic process. Their structures confirmed by 1- and 2-DNMR, FTIR, and their masses were validated by high resolution-mass spectrometry (HRMS). A number of these compounds showed promising MIC_{90} activities against H37Rv *Mtb* strain and also showed appreciable cytotoxicity.[3]

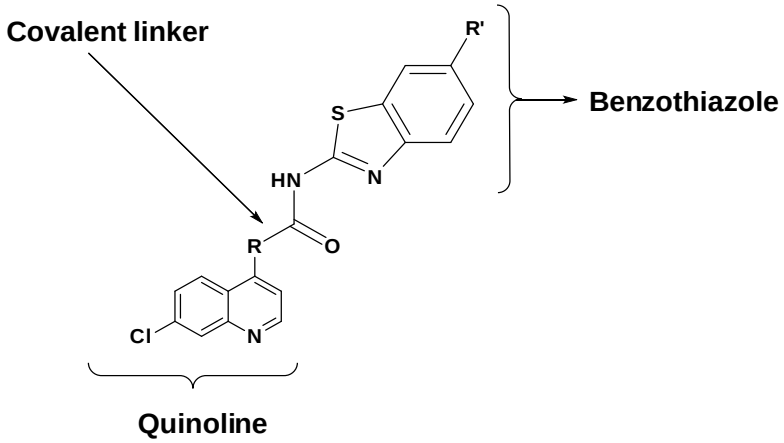

Figure 1: the targeted Quinoline-urea-benzothiazole hybrid

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P28: Cholesterol Dynamics in Cardiovascular Disease: A Computational Study on Lipid behaviour within Biological Systems

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Keywords: Cholesterol, Computational study, Cardiovascular disease, Lipid dynamics.

In this computational study, sophisticated molecular modeling and simulation techniques were employed to explore the intricate dynamics of cholesterol molecules within biological systems [1, 2]. Cholesterol's pivotal role in membrane structure and cellular function, closely associated with various diseases, particularly cardiovascular disorders, was investigated. Through comprehensive computational analyses, the interactions, transport mechanisms, and spatial distribution of cholesterol within lipid bilayers and cellular environments were scrutinized. The study aimed to unravel the molecular intricacies governing cholesterol's behavior and its influence on membrane properties, shedding light on the physiological and pathological implications of cholesterol within living systems. The insights gained from this computational study had the potential to inform therapeutic strategies targeting cholesterol-related disorders and advance the fundamental understanding of lipid biology.

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P29: Exploring the Impact of Alkyl Chains on the Photochromic Behaviour and Liquid Crystallinity of Azobenzene Compounds

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Keywords: Azobenzene, Liquid Crystals, Photochromic effect.

Azobenzene-based compounds have garnered significant attention in recent years due to their remarkable photochromic properties and potential applications in advanced materials[1]. This study investigates how the addition of alkyl chains influences the photochromic behaviour and liquid crystalline properties of azobenzene derivatives. By systematically varying the length and structure of alkyl chains attached to the azobenzene core, we aimed to elucidate the structure-property relationships governing these intriguing molecules. Ethyl 4-aminobenzoate was coupled with phenol in the presence of sodium nitrate to produce ethyl 4-[(E)-(4-hydroxyphenyl) diazenyl] benzoate which was condensed with appropriate bromo-alkyl chain to form ethyl 4-[(E)-(4-alkylphenyl) diazenyl] benzoate which was then reduced to form the desired product 4-[(E)-(4-alkylphenyl) diazenyl benzoic acid. The structures were characterized by means of NMR and IR, UV-vis spectroscopy, DSC, and POM. Our findings reveal a complex interplay between the alkyl chain length, photochromic efficiency, and liquid crystalline phase transitions. We observed that longer alkyl chains tend to enhance the stability of the *cis* isomer, resulting in prolonged photochromic lifetimes. Furthermore, the presence of alkyl chains influenced the phase transition temperatures, leading to variations in liquid crystalline behavior.

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P30: Method development, validation, and oral acute toxicity of a quinoline-benzothiazole hybrid compound

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Keywords: LC-MS/MS, preclinical, chromatography, mass analysis

A quinoline-benzathiozole hybrid compound was found (Figure 1) to display antimicrobial activity *in vitro* (Moodley et al., 2022). A LC-MS/MS method for analysis of this compound in plasma was developed and validated to determine the pharmacokinetic parameters in rats. The method development included a recovery study evaluating different sample preparation methods and a column study. Protein precipitation was found to be the method that produced the highest recoveries, and a polar C-18 column was found to have the highest column efficiency. Method validation was performed according to the European Medicines Agency guideline for bioanalytical validation. The accuracy, precision, matrix effects, specificity, stability, and dilution integrity validation parameters all fell within the acceptable statistical values stipulated by this validation guide. An oral acute toxicity study was performed at 100 mg/kg to determine the safety dosage that could be used during the pharmacokinetic study. This concentration was deemed to be safe since no animals died after the 14-day evaluation period. Therefore, this compound could be used in a future pharmacokinetic study.

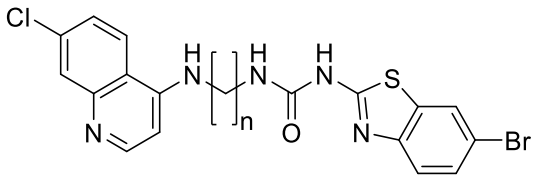

Figure 1: Structure of quinoline-benzathiozole where n=3

Acknowledgements
NRF for funding
Dr Matshawandile Tukulula

1. World Malaria Report 2021. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.
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P31: Synthesis of novel 6, 8-disubsituted-chromone-3-carboxylic acid derivatives

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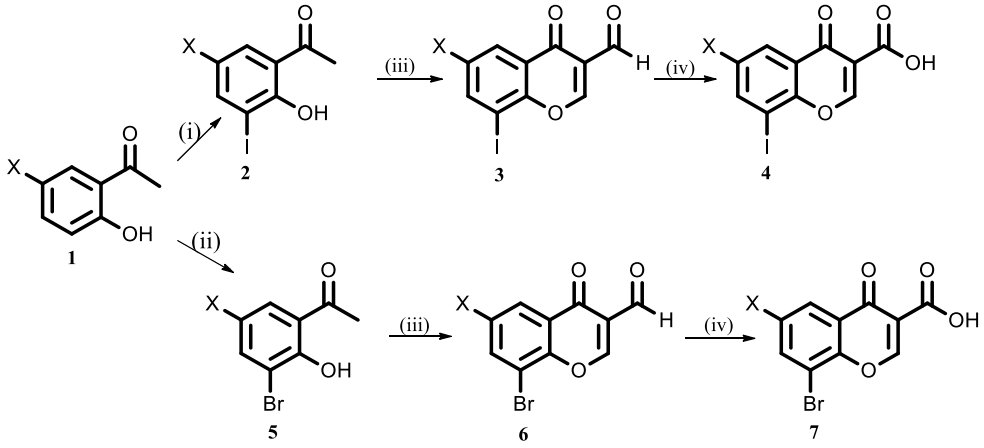
Keywords: Chromones, Synthesis, Chromone-3-carboxylic acids

Chromone consists of a substituted keto group on the pyran ring and a benzopyran ring structure fused together.[1] They are found in the chemical structure of flavonoids, a class of naturally occurring compounds that are currently of interest because of their biological activity and classified as prevailed structure for the development of novel pharmacologically interesting compounds in drug discovery.[2] The current studies shows that chromones have various range of pharmacological applications such as anti-cancer agents, anti-HIV agents, anti-tuberculosis agents,and many others.[3] In this project, novel 6,8-disubstituted chromone-3-carboxylic acid derivatives were synthesized, characterized by (^{1}H and ^{13}C) NMR and FTIR spectroscopies. The scheme 1 below shows the synthetic route of the presentation.



Scheme 1: Reagents and conditions: (i) NIS,AcOH, reflux,2h (ii) NBS, MeOH ,rt ,3h (iii) DMF-POCl3, rt, 12h (iv) NaClO2, Sulfamic acid, rt, 24h

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P32: Green synthesis of silver nanoparticles mediated *dacryodes edulis* stem bark for the treatment of the SARS-COV-2.

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BACKGROUND AND OBJECTIVES: The Covid-19 pandemic caused by SARS-CoV-2 has led to serious economic damage, burdening the healthcare systems, and depriving millions of people of their livelihoods. The need for effective antiviral medicines with multifunctional, target-specific, and nontoxic properties during the Covid-19 pandemic highlighted the importance of drug discovery. The aim of the study was to green synthesize silver nanoparticles (AgNPs) using *Dacryodes edulis* stem bark water extract for the treatment of SARS-CoV-2.

METHODS: Different parameters like temperature, time, silver nitrate concentration and concentration of the stem bark extract were optimized to determine the best possible reaction conditions for the synthesis of AgNPs. Various characterization techniques were employed such as; UV-vis, TEM, SEM, DLS particle wave analyzer, FTIR and EDX.

RESULTS: The synthesized AgNPs in solution have shown maximum absorption between 430 - 460 nm. Micrographs from the TEM confirmed the nanoparticle sizes ranged from 10 to 90 nm; the image showed a quasi-spherical to spherical shape. Studies of SEM micrographs showed that the nanoparticles have a non-smooth yet spherical form. The PDI values of the synthesized AgNPs ranged from 0,0383 to 0,807, the zeta potential ranged between -19,5 to 0,3 mV. The Fourier-Transform Infrared (FTIR) Spectroscopy was used to confirm the existence of various functional groups responsible for reducing and stabilizing during the biosynthesis process. The results from EDX confirmed the presence of Ag in the sample.

CONCLUSION: The developed method for the AgNPs synthesis using *D. edulis* is an eco-friendly and non-toxic nanodrug delivery system. The results of the AgNP synthesis indicate that silver is a promising therapeutic agent because of its small size and shape. Further studies should be done on the encapsulation and delivery of AgNPs.

P33: Synthesis and Characterization of Perylene Tetracarboxylic Bisimide Derivatives for Advanced Solar Energy Harvesting

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Keywords: PTCBI, solar energy, harvest, optical, electronic, thermal.

The demand for efficient and sustainable solar energy conversion technologies continues to drive innovation in material science. Perylene tetracarboxylic bisimide (PTCBI) derivatives have emerged as promising candidates for their exceptional optoelectronic properties and tunable molecular structures.[1,2] This study explores the synthesis and in-depth characterization of two PTCBI derivatives varying in alkyl chains, where n= 4 & 8, with a specific focus on their applicability in high-performance solar energy harvesting applications.

The characterization of these materials involves a comprehensive study of their optical, electronic, and thermal properties. UV-vis spectroscopy was employed to assess the absorption spectra for their potential for light harvesting. Thermogravimetric analysis (TGA) was used to investigate their thermal stability which is critical for optimizing their performance in energy harvesting applications. Density functional theory (DFT) calculations and molecular dynamic simulations provided valuable information on the intermolecular interactions and the potential for efficient charge separation and transport.

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P34: Synthesis of ulopterol and meranzin hydrate and their analogues as potential antibacterial agents.

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Keywords: Antibactial agents, coumarins, meranzin hydrate, *Muraya paniculata* and *Murraya exotica*

Coumarins and their derivatives have been investigated and show suitable biological activities against the anti-inflammatory, anti-cancer, antimicrobial, etc.[1] Ulopterol and meranzin hydrate are active coumarin derivatives with a broad spectrum of pharmacological properties, making them excellent antibacterial, antidepressant, anticoagulant, and anti-atherosclerosis agents.[2] From the consulted literature, ulopterol can be found on the leaves of *Toddalia asiatica*[3] and the fruit and roots of *Prangos uloptera* DC[4]. Meranzin hydrate has been isolated from *Muraya paniculata* and *Murraya exotica*.[2,5] This project targets the total enantioselective synthesis of these two natural products, ulopterol (**1**) and Meranzin hydrate (**2**), and their analogues as potential antibacterial agents (**figure 1**).

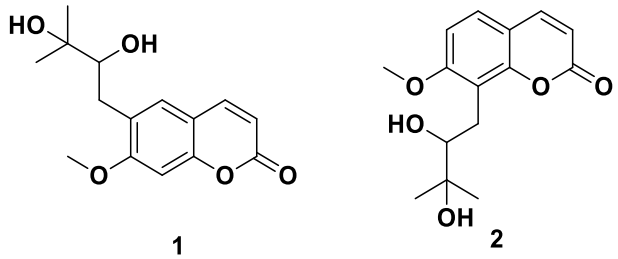

Figure 1. Chemical structures of ulopterol (**1**) and meranzin hydrate (**2**).
Keywords: coumarins, ulopterol, meranzin hydrate, antibacterial activity

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P35: Design, synthesis, and molecular modelling of aryl substituted 2-(4-(sulfonyl) styryl)quinazolin-4(3*H*)-ones as potential anticancer agents.

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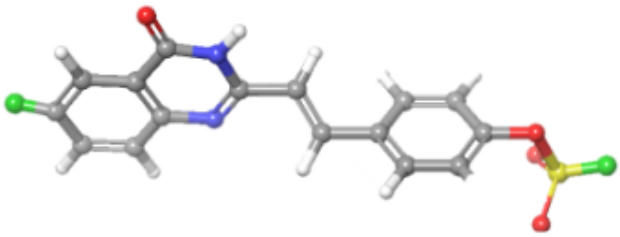
Keywords: Quinazolinone, 2-(4-(sulfonyl)styryl)quinazolin-4(3*H*)-one

Cancer encompasses a wide range of diseases characterized by irregular cellular proliferation that can infiltrate various areas of the body, breaking down and disrupting normal tissue and organ functioning[i]. The current available drugs are compromised by numerous side effects and development of resistance[ii]. In this study, we aim to synthesize styryl-dihydroquinazolinone[iii] derivatives for biological evaluation against cancer.

The target compounds were achieved through reaction of iodination of 2-aminobenzamide to yield 5-iodo-2-aminobenzamide, followed by a nucleophilic substitution acetylation reaction, resulting in 2-aceto-5-iodobenzamide. The resulting product underwent cyclization under reflux conditions forming 2-methylquinazolin-(3*H*)-one. Salicylaldehydes were sulphonated to afford four intermediate derivatives, that were subsequently reacted with 2-methylquinazolin-4(3*H*)-one to afford sulfonyl styrylquinazolin-4(3*H*)-ones through condensation reaction under reflux conditions. Application of Suzuki coupling reaction using six different boronic acids under inert conditions afforded novel 6-aryl (2-(4-(sulfonyl)styryl)quinazolin-4(3*H*)-one derivatives. Synthesized compounds were characterized using a nuclear magnetic resonance (^{1}H and ^{13}C-NMR), infrared spectroscopy (IR), and mass spectrometry (MS) techniques, computational and biological studies.



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P36: Design and synthesis of quinoline-pyrimidine inspired hybrids as potential plasmodial inhibitors

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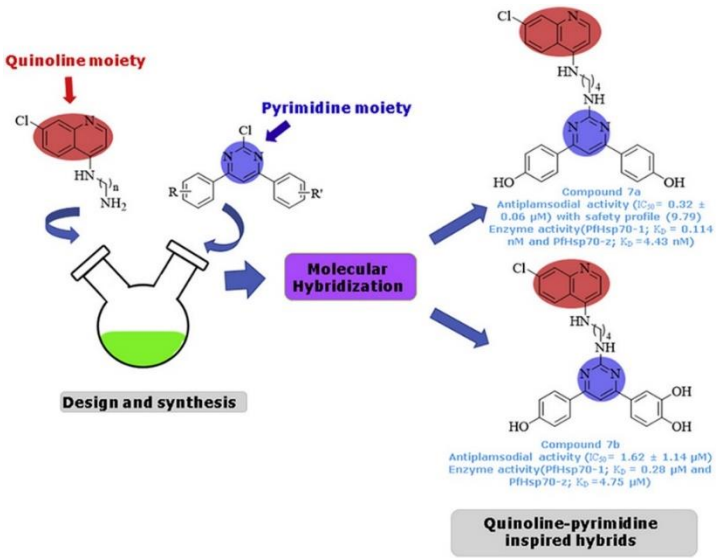
Keywords: Quinoline, Pyrimidine, Antimalarial agents, *Plasmodium falciparum.*

Presently, artemisinin-based combination therapy (ACT) is the first-line therapy of *Plasmodium falciparum* malaria[1-4]. With the emergence of malaria parasites that are resistant to ACT, alternative antimalarial therapies are urgently needed. In line with this, we designed and synthesised a series of novel N-(7-chloroquinolin-4-yl)-N'-(4,6-diphenylpyrimidin-2-yl)alkanediamine hybrids **(6a-7c)** and evaluated their inhibitory activity against the NF54 chloroquine-susceptible strain as a promising class of antimalarial compounds. The antiplasmodial screening revealed that seven analogues showed promising to good activity with half-maximal inhibitory concentration (IC_{50}) = 0.32 µM-4.30 µM. Compound **7a** with 1,4-diamine butyl linker and 4-hydroxyl phenyl on fourth and sixth position of pyrimidine core showed the most prominent activity with an IC_{50} value of 0.32 ± 0.06 µM, with a favourable safety profile of 9.79 to human kidney epithelial (HEK293) cells. We further investigated the binding affinities of the molecules to two essential cytosolic *P. falciparum* heat shock protein 70 homologues; PfHsp70-1 and PfHsp70-z. Compound **7a** exhibited the highest binding affinity for both PfHsp70s with K_D in a lower nanomolar range (4.4-11.4 nM). Therefore, we speculate that PfHsp70-1 is one of the targets of these inhibitors. The bioisoteric replacement of the groups at phenyl ring at the fourth and sixth position of the pyrimidine core had a constructive association with antiplasmodial activity.

Graphical Abstract:



P37: Safety-Catch Protecting Group Scheme for Solid-Phase Peptide Synthesis

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Keywords: Solid-phase peptide, safe-catch, Leu-enkephalin amide, Mtbh

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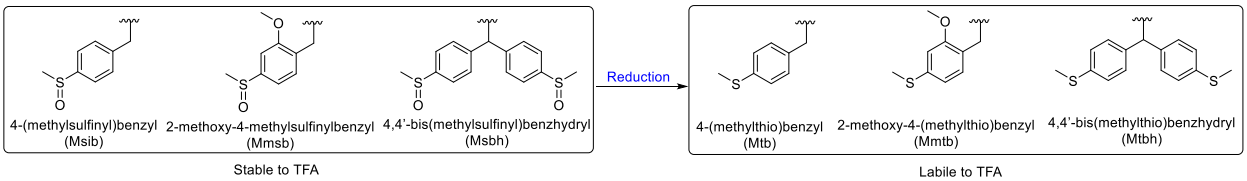
In the field of solid-phase peptide synthesis (SPPS), the challenge of synthesizing difficult peptides can be achieved with innovative solutions using safety catch protecting groups and safety-catch linkers. These chemical species, stable under acidic conditions, can be activated into acid labile forms either chemically or photochemically. Our research hunts into this domain, focusing on peptide safety catch protected methodologies. In this search, we successfully synthesized a range of amino acids (AAs) – Tyrosine, Serine, Threonine, Glutamic acid, Aspartic acid, and Lysine – protected with Msbh, Msib, and Msz groups [Fmoc-AA(Msbh/Msib/Msz)-OH]. Our investigations began by studying the reactivity of the sulfide-reduced form of Msbh, Mtbh, which exhibited notable reactivity with amino acid hydroxy groups. The resulting attachment with Mtbh led to the oxidation of protected amino acids to Msbh protected AAs. Comparatively, Mtb and Mtz groups showed higher reactivity than their Msib and Msz counterparts. Upon conducting several experiments on stability and lability towards TFA (up to 95%), deprotection was not observed. These protecting groups are stable to acidic conditions due to the presence of the sulfoxide groups in their chemical structures. Using these newly protected AAs, we synthesized Leu-enkephalin amide analog peptides. Cleavage from the resin was achieved using a TFA-triisopropylsilane (TIS)-H_2O cocktail, resulting in peptides with acceptable purity as confirmed by HPLC and LCMS analyses. The absence of completely unprotected peptides highlighted the sulfinyl group's stability to TFA. The subsequent removal of the sulfonyl protecting group followed a two-step process: sulfoxide to sulfide reduction involved consecutive treatments with Me_3SiCl (20 eq.)-Ph_3P (10 eq.) in THF for 1 h, followed by the cleavage step as previously described. This new concept of protecting groups may potentially facilitate the synthesis and manipulation of difficult peptides. Furthermore, the synthetic steps for the amino acid-Msbh, Msib, and Msz protected can be scaled up and made commercially available for further use in the synthesis of difficult peptides.



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P38: Identification and SAR evaluation of β-haematin inhibiting coumarins active against chloroquine-resistant *Plasmodium falciparum*

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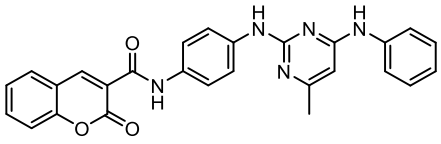
Keywords: *Plasmodium falciparum*, haemozoin inhibition, coumarin

Plasmodium falciparum, the most virulent of the malaria-causing *Plasmodia*, has developed resistance to several frontline antimalarials, necessitating ongoing investigations into next-generation chemotherapies.[1] The non-genomic nature of haemozoin, the product of *Plasmodium*'s haem detoxification pathway, makes it an attractive choice for target-based drug design. A virtual screen for new β-haematin (synthetic haemozoin) inhibiting antimalarial agents identified the coumarin-containing compound **1** as having sub-micromolar activity against chloroquine-resistant *P. falciparum*.[2] Unfortunately, this compound is not commercially available in sufficient quantities to allow in-depth mechanistic and biological investigation, nor has a synthetic route been reported. Accordingly, we present here, the development of a concise, and efficient synthesis for compound **1** as well as a series of analogues, specifically designed for SAR analysis. These compounds represent a new chemotype of β-haematin inhibiting antiplasmodials with substantial potential for further development.



Compound **1**

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P39: The synthesis and evaluation of 3-benzoylbenzofurans and their pyrazole derivatives against HIV-1 infections and cancer.

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Keywords: 3-Benzoylbenzofurans, Pyrazoles, HIV-1 pseudoviruses, cancer.

The human immunodeficiency virus-1 (HIV-1) remains one of the leading global epidemics in the world. The HIV/AIDS epidemic is particularly dominant in Eastern and Southern Africa, as is evident by the 670 000 annual new infections in this region alone, compared to 1.5 million global annual new infections.[1] HAART is an effective treatment for controlling HIV-1 infections; however, severe adverse events and the emergence of drug resistance have been major challenges.[2] Lenacapavir, a pyrazole-based drug, was FDA-approved in 2022 and has been proven to be the most potent HIV-1 inhibitor thus far.[3] Numerous experimental pyrazole compounds have demonstrated high potency against HIV-1 infections and have been shown to have minimal cytotoxicity, thus making them attractive candidates for HIV-1 treatment.[4] In this study, the 3-benzoylbenzofurans that were previously shown to inhibit the proliferation of breast cancer cells were converted into pyrazoles and investigated for anti-HIV-1 and anti-cancer activities.[5] Our synthesis method involved methylating the 5-hydroxy group of 3-benzoylbenzofurans, which produced the intermediates from which the pyrazoles were derived. The methylated benzofurans were discovered to be cytotoxic in TZM-bl cells, while the pyrazole derivatives showed mild cytotoxicity. Some benzofurans and pyrazoles demonstrated promising anti-HIV activities when tested against Q23 and CAP210 pseudoviruses. The cytotoxic benzofurans demonstrated high potency against cervical cancer and hepatic cancer cells and were also demonstrated to be potent antioxidants using a DPPH assay. Together, these results demonstrate the potential of benzofurans and pyrazole derivatives for further development as antiretrovirals and anti-cancer treatment.

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P40: Extraction and anti-cancer evaluation of metabolites from southern African plants

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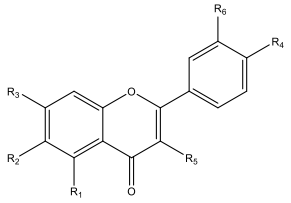
Keywords: cytotoxicity, flavonoids, MTT assay, synergism, isobolog

Our ancestors have used medicinal plants to promote health and treat disease including cancer.[1] In this study we have investigated the anti-cancer activity of extracts prepared from medicinal plants *Dodonaea viscosa*, *Tulbaghia violacea* (wild garlic) and *Allium sativum* (table garlic). *D. viscosa* is an evergreen shrub, that grows endemically in tropical and subtropical regions of Africa, Australia, and Asia. Extract preparations from all of these plants have been shown to have anti-proliferative activity against liver, breast, and colon cancer cells.[2,3] *D. viscosa*'s activity is attributed to the phytochemicals present in the extracts which includes flavonoids, alkaloids, terpenoids and sterols.[4,5] The activity of *A. sativum* and *T. violacea* is attributed to the organosulfur compounds found therein.[3]

Seven methoxylated flavonoids were isolated through silica-gel column chromatography from *D. viscosa* plant material. Bio-assay guided fractionation was also employed to narrow down active fractions along with HPLC-MS^E analysis to tentatively identify active compounds. Five flavonoids (**Figure A**) were tested for cytotoxicity against the MDA-MB-231 (triple-negative breast) cancer cell-line using the MTT-assay. From the tested compounds, penduletin (**3**) showed the largest inhibitory effect (50.2 ± 15.2% viability) at 200 µM. *D. viscosa* (22.7 µg/mL) and both garlic extracts (28.5 µg/mL) displayed synergistic effects on the MDA-MB-231 breast cancer cells when treated in combination with the cancer chemotherapeutic doxorubicin (2.5 µM). This study demonstrates that extracts from the traditional plants *D. viscosa*, *A. sativum* and *T. violacea* have the potential to be developed as adjuncts in breast cancer chemotherapy.



1. 5-hydroxy-3,6,7,4'-tetramethoxy-flavone: R_1 = OH; $R_{2,3,4,5}$ = OMe; R_6 = H
2. santin : $R_{1,3}$ = OH; $R_{2,4,5}$ = OMe; R_6 = H
3. penduletin : $R_{1,4}$ = OH; $R_{2,3,5}$ = OMe; R_6 = H
4. kampferol 3,7,4'-trimethyl ether : R_1 = OH; R_2 = H; $R_{3,4,5}$ = OMe; R_6 = H
5. viscosine : $R_{1,3,4}$ = OH; $R_{2,5}$ = OMe; R_6 = H
6. kaempferol : $R_{1,3,4,5}$ = OH; R_2 = H; R_6 = H
7. quercetin : $R_{1,3,4,5,6}$ = OH; R_2 = H

Figure A: Chemical structures of isolated flavonoids (1-5) from D. viscosa and standards (6-7) used in the study.

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P41: The selective reduction of a Morita-Baylis-Hillman adduct-derived ketone using various ketoreductase enzyme preparations

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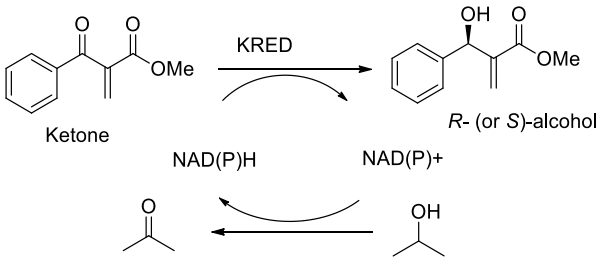
Keywords: Morita-Baylis-Hillman reaction, ketoreductases, selective reduction.

The preparation of enantiopure Morita-Baylis-Hillman (MBH) adducts remains a challenge in organic chemistry. MBH adducts are highly functionalised and act as key intermediates in the preparation of compounds of medicinal importance. MBH adducts are prepared in racemic form by reacting various aldehydes and activated alkenes in the presence of DABCO; a reaction that was reported in 1972 by Baylis and Hillman[1] and in 1968 by Morita *et al*.[2] Enantiopure MBH adducts can be obtained by employing enzymatic kinetic resolution (EKR). This technique has previously been successfully demonstrated in our group, amongst others, using lipases in either hydrolysis or transesterification reactions.[3] As these methods only allow 50% of each enantiomer to be obtained, our interest grew in exploring other enzymatic methods for the synthesise of enantiopure MBH adducts where theoretically 100% of the desired enantiomer could be obtained.

Dehydrogenase enzymes can be employed on prochiral substrates to obtain optically pure compounds, by reducing carbon-carbon double bonds or carbonyl groups of ketones. Ketoreductases have been used historically to obtain enantiopure secondary alcohols on an industrial scale. Ketoreductases are NAD(P)H-dependent enzymes and thus require nicotinamide as a cofactor. [4] This project focuses on employing ketoreductase enzymes to selectively reduce ketones derived from Morita-Baylis-Hillman (MBH) adducts in order to obtain these adducts in enantiopure form (Scheme 1).



Scheme 1

Results obtained using various ketoreductase enzyme preparations to selectively reduce MBH ketones to the corresponding alcohol compounds will be reported. Good enantioselectivity was observed using a range of different ketoreductases, however, reactions were complicated by the formation of an unexpected by-product, which was characterised employing single crystal x-ray crystallography techniques. Methods to minimise by-product formation are currently being investigated.

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P42: Design, synthesis and investigation of photophysical and electrochemical properties of precursor materials containing alkylated 1H-benzo[d]imidazol-6-yl) as π-spacer for use in photovoltaic applications

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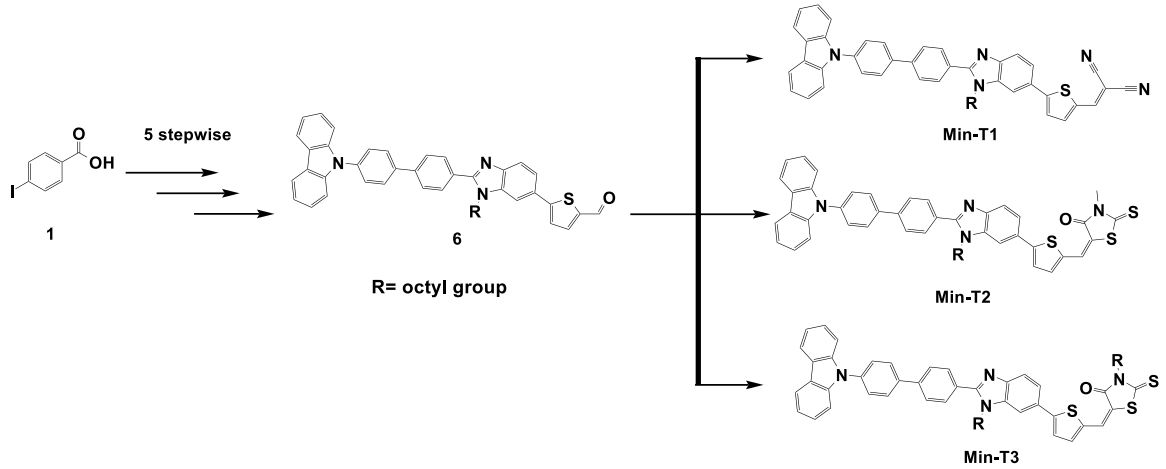
Keywords: Small-molecule; FTIR; NMR, LCMS; photophysical properties, electrochemical properties

In recent times, there has been significant interest in linear-conjugated small molecules, driven by their versatile applications in various fields such as light-emitting diodes, thin-film transistors, and solar cells [1–3]. The benefits of using these small molecules include their lightweight nature, cost-effectiveness, simple chemical modification, outstanding absorption properties, and easy fabrication [4–6].

In this study, we designed and synthesized three linearly conjugated small-molecule compounds, **Min-T** (**1-3**), using a seven-step sequential reaction, as shown in Scheme 1. Their structural properties were validated and verified by various analytical techniques, including 1D and 2D NMR, FTIR, elemental analysis, and LC-MS spectrometry. Subsequently, their photophysical and electrochemical properties are currently being investigated. The potential of these three small-molecule compounds as materials for organic solar cells will be evaluated.



Scheme 1

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P43: New analogs of the Cecropin A and Melittin B hybrid CA(1–7)M(2–9) with improved properties

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University of KwaZulu-Natal, South Africa

Keywords: Antibicrobial pesticides, hemolytic activity, cecropin, melittin

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The rapid emergence of antimicrobial resistance to classic antibiotics has rekindled interest in the development of new classes of antimicrobial drugs with different modes of action. In this sense, antimicrobial peptides (APMs) have attracted great interest due mainly to their broad-spectrum activity and low resistance induction. Nevertheless, AMPs have several drawbacks that should be overcome as their short half-life because of the degradation by proteases, hemolytic activity or toxicity for the host. Hybrid peptides from cecropin A (CA) and melittin (M) have attracted the interest of the research community for decades. In the present work we will discuss the synthesis, antibacterial activity, toxicity and protease stability of several new analogs of the pentadecapeptide CA(1−7)M(2−9) [H-KWKLFKKIGAVLKVL-NH_2]. Whilst the substitutions of Lys residues by Arg does not show relevant effect, the substitution by Orn improve considerably the proteolytic stability of the peptide without being detrimental for the antimicrobial activity and toxicity. A disulfide cyclic version of the sequence by adding Cys residues at both ends also showed improved properties.

P44: Photolytic of azides and their application using a continuous photochemical reactor

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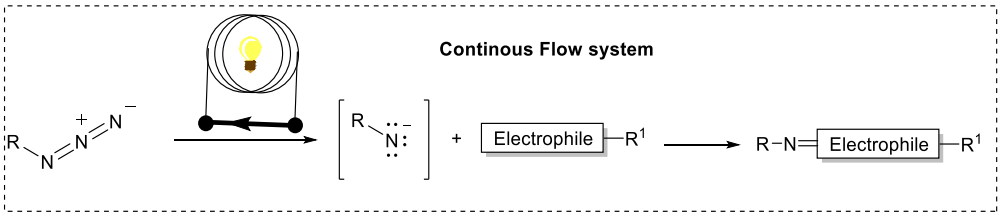
Keywords: Photolytic reactions, photochemical reactor, flow chemistry, azides, nitrenes.

Flow chemistry provides many opportunities for improving or discovering transformations that are green, efficient with less energy consumption, shorter production times, safer, and many others.[1] Many improvements and discoveries on flow systems focus more on developing reactors that mitigate the challenges encountered in conventional methods.[1] Among others, photochemical reactions in flow chemistry have enormously shown reduction of feedstock, and are conducted easier, safer, and greener.[2] Additionally, flow photochemical reactions undergo uncommon mechanisms, which are impossible with conventional methods.[1,2] Photochemical reactions commonly results in rearrangement, reduction, oxidation, and photolysis reactions.[1,2] Hence, the application of azides in flow chemistry especially in photolytic reactions has gained momentum. This is due to the nature of azides, of not being stable naturally; they are susceptible to decomposition toward the exposure to light including visible light and mostly produce nitrene intermediates and nitrogen gas as a co-product.[3] The resultant nitrene intermediates have been useful, and are utilized for transformation such as sulfur imidation, amination of alkyl groups through C-H activation, and aziridination of olefins and many others.[4] However, due to the hazardous nature of azide chemistry, certain transformations are forbidden in conventional batch synthesis hence limiting researchers. Herein, we take advantage of the inherent safety profile of continuous flow chemistry technology to safely access nitrenes intermediates through photolysis of azides and subsequently transform them with different electrophiles.



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P45: Machine learning chemical space exploration of JNK3 inhibitors for Alzheimer's disease drug discovery

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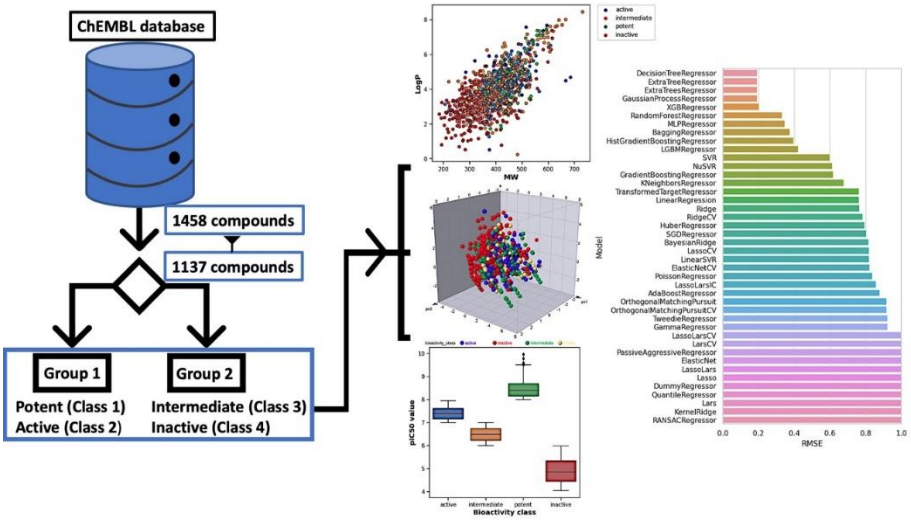
Keywords: QSAR modelling, Lipinski's descriptors, ChEMBL-33, JNK3 bioactivity, machine learning.

Alzheimer's disease (AD) is a challenging neurodegenerative disorder instigating cognitive impairment.[1] Accumulation of β-amyloid (Aβ) plaques and neurofibrillary τ tangles are primary pathophysiologies of AD.[2] C-Jun *N*-terminal kinase 3 (JNK3) expressed in the brain facilitates the conversion of amyloid precursor proteins (APP) into Aβ.[1] Additionally, JNK3 participates in the maturation of τ tangles.[1] Therefore, JNK3 is a druggable target for the development of anti-AD inhibitors. Herein, structure-activity relationship, and JNK3 inhibitor landscape were studied through cheminformatics and machine learning.[3] A dataset of inhibitors of the disease target was acquired through ChEMBL-33. Lipinski's descriptors were used for chemical space exploration to acquire the bioactivity data of the compounds. Further, quantitative structure-activity relationship (QSAR) model was developed employing PubChem fingerprints.[3] Python's Lazy Predict library was used to evaluate the model based on the root mean square error (RMSE), Pearson's correlation (R^2) and modelling time.[4]



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P46: Reductive biocatalysis of prochiral ketones to alcohols using a variety of yeasts

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Keywords: Biocatalysts, yeast, whole-cell

Whole-cell biocatalysis for the reduction of ketones to their corresponding chiral alcohols represents a potentially highly economical and "green" method to produce the building blocks required for the stereoselective production of pharmaceuticals [1]. The use of whole-cell biocatalysts is advantageous over chemical catalysts because biotransformations generally proceed more chemo- and stereoselectively, are done using water as solvent and produce less hazardous waste [2].

Yeast is a popular whole-cell biocatalyst due to its potentially much higher volumetric capacity when compared to bacteria. The use of baker's yeast for asymmetric reduction of ketones is well known [3]. Alternative yeasts such as *L. kefir* have also been reported to enantioselectively reduce **1** to **2** as shown in **Scheme 1** [4]. Compound **2** is a key intermediate for the synthesis of HMG-CoA reductase inhibitors, a class of compounds known to lower cholesterol levels in human blood.

1 **2**

Scheme 2: Reduction of ethyl 4-chloro acetoacetate **1** to ethyl (*S*)-4-chloro-3-hydroxy butanoate **2**.

Herein, we report the interesting outcome of using seven different yeast strains, most of which unusual and rare, for the whole-cell reduction of various alkyl ketones and diketones.

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P47: Green and Sustainable approach of palladium-catalyzed C-H olefination of Imidazo[1,2a] pyridine carboxamide.

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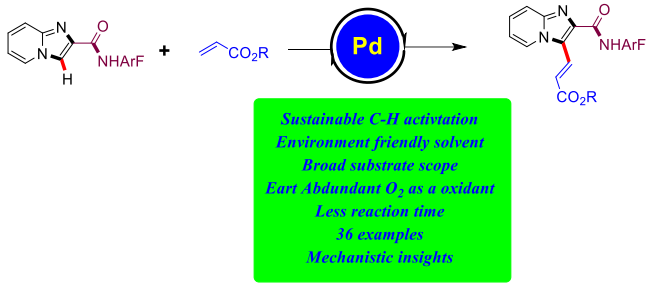
Keywords: 16th Frank Warren, Abstract, Conference.

The last two decades have witnessed, significant advancement in transition metal-catalyzed oxidative C-H alkenylation reactions via C-H bond activation which resulted in many groundbreaking discoveries[1,2]. The cleavage of strong C-H bonds and controlling site selectivity are two major challenges that always appeared in the C-H alkenylation reactions. Indeed, desired site selective C-H bond cleavage has been accomplished by a proper combination of ligand and directing group (DG)[3,4]. The advancement of sustainable chemistry and changes in the economy are strongly intertwined. In particular, reaction time, cost savings, moderate temperatures, and generation of fewest by-products are frequently achieved by using catalytic processes. Herein, we report the C3 olefination of imidazo[1,2-a] pyridine by C-H activation with acrylates in the presence of Pd (II) catalyst with Cu $(OAc)_2 \cdot H_2O$ as the oxidant in an ethanol/water mixture rather than using non-ecofriendly solvents. This palladium (II)-catalyzed transformation was also shown to be profitably performed using O_2 as an oxidant. Additionally, this process showed a promising approach regarding substrate scope. Several control experiments and mechanistic studies indicated that anilide DG is essential for this water tolerant pd catalyzed C-H olefination. Further this protocol is applicable for gram scale synthesis.



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P48: Exploring the tumour extracellular environment as a new mode of heat shock protein (HSP) 90 inhibition

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Keywords: Heat shock protein 90, Extracellular inhibition, Cancer.

Heat shock protein (HSP) 90 remains a valuable target for cancer therapy as it regulates various oncoproteins. Unfortunately, targeting intracellular HSP90 has proven not to be a viable chemotherapeutic approach, mainly limited by the compensatory heat shock response (HSR) induction, triggering HSP70 overexpression. Alternatively, targeting extracellular HSP90 has been postulated as a promising anti-cancer strategy, devoid of the drawbacks associated with intracellular HSP90 inhibition.[1]

In this study, we synthesized cell-impermeable analogues of the known HSP90 *N*-terminal inhibitor **SNX-2112**, all of which were modified to include a polar sulfonate (**1,2**) or phosphonate group (**3,4**) at the end of an alkyl chain (**Figure 1**). Hypothetically, introduction of polar alkyl groups would inhibit cell penetration thus limiting them to the extracellular environment.

Consistent with our hypothesis; preliminary biological assessments demonstrated that our compounds did not inhibit intracellular HSP90, but inhibited HSP90 ATPase to a similar extent as the parent compound, **SNX-2112**. Furthermore, our analogues displayed potent cytotoxicity against a *HeLa* cell line, without stimulating HSP70 expression, a marker of the compensatory HSR induction. These preliminary data support the feasibility of targeting extracellular HSP90 as a novel anticancer strategy.

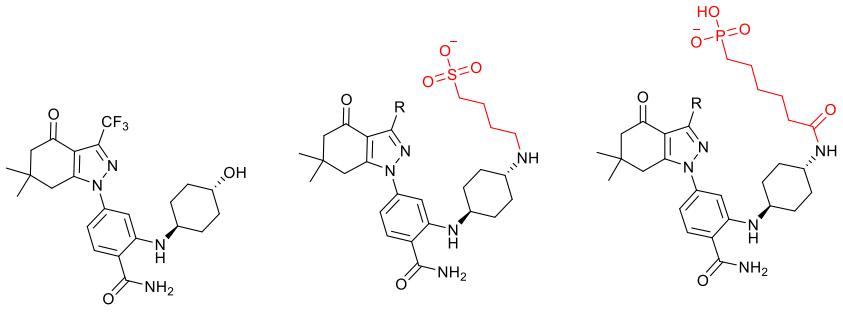

Figure 1: Cytotoxicity data: Average pIC_{50} values of the synthesised compounds against a *HeLa* cell line

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P49: Synthesis of imidazopyridazine and pyrazolopyrimidine derivatives as potential inhibitors of *Plasmodium* kinases PI4K and PKG.

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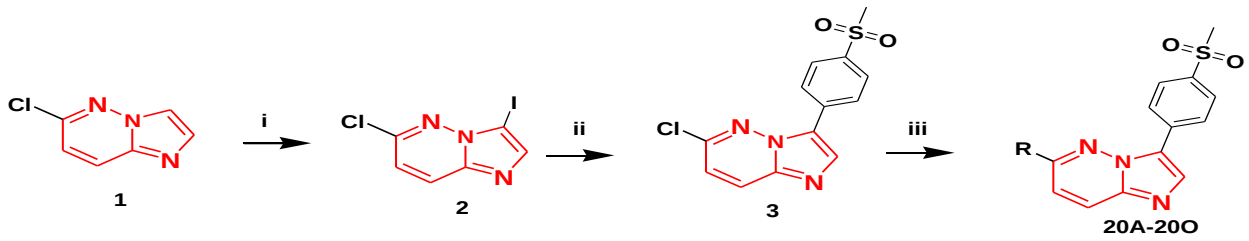
Keywords: imidazopyridazine, pyrazolopyrimidine, NF54 strain, *Pf*PKG, *Pv*PI4Kβ,.

Malaria is a disease that is caused by various *Plasmodium* species, with *Plasmodium falciparum* and *vivax* being the most prevalent. The disease is usually mostly severe in pregnant women and children under the age of five. The 2020 World Malaria Report from WHO estimated 241 million new malaria cases and 627000 malaria deaths globally.[1] Emergence of resistance towards previously effective anti-malarial drugs, has resulted in an urgent need for the development of new drugs with new modes of action. A series of imidazopyridazine and pyrazolopyrimidine derivatives have been reported to be potent against sensitive (NF54) strain of the human malaria parasite *P.falciparum*.[1] In this study we focused on synthesizing a new library of imidazopyridazine and pyrazolopyrimidine derivatives, with substituents at 3- & 6- positions and 3- & 5- positions respectively. The compounds were successfully synthesized and characterized by NMR and HRMS. Their percentage yields ranged from 38% to 75%. All the imidazopyridazine compounds were evaluated for their *in vitro* antiplasmodial activities against NF54 strain and inhibitory activity against *Pf*PKG and *Pv*PI4Kβ. The pyrazolopyrimidine compounds were only evaluated for their *in vitro* antiplasmodial activity against the NF54 strain. Selected compounds demonstrating an activity with IC_{50} of less than 0.5 μM against NF54 strain were evaluated for cytotoxicity assays.



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P50: Reduction of α, β-alkynyl carbonyl compounds using $SnCl_2$ and other metal salts.

U. Ralepelle [a], W. Nxumalo [a], H. Chauke [b], I. Cukrowski [c]

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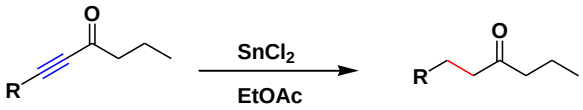
Keywords: 1-(6-nitroquinoxalin-2-yl)hex-1-yn-3-one, α, β - alkynyl carbonyl, reduction, $SnCl_2$, heteroaromatic.1

The development of an efficient method for the reduction of α, β - alkynyl carbonyl compounds, is mostly important in organic synthesis, playing a crucial role in the synthesis of pharmaceuticals, and other valuable chemicals.[1] Tin (II) chloride ($SnCl_2$) mediated reduction of alkyne to their corresponding alkane has not been reported in literature. In our research group, the reduction of 1-(6-nitroquinoxalin-2-yl)hex-1-yn-3-one using Tin (II) chloride was found to reduce both the nitro group and alkyne functionality to primary amine and alkane, respectively.[2] As a result, we decided to synthesize various quinoxaline, pyridine, pyrimidine, and pyrazine containing the conjugated α, β - alkynyl carbonyl functionality and investigate the reduction of the conjugated α, β - alkynyl carbonyl groups using commercially available $SnCl_2$ and other metal salts known to reduce the nitro group, such as iron (Fe) and zinc (Zn). The developed method was optimized varying parameters such as reaction time, temperature, and equivalence of $SnCl_2$ using different solvents. The reduction of conjugated α, β - alkynyl carbonyl using $SnCl_2$ is limited to specific heteroaromatic molecules.



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P51: Synthesis of sulfonylureas as potential anti diabetic drugs

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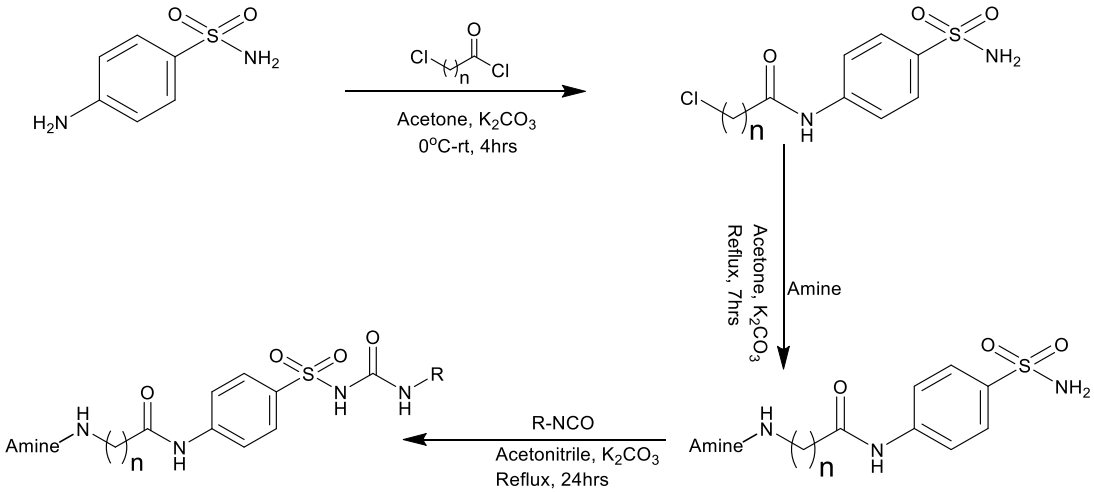
Keywords: Diabetes, Sulfonylureas, anti-diabetic drugs biological screening.

Diabetes mellitus (DM) which is commonly referred to as diabetes is a worldwide disease that is characterized by high levels of blood glucose [1]. In 2014, 422 million people were living with diabetes and from the studies it showed that diabetes has been rising rapidly in low middle income than in high income countries[2]. The primary action of sulfonylureas is through the stimulation of insulin secretion[3]. Our objective is to synthesize, purify, characterize sulfonylureas and biological screening of antidiabetic activities. Our Target compounds will be obtained in a three step synthesis starting from the commercially available sulfanilamide as shown in reaction scheme 1 below.



Synthetic scheme 1.

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P52: Bio-renewable based synthesis of anthraquinone-centered natural products

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Keywords: Anthraquinones, anacardic acid, cardanol, emodin, aloe-emodin, rhein

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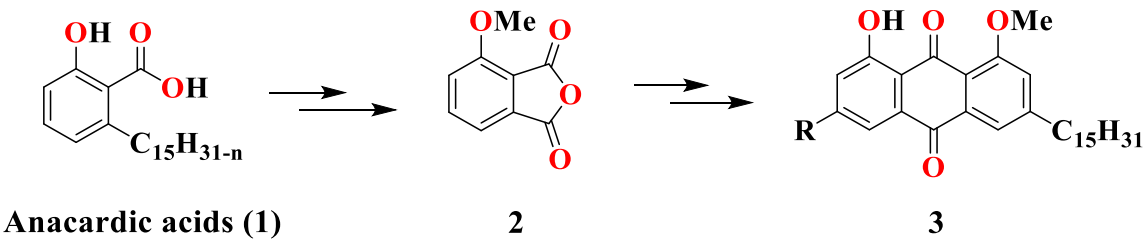
Biomass resources such as agricultural residues and food processing waste have become a source of building blocks for the synthesis of organic compounds[1]. This is as a result of the diminishing fossil fuel reserves[2]. Over the past few years, biomass derived phenols extracted from lignin and cashew nutshell liquid (CNSL) have been utilized in the synthesis of bioactive compounds such as anthraquinones[3]. Anthraquinones are an interesting group of natural products that exhibit a wide range of biological activities such as antibacterial, anticancer, antifungal, antiplasmodial and anti-viral activities[4,5].

Herein, we describe the synthesis of anthraquinone-centered rhein and emodin derivatives utilizing CNSL based anacardic acids and cardanols as chemical building blocks (**Scheme 1**). 3-Methoxypthalic anhydride **2** was successfully synthesized as an advanced precursor from anacardic acids **1** utilizing a series of chemical transformations. Treatment of the 3-methoxypthalic anhydride **2** with various Lewis acids in the presence of hydrogenated cardanol advanced a Fries rearrangement and subsequent Friedel-Crafts type reaction to afford anthraquinones **3** (R = H or CH_3) which serve as key precursors for the total synthesis of natural products, emodin, aloe-emodin and rhein.



Anacardic acids (1) **2** **3**

Scheme 1: The bio-renewable synthesis of anthraquinone-centered natural products.

References:

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P53: A batch-flow hybrid approach for the synthesis of the Schistosomiasis treatment praziquantel

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[c] *Department of Chemistry, University of Pretoria, 0028, South Africa; Darren.riley@up.ac.za*

Keywords: Neglected tropical diseases; Schistosomiasis; Praziquantel; Flow chemistry; Micro-fluidics; Pharmaceutical process development

Neglected Tropical Diseases (NTDs) are a diverse group of infectious conditions that predominantly affect the poorest people residing primarily in the tropical regions of the globe. Schistosomiasis is a NTD affecting >200 million people globally with >700 million at risk,[1] with >80% of occurrences in sub-Saharan Africa. Praziquantel is a prescription de-worming medication used to prevent infections from Schistosoma worms. In 2019, the WHO reported that approximately 236.6 million people needed preventative treatment, however, only ~105.4 million (44.5%) had access to the medication.[2] Consequently, an innovative batch-flow hybrid 3-step approach for the synthesis of racemic praziquantel has been demonstrated. The first step is a modified Hofmann procedure for the preparation of 2-isocyanoethylbenzene **1** (Figure 1), which was performed on a micro-reactor platform achieving increased yields when compared with pre-existing batch methodologies with similar chemistry. The produced 2-isocyanoethylbenzene **1** is noxious and exhibits potential safety hazards which are ultimately reduced when synthesised under flow conditions. The second step is a 4-component Ugi reaction optimised under continuous flow conditions in methanol affording N-(2,2-dimethoxyethyl)-N-(2-oxo-2-(2-phenethyl-amino)ethyl)cyclohexanecarboxamide **2**. This step achieves comparable yields to previously reported batch conditions but with a significant decrease in reaction time (1 h vs. 48 h). The final conversion to praziquantel **3** is performed solventless with the use of a green acid, methanesulfonic acid (Figure 2) with the entire 3-step procedure affording praziquantel **3** in an overall yield of 41% (1 g scale) with a total reaction time of 7.25 h.

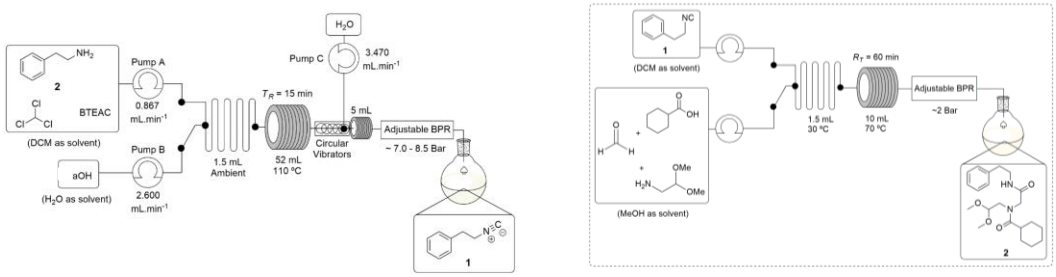

Figure 1: *Step 1 (outlined in red on the left) and Step 2 (outlined in black on the right) developed under continuous flow conditions for the preparation of **1** and **2**.*

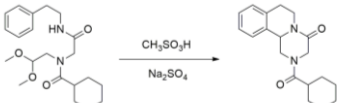

Figure 2: *Final Step 3 for the conversion of **2** to the desired praziquantel **3**.*

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P54: Synthesis of Quinoxaline Derivatives and Evaluation of their Biological Activity against Tuberculosis

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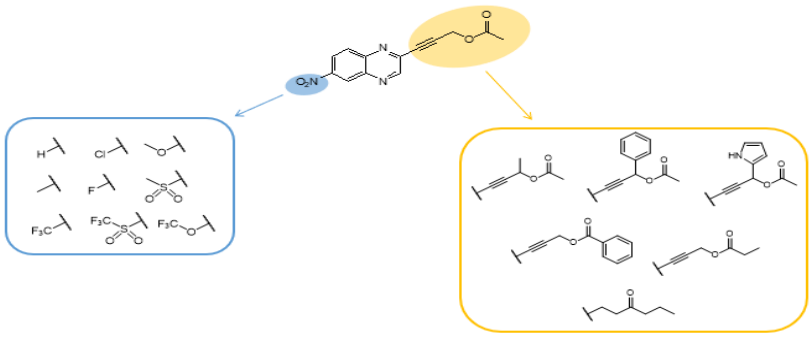
Keywords: Quinoxaline, Mycobacterium tuberculosis

Quinoxaline derivatives have gained significant attention in medicinal chemistry due to their versatile pharmacological properties such as antitumor, anti-inflammatory[1], antimicrobial[2] and antiviral[3]. This study explores the synthesis of quinoxaline derivatives to evaluate their potential activity against tuberculosis (TB). The motivation behind this research stems from the discovery of 3-(6-nitroquinoxalin-2-yl) prop-2-ynyl acetate from our research group, which has shown promising activity against TB with a minimum inhibitory concentration (MIC) of 1.8 µM, cytotoxity IC_{50} of 13.5 µM and solubility of 195 µM. The goal is to find improved treatment for TB, by synthesizing and testing various quinoxaline scaffolds and structures, with the hope to identify compounds with higher efficacy against TB. The synthesized compounds were evaluated against Mycobacterium tuberculosis, using broth micro dilution method[4]. The MIC of the prepared compounds was determined, and their anti-mycobacterial activity were compared with standard drugs in use for TB treatment.



UL Code / H3D Number	KL-85 / H3D-021912
cLogP MW TPSA	0.84 271.2 102
TB MIC (7H9 ADC Glu Tw) Original / H3D (µM)	**1.8 / 1.8**
Cytotox IC50 Original / H3D (µM)	**13.2 / 6.8**
Solubility (µM)	**195**

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P55: Towards the synthesis of hydroxylated polyamines

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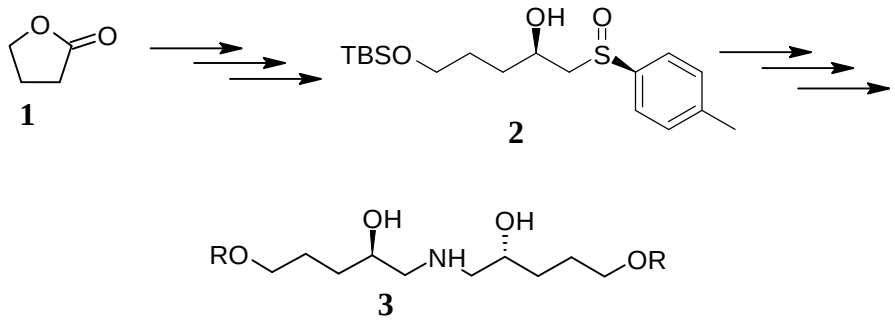
Keywords: Polyamines, sulfoxide.

Polyamines are described as aliphatic organic compounds with two or more primary amine substituents, connected by one or more methylene linkages within their structure.[1] Biological properties exhibited by this class of compounds has seen them being incorporated into different chemotherapeutic strategies for various diseases as either drug vectors or therapeutic agents. Interestingly, substitution of the methylene linkage of polyamines is not commonly observed in the naturally occurring substrates. Identification and characterisation of a polyamine toxin, pavettamine, with a five-carbon linker having a 1,3-*syn*-diol functionality piqued our interest and led us to develop methodologies for synthesising reduced functional analogues of this unusual compound.[2] A synthetic route towards the hydroxylated polyamines starting from commercially available small molecules like γ-butyrolactone **1**(**Scheme1**) will be discussed. The sulfoxide chiral auxiliary was employed for stereochemical control and this approach afforded intermediate **2** which was further transformed yielding precursor polyamine **2**.



Scheme 3: Synthetic approach to hydroxylated polyamines

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2. M.L. Bode, P.J. Gates, S.Y. Gebretnsae and R. Vleggar, *Tetrahedron*, 2010, **66**, 2026.

P56: Synthesis and evaluation of flexible pyrimethamine analogues as antifolates targeting drug resistant malaria.

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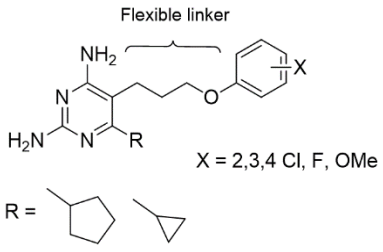
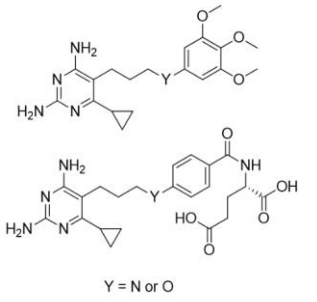
Keywords: Malaria, Drug development, computational modelling

Point mutations in the active site of the dihydrofolate reductase – thymidylate synthase (DHFR-TS) enzyme found in the malaria causing parasite *Plasmodium falciparum* render current class II antifolates ineffective. The prevalence of drug resistant *P. falciparum* strains highlights the need for the development of new molecules to combat drug resistant malaria. Previous work done by A. Rousseau et al.[1] identified that modifying existing drugs by adding a flexible linker allows for compounds to remain effective despite active site mutations. In this work, in-silico methods are employed to assess what effect modifying various functional groups, around a conserved flexible template, has on the binding ability against the drug resistant enzyme. Based on these results a large library of first-generation analogues was successfully synthesized by adapting partially established procedures. These compounds were then evaluated against drug resistant strains in-vitro in single enzyme and whole cell assays. The results of the single enzyme assay were very promising, with our molecules inhibiting *Pf*DHFR in the low nanomolar range. The results from the whole cell assay, however, were less favorable, with K_i values in the low micromolar range. This suggests that while our compounds are very potent binders of the enzyme, there may be some pharmacokinetic problems which limit their efficacy in the cellular environment. This led us to design a second generation of analogues, assisted by in-silico modelling and taking inspiration from other antifolate drugs, with the aim of addressing these concerns. The synthesis of these compounds is currently underway.

First generation analogues



Selected second generation analogues



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P57: Synthesis of Sulfonated (poly ether- ether ketone) membranes for Iron Redox flow battery

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Keywords: Redox flow battery, Water uptake, Ion exchange capacity.

This study focuses on synthesis and characterization of sulfonated poly(ether ether ketone) (SPEEK) membranes for application in Iron redox flow batteries (FeRFB). The sulfonation degree influenced by varying time, sulfonic acid group ($-SO_3H$) enhanced synergistic proton transport channel were formed, showing a trade-off balance between ion exchange capacity and mechanical, thermal and chemical stability.[1,3]. The Ion Exchange Capacity (IEC) ranged from 0.88 (IEC) mequi/g-1@25°C to 2.05 (IEC) mequi/g-1@25°C[2,3]. Electrochemical impedance measurements, as evidenced from Nyquist plots, were performed using a test cell with dimensions of 5x5 cm, an active area of 2.9x2.9 cm, and a sinusoidal excitation voltage of 1.2V in 1M H_2SO_4. Remarkably, even at a high current density of 100 mA cm^{-2}, minimal polarization settling at 1.4V was observed. This work offers promising insights into the development of SPEEK membranes for efficient and durable FeRFBs[3].

P58: Design, synthesis and evaluation of anti-HIV and antiplasmodial activities of some hydroxypyridinone-aminoquinoline derivatives

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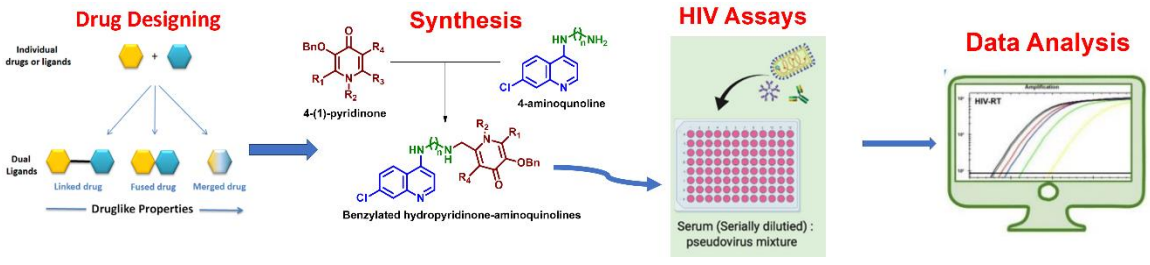
Keywords: Co-infection, HIV-AIDS, Malaria, Hydroxypyridinone-Aminoquinolines.

In malaria-endemic regions, HIV-AIDS infection increases the risk of malaria infection. That being so, malaria and HIV coinfection are common in the sub-Saharan region. Given the overlap of their geographic distribution and resultant rates of coinfection, interactions between the two diseases pose major public health problems[1].

Hydroxypyridinone-aminoquinoline derivatives are hybridized compounds, whereby the quinoline scaffold which is known anti-malarial active and the pyridinone scaffold which is anti-HIV are conjugated. Drug conjugation whereby two pharmacophores are covalently fused together with a sophisticated linker to create a single molecule with multiple pharmacological targets has proved to be a working strategy, and one moiety can counterbalance the side effects caused by another[2-3].

The 2 series of HPO-AQ compounds, maltol-derived and kojic acid-derived, were synthesized, characterized by a combination of spectroscopic techniques, namely, Nuclear Magnetic Resonance (NMR), Fourier Transform Infrared Spectroscopy (FT-IR), Liquid Chromatography-Mass Spectrometry (LC-MS) and also biologically evaluated.

This presentation will focus on the anti-HIV activity of some of the compounds which exhibited good percentage inhibitions against HIV reverse transcriptase as well as the protease enzyme.



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P59*: In Silico* study of DNA metabolic enzymes for cancer treatment

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Keywords: Polymerase theta, Topoisomerase II beta, Etoposide, RP-6685.

Cancer remains a severe hazard to human health, accounting for the second biggest cause of mortality worldwide. Cancer cells can initiate, spread, lodge, and grow in various tissues and organs throughout the body, with the lungs, prostate, colorectum, stomach, and liver being the five most common sites of cancer in men, and the breast, colorectum, lungs, cervix, and stomach being the five most common sites of cancer in women [1]. While extensive genetic, molecular, and cancer metabolism research has resulted in significant advances and landmark discoveries, much remains to be discovered about cancer metabolism [2]. Anti-cancer drugs and chemotherapy are currently experiencing significant hurdles due to drug resistance, chemical instability, and dose-limiting side effects. DNA metabolic enzymes are appealing synthetic deadly targets for drug development. In this study, several therapeutic candidates derived from etoposide and RP-6685, which are recognized for their antiviral activity against topoisomerase II beta and polymerase theta (which are DNA metabolic enzymes) respectively, were investigated using *in silico* evaluation (physicochemical characteristics and ADMET), molecular docking, and molecular dynamics. The binding interactions of 400 etoposide derivatives against the human topoisomerase II-DNA complex and 500 RP:6685 derivatives against polymerase theta complex were investigated using molecular docking. The anticancer properties of the most promising candidates were evaluated using MD simulations for 100 ns computations for 3QX3 and 100ns for 8E23.

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P60: Determining the Optimal Reaction Pathway for Methanol Production Prior to Extensive Design Decisions – Application of the ASSF Tool

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Keywords: 16th Frank Warren, Abstract, Conference.

An integral cog in the design and development of sustainable chemical processes, includes the identification of promising and feasible reaction pathways. Often this requires the use of extensive design resources. Furthermore, with the rapidly expanding database of reaction pathways, it is exceedingly difficult to build economically and environmentally sound manufacturing processes, with manual analysis of all pathways within any given database proving to be a time-consuming task. With the exception of the reactor system, high-cost elements in a process include the unit operations required to meet reaction and separation conditions, as well as the necessary separation systems required to achieve marketable purity.

The Automated Systematic Synthesis Framework (ASSF) tool presented herein, is a novel rapid screening tool bridging the gap between the scale up of laboratory processes, process design, and the subsequent economic and environmental analysis. The application of this tool allows for generic process structures to be developed, analysed and ranked in order of their overall feasibility.

The potential and novelty of the ASSF tool is demonstrated through its application to a case study focused on the production of methanol via the hydrogenation of carbon dioxide. This case study not only looks at green hydrogen storage, but also at the production of an alternative, cleaner fuel source. To ensure reliability of the tool developed, the ASSF tool was validated and verified against existing established engineering software platforms, including CHEMCAD and W-EcoMP, noting a minor 6% deviation in capital costs in a fraction of the runtime, and with less user input required.

P61: Synthesis of polysubstituted pyrroles via enaminone intermediates

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Keywords: Enaminones, pyrroles, polysubstituted pyrroles.

Polysubstituted pyrroles are compounds with substituents on the heterocyclic pyrrole nucleus that play an important role in medicinal chemistry because of their broad pharmaceutical spectrum. Pyrrole-containing compounds have previously been reported to have biological activities such as anticonvulsant, antiviral, anti-analgesic, antibacterial, anti-inflammatory, and antitumor properties.[1] The purpose of the research was to investigate the synthetic efficiency of using enaminones prepared by the Eschenmoser sulfide contraction reaction of thioamides to make polysubstituted pyrrole derivatives. The design was to preposition substituents on a pyrrole ring with each reaction step aiming for the desired outcome (Figure 1). Schmidt reaction conditions were used to successfully synthesize *N*-methylacetamide with a poor yield of 25% and *N*-phenylacetamide with a moderate yield of 66%. The synthesized amides were then converted into thioamides; *N*-methylethanethioamide (m/z of 89) and *N*-phenylethanethioamide (m/z of 151) were synthesized in a thiation reaction in THF using phosphorus pentasulfide (P_2S_5) with a moderate to good yield of (40-80 %). The enaminones, (*E*)-3-(methylamino)-1-phenylbut-2-en-1-one (m/z of 175) and (*Z*)-1-phenyl-3-(phenylamino)-but-2-en-1-one (m/z of 237) were synthesized via the Eschenmoser sulfide contraction reaction of the thioamides.

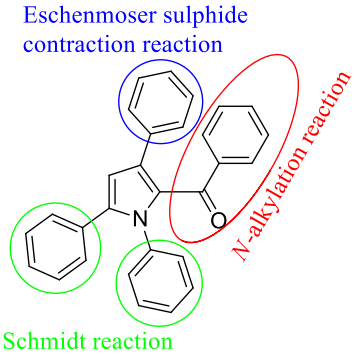

Figure 1: Pyrrole ring substituents' installation reactions.

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P62: Towards a bio-renewable based synthesis of flavonoids and benzofuro[3,2-b]chromenones as potential UV absorbers.

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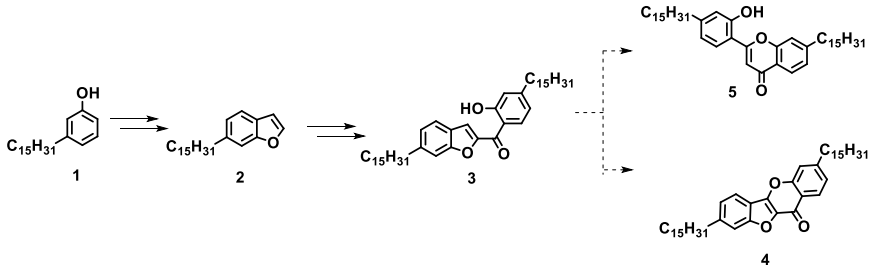
Keywords: Benzofuro[3,2-b]chromenones, cardanol, flavonoids, UV absorbers.

Biomass-derived renewable starting materials offer useful advanced building blocks for organic synthesis as they have a high degree of functionalization[1]. This relieves pressure on the exhaustion of petrochemical deposits[1]. Recently, non-edible cashew nutshell liquid (CNSL) waste has been utilized for the synthesis of different classes of UV absorber molecules[2,3].

In this poster, we will discuss how CNSL-derived phenolics could be used as precursors in the synthesis of flavonoids and benzofuro[3,2-b]chromenones as potential UV absorbers. These classes have also been reported to have a wide range of biological activities such as anti-inflammatory, anti-bacterial, and anti-cancer activity[4,5,6].

Subjecting cardanol **1** through a series of chemical reactions afforded benzofuran intermediate **2** (**Scheme 1**). The benzofuran **2** was subsequently converted to the hydroxy benzylbenzofuran **3** via a Friedel Crafts reaction with a carboxylic acid derived from cardanol **1** followed by deprotection. With this key intermediate in hand, we envisage that an oxa-Michael addition of **3** could furnish the benzofuro[3,2-b]chromenone **4**, and if the oxa-Michael reaction is followed by a furan ring opening could give the desired flavonoid **5,** completing the synthesis.



Scheme 1: Synthesis of flavonoids and benzofuro[3,2-b]chromenones.

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P63: Synthetic Possibilities for Hemilabile Ligands: A Case Study of Decacyclo[10.8.1^{5,8}.0^{2,11}.0^{4,9}.0^{13,20}.0^{15,18}]-heneicosane-3,10,14,19-tetraone.

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Keywords: Pentacycloundecane, Grubbs pre-catalyst, cyclo-addition, hemilabile ligands

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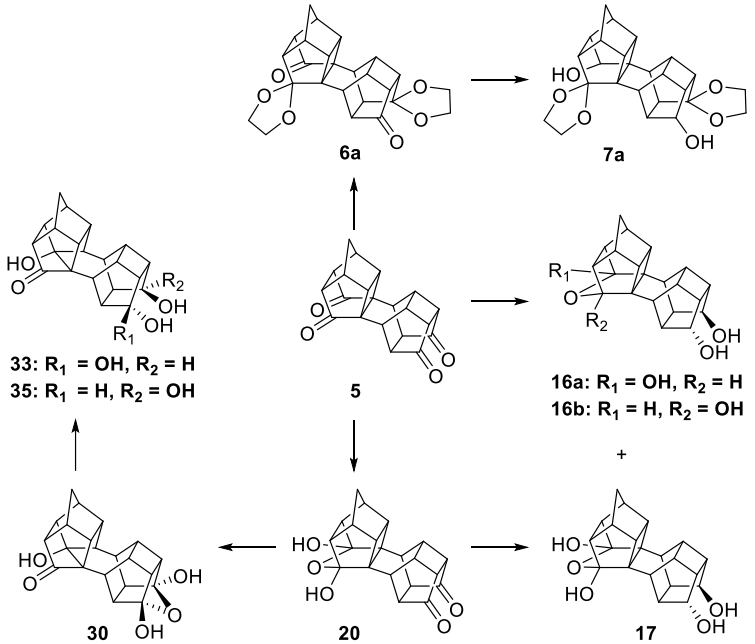
As proof of the synthetic possibilities for hemilabile ligands the chemistry of decacyclo[10.8.1^{5,8}.0^{2,11}.0^{4,9}.0^{13,20}.0^{15,18}]heneicosane-3,10,14,19-tetraone (**5**) was investigated. Reacting **5** with ethylene glycol under acid conditions gave the expected di-acetal protected ketone (**6**) as four possible isomers. Reduction of these isomers to produce the dialcohol ketal (**7**) was only possible with $LiAlH_4$, after $NaBH_4$, Luche's, and Meerwein-Ponndorf-Verley reduction methods were unsuccessful. Deprotection of **7** to the hydroxyl ketone (**8**) derivative was not possible under reflux with a 25% HCl solution. To evaluate the reactivity of **5**, and investigate alternative synthetic routes to Grubbs pre-catalysis, **5** was treated with the reducing agents i) $NaBH_4$, ii) glacial AcOH, Zn and iii) 80% AcOH/H_2O/Zn mixture, which resulted in various reduction products. The AcOH/H_2O/Zn reduction resulted in various products and a further investigation into the mechanism is given within this report.



P64: An investigation of the herbicidal activity of plant *Artemisia afra* Jacq. ex Willd.

Delisile Fortunate Zulu[a], Fanie van Heerden[a], Muvhango Rasalanavho[a]

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Keywords: Herbicides, *Artemisia afra*, Phytotoxicity.

Most synthetic herbicides that are used to control weeds in the agricultural sector can cause environmental pollution.[1] Identifying and quantifying natural products from plant extracts that can be used to control weeds can assist in the development of natural herbicides. In this project, extracts from the plant *Artemisia afra* Jacq. ex Willd., belonging to the Asteraceae family, were assayed for phytotoxicity to find biologically active compounds that can be used as alternatives to currently used synthetic herbicides. The DCM-MeOH crude extract showed positive inhibition on the germination of vegetable seeds, lettuce (*Lactuca sativa*), and radish (*Raphanus sativus*). This crude extract was further fractionated, resulting in two fractions that were active, i.e. giving 0% germination on *L. sativa*. Our results showed that the extracts inhibited the germination of seeds in the following order: DCM-MeOH extracts (leaves and stem) > methanol extracts (leaves and stem) > hexane extracts (leaves and stem). All the crude extracts inhibited the germination of lettuce seeds more than the radish seeds. From our results, we concluded that the plant *Artemisia afra* is a possible source of natural herbicides. The next step in our project is to isolate and carry out structural elucidation of the active compounds.

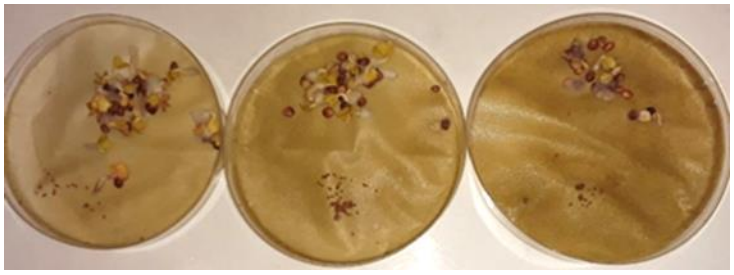

Figure 1. Phytotoxic bioassay of the DCM-MeOH crude extract on *L. sativa* (lettuce) seeds

1. C. Y. Ojemaye, C. T. Onwordi, D. M. Pampanin, M. O. Sydnes, and L Petrik, *Sci. Total Environ*, 2020,**738**,140346

P65: Identification of anti-inflammatory compounds from South African plant species

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Keywords: Anti-inflammation, COX-2, *Siphonochilus aethiopicus, Harpephyllum caffrum*

In South Africa, many medicinal plants are used for pain treatment, rheumatism, and other inflammatory diseases. The anti-inflammatory activity of crude extracts of some indigenous plants has been reported.[1] However, in these investigations, active compounds have not been identified. Knowing the structures of the active chemical compounds is essential to understanding the activities of anti-inflammatory plants and developing local medicinal plants as anti-inflammatory medicines. This study aims to identify compounds in plant extracts that are inhibitors of cyclooxygenase-2 (COX-2) and lipoxygenase-5 (LOX-5), enzymes that are part of the inflammation cascade. Several plants traditionally used for anti-inflammatory treatment (pain relief) were selected for this study. These plants were collected from the UKZN botanical gardens, and these include *Siphonochilus aethiopicus*, *Harpephyllum caffrum*, *Burchellia bubalina*, *Leonotis leonorus*, *Podocarpus elongatus*, *Podocarpus falcatus*, *Rapanea melanophloeos*, *Dais cotinifolia*, *Trichilia emetica,* and *Turraea floribunda*. Lead-like extracts were prepared from each plant, and the lead-like extracts were subjected to a 96-well plate bioassay to identify the plants that inhibit the enzyme COX-2. The results from this assay showed that the rhizomes of *Siphonochilus aethiopicus* were the best inhibitors of COX-2, with 47.3% relative inhibition compared to celecoxib (a nonsteroidal anti-inflammatory drug). *Harpephyllum caffrum* had the second highest COX-2 inhibition, with 45% and 42% relative inhibition in the plant's stems and leaves, respectively. *Burchellia bubalina* had the third highest inhibition, with a percentage relative inhibition of 44.1%. *Siphonochilus aethiopicus* and *Harpephyllum caffrum* were selected for further studies and isolation of compounds. So far, two sesquiterpenoid lactones, including **1** (**Figure 1**), have been isolated from *Siphonochilus aethiopicus* using column chromatography and characterized using 1D and 2D NMR, IR, and X-ray crystallography.

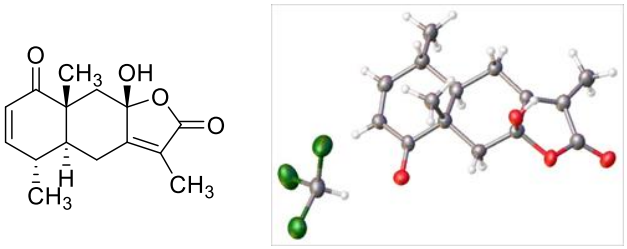

Figure 1: X-ray crystallography structure of **1**.

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P66: Synthetic review and characterization of new psychoactive compounds (NPC) for potential use by the law enforcement agencies

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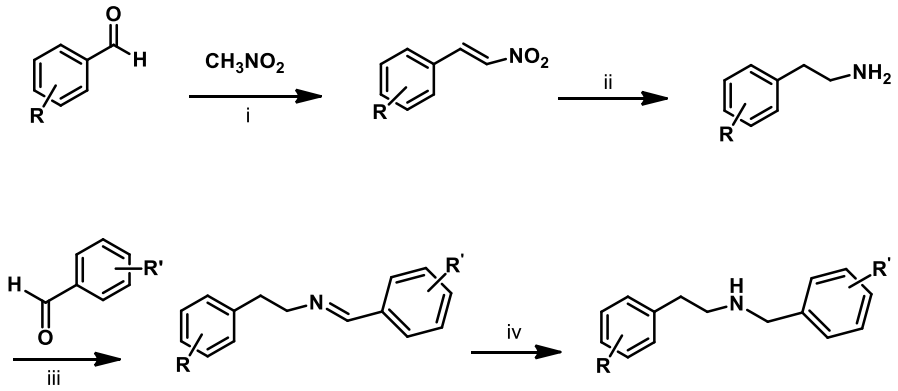
Keywords: New psychoactive compounds, NBOMes, chromatographic techniques

Drug trafficking has triggered a lot of attention in the law enforcement agencies worldwide. An unfortunate challenge that mostly affect South Africa, is a preferred destination for smuggling of illicit drug particularly synthetic psychoactive compounds. These illicit compounds are tremendously produced and made readily available on the black market. Therefore, law enforcement agencies rely on characteristic information obtained from different chromatographic techniques to identify these compounds. *N*-Methoxybenzyl (NBOMes) are synthetic psychoactive substances well known for their high potency and derived from different phenethylamine derivatives. We hereby report our progress in the synthesis of different NBOMes derivative [1] and their characterization [2]. These could potentially be used by Law Enforcement agencies for identification purposes.



Scheme 1: i) Toluene, 110 ̊C, ii) $LiAlH_4$; THF, 66 ̊C iii) $NaBH(OAc)_3$, 1.2-DCE, rt iv) gl. AcOH

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2. Af Abdel-Magid, KG Carson, BD Bruce, CA Maryanoff, RD Shah, *J. Org. Chem.*, **1996**, 61, 3849-3862

P67: Phytochemistry and Cytotoxicity Studies from *Clerodendrum Glabrum* and *Combretum Nelsonii* Roots against the Breast and Colon Cancer Cell Lines.

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Keywords: *Clerodendrum glabrum*, *Combretum nelsonii*, Cytotoxicity, Caco-2, MCF-7, VERO

Cancer remains to be a major cause of death across the world. Despite various treatments of cancer existing, it is essential to improve new cancer treatment strategies. Traditional medicinal plants such as *Clerodendrum glabrum* and *Combretum nelsonii* have promising chemical constituents which can combat cancer disease. [1-2]. The focus of the study was to isolate compounds from both plant species, evaluate their *in vitro* cytotoxicity against **colorectal and** breast cancer cell lines. Sequential extraction method was used to extract both plant species. The dichloromethane crude extracts (*C. glabrum*, 18.65 g and *C.nelsonii*, 23.87 g) were separated and purified using Column Chromatography. Nuclear Magnetic Resonance (NMR), Mass Spectroscopy (MS), Infrared (IR), melting point and optical rotation were used to characterize the isolated compounds. The cytotoxicity and anticancer efficacy of the extracts and isolated compounds were evaluated by using the colorimetric 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. *C. glabrum* root extract led to the isolation of 12-hydroxy-abieta-8,11,13-triene (**1**), 12-hydroxy-8,12-abietadiene-11,14-dione (**2**) and 3*β*-olean-12-en-3-yl-palmitate (**3**), while *C. nelsonii* afforded the previously reported 3,4,5-trimethoxy-2',3'hydroxyl-4'methoxy-stilbene (**4**), mixture of two stilbene derivatives, combretastatin A-1-2'-*O*-*β*-*D*-glucopyranoside (**5a**) and combretastatin B-1-2'-*O*-*β*-*D*-glucopyranoside (**5b**). Stigmasta-5,22-dien-3*β*-ol (**6**) was found common in both plant species as seen in **Figure 1**. Compound (**1**) exhibited high toxicity against the Caco-2 at LC_{50} of 24.3 µg/mL and moderate activity against MCF-7 at 48.4 µg/mL. Compound (**4**), (**5a** and **5b**) showed moderate activity against the MCF-7 at LC_{50} 72.0 and 44.1 µg/mL respectively. The results showed that *C. glabrum and C. nelsonii* are potential sources of bioactive compounds.

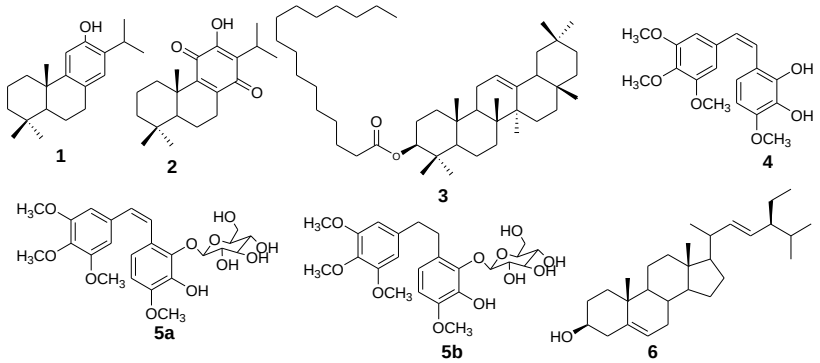

Figure 1: Compounds isolated from *Clerodendrum glabrum* and *Combretum nelsonii* roots.

1. S.M. Hercules, M. Alnajar, C. Chen, S.M. Mladjenovic, B.A. Shipeolu, O. Perkovic, G.R. Pond, L. Mbuagbaw, K.R. Blenman and J.M. Daniel. *BMJ Open*, 2022, **12**, e055735.
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P68: Synthesis of imidazo[1,2-*a*]pyridin-3-amine derivatives with heteroatom linkers as potential HIV-1 reverse transcriptase inhibitors

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Keywords: imidazo[1,2-*a*]pyridines, NNRTIs, Groebke-Blackburn-Bienaymé reaction

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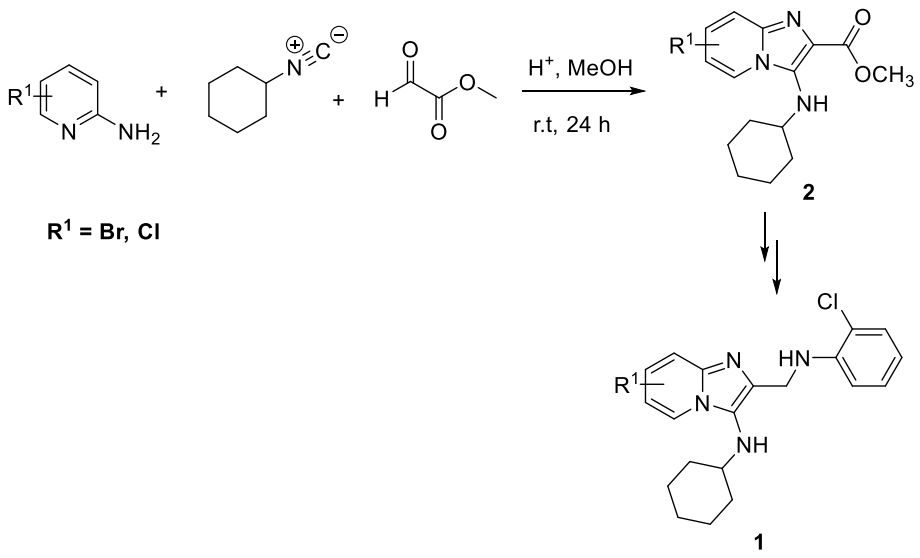
The imidazo[1,2-*a*]pyridine scaffold continues to play a significant role in our daily lives due to the broad range of biological activities it displays such as antineoplastic, antimicrobial, antiviral, anticonvulsant, antidiabetic, anti-insomia, proton pump inhibitory as well as insecticidal activity.[1,2] Previous studies in our laboratory led to the discovery of novel imidazo[1,2-*a*]pyridine derivatives with appreciable antiviral activity against wild-type HIV-1, with an IC_{50} value of 0.18μM and a selectivity index of 867.[3] The objective of this study was to improve the antiviral activity of the compounds against mutant viral strains by using heteroatom linkers to reduce rigidity and to enable the compounds to be more flexible in order to counter the various viral mutations. The preparation of these compounds, such as **1** (Scheme 1), will be discussed. The first step was the preparation of an ester **2** (Scheme 1) using the Groebke-Blackburn-Bienaymé reaction and subsequent structural modifications led to the desired products (**1**).



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P69: Synthesis and characterisation of functionalised indolin-2-ols and their application as antimalarial agents

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Keywords: Cipargamin, Spiroindolone, Malaria, Lead optimization, Antimalarials

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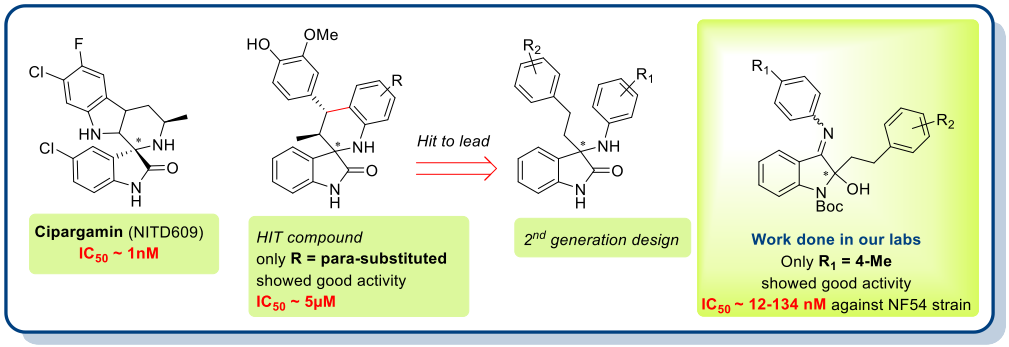
The discovery of Cipargamin, a potent antimalarial agent, has resulted in a growing body of research concerning the compound's spiroindolone scaffold and its application in the treatment of malaria. Cipargamin was identified as a lead compound due to its novel mode of action, transmission blocking potential, and compelling antimalarial activity (IC_{50} = 0.5-1.4 nM against *P. falciparum in vitro*).[1] One of the greatest challenges in the treatment of malaria includes the emergence of drug resistance. Cipargamin showed activity against multi-drug resistant malaria strains due to its novel mode of action. Previously Rousseau *et al.* developed a series of 3',4'-dihydro-1'*H*-spiro(indoline-3,2'-quinolin)-2-ones which bear the spiroindolone scaffold, of which only para-substituted analogues displayed activity in the micromolar range *in-vitro*.[2] Further optimization included a virtual ring opening to afford 3-amino-3-phenethyl oxindoles, which were designed to have improved flexibility. However, the attempted preparation of 3-amino-3-phenethyl oxindoles via Grignard addition to isatin derived ketimines gave rise to unusual reactivity which yielded 2-phenethyl-3-imino indol-2-ols. Despite this, the prepared 2-phenethyl-3-imino indol-2-ols displayed improved antiplasmodial activity in the nanomolar range against the NF54 strain of *P. falciparum* (12.6–134.7 nM), however, the compounds were found to be unstable. Due to the observed efficacy of the previously synthesized compounds *in vitro*, the work herein focuses on expanding the library of existing analogues by optimizing the structure-activity relationship data generated previously. This work specifically explores the synthetic viability of the preparation of analogues with improved stability and antiplasmodial activity.



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P70: Phytochemical investigation of secondary metabolites from *Pappea capensis* for anticancer properties

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Introduction: Cancer is a global threat severely affecting the human population. The number of cancer cases and deaths continues to grow each year[1]. Due to lack of effective treatments against this disease, researchers have turned their attention towards naturally-derived compounds as they are considered to have less side effects. The aim of the study was to extract, isolate and identify bioactive compounds from *Pappea capensis* and test them against several cancer cell lines.
Material and methods: The plant materials were purchased from Grow wild Indigenous plants Nursery in Midrand. The aerial parts of the plant were dried and ground to a fine powder and sequentially extracted with organic solvents hexane (100%), dichloromethane (100%), ethyl acetate (100 %) and methanol (100%). Dichloromethane crude was fractionated by gradient elution. Main fractions were purified by column chromatography and thin layer chromatography. The isolated compounds were characterized by nuclear magnetic resonance (NMR) and infrared spectroscopy.
Results: Four compounds were isolated from the dichloromethane crude. To date, three of the four compounds have been identified to be Lupeol (**1**) and a mixture of α-Amyrin (**2**) and β-Amyrin (**3**) shown in Figure 1.
Conclusion: of the four compounds isolated from the dichloromethane crude, three of them have been successfully identified. Crude extracts and isolated compounds will be evaluated for *invitro* anticancer properties.

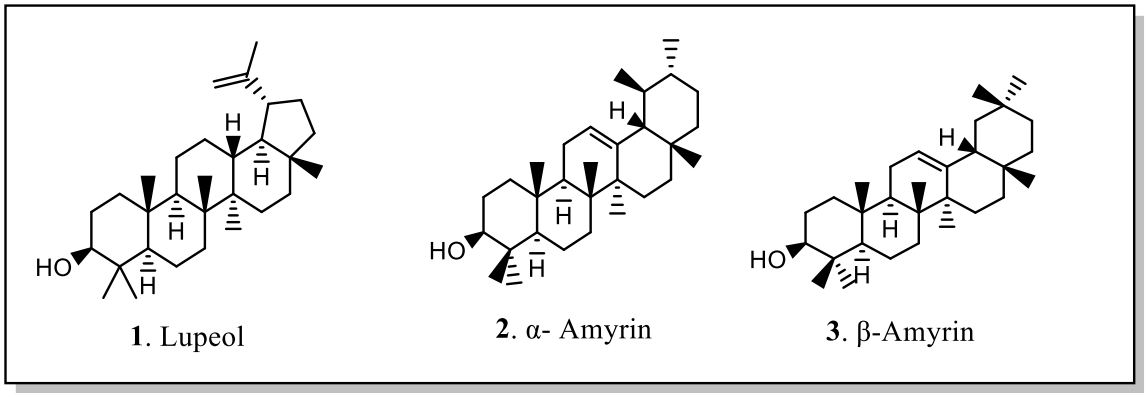

Figure 1: Structures of isolated compounds

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P71: A Green and Efficient Synthesis of Ethambutol

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Keywords: Ethambutol.

(S-S)-Ethambutol (**Figure 1**) has been instrumental in the treatment and control of tuberculosis (TB). It is among the first-line antibiotics used due to its selectivity and high potency against *Mycobacterium tuberculosis*. The chemotherapeutic agent act by inhibiting mycobacterial arabonosyl transferases, enzymes involved in bacterial cellwall biosynthesis.[1]

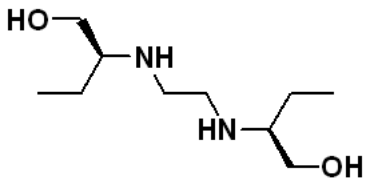

Figure 1. Ethambutol

Current literature synthetic methods of ethambutol involve alkylation reactions, which make use of alkylating reagents such as 1,2-dichloroethane known for the toxic nature.[2] In pursuit of our research project aimed at stereoselective synthesis of ethambutol, we report herein our progress on a green and efficient methodology towards this compound with antimycobacterial significance.

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2. V. Yufryakov, M. Tsvetikova, N. Bystrova and K. Kochetkov, *Russ. Chem. Bull*., 2023, **72**, 1268

P72: The synthesis of bridged disaccharides

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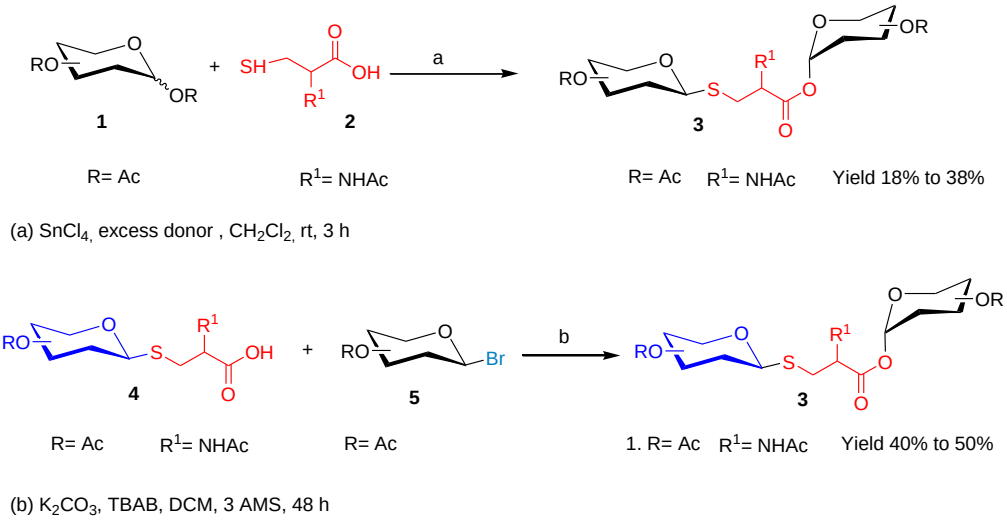
Keywords: Cysteine bridged disaccharide, and Mycothiol analogues.

In 2014 Nkambule and co-workers reported the serendipitous synthesis of a cysteine bridged disaccharide, which is an analogue of Mycothiol (MSH).[1] The synthetic analogues of MSH are potential inhibitors of MSH biosynthesis and may be a key to the development of more efficacious treatments against tuberculosis (TB).

The current method to synthesize cysteine-bridged disaccharide uses an excess of the peracetylated donor, but that only gives symmetrical disaccharides. To make asymmetrical disaccharaides we envisioned the approach shown in Scheme 1 where a cysteinyl sugar reacts with a different glycosyl donor**.**



Scheme 1: Synthesis of cysteine bridged disaccharides

In conclusion, we can synthesize the both symmetrical bridged disaccharides and asymmetrical bridged disaccharide using the new approach. In this presentation the latest development, results, and an overview will be discussed.

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1. NOKWEQU, M. G., NKAMBULE, C. M., GAMMON, D. W. *S. Afr. J. Chem*., 2014, 67, 180-183.

P73: Reaction-enhanced solvent extraction of carboxylic acids from aqueous solution using hydroxyl-functionalized ionic liquids

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[b] *SMRI/NRF SARChI Research Chair in Sugarcane Biorefining, School of Engineering, University of KwaZulu-Natal, Howard College Campus, Durban, South Africa, E-mail: starka@ukzn.ac.za*

Keywords: Carboxylic acids, fermentation, reactive extraction, ionic liquids, separation.

Carboxylic acids can be produced through chemical synthesis or biochemical processes such as fermentation. The depletion of petroleum reserves, increasing sustainability concerns, and adoption of bio-based chemicals favour the production of carboxylic acids via fermentation. Furthermore, some carboxylic acids have complex structures and are derived solely from fermentation. The major drawback of fermentation is low productivity due to end-product inhibition, which complicates the recovery of the carboxylic acids from the broth. Separation costs constitute nearly 50% of the overall costs in biorefineries.[1] The conventional recovery of carboxylic acids from aqueous solutions using calcium hydroxide is characterized with stoichiometric production of waste sludge.[2] Methods such as adsorption, dialysis, ion exchange, and liquid-liquid extraction are hindered by low efficiency, high energy requirements and extreme costs.

Reactive extraction offers an intensified alternative for the recovery of carboxylic acids from aqueous solution.[1] Conventional reactive extraction of carboxylic acids is achieved using organic solvents such as long-chain tertiary amines, which are toxic, volatile, and difficult to regenerate. The use of ionic liquids (ILs) for sustainable development is an area of active research. The tunable chemistry of ILs present a competitive advantage for their use as an alternative solvent for reactive extraction processes.[2] This study details a proof of concept of the application of a hydroxyl-functionalized IL for the reactive extraction of carboxylic acids from aqueous solution. The underlying extraction mechanism takes advantage of the reactivity of the carboxylic acids as well as the hydroxyl functional group in the IL. The major bottlenecks to be addressed include preparation of a functionalized IL, phase miscibility, extractability of the carboxylic acid, and solvent regeneration.

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P74: Synthesis of 5-substituted-4,6-diaminopyrimidine derivates as potential inhibitors of P*f*CDK1 and P*f*CDK4 for malaria treatment and transmission-blocking

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Keywords: Malaria, *Plasmodium falciparum*, *Pf*CDPK4, *Pf*CDPK1, 4,6-diaminopyrimidines

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Efforts made to reduce and/or eliminate malaria globally have continuously been undermined by the spread of drug resistant *Plasmodium falciparum* parasites. Thus, the development of new antimalarial agents with novel targets, especially those that block transmission is vital in the fight against malaria. *Plasmodium falciparum* calcium-dependent protein kinase 4 (*Pf*CDPK4) has been identified as an ideal target for the development of potent and selective transmission blocking agents[1-3]. Taking advantage of the high sequence homology of CDPKs, we explore the potential of 5-substituted-4,6-diaminopyrimidine derivatives as inhibitors of both *Pf*CDPK4 and *Pf*CDPK1 for malaria transmission-blocking and treatment, respectively. We also look at how the nature (i.e., C, N, or O), length and flexibility of the linker between the pyrimidine scaffold and the 5-substituent affects the compound performance.

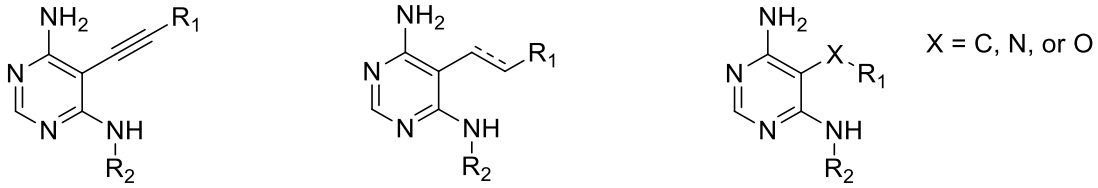

Figure 2: General structures of the explored 5-substituted-4,6-diaminopyrimidine derivatives.

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P75: Synthesis of fused bicyclic rings via cyclodehydration of triols using catalytic dibutyltin oxide

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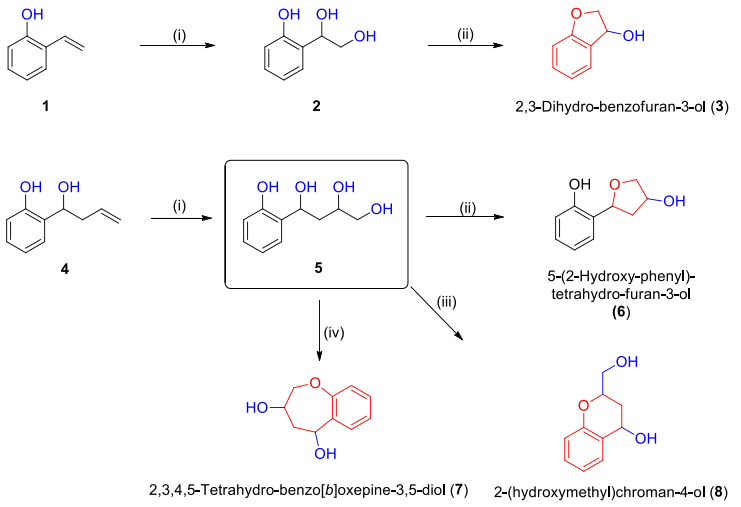
Keywords: Bicyclic compounds, chromanoids, cyclodehydration, flavonoids and oxepines.

Bicyclic compounds are found widely in natural and pharmaceutical products.[1] These include flavonoids, chromanoids, benzoxepines which have benzofuran, benzopyran and oxepine moieties, respectively. Compounds with these three moieties have been reported to exhibit a wide range of biological properties including antimicrobial, anticancer, antioxidant, and anti-inflammatory. [2]

Medicinal chemists extract compounds with complicated structures from plants, but that can be a tedious process and often with low yields of the desired product and requires a lot of reagents and solvents. Some of the target compounds contain fused cyclic rings and many other functional groups, thus posing a serious synthetic challenge to chemists. Our hypothesis is that benzofurans, benzopyrans, and oxepines can be synthesized by cyclodehydration from various polyhydroxylated molecules as shown on scheme 1.[3]



Conditions: (i) NMO, Ac_2O-H_2O (5:1), OsO_4 (cat), 24 h, 0-25 °C. (ii) 1. TBSCl, DMF, RT, 3 h. 2. *p*-TsCl, Bu_2SnO, Et_3N, CH_2Cl_2 reflux, 3.5 h. 3. HCl, MeCN/H_2O, RT, 3h. (iii) 1. BzCl, Bu_2SnO, Et_3N, CH_2Cl_2 reflux, 3.5 h., 2. *p*-TsCl, Bu_2SnO, Et_3N, CH_2Cl_2 reflux, 3.5 h. 3. K_2CO_3, MeOH/THF, RT, 2 h. (iv) *p*-TsCl, Bu_2SnO, Et_3N, CH_2Cl_2 reflux, 3.5 h.

Scheme 1: Synthesis of fused bicyclic rings using cyclodehydration.

1. Jha, A.K., Inani, H. & Easwar, S. 2018. *Tetrahedron Letters*, **59**: 2356-2359.
2. Shamsuzzaman, H.K. 2015. *European Journal of Medicinal Chemistry*, **97**: 483-504.
3. Gamedze, M.P., Maseko, R.B., Chigondo, F. & Nkambule, C.M. 2012. *Tetrahedron Letters*, **53:** 5929-5932.

P76: The synthesis and characterization of novel Guerbet-type and linear N-alkyl amino acid surfactants

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Keywords: Guerbet, amino acid, alkyl amino acid surfactants.

In the past decade, amino acid surfactants have been increasingly used in various industries as environmentally friendly formulation agents. Surfactants are used in the agricultural, cosmetic, pharmaceutical, and food industries to enhance the solubility and stability of the active component. However, there has been limited research on the synthesis of acidic *N*-alkyl amino acid surfactants. To the best of our knowledge, the synthesis and application of Guerbet-type amino acid surfactants have not been investigated.

In this study, two different synthesis routes were employed to synthesize 13 different *N*-alkyl surfactants. The synthesis of three linear *N*-alkyl iminodiacetic acid surfactants and 10 unique Guerbet-type *N*-alkyl amino acid surfactants was successfully carried out. The synthesis was performed with high purity and yields exceeding 90%. NMR elucidation of the surfactants and their starting materials is discussed. Grant-Paul parameters were calculated for the α, β, and γ carbons of the surfactants. These parameters can be used in the future to make predictions about the ^{13}C NMR shifts of similar amino acid surfactants. Furthermore, the relationship between NMR resolution, sample concentrations, and surfactant aggregation is discussed.

P

P77: Quantitative analysis of wet process phosphoric acid reaction by spectroscopic techniques

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Keywords: Phosphoric acid, Wet process phosphoric acid, Wet chemistry

Phosphoric acid is one of the essential minerals due to its widespread industrial use and production [1]. It is frequently used in the food and beverage industry to increase acidity and flavours, particularly in carbonated drinks like cola and to make fertilizers like phosphate fertilizers [2]. In this study, we study the P_2O_5 concentration of phosphoric acid purification using the wet process reaction method by using a UV-visible technique. Other impurities concentrations were also measured using inductively coupled plasma optical emission spectroscopy (ICP-OES) [3,4]. The quantification of P_2O_5 results by UV-visible techniques was 50.8% for wet process phosphoric acid (WPA) and 39.3% for raffinate (Organic matter). The P_2O_5 results for the stripped aqueous phase was 9,26%. ICP-OES results revealed that other elements with high concentrations were Al, Ca, Fe, and Mg with 7780,54, 1243,65, 5161,39, and 9738,45 mg/L respectively. The metal concentrations after extraction for Al, Ca, Fe, and Mg were successfully reduced to 9603, 3972, 6003, and 12571 mg/L, respectively.

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2. J Chem, Ji-guang Li, Yu-feng Hu, Shu-feng Sun, Yan-sheng Liu, The Journal of Chemical Thermodynamics, 42.7 (2010), 904–8
3. Changwen Ye a ∗ and Jun Li B', August, 2012
4. Wu, Shengxi, Liangshi Wang, Patrick Zhang, Hassan El-shall, Brij Moudgil 'AC PT CR' 2017

P78: Development and application of "tag, capture, and release" derivatizing protocol for alcohols

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Keywords: Fluorous tags, diols/triols, benzotriazoles and tin catalyst

Bioactive 1,2,4-triol compounds can either be extracted and isolated from avocado fruit, or be synthesized for medicinal, nutritional and cosmetic applications [1,2]. However, the extraction, isolation and purification of these compounds is tedious and inefficient. So the main objective of this study was to develop a cost effective, environmentally friendly and efficient method for the extraction, isolation and purification of triol compounds from a matrix or reaction mixture via the "tag, capture and release" derivatization protocol. In this study fluorous tags (**1**, **2** & **3)** shown in Figure **1** were synthesized and characterized by mp, TLC, IR and NMR. The tags were used in the tin-mediated acylation reactions of diols and triols as shown in Scheme 1.

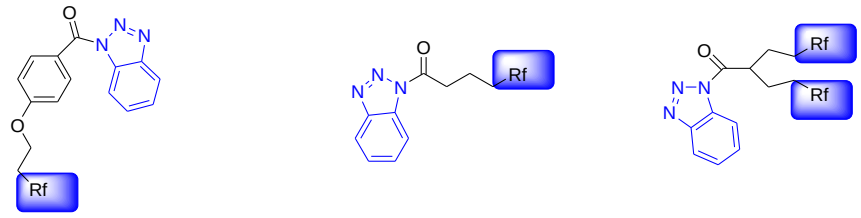
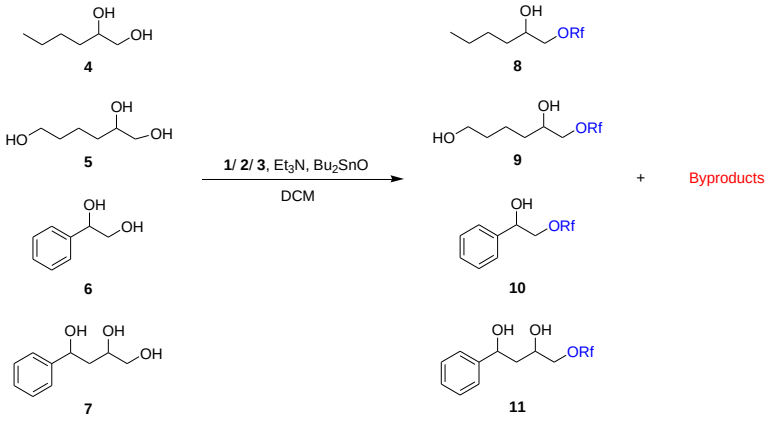


Figure 1. Flourous tags (BtORf)



Scheme 1. Acylation reactions of diols and triols with fluorous tags.

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P79: The synthesis and structural evaluation of *S,O*-bidentate ligands, and their tricarbonyl Re(I) complexes as anti-cancer agents

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Keywords: *S,O*-bidentate ligands, rhenium, anti-cancer

Platinum-based drugs are the drug of choice for cancer therapy; however, these compounds causes severe side effects, and patients develop resistance to this treatment. Therefore, alternate metal-based cancer drugs are needed due to the increase in the statistical number of new cancer cases diagnosed. The coordination chemistry of rhenium has been continuously improving in recent years due to its importance in biological applications particularly the *fac*-$[M(H_2O)_3(CO)_3]^+$ (M = Re) synthon developed in 1998[1]. This tricarbonyl precursor is appealing not only because of its potential use in therapeutic radiopharmaceuticals but also because of its coordinated water molecules, which can be easily substituted with appropriate novel ligand systems[2], which are advantageous for the development of new anticancer drugs. These ligands have received a lot of attention as highly customizable ligands in various applications[3] and this is due to the distinct properties, that allow them to coordinate as a bidentate ligand to the rhenium metal ion. In this study, various *S,O* bidentate ligands and rhenium(I) complexes containing H_2O on the axial position were synthesized using a *fac*-$[Re(CO)_3]^+$ core. The synthesis, characterization (IR, NMR, MS, XRD, and UV-Vis), and in vitro anticancer studies obtained are reported in **Figure 1**.

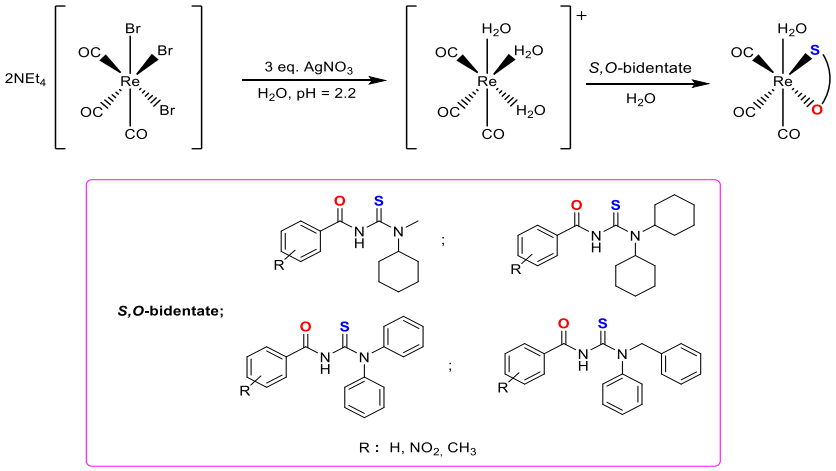

Figure 1: Schematic illustrations of various *S,O*-bid ligands and the synthesis of Re(I) tricarbonyl complexes

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P80: Synthesis and characterization of amino ferrocenyl heterocyclic and cyclopentane-dicarboxylate ligands

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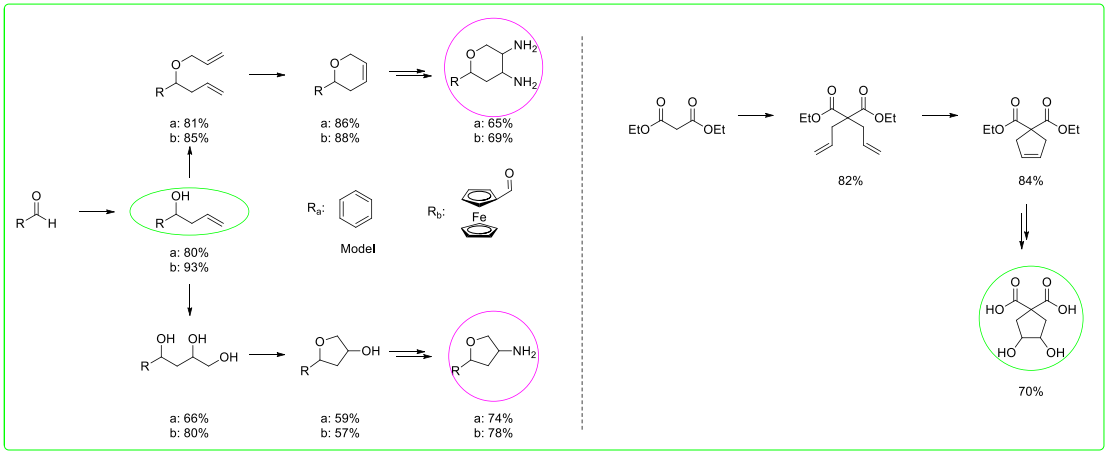
Keywords: Cancer, Tetrahydrofurans, Tetrahydropyrans, Dicarboxylate ligand.

Cancer ranks as the second most common cause of natural death.[1] Platinum anticancer agents remain to be the primary approach for the treatment of cancer however they are largely compromised by drug resistance and toxicity.[2] Recently, the incorporation of bioactive ligands into metals has emerged as an effective strategy to enhance their bioactivities and modulate their toxicities.[3] We are interested in the design of ferrocene containing heterocyclics (tetrahydrofurans and tetrahydropyrans) and dicarboxylate ligands which are potential ligands for coordination into metal centres. The THF and THP scaffolds are common in natural products that exhibit potent bioactivities including anticancer, antimalarial, and/or antifungal.[4] In this work we report the synthesis and characterization of ferrocenyl heterocyclics and cyclopentane-dicarboxylate; we postulate that the ferrocenyl heterocyclics will be potent by taking advantage of ferrocene's cytotoxicity, tunable redox and lipophilic characteristic.



The key steps to obtaining THFs involve homoallylation, dihydroxylation, cyclodehydration sulfonylation, mesylation, azidation and Staudinger reduction. While those for obtaining THPs include allylation, Grubbs-metathesis, and alkene-amination. The preparation of cyclopentane-dicarboxylate followed similar approach to THP synthesis and was obtained in moderate yields. All the synthesised compounds were characterized by IR and NMR (1D & 2D).

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P81: Rapid Method for Iodination of Phloroglucinol Derivatives

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Keywords: Electrophilic Iodination Reactions, Metal-Catalyzed Reactions, Phloroglucinol

In numerous metal-catalyzed coupling reactions, such as Heck, Sonogashira, Ullman, and many others, iodinated aromatic compounds play a significant role.[1,2] A handful of pharmaceutical drugs and some X-ray contrast media contains iodinated aromatic compounds.[1,3] Iodination is often achieved by electrophilic substitution reactions. Although it has a low reactivity and produces hydrogen iodide during the iodination of aromatic compounds, elemental iodine is known as a low-cost reagent. Owing to its advantage of atom economy and ease of oxidation into the iodonium species, elemental iodine is still a useful reagent. However, there is a variety of iodinating reagents in the market. Bis(pyridinium)iodinium(I)tetrafluoborate(IPy2BF4), Iodine monochloride (ICI), *N*-iodosuccinimide (NIS), and 1,3-diiodo-5,5-dimethylhydantoin(DIH) are examples of typical iodinating reagents.[4] In this poster, we describe how several iodinating agents were used to iodinate the phloroglucinol moiety and its derivatives.

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P82: PHYTOCHEMISTRY, CHEMICAL, AND BIOPHARMACEUTICAL PROFILING OF *HALLERIA LUCIDA* FOR ANTICANCER PROPERTIES

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Keywords: *Halleria lucida*; triterpenoid; steroid.

Introduction: Cancer is one of the leading causes of death in the 21st century but, conventional treatments have serious side effects and are often associated with multidrug resistance, leading to treatment failure.[1] Finding new chemotherapeutic agents that are more effective than traditional drugs which can overcome drug resistance and metastasis is crucial to improving the survival of cancer patients. Nanoparticles (NPs) and liposomes containing anti-cancer drugs are a promising alternative to conventional dosage forms due to their targeted drug delivery.[2] *Halleria lucida*, a medicinal plant with anticancer properties, is commonly found in South Africa's eastern coastal region.[3] The purpose of this phytochemistry phase of the project was to sequentially extract active chemicals from *Halleria lucida L*. leaves using hexane, dichloromethane, ethyl acetate, and methanol.

Methods and Materials: Active chemicals were sequentially extracted from 835.45g of *Halleria lucida L* leaves using hexane, dichloromethane (DCM), ethyl acetate, and methanol to extract. The crude extract of dichloromethane (DCM) (62.23g) was then used. Structures of these compounds were established using 1D and 2D NMR, IR, melting points, and comparison with literature values. Effects of the crude extracts and separated chemicals on triple-negative breast cancer cells (HCC70) were examined *in vitro*. Nano-formulation using active chemicals is currently in progress using chitosan and liposomes as nano-capsules.

Results and Discussions: Seven compounds were isolated and identified, of which four of these were pentacyclic triterpenoids belonging to the oleanane class, which included β-amyrin **(1)** (353.3 mg, 0.56% w/w), β-amyrin acetate **(2)** (76.5 mg, 0.123%), erythrodiol **(3)** (166.2 mg, 0.267% w/w), and oleanolic acid **(4)** (21.0 mg, 0.034% w/w). Additionally, a taraxerane-type pentacyclic triterpenoid known as marsformoxide B **(5)** (38.7 mg, 0.062% w/w), a lupane-type pentacyclic triterpenoid called lupa-12, (20)29-diene-3β,28-diol **(6)** (24.2 mg, 0.039% w/w), and a steroid named stigmasterol **(7)** (63.3 mg, 0.010% w/w) were isolated and identified. For each drug (50 μg/mL), the data obtained show the percentage of cell death as follows: DCM crude (78.52±2.22)%, β-amyrin (41.72±0.56)%, β-amyrin acetate (41.72±0.56)%, erythrodiol (54.46±0.90)%, oleanolic acid (78.52±2.22)%, marsformoxide B (47.16±0.63)%, lupa-12, (20)29-diene-3β,28-diol (56.17±1.41)%, and stigmasterol (56.17±1.41)%.

Conclusion: Seven isolated compounds were successfully identified through spectroscopic techniques and literature data.

Acknowledgments: I would like to acknowledge TUT Natural Products & Organic Chemistry Research and TUT Biopharmaceutical & Nanomedicine Research groups.

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P83: Synthesis of sulfamethazine derivatives as inhibitors of corrosion on aluminum metal in HCl medium.

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Keywords: Corrosion, Corrosion inhibitor, Sulfamethazine, Reductive amination.

Corrosion is the gradual deterioration of metals caused by the action of air, moisture, or a chemical reaction (such as an acid) on their surface. Corrosion is a global problem that strongly affects natural and industrial environments. Chemical industries can experience uncontrolled humidity, corrosive acids, bases, and gases which are the primary causes of corrosion in industrial environments. Corrosive acids such as HCl or H_2SO_4 results in the accumulation of corrosion products such as rust, which can pollute water bodies, The presence of rust causes harmful processes that affect the economy and the environment, also the efficiency of the industry and the durability of the infrastructure assets [2]. Therefore, it's essential to develop organic inhibitors that are eco-friendly to help reduce the effect of corrosion. Sulfamethazine derivatives were synthesized and evaluated as potential corrosion inhibitors for aluminum metal under an HCl corrosive medium. Sulfamethazine derivatives can be effective corrosion inhibitors because they contain heteroatoms with lone electron pairs and moiety with π-electrons (aromatic rings and multiple bonds) that can interact with the d-orbitals of the metal, favoring the adsorption process [1]. Three (3) sulfamethazine derivatives were synthesized via reductive amination reaction, purified using flash chromatography, and structures confirmed using F-TIR, ^{1}H-NMR, and ^{13}C-NMR. The compounds were tested as corrosion inhibitors for the aluminum metal in **1** M HCl at various temperatures (30, 40, and 50 °C). The best inhibition efficiency obtained was **91%** for N-(2-hydroxy-5-nitrobenzyl) sulfamethazine at **30 °C** and a concentration of **$4.5x10^{-3}$M**, while sulfamethazine showed an inhibition efficiency of **50%**.

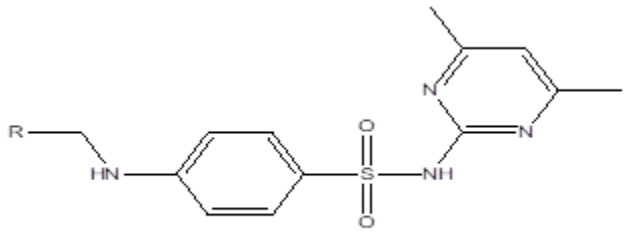

Figure 1: General structure of sulfamethazine derivatives

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P84: Mycochemical analysis and structural elucidation of compounds from an indigenous mushroom species, *Termitomyces sagittiformis*

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Keywords: *Termitomyces sagittiformis*, Ergosterol, Glycosphingolipid, Linoleic acid, Mannitol.

Termitomyces sagittiformis is an edible mushroom from the well-known genus of Basidiomycetes that forms a symbiotic relationship with the wood-destroying termites and is found in many parts of Africa and East Asia.[1, 2] Human beings have used mushrooms as a source of food and medicine for many centuries and some species played a role in traditional ceremonies. Like vascular plants, mushrooms produce secondary metabolites believed to be used as a form of communication amongst fungi or between fungi and other species, recognition of pathogens, signal transduction, cell differentiation, and exhibit antihepatotoxic, antitumor, antifungal, antiviral, neuritogenic, and immunoregulatory activities.[3] Natural Product Chemists are interested in the isolation and structural elucidation of bioactive secondary metabolites from organisms, including mushrooms, which are beneficial to the livelihood of humans. The aim of this study was to identify bioactive molecules with nutraceutical properties from the mushroom species, *L. sagittiformis*. Secondary metabolites and bioactive molecules include polysaccharides, terpenoids, steroids, nucleobases, and glycoproteins.[4] In addition to other compounds, we were able to isolate and carry out structural elucidation of the well-known sterol found in mushrooms, ergosterol, Figure 1, using ^{1}H NMR, ^{13}C NMR, COSY, HSQC, HMBC, GC-MS spectral techniques.

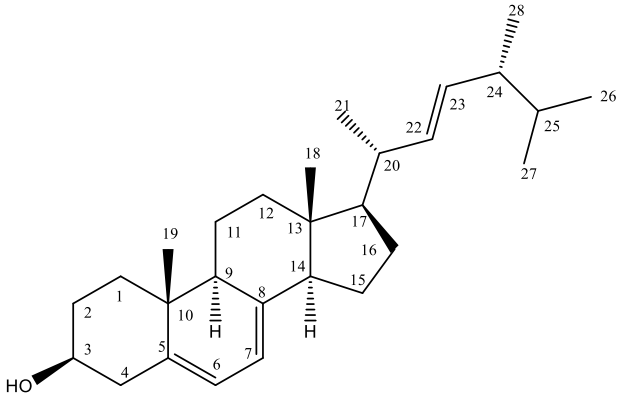

Figure 1. Chemical structure of ergosterol

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P85: Antidiabetic Activity of Methyl Gallate from *Mezoneuron benthamianum* Leaf: Structural modification and in-silico studies

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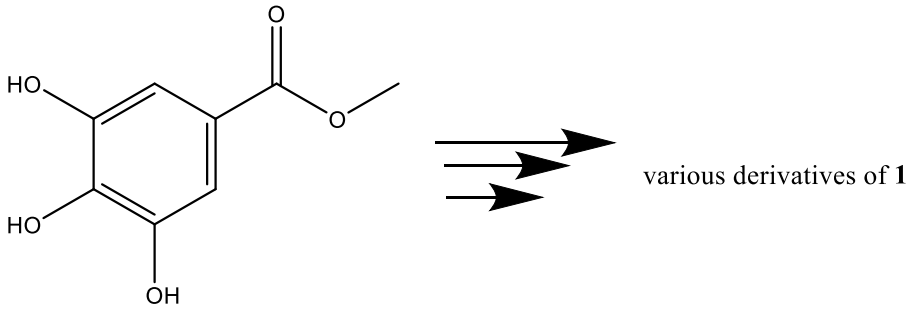
Keywords: *Mezoneuron benthamianum*, methyl gallate, α-amylase, in-vitro, in-silico.

Mezoneuron benthamianum is a climbing shrub that has traditionally been used to cure malaria, bacterial, fungal, and inflammatory disorders in West Africa.[1-2] The antidiabetic activities of the isolated compounds from *M. benthamianum* leaf are investigated in this work. The pulverized leaf (1 Kg) was extracted by maceration with dichloromethane and methanol successively to give the dichloromethane and methanol extracts. Column chromatography fractionation of the methanol extract led to the isolation of a compound **1** (methyl gallate).

The α-amylase inhibitory activity of methyl gallate (IC50 = 43.9 μg/ml) demonstrated that it is more active than the standard antidiabetic drug acarbose (IC50 = 378.2 μg/ml). In silico studies of methyl gallate when docked into the active site of the targeted diabetic proteins: human pancreatic alpha-amylase, pig pancreatic alpha-amylase and tetrameric 11B-HSD1 oxidoreductase enzyme, showed that methyl gallate had good interactions with the target proteins, with binding affinities of -4.8, -4.8 and -6.5 Kcal/mol, respectively, when compared to arcabose with binding affinities of -5.9, -5.5, -6.5 Kcal/mol, respectively. These intriguing in vitro and in silico activities of methyl gallate influenced our decision to further probe the structural derivatives of methyl gallate in order to improve both antidiabetic activity and pharmacokinetic features.



Compound **1**
(methyl gallate)

1. Jansen O, Tchinda AT, Loua J, Esters V, Cieckiewicz E, Ledoux A, Toukam PD, Angenot L, Tits M, Balde AM, Frédérich M, *J Ethnopharmacol Antiplasmodial activity of Mezoneuron benthamianum leaves and identification of its active constituents*, 2017, **203**, 20.
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P86: Exploring possible inhibitors targeting the SARS-CoV-2 MP^{RO} enzyme extracted from *Dacryodes edulis* stem bark

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Keywords: *Dacryodes edulis*, ethnomedicine, SARS-CoV-2.

In the relentless pursuit of effective therapeutics against SARS-CoV-2, the causative agent of the ongoing COVID-19 pandemic, researchers have turned their attention toward natural compounds with potential inhibitory properties. One such avenue of investigation involves exploring the medicinal properties of *Dacryodes edulis*, a plant known for its diverse range of bioactive compounds. *Dacryodes edulis* is a plant that is indigenous to the Gulf of Guinea and is widely used in ethnomedicine to treat a range of ailments such as tonsilitis and fever which arise from viral infections[1]. The aim of the study was to identify bioactive compounds extracted from *Dacryodes edulis* and test them against the SARS-CoV-2 M^{PRO} enzyme.

The plant material was sequentially extracted by maceration with four different solvents in the order of increasing polarity, i.e., Hex, DCM, EtOAc, and MeOH. The extracts were then tested for phytochemicals and then fractionated by column chromatography using different solvent systems starting from less to more polar (e.g., 100% Hex, 90 Hex:10 DCM, etc). The resulting unknown compounds were subjected to characterization techniques. The column chromatography of the hexane crude extract afforded five pure compounds. The techniques have confirmed compounds to be Lupeol acetate, Lupeol, and β-amyrin (Figures 1,2, and 3).

Five compounds have been successfully isolated and identified. These compounds are going to be tested against the SARS-CoV-2 M^{PRO} enzyme.

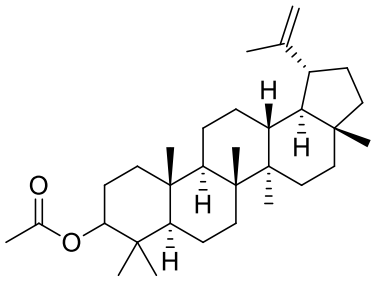

Figure 1. Lupeol acetate

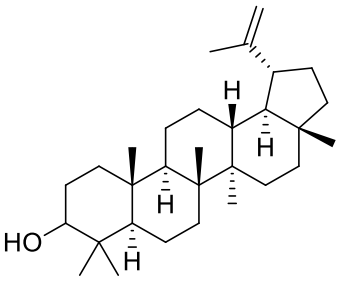

Figure 2. Lupeol

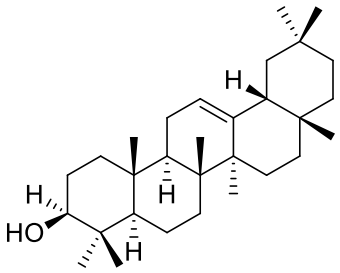

Figure 3. β-amyrin

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P87: Pharmacophore modelling, QSAR study, insilico ADME prediction of N-phenylphenoxyacetamide derivatives, oxadiazole compounds and N-substituted tropinones with the potential of EthR inhibition.

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Keywords: Tuberculosis, MDR-TB, Ethionamide, EthR inhibitors.

Purpose: Tuberculosis (TB) is one of the leading infectious diseases, about one-quarter of the global population is infected with TB. Multi-drug resistant (MDR) TB remains a threat to health security, with a treatment success of 59% reported in 2018. MDR-TB requires extensive treatment with second-line TB treatment for 24-48 months. Ethionamide (ETH), a second line TB drug is a prodrug that is activated by the enzyme ethA inside the mycobacteria. ethA is regulated by the transcription regulator ethR, the repressor gene ethR is involved in the resistance of ETH to Mycobacterium tuberculosis. One of the strategies to boost ETH is to inhibit ethR to increase the activity of the drug. This study will focus on the Pharmacophore, Quantitave Structure-Activity Relationships (QSAR) and absorption, distribution, metabolism, excretion, toxicity (ADMET) of N-phenylphenoxyacetamide derivatives which inhibit ethR.
Methods: Over 50 biologically active compounds (N-phenylphenoxyacetamide derivatives, oxadiazole compounds and N-substituted tropinones) which are ethR inhibitors were taken from literature studies and used in this current study. Pharmacophore, QSAR and ADMET properties were calculated using the Schrödinger's Suite.
Results: Scored based on phase hyposcore, the AADRR_1 (A- H bond acceptor, D- H bond donor, R – benzene ring) hypothesis is the best hypothesis in this analysis characterized by high survival score (5.100474) for N-phenylphenoxyacetamide derivatives. Most compounds have good gastrointestinal absorption, QPPCaco > 500.
Conclusions: N-phenylphenoxyacetamide derivatives, oxadiazole compounds and N-substituted tropinones are promising compounds in the drug development of Ethionamide based on the in silico ADMET results. Further in vitro studies are needed to validate the results obtained in this study.

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P88: Synthesis of Sulfamezarine derivatives as potential corrosion inhibitor of zinc metal in 1 M sulphuric acid solution

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Keywords : Corrosion, organic inhibitors, Sulfamezarine.

Corrosion is the process of material decay caused by physical or chemical interactions with the environment[1]. Zinc is a very important metal used in a wide range of applications by various industries, and it is also very active metal hence it corrodes faster in aqueous solution. Thus, use of corrosion inhibitors is often a good solution to prevent corrosion phenomena and to provide a more acceptable life time of metallic structures. Therefore, organic compounds are used as corrosion inhibitors because they contain atoms (nitrogen, oxygen, sulfur and phosphorous), aromatic ring or triple bonds that reduce corrosion attack in aqueous solutions[2]. In this study, three (3) derivatives of sulfamezarine were synthesized, and characterized by NMR, FTIR and MS. The derivatives were evaluated as corrosion inhibitors of zinc due to 1 M H_2SO_4 at different temperatures (30, 40, and 50 °C). Both the sulfamezarine and its derivatives have shown best inhibition of about 65% at different temperatures which implies that the effect of temperature on inhibition is prominent.

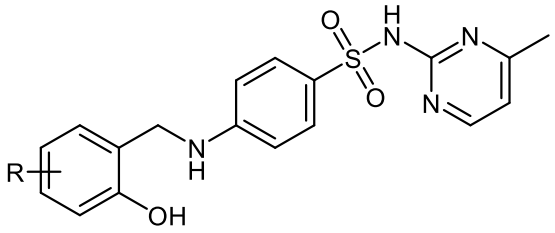

Figure: A general representation of the sulfamezarine derivatives.

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P89: Synthetic studies and biological evaluation of chromone-based derivatives

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Keywords: Synthesis, chromones, Tuberculosis, Malaria

Chromones(4*H*-1-benzopyran-4-ones) are a group of naturally occurring compounds that are ubiquitous in nature,[1] and are widely found in different plant parts, ranging from the flower petals, to leaves, stems, roots and barks of trees. These plant parts have all been used by traditional healers worldwide to relieve various ailments. These compounds exhibit broad spectrum pharmacological properties ranging from antibacterial, antiviral, antifungal, anti-inflammatory, etc[1,2] or exhibit interesting chemical reactions. Chromone-based derivatives have been used as a precursor to synthesize a diversity of heterocyclic systems due to the presence of an α,b-unsaturated keto-function.The rigid bicyclic chromone moiety has been classified as a priviledged structure in the drug discovery.[3,4]

The presentation will focus on the progress made on the synthetic studies and biological evaluation of chromone derivatives as potential lead compounds for the treatment of diseases such as Mycobacterium tuberculosis, Malaria, and Diabetes.

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P90: Easy access to the synthesis of 4,5-dihydrooxazole/5,6-dihydro-4*H*-1,3-oxazine derivatives *via* carboxamides

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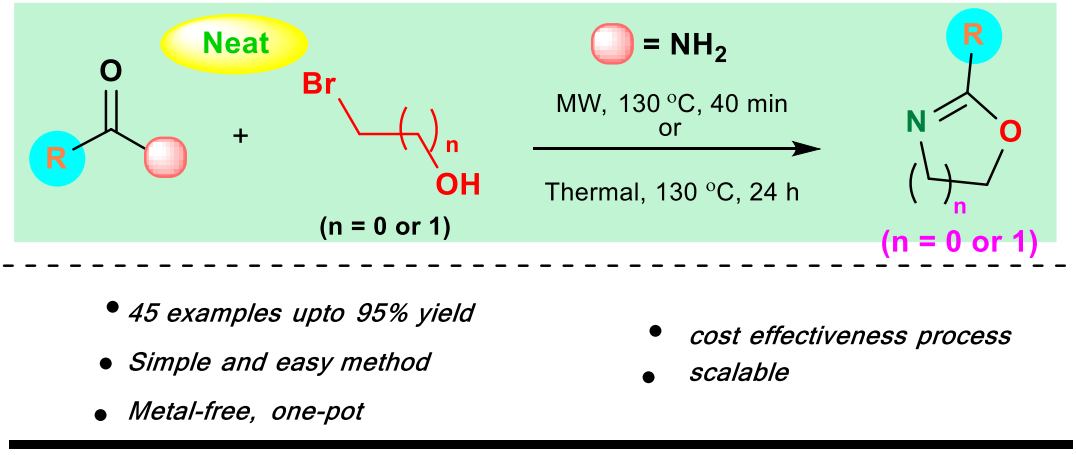
Keywords: carboxamide, haloalcohols, dioxazine, oxadiazine, oxazine, and oxazoline.

Oxazole is a nitrogen and oxygen containing five membered rings with versatile biological profile. It's unsaturated analogue, oxazoline has gained attention of many researchers due to its wide scope in the field of pharmaceutics, medicine, agriculture as well as polymer chemistry. It has also displayed activities like anti-cancer, antimicrobial, antitubercular agent, Prostacyclin receptor antagonists, CNS agent and many more. With this background, we interested to work on economical, greener, and one-pot synthesis of 2-oxazolines from commercially available starting materials. In this, one-step reaction of carboxamide with bromoethanol in microwave at 130 °C for 40min (Thermal heating at 130 °C for 24 h) affording 2-oxazoline analogues in absence of base, catalyst, and solvent. The scope of the present synthetic approach was further investigated by selecting various haloalcohols and amide derivatives for synthesizing other heterocycles like oxazine, dioxazine, and oxadiazine etc.. Proposed reaction mechanism for these conversions suggests in-situ dehydrohalogenation followed by dehydration resulting into desired compound in quality and quantity (up to 90% yield). Structures of the final compounds were confirmed by analytical techniques such as NMR (^{1}H, ^{13}C, HMBC, & HSQC), and FT-IR.

Graphical Abstract:



P91: Bioactive Arylnaphthalide Lignans from *Justicia depauperata*

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Keywords: *Justicia depauperata*, Arylnaphthalide, cytotoxic

Abstract: Phytochemical investigation of *Justicia depauperata*, a Cameroonian medicinal used in folk medicine for the treatment of jaundice, liver affections and to cure certain cancers[1], led to the isolation of eleven new arylnaphthalide lignans (**1**−**11**), together with seven known compounds (**12**−**18**). Their structures were elucidated mainly by extensive spectroscopic analysis and mass spectrometry. Compounds **6** (IC_{50} = 4.06 μM) and **9** (IC_{50} = 9.44 μM) displayed significant cytotoxic activity against cervix carcinoma cell line KB-3-1, and were four and two times, respectively more active than griseofulvin (IC_{50} = 19.3 μM) used as the reference drug. Additionally, the extract, fractions, and some of the isolates were screened for their antibacterial and antioxidant activity. The results of the antioxidant screening showed that compounds **9** and **14** exhibited good activity with IC_{50} values of 84.5 and 41.2 μM respectively. Furthermore, compound **14** with an IC_{50} value of 41.2 μM was more active than trolox used as reference (IC_{50} = 68.0 μM). Regarding the antibacterial test, compound **6** showed the best activity in all the selected strains (MIC ranging from62.5 to 31.25 μg/mL) excepted *Pseudomonas aeruginosa* HM801. Furthermore, compound **12** showed the best activity (MIC = 15.6 μg/mL) against *P. aeruginosa* HM801.Compounds **6** and **9** which displayed promising cytotoxic activity, were also docked and the results obtained supported and delivered further insights on their cytotoxicity.

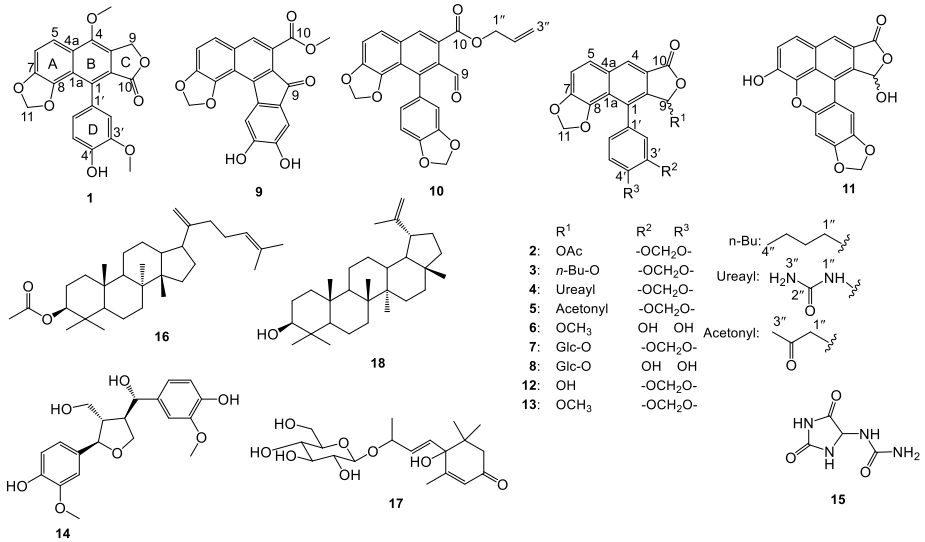

Figure 1. Structures of compounds **1**−**18** from *Justicia depauperata*.

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P92: HYBRIDIZATION OF AIDS AND TB DRUGS

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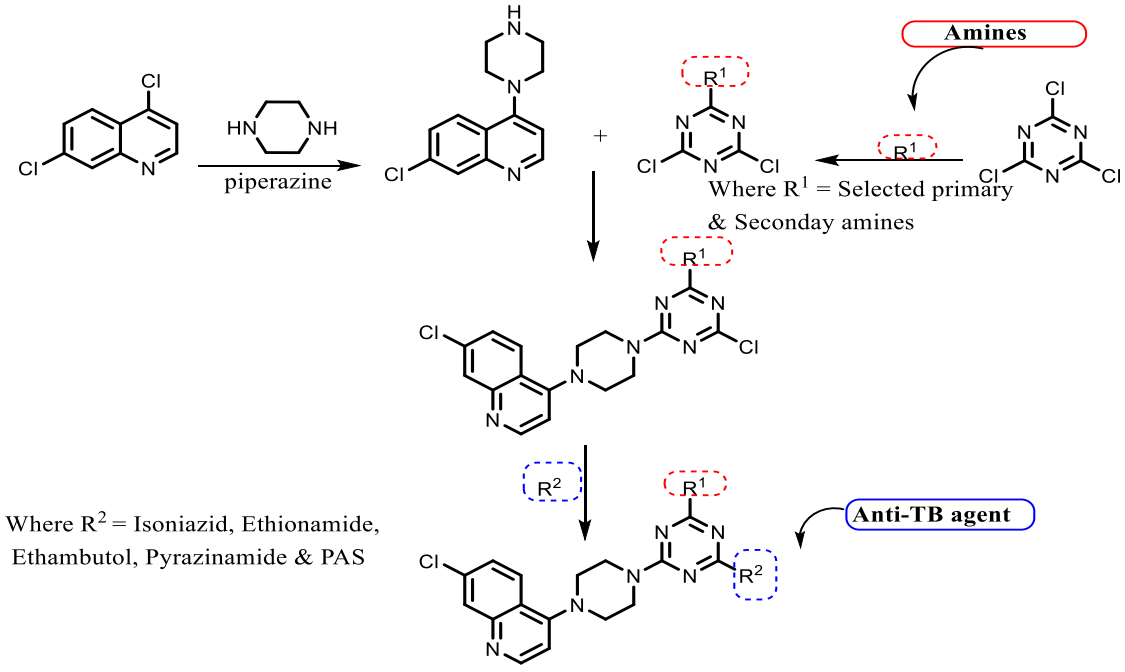
Keywords: 1, 3, 5-triazine, hybridization, TB, quinoline.

Tuberculosis (TB) is one of the leading causes of mortality rate worldwide.[1] Although there are already a handful of anti-TB drugs which are in use presently, drug resistance against many existing TB drugs and lack of treatment adherence due to excessive pill burden, remains a major problem. Hence this project is aimed at synthesizing novel hybrid potential anti-TB drugs. The new proposed potential drugs will be obtained by using a hybridization process (i.e. combining two or more drugs into a single chemical entity to form a hybrid drug). 1, 3, 5 triazine will be used as a middle linker of known amines, 4-aminoquinolines and TB drugs. Nucleophilic substitution will be used as a general reaction of this project. [2]



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P93 The use of blended and single essential oils in management of anxiety and stress.

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Keywords essential oils, lavender, Bergamot, chamomile, single and blended

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This study explores the therapeutic potential of both single essential oils, including lavender, chamomile, and bergamot, and blends of essential oils in managing anxiety and stress. Essential oils, known for their aromatic and healing properties, have a rich history dating back to ancient civilizations. These oils are extracted from various plant parts and have been used for centuries in diverse cultures for their potential emotional and physical benefits. This research draws inspiration from the historical and geographical origins of these essential oils. Lavender, with its Mediterranean roots, has a history steeped in its calming properties, while chamomile, utilized in ancient Egypt, is associated with relaxation and soothing effects. Bergamot, known for its citrusy allure, finds its origins in the Calabrian region. A randomized controlled trial will be conducted, involving participants who report symptoms of anxiety and stress. The intervention methods will encompass various application methods, including inhalation, topical application, and aromatherapy. Blended essential oils, inspired by ancient practices and carefully formulated to leverage the unique properties of each constituent oil, will be used alongside single essential oils. The study will utilize standardized instruments to assess anxiety and stress levels both before and after the intervention. This research aims to determine whether single and blended essential oil combinations. The findings of this research will not only enhance our understanding of the practical applications of essential oils for emotional well-being but will also pay homage to the historical and cultural roots of these natural remedies. This insight may be of great value to individuals seeking ancient-inspired, natural remedies for managing anxiety and stress

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Fradelos E., Komini A, The Use of Essential Oils as a Complementary Treatment for Anxiety, 2014. *American Journal of Nursing Science*, 4: 1-5

P94: Identification of alpha-glucosidase inhibitors from indigenous plants

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Keywords: *scleracarya birrea*, diabetes, lead-like.

Diabetes mellitus, also known as diabetes, poses a great threat to global health due to the exponential death rates caused by the disease. The rising prevalence of diabetes calls for innovative therapeutic approaches needed for maintaining diabetes.[1,2] Traditional medicines (derived from plants and animal extracts) have gained considerable attention as an alternative and affordable treatment. Isolated plant compounds and their modification have given possible candidates and drugs, i.e., Metformin, an antidiabetic drug isolated from Galega officinailis.[3]

Sclerocarya birrea (A.Rich.) Hochst., also known as Morula, has been reported as one of the medicinal plants with antidiabetic activity.[4] However, bioactive compounds responsible for the activity have not yet been reported until recently. Maharaj et al.[5] identified eight compounds responsible for the antidiabetic activity, from which three were isolated and further tested. This study is conducted further to understand the uses of this plant in enzyme-inhibition studies. Lead-like small-scale (300mg) extraction was prepared from plant material. Conducted the α-glucosidase inhibitory assay for plant extract. The extract was confirmed active. Method development and fractionation of the extract into a 96-well plate was performed using high-performance liquid chromatography. The plate was then subjected to enzyme-inhibition studies. The active wells will be analysed by LC-MS-MS to determine the structures of the active compounds. The unknown compounds will be isolated by preparative HPLC, and the structures will be determined by NMR and MS.

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