



Southern  
African  
Training  
Academy



# 1<sup>st</sup> International Conference on Clinical Trial and Innovative Therapeutics



July 24-26th, 2017. Cape Town Lodge, Cape Town, South Africa

Organised by

**The Southern African Training Academy and  
The Larkin University**

# Southern African Training Academy - Larkin University



Southern  
African  
Training  
Academy

**1<sup>st</sup> International Conference on Clinical Trial & Innovative  
Therapeutic 24 – 26<sup>th</sup> July 2017, Cape Town (South Africa)**



## Programme and Abstracts

**July 24-26, 2017, Cape Town Lodge, Cape Town, South Africa**

# Disclaimer

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The information presented in this book of program and abstracts is as accurate as submitted by the authors. The ideas, opinions, and views presented in this book do not necessarily reflect those of SATA Conference. The organizer committee accepts no liability whatsoever for any claim that may arise from any of these abstracts.

This book is produced by the local organizing committee of this conference and first published in South Africa.

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## Welcome Message from the Conference Chairman

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**Prof. Kensese S. Mossanda**

In our perspective to build up a platform for the exchange of researchers between various institutions for the dissemination of knowledge generated by academics, researchers and postgraduate students, the 1st International Conference on Clinical Trial and Innovative Therapeutic” has been conjointly organized by the South African Training Academy (SATA – South Africa) and the Larking University (USA) from 24 to 26 July 2107 in Cape Town.

Our society is beset with numerous challenges that require indeed a collaborative approach which should collate information from many varied sources.

This conference has therefore gathered academics and scientists from India, USA, and various African countries for showcase presentations resulting from growing and conducive environments created for research enhancement.

26 renowned academics and researchers have been invited as keynote/plenary/contributing speakers to make presentations as follows:

1. Prof. Anupam Bishayee – Larkin University (Miami, USA)
2. Prof. Kensese Mossanda – SATA (Johannesburg, South Africa)
3. Prof. Theeshan Bahorun – Mauritius Research Council (ANDI CBBR, Reduit Mauritius)
4. Prof. Sanjay K Srivastava – Texas Tech University (Amarillo, USA)
5. Prof. John I Anetor – University of Ibadan (Ibadan, Nigeria)
6. Prof. Manju Ray – Bose Institute (Kolkata, India)
7. Prof. Hiranmoy Das - Texas Tech University (Amarillo, USA)
8. Dr. Tchokonte-Nana – Stellenbosch University (Stellenbosch, South Africa)
9. Dr. Deepak Bhatia – Shenandoah University (Ashburn, USA)
10. Ms. Tebogo Sebata – Pfizer (Johannesburg, South Africa)
11. Dr. Weheeda bux – Sprim (Johannesburg, South Africa)
12. Dr. Eugene J Ndebia – Walter Sisulu University (Mthatha, South Africa)
13. Dr. N’yunyi Katumba – University of South Africa (Johannesburg, South Africa)
14. Mr. Arniban Roy – Bose Institute (Kolkata, India)
15. Dr. Graham Chakafana – University of Venda (Thohoyandou, South Africa)
16. Dr. Retsilisitsoe R Moholisa – University of Cape Town (Cape Town, South Africa)
17. Dr. Lloyd Tanner – University of Cape Town (Cape Town, South Africa)
18. Dr. Shivan Chetty – University of Cape Town (Cape Town, South Africa)
19. Dr. Teke Apalata – Walter Sisulu University (Mthatha, South Africa)
20. Dr. Dominic Targema Abaver – Walter Sisulu University (Mthatha, South Africa)
21. Dr. Nambatya Winnie – Mulago National Referral Hospital (Kampala, Uganda)
22. Dr. Ewura Seidu Yahaya – University of Pretoria (Pretoria, South Africa)
23. Ms. Pumla Mesatywa – Stellenbosch University (Stellenbosch, South Africa)
24. Dr. Simona Kucerikova – ProClinicalLife Sciences Recruitment (London, UK)
25. Dr. Eugene J Ndebia – Walter Sisulu University (Mthatha, South Africa)
26. Ms. Mirabel Nanjoh – SATA (Johannesburg, South Africa).



In the era of drug resistance and search for better therapeutic focusing on specific target for better efficacy and less toxicity, no better theme could have been selected than the one above mentioned. This theme is relevant in terms of addressing issues impinging on Clinical Trial and Innovative Therapeutic and beyond.

Height presentations have been clustered into the following 10 related subthemes:

- Track 1: Bioprospecting and drug development
- Track 2: Preclinical research
- Track 3: Pharmacognosy and phytochemistry
- Track 4: Pharmacokinetics and pharmacodynamics of the drugs
- Track 5: Clinical research and trials on different diseases
- Track 6: Clinical data management and statistics
- Track 7: Clinical research and trials on different medical devices
- Track 8: Therapeutic drug monitoring and drug quantification
- Track 9: Toxicogenomics challenges and applications
- Track 10: Pharmacovigilance and drug safety.

About 27 oral and 13 posters will be presented during this conference.

The afternoon of the past day will be devoted to the organization of a workshop titled: “Modern drug discovery and development from traditional medicinal plants: Pros and cons for commercialization in the African market.”

Participants will be having an opportunity to engage discussion on the strategies for developing drugs from African medicinal plants which have been proven to be less toxic and more effective.

It is expected that the platforms offered by this conference will assist in advancing the frontiers of knowledge concerning clinical trial and innovative therapeutics.

I would like to extend my gratitude to the guest speakers who were committed to make this conference successful despite financial burden that we have encountered during the preparation of this conference.

I also acknowledged the courage and the determination of the LOC members who have accepted to work all day long for the success of this event which should be considered as the first step of a multilateral collaboration between African and overseas institutions.

It is my pleasure to welcome all delegates from many different countries to this “1<sup>st</sup> International Conference on Clinical Trial and Innovative Therapeutic” and I wish you a successful and enjoyable visit to the Cape Town.

After the academic activities, participants are welcome to spend a day or two in the beautiful city of Cape Town.

As you all know, Cape Town is a coastal city in South Africa with its Table Mountain and Victoria and Alfred Waterfront. It is one of the most multicultural cities in the world, reflecting its role as a major destination for immigrants and expatriates to South Africa.

Considered as the best place in the world to visit, this city located on the shore of Table Bay attract a lot of visitors not only for the Table Mountain but also for the busy harbor and boats heading for Robben Island, the notorious prison that once held Nelson Mandela, which is now a living museum.

May all delegates find this conference exciting and encouraging as we all pursue the production of new knowledge which will play such a critical role in the bright development that surely lies ahead for Africa.

# CONFERENCE PROGRAM

## Day 1: 24 July 2017

Time	Event
8:00-9:00	Registration
9:00-9:30	Inaugural address, welcome speech by the Chair and Co-chair of the conference. Presentation of Keynote and Plenary Speakers; Overview of the Program
9:30-10:15	Keynote talk 1: Prof. Anupam Bishayee - Larkin University (Miami, USA) Pomegranate: A unique fruit with extraordinary cancer preventive and therapeutic potential
10:15-10:50	Plenary talk 1: Prof. Sanjay K Srivastava – Texas Tech University (Amarillo, USA) Melanoma therapy: Challenges and options
10:50-11:00	Group photos
11:00-11:30	Networking session/tea break/poster session
	Morning Session Moderator: Prof. Anupam Bishayee
11:30-11:55	Prof. Manju Ray - Bose Institute (Kolkata, India) Journey of methylglyoxal in cancer therapy: Bench to bedside
11:55-12:20	Dr. Deepak Bhatia - Shenandoah University (Ashburn, USA) CARG-driven GADD45 $\alpha$ : A suicide gene therapy for nonsmall cell lung carcinoma
12:20-12:45	Prof. Hiranmoy Das - Texas Tech University (Amarillo, USA) Development of human adult stem cell therapeutics for degenerative diseases
12:45-13:10	Prof. John I Anetor - University of Ibadan (Ibadan, Nigeria) Toxicogenomics: The promise and hurdles in developing countries
13:10-14:00	Lunch
	Afternoon Session Moderator: Prof. Sanjay K Srivastava
14:00-14:25	Ms. Tebogo Sebata – Pfizer (Johannesburg, South Africa) From unconscious bias to conscious inclusion – Key to transformation and capacity building
14:25-14:50	Ms. Tebogo Sebata – Pfizer (Johannesburg, South Africa) Clinical research in children
14:50-15:15	Dr. Eugene J Ndebia – Walter Sisulu University (Mthatha, South Africa) Data management in clinical trials
15:15-15:40	Mr. Arniban Roy - Bose Institute (Kolkata, India) Preclinical studies of nanofabricated methylglyoxal; combination with conventional chemotherapeutic drugs and effects on cancer stem cells
15:40-16:10	Networking session/tea break/poster session End Day 1

## CONFERENCE PROGRAM

### Day 2: 25 July 2017

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Time	Event
9:00-9:45	Keynote talk 2: Prof. Theeshan Bahorun - Mauritius Research Council (ANDI CBBR, Reduit Mauritius) Clinical research and trials in Mauritius: The case of functional foods in the management of cardiovascular diseases and diabetes
9:45-10:25	Plenary talk 2: Prof. John I Anetor - University of Ibadan (Ibadan, Nigeria) Redefining therapeutic drug monitoring and quantitative drug assay: Promise and significance for growing global drug resistance
10:25-10:50	Networking session/tea break/poster session
	Morning Session Moderator: Prof Theeshan Bahorun
10:50-11:15	Dr. N'yunyi Katumba – University of South Africa (Johannesburg, South Africa) Neuropharmacology in cerebrovascular accident: A stepwise preclinical research process
11:15-11:40	Dr. Shivan Chetty – University of Cape Town (Cape Town, South Africa) The use of human cytolytic fusion proteins for targeted immunotherapy
11:40-12:05	Ms. Mirabel Nanjoh - SATA (Mthatha, South Africa) Morbidity and mortality trends for non-communicable diseases in ORTDM-EC-SA
12:05-12:30	Dr. Retsilisitsoe R Moholisa – University of Cape Town (Cape Town, South Africa) Model-based pharmacokinetic-pharmacogenetic analysis of lopinavir and nevirapine in a cohort of South African children infected with HIV
12:30-12:55	Dr. Lloyd Tanner – University of Cape Town (Cape Town, South Africa) An <i>in vitro</i> model for drug accumulation at the target site
12:55-14:00	Lunch
	Afternoon Session Moderator: Prof. Kensesse Mossanda
14:00-14:25	Dr. Teke Apalata – Walter Sisulu University (Mthatha, South Africa) Antimicrobial resistance: The missing puzzle piece
14:25-14:50	Dr. Dominic Targema Abaver – Walter Sisulu University (Mthatha, South Africa) Human immunodeficiency virus and acquired immune deficiency syndrome prevention practices in correctional centres in the Eastern Cape, South Africa
14:50-15:15	Dr. Nambatya Winnie - Mulago National Referral Hospital (Kampala, Uganda) Toxic epidermal necrolysis associated with lamotrigine
15:15-15:40	Dr. Ewura Seidu Yahaya – University of Pretoria (Pretoria, South Africa) Comparative effect of three wound healing ethnomedicinal extracts on fibroblast migration and reactive oxygen species release <i>in vitro</i>
15:40-16:20	Networking session/coffee break End of Day 2



## CONFERENCE PROGRAM

### Day 3: 26 July 2017

**Moderator: Dr. Teke Apalata**

Time	Event
9:00-9:50	Keynote talk 3: Prof. Kensesse Mossanda – SATA (Johannesburg, South Africa) DNA damage induced by oxidative stress in hepatic iron overload disease, esophageal and prostate cancers
9:50-10:25	Plenary talk 3: Dr. Tchokonte-Nana – Stellenbosch University (Stellenbosch, South Africa) A translational challenge to mimic diabetes in islet cell therapy
10:25-10:55	Networking session/tea break/poster session Morning Session Moderator: Dr. Teke Apalata
10:55-11:20	Ms. Pumla Mesatywa – Stellenbosch University (Stellenbosch, South Africa) Gastric ulcer healing properties of <i>Ledebouria ovatifolia</i> (Baker) Jessop
11:20-11:45	Dr. Eugene J Ndebia – Walter Sisulu University (Mthatha, South Africa) The effect of <i>Helicobacter pylori</i> on the pattern of gastroesophageal reflux in a rural population of South Africa
11:45-12:10	Dr. Graham Chakafana – University of Venda (Thohoyandou, South Africa) Validation of molecular diagnosis of hepatitis B virus and human papillomavirus from clinical samples at Parirenyatwa Hospital (Harare) using nested PCR
12:10-12:35	Dr. Simona Kucerikova – ProClinical Life Sciences Recruitment (London, UK) The effect of vitamin E succinate and etoposide on MDA-MB-231 breast cancer cell line viability
12:35-13:30	Workshop - Debate “Modern drug discovery and development from traditional medicinal plants: Pros and cons for commercialization in the African Market” Facilitators: Prof. Kensesse Mossanda and Prof. Anupam Bishayee
13:30-14:00	Closing Ceremony Conference Chair and Co-Chair Closing Ceremony Speech Vote of Thank Introduction of the Next Conference “Clinical and Basic Sciences Research”
14:00	Lunch
Tour: Visit Cape Town (more information on this will be announced on site)	
End of Day 3	

## Poster Presentations

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Mr. Wa Ilunga Evodie – Université de Lubumbashi (Lubumbashi, Republic Democratic of Congo) Phytochemical and biological screening of 36 plant species for tuberculosis use in lubumbashi
Mr. Wa Ilunga Evodie – Université de Lubumbashi (Lubumbashi, Republic Democratic of Congo) Ethnobotanical survey of some plant species used against the tuberculosis in lubumbashi and its surroundings
Dr. Ayissi Mbomo Rigobert Espoir – Université de Yaounde I (Yaounde, Cameroon) Medicinal plants real or placebo properties? The case of <i>Mimosa pudica</i> empirically used in cameroon to treat anxiety and depression
Dr. Valerie Etoundi – Université de Yaounde I (Yaounde, Cameroon) Effect of efavirenz on day 7 plasma lumefantrine concentration during coinfection of <i>Plasmodium</i> sp. and HIV-1 in Cameroonians adults
Dr. Kalunga Muya Richard – Université de Lubumbashi (Lubumbashi, Republic Democratic of Congo) Evaluation of the acute toxicity of <i>Garcinia huillensis</i> Baker, a plant used against urogenital schistosomiasis in Haut-Katanga, Republic Democratic of Congo
Dr. Kalunga Muya Richard – Université de Lubumbashi (Lubumbashi, Republic Democratic of Congo) Evaluation of the molluscicidal activity of some plants collected in Lubumbashi and surroundings (Republic Democratic of Congo)
Dr. Petnga Saint-Just – Université de Yaounde I (Yaounde, Cameroon) Intramuscular based insulin protocol: A safe approach to hyperglycemic emergencies in limited resources settings
Dr. Mbuyi Kalonji – Université de Lubumbashi (Lubumbashi, Republic Democratic of Congo) An ethnobotanical overview of some plants known to be antimalarial used in the city of Lubumbashi and its surroundings, Upper Katanga province, Republic Democratic of Congo
Dr. Mbuyi Kalonji – Université de Lubumbashi (Lubumbashi, Republic Democratic of Congo) Phytochemical study of some plants considered antimalarial used in the city of Lubumbashi and its surroundings
Dr. Raicha Namba – Université de Yaounde I (Yaounde, Cameroon) Metabolic effects of add-on probiotics supplementation in uncontrolled Type 2 diabetes mellitus patients
Ms. Bokop Fotso Carine – Walter Sisulu University (Mthatha, South Africa) Incidence and risk factors associated with post-operative infections among neurosurgical patients admitted in a public tertiary teaching hospital in the Eastern Cape province, South Africa
Dr. Idrissa Abame – Université de Yaounde I (Yaounde, Cameroon) Place of procalcitonin in the early diagnosis of infections in patients with chemo-induced severe neutropenia at Yaounde General Hospital

### Keynote Speakers

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**Professor Anupam Bishayee**

Dr. Anupam Bishayee is a Professor and Founding Chair at Department of Pharmaceutical Sciences of Larkin University College of Pharmacy (Miami, Florida). Dr. Bishayee has 25 years combined experience in pharmaceutical education, research, teaching, and administration. He received his Bachelor of Pharmacy (B.Pharm.), Master of Pharmacy (M.Pharm.), and Ph.D. in Pharmacy from Jadavpur University, Kolkata, India. Dr. Bishayee performed postdoctoral research at Rutgers University, Newark, New Jersey (formerly University of Medicine and Dentistry of New Jersey) and completed a fellowship in Academic Medicine from Northeast Ohio Medical University (NEOMED, Rootstown, Ohio). Dr. Bishayee's primary research interest during the past two decades encompasses cancer biology, cancer therapeutics, and cancer prevention. His laboratory is involved in investigating chemopreventive and therapeutic effects of various medicinal plants, natural products, dietary and synthetic agents using various preclinical models of cancer, including breast and liver cancer, and underlying mechanisms of action. The various projects of Dr. Bishayee are funded by the National Institutes of Health as well as private pharmaceutical and biotechnological companies. Dr. Bishayee has published at least 143 original research papers and authoritative review articles, mostly in high-impact, peer-reviewed journals and 12 book chapters, and delivered >25 invited presentations at various national and international scientific meetings. Dr. Bishayee is serving as Editor-in-Chief of the Journal of Natural Products in Cancer Prevention and Therapy as well as editorial board member and reviewer of >60 reputed journals.



**Professor Theeshan Bahorun**

Professor Theeshan Bahorun is currently National Research and Innovation Chair in Applied Biochemistry under the Mauritius Research Council and Head of the ANDI Centre of Excellence for Biomedical and Biomaterials Research. He has more than 20 years of experience in biomedical research on bioactive components of dietary/plant-based factors (phytochemicals), functional foods, oxidative stress mechanisms, molecular nutrition, chemopreventive strategies in diabetes, cancer and cardiovascular dysfunctions and clinical research. His seminal publications in Toxicology *In Vitro*, Toxicology, Journal of Agricultural and Food Chemistry, Food Research International, Free Radical Research, Biofactors, and his recent works published in Food Science and Nutrition, Mutation Research, Preventive Medicine, Pharmaceutical Biology, Biomed Research International, Life Sciences and Food and Function are indicative of his span of work with a strategic approach combining the latest scientific technologies in biochemistry and molecular biology to

## GUEST SPEAKERS BIOGRAPHY

culminate to applied preclinical and clinical trials addressing the pertinent problems of diabetes and cancer in Mauritius and neighboring islands. He has been the Chairman of the Food and Agricultural Research Council and is currently the President of the Board of Governors of the University of Technology, Mauritius, the Chairperson of the Board of Directors of Polytechnics Mauritius, the President of the Society for Free Radical Research Africa (SFRR-Africa) and Vice President of the International Association of Medical and Biomedical Researchers. He is the author/co-author of 120 peer-reviewed publications and 79 peer reviewed communications in international conferences. In 2010, he was awarded the CV Raman Senior Fellowship for African researchers by the Government of India. In 2013, he received the Best Mauritian Scientist Award. He has been elevated to the rank of Grand Officer of the Star and Key of the Indian Ocean (G.O.S.K) on 12 March 2015 by the Government of Mauritius for his contribution to Scientific Research and Education. In 2016, he received the Project Leadership Certificate Hall of Fame Award for exemplary leadership in guiding the University of Technology, Mauritius Talent development program.



**Professor Kensese Mossanda**

Professor Kensese Mossanda a degree in Pharmacy; 3 Master's degrees in Tropical Medicine and Biology, Clinical Biology and Food sciences and a PhD in Pharmaceutical Sciences (Biochemistry and Toxicology) from the State University of Liege, Belgium. His previous appointments include postdoctoral fellow in many universities in Europe, USA, Asia, and Africa; Professor, Dean of Faculty of Pharmacy, and Head of Clinical Biology Department at the University of Kinshasa, Congo. He has been awarded the Seoul National University (South Korea) prize for an outstanding lecture in 2003 as well as the "Dakota" award (Kyoto-Japan). During the past two decades, he has been awarded more than 25 scholarships, bursaries and fellowships to attend conferences, congresses, and workshops. He was acting as Research Coordinator at the Walter Sisulu University (South Africa) for the past 6 years, and he is presently supervisor of postgraduate students and external examiner of masters and PhD dissertations from various South African Institutions and abroad.

Professor KSA Mossanda is member of various scientific and professional societies and reviewer of more than 10 African and international journals. His is also serving as Executive Director of PROMETRA-South Africa (an organization for the Promotion of Traditional Medicines) and member of South African platform on Bioprospecting and Product Development. He was also the chairperson of the 26<sup>th</sup> African Health Sciences Congress in 2006.

He is the Chair of the International conferences, workshops, and courses organized by the Southern African Training Academy (SATA).

His research expertise includes biochemistry, toxicology, carcinogenesis, mutagenesis, traditional medicine, chemoprevention, and anti-inflammatory activities of medicinal plants; he has published 75 papers in peer-reviewed journals and refereed/peer-reviewed conference proceedings, 3 chapters in book and 1 book.

### Plenary Sessions

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**Professor Sanjay K. Srivastava**

Dr. Sanjay K. Srivastava is a Distinguished Professor and Chairman of Department of Immunotherapeutics and Biotechnology at the Texas Tech University Health Sciences Center, Texas, USA. He is also the Associate Dean for Sciences at the same institution. Dr. Srivastava has published around 150 papers in high impact journals, numerous abstracts and book chapters, has several patents, and is the editor of three books on cancer. His research has been continuously funded by the National Cancer Institute, NIH. Dr. Srivastava is a recipient of several prestigious awards. His research work has been featured by news agencies including BBC, MSNBC, CBS, ABC, and Science News.

Dr. Srivastava's laboratory has been working on pancreatic cancer, breast cancer, ovarian cancer, brain cancer and melanoma, and demonstrated that some of the dietary agents, such as piperlongumine, capsaicin, cucurbitacin B, benzyl isothiocyanate, phenethyl isothiocyanate, diindolylmethane and curcumin, suppress the growth of primary, and metastatic tumors by inhibiting various oncogenic signaling pathways. The main theme of his research is directed toward understanding the mechanisms that underlie the cellular and molecular basis of cancer and evaluating novel anticancer agents against various types of cancers. Ongoing studies along these lines in Dr. Srivastava's laboratory will identify novel targets to develop new therapies for cancer.



**Professor John Anetor**

Professor John Anetor is a Clinical Biochemist (Chemical Pathologist); received his doctorate from the University of Ibadan, Nigeria, where he is currently a Professor of Chemical Pathology and Honorary Specialist Adviser (Consultant) to the University College Hospital, Ibadan. Professor Anetor had his postdoctoral training at the Pathology Department, Osaka City University Medical School, Japan. He is a fellow of many learned and professional societies, including the Royal Society of Chemistry, American College of Nutrition, Institute of Biomedical Science (UK) and Member Association of Clinical Biochemistry and Laboratory Medicine (U.K), and Society of Toxicology (SOT) (USA). His field of research includes clinical and environmental toxicology, chemical carcinogenesis, applied nutrition with special interest in ameliorating toxic states with micronutrients as well as oxidative stress. He has published over 110 peer-reviewed papers in reputable journals and is on the editorial board of many journals.



## GUEST SPEAKERS BIOGRAPHY



**Dr. Tchokonte-Nana**

Dr. Tchokonte-Nana Venant, Anatomist and histologist, is an educator and researcher. He is currently the leader of the Islet and MSK research group at the Stellenbosch University, Faculty of Medicine and Health Sciences. Dr. Tchokonte-Nana is an affiliate Mentor at the African Academy of Sciences (AAS) and the South African Consortium for Research Excellence (SACORE). He is an appointed Visiting Professor of Anatomy at African Universities and Istinye Medical University in Turkey; a Visiting researcher at the University British Columbia, Vancouver in Canada-2013.

Dr. Tchokonte-Nana interest lies in the field of beta cells replacement therapy. He has worked and published in Reproductive Medicine and Islet regeneration following the duct ligation procedure. His achievements include research in the chronobiology of gene expression pattern in developing pancreas in PDL rat model; 2012 finalist of “New Voices in Science” oral and written competitions; a review of the 5<sup>th</sup> Edition of Atlas of Human Anatomy by Netter.

Dr. V Tchokonte-Nana is a recipient of a number of research grants, locally and internationally. He is a reviewer and evaluator for NRF (National Research Foundation) and MRC (Medical Research Council) grant proposals; an editorial Scholar board member for WebMedCentral online journal and a reviewer of a number of research Journals. He is a founding member of Islet Society Meeting (based in Sweden), a founding member and Secretary General of the African Association of Anatomists, a member of the Anatomical Society of Southern Africa, a member of Advances in Stem Cell Discovery Society.

Dr. Tchokonte-Nana is a supervisor and mentor to a number of postgraduate students locally and internationally.

### Oral Keynote Abstracts

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#### Pomegranate: A Unique Fruit with Extraordinary Cancer Preventive and Therapeutic Potential

Anupam Bishayee

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**Background and Purpose:** Pomegranate (*Punica granatum*), an ancient, mystical, and unique fruit, is gaining incredible attention because of its numerous health benefits. However, the effect pomegranate on breast cancer is not completely elucidated. The purpose of this study was to investigate the mechanism-based cancer preventive potential of a novel pomegranate formulation (pomegranate emulsion) against 7,12-dimethylbenz(a)anthracene (DMBA)-induced rat mammary tumorigenesis. **Methods:** The rats were administered per os (p.o.) with PE at various doses (0.2-5 g/kg) 3 times/week, starting 2 weeks before and 16 weeks following DMBA (50 mg/kg, p.o.) treatment. Following this regimen, rats were sacrificed and breast tumors were excised. Tumor samples were subjected to histopathological, immunohistochemical, and reverse transcription polymerase chain reaction analysis. The Fisher's exact probability test was used to analyze tumor data, and one-way analysis of variance was employed for other endpoints. **Results:** PE exhibited a notable reduction of DMBA-induced mammary tumor incidence, total tumor burden, and reversed intratumor histopathological alterations. PE suppressed abnormal cell proliferation and induced apoptosis in mammary tumors in a dose-dependent manner. PE increased intratumor Bax expression, decreased Bcl-2 expression, and registered a proapoptotic shift in Bax/Bcl-2 ratio. The gene expression studies confirmed the aforementioned results and also showed PE-mediated upregulation of Bad, caspase-3, caspase-7, caspase-9, poly (adenosine diphosphate ribose) polymerase, and cytochrome C. PE downregulated the expression of estrogen receptors (ER- $\alpha$  and ER- $\beta$ ), cyclin D1 and  $\beta$ -catenin. Finally, PE decreased the expression of cyclooxygenase-2 and nuclear factor- $\kappa$ B and increased the expression of nuclear factor erythroid 2p45 (NF-E2)-related factor 2 (Nrf2). **Conclusions:** Our study demonstrates for the first time that PE exerts chemoprevention of chemically-induced mammary tumorigenesis by suppressing abnormal cell proliferation, inducing apoptosis, impeding inflammatory cascades as well as augmenting Nrf2 signaling. Multitargeting pomegranate bioactive phytochemicals could be developed as complex drug to prevent and treat breast cancer which is a complex and dismal disease.

#### Clinical Research and Trials in Mauritius: The Case of Functional Foods in the Management of Cardiovascular Diseases and Diabetes

Theeshan Bahorun

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Diabetes and cardiovascular diseases are noncommunicable diseases that have a worldwide prevalence estimated to increase alarmingly to attain 380 and 27 million deaths, respectively by 2025. The incidence of these diseases has also attained alarming proportions in many island states such as Mauritius. Previous agreed global sustainable development resolutions underscores the "primary health needs of the world's population" as "integral to the achievement of the goals of sustainable development and primary environmental care," and identifies "preventive and curative health facilities, accessible to all" as a critical component of sustainable development and green economy advancement. There are therefore increasing interests to find therapeutic means to improve health conditions. In this regard, the biopotency and antioxidant prophylactic properties of functional foods, nutraceuticals, and plant biofactors have been the main interests of our group, with emphasis these recent years, on molecular nutrition mechanisms and clinical supplementations. This presentation will focus on the methodologies and outcomes of clinical trials in the context of adjunct therapy and health sustainability and will be supported by data from prospective randomized controlled studies on ischemic, normal and prediabetic populations. The effects of black tea, fermented papaya preparation, and green tea will be comprehensively discussed with regard to their significant contribution to decrease independent diabetic and cardiovascular risk factors and biomarkers and to improve the overall antioxidant status in humans.

**Key words:** Type 2 Diabetes, Cardiovascular Diseases, Functional Foods, Clinical Trials, Molecular Nutrition, Antioxidants, Biomarkers

## ABSTRACTS

### DNA Damage Induced by Oxidative Stress in Hepatic Iron Overload Disease, Esophageal and Prostate Cancers

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**Introduction:** Excessive intake of dietary iron as a result of drinking home-brewed in iron pots constitutes an important factor leading into hepatocellular carcinoma (HCC) (incidence: 23-26%). Due to the *Helicobacter pylori* infection and other nonelucidated factors, squamous cell carcinoma of the esophagus (SCCO) has become the most common cancer in black Southern African men (incidence: 14.5%). Prostate cancer (PC) is the second leading cause of cancer-related death in men in Western countries. **Objective:** This study aims to demonstrate the implication of oxidative stress in the extent of DNA damage during the progression of these types of cancer. **Methods:** Oxidative stress was estimated by measuring lipid peroxides, thiobarbituric acid reactive substances, and isoprostane using classical methods whereas superoxide dismutase and glutathione peroxidase activities were assessed using kits commercially available. Level of 8-hydroxy-2'-deoxyguanosine (8-OH-dG) measuring the extent of DNA damage and that of 4-hydroxy-2'-nonenol measuring the extent of the lipid-peroxidation were evaluated by enzyme-linked immunosorbent assay method. **Results:** Consistent correlation has been observed between DNA damage by the presence *in situ* (biopsies) of 8-OH-dG, the level of this metabolite in serum/plasma, and the extent of oxidative stress biomarkers in SCCO, HCC, and PC. **Conclusion:** Despite our progress in earlier detection of these types of cancer, their etiology still remains not very well understood resulting in a partial efficiency of their prevention. The capacity of free radicals to damage DNA molecule and to overexpress some oncogenes suggests their implication in the etiology of these types of cancer and justifies the use of antioxidant compounds modulating the expression of these genes for their prevention.

**Key words:** *Helicobacter pylori*, Lipid Peroxides, Thiobarbituric Acid Reactive Substances, Isoprostane, Superoxide Dismutase, Glutathione Peroxidase, 4-hydroxy-2'-nonenol, 8-hydroxy-2'-deoxyguanosine

## Oral Plenary Session Abstracts

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### Melanoma Therapy: Challenges and Options

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Malignant melanoma is a significant problem for Caucasian population in the western countries. Mutations in BRAF gene in 60% of patients are responsible for developing resistance to BRAF inhibitors. Our results delineated the mechanism of resistance and identified a suitable drug combination to overcome the resistance. Treatment of BRAF mutant melanoma cells with vemurafenib or dabrafenib (BRAF inhibitors) alone or in combination with trametinib (MEK1/2 inhibitor) resulted in induced expression of Mcl-1. Melanoma cells resistant to BRAF inhibitors exhibited substantial expression of Mcl-1 as compared to sensitive cell lines. Silencing of Mcl-1 using siRNA completely sensitized resistant cells to growth suppression and induction of apoptosis by BRAF inhibitors. Vemurafenib resistant A375 xenografts showed substantial tumor growth inhibition in mice when treated with a combination of vemurafenib and Mcl-1 inhibitor or siRNA. Immunohistochemistry and western blot analyses confirmed enhanced expression of Mcl-1 and activation of ERK1/2 in vemurafenib-resistant tumors, whereas the level of Mcl-1 or p-ERK1/2 was reduced in the tumors of mice treated with either of the combination. Biopsied tumors from the patients treated with or resistant to BRAF inhibitors revealed overexpression of Mcl-1. These results suggest that the combination of BRAF inhibitors with Mcl-1 inhibitor may have therapeutic advantage to melanoma patients with acquired resistance to BRAF inhibitors alone or in combination with MEK1/2 inhibitors.

## ABSTRACTS

### Redefining Therapeutic Drug Monitoring and Quantitative Drug Assay: Promise and Significance for Growing Global Drug Resistance

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**Background and Purpose:** There is currently great global concern about drug efficacy, resistance, and misuse. Therapeutic drug monitoring (TDM) was introduced for many decades to at least in part address these concerns. The aim of TDM is essentially to aid clinical decisions in the choice of drug dosage to provide optimum treatment for a particular pathological state as well as avoid iatrogenic toxicity. Although, TDM has an accepted place in enhancing optimization of therapy in select cases this is often usually a last resort. **Comment:** The current growing drug resistance calls for redefining and expanding TDM and drug quantification which appears to hold great promise with far reaching significance. This presentation examines traditional concepts in TDM and drug analysis and the need to make some adjustments which may curtail the disturbing pace of drug resistance. Although apparently unconventional, it may be beneficial to conduct TDM on all patients at least at the onset of treatment with antibiotics. TDM is usually thought not helpful in routine monitoring of patients, but there are creative ways to go about this. It may be useful on limited basis in detecting poor adherence or poor pharmacokinetics and pharmacodynamics, signaling unfolding resistance. Although TDM has traditionally been considered to be only useful for drugs that have poor correlation between dose and pharmacological effects, there appears to be a palpable need to extend this practice to many other drugs and supplements; the micronutrients, particularly iron (Fe) in today's clinical practice. **Conclusion:** The challenge of drug ineffectiveness and resistance calls for a re-examination of current practices, particularly in TDM and drug assays including key micronutrients. This appears a creative approach to the refractory drug resistance imbroglio, particularly with antibacterial agents, though the occult trends in other types of therapeutics are unexplored, calling for proactive measures by the scientific community.

### A translational Challenge to Mimic Diabetes in Islet Cell Therapy

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For translational studies in diabetes mellitus, laboratory animals are often used to mimic diabetes which is characterized by a chronic hyperglycemia, due to the insufficient production of insulin by the pancreatic beta. Many diabetic animal models are commercially available in which diabetes has been induced by a chemical compound, a high fat diet or a virus. However, how do we choose a model for a nonobesity or obesity diabetes research? Do any of these models mimic the physiology of diabetes in the human? What could be the challenges of these models in diabetes research (e.g., streptozotocin-induce diabetes)? These are some of the questions we will attempt to answer during our talk.

24 July 2017

Morning Session

Time: 11:30-11:55

## Journey of Methylglyoxal in Cancer Therapy; Bench to Bedside

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**Background and Purpose:** Anticancer properties of methylglyoxal documented by Nobel laureate Albert Szent-Györgyi encouraged us to undertake systematic investigations on the toxicity, pharmacokinetics, and mechanism of action methylglyoxal. Our preclinical, toxicology/safety studies were assessed by administering through three different routes to four different species of animals at a dose of 15 times higher than the therapeutic dose which did not lead to any adverse effect highlighting safety of the drug. We also demonstrated that methylglyoxal specifically kills malignant cells only through cessation of energy production by glycolysis and mitochondrial oxidative phosphorylation preventing tumor cell proliferation and effectuating cell death. With permission from the Drug Controller General of India, clinical trial was carried out where methylglyoxal based anticancer formulation was administered orally to diverse groups of 105 terminally ill patients suffering from different malignancies which established the efficacy of methylglyoxal. **Methods:** The Phase I/II trial was completed in four periods. 24, 46, 16, and 19 patients were treated with methylglyoxal between the year 2000-2001, 2000-2005, 2005-2008, and 2008-2013 with permission from the regulatory authorities. **Results:** Among the 105 patients treated with methylglyoxal, complete remission was observed in 48 patients and partial remission in 26 patients. Among the remaining patients at least 12 patients lost follow-up. The treatment was found to be especially effective for adenocarcinoma of urinary bladder, breast, uterus, esophageal and gastrointestinal tract cancers. Several vital biochemical, radiological, and other parameters were tested in patients who received treatment for a long time implicated no toxicity as per the parameters studied. Most importantly, it ceases bleeding and relieves pain. **Conclusions:** All the results showed great promise of methylglyoxal treatment and demanded further improvisation of the methylglyoxal-based therapeutics. The methylglyoxal-based formulation is now on the way to Phase III clinical trial.

24 July 2017

Morning Session

Time: 11:55-12:20

## CAR<sub>G</sub>-Driven GADD45 $\alpha$ : A Suicide Gene Therapy for Non-small Cell Lung Carcinoma

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A novel suicide gene therapy vector, pE9NS.G45 $\alpha$ , was engineered by cloning growth arrest and DNA damage-45 alpha (GADD45 $\alpha$ ) cDNA downstream to the synthetic CAR<sub>G</sub> promoter E9NS containing nine repeats of CAR<sub>G</sub> element with modified core A/T sequence. GADD45 $\alpha$  is a nuclear protein often upregulated by environmental stresses and DNA-damage agents to induce growth arrest and apoptosis, and CAR<sub>G</sub> elements are the chemo/radio-responsive region in the Egr-1 promoter. By being connected with the inducible promoter, the expression of therapeutic target could be nicely controlled to perform cytotoxic effects. Here, we evaluated and compared the efficacy of our suicide gene therapy vector with chemotherapeutic drugs and radiation against resveratrol in non-small cell lung cancer (NSCLC) cell lines. All the combinations successfully activated promoter E9NS to drive the expression of GADD45 $\alpha$ , and subsequently reduced cell viability and induced apoptosis regardless of p53 status. Our study demonstrates that GADD45 $\alpha$ -targeted suicide gene therapy sensitizes NSCLC cells to cisplatin, resveratrol, and radiation.



24 July 2017

Morning Session

Time: 12:20-12:45

## Development of Human Adult Stem Cell Therapeutics for Degenerative Diseases

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Stem cells possess unique characteristics such as self-renewal capability, multi-lineage differentiation abilities, and regenerative potential, which make them different from other cell types in the body. Stem cell therapy using autologous stem cells to treat degenerative diseases is promising; however, the limited availability and compromised quality of progenitor cells in aged and diseased patient's constraint its therapeutic potential. Among the adult stem cells, the use of human umbilical cord blood-derived stem cells is advantageous as the cord blood is easy to collect, harmless to donor, ethical, and ontogenetically primitive, with reduced risk of developing graft-versus-host disease, and can be stored in cord blood bank. However, a single cord unit does not ensure enough stem cells, which limits the clinical application of this stem cell source. We have developed and patented a nanofiber-based *ex vivo* stem cell expansion technology, which not only preserves stem cell characteristics but also provides essential number of functional stem cells. Furthermore, these nanofiber-expanded stem cells could be genetically modified to enhance their therapeutic potential. We provide that evidence of the therapeutic efficacy of the nanofiber-expanded stem cells in various preclinical models includes hind limb ischemia, myocardial ischemia, osteoporosis, Parkinson's disease, and cutaneous wound. We also defined molecular mechanisms by which stem cells regenerate tissues in various degenerative disease models. This body of work shows the promising potential of nanofiber-expanded stem cells for clinical application in various degenerative diseases.

24 July 2017

Morning Session

Time: 12:45-13:10

## Toxicogenomics: The Promise and Hurdles in Developing Countries

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**Background and Purpose:** A notable peculiarity of the industrializing developing countries is the absence of regulatory policies and measures to effectively control the enormous amount of chemical substances released into the environment. Exquisite technologies for better understanding and early intervention are required. Toxicogenomics; combination of toxicology and genomics is one such emerging vital tool. Despite the immense potential benefits, toxicogenomics remains poorly recognized in many developing countries. **Comments:** The enormous genetic knowledge derivable from toxicogenomics has pushed the science of toxicology beyond traditional boundaries, incorporating genes and proteins in the biochemical pathways toward manifestation of disease. Thousands of genes and proteins can now be examined simultaneously; to carefully map the effects of a toxic chemical as a function of dose and duration of perturbation in clusters of expressed genes and proteins. Toxicologists and environmental scientists in resource poor countries though have explored the effects of chemicals on human health for a long time; only measurable progress has been achieved toward ameliorating adverse effects. Progress in this area has largely paralleled the level of scientific knowledge and technology. To rise from the challenge of using obsolete, less efficient technologies of the past, there is need to embrace toxicogenomics. This will ensure the development of efficient, cost-effective and comprehensive strategies in predicting and preventing toxic response in populations. Realizing the goals of toxicogenomics requires long-term efforts, the magnitude of which far exceeds the resources of any single institution. Pooling of facilities, collaborative research agreements and resource contracts are needed. **Conclusion:** Toxicogenomics, though still in its early days holds huge potential benefits. The breadth and scope of knowledge derived from it permits better understanding of the underlying mechanisms of chemical-induced diseases and drug discovery, thus a critical platform for developing interventional and remedial strategies to halt the disease process and very promising though a number of hurdles need scaling in the developing countries.

24 July 2017

Afternoon Session

Time: 14:00-14:25

### From Unconscious Bias to Conscious Inclusion – Key to Transformation and Capacity Building

**Tebogo Sebata**

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Every day we make countless decisions without realizing it. Researchers call this “unconscious bias.” We are faced with around 11 million pieces of information at any given moment, according to Timothy Wilson, professor of psychology at the University of Virginia and author of the book *Strangers to Ourselves: Discovering the Adaptive Unconscious*. The brain can only process about 40 of those bits of information so it creates shortcuts and uses past knowledge to make assumptions. We are so powerfully guided by the things we expect to be true in the world. “Most of us believe that we are ethical and unbiased. We imagine we’re good decision makers, able to objectively select suitable sites for our company studies, size up a job candidate or a venture deal and reach a fair and rational conclusion that’s in our, and our organizations, best interests, however, research indicates differently. In reality, most of us fall woefully short of our inflated self-perception.” All throughout the day, we send subtle messages to the people around us through our body language, word choice, and behavior. Derald Wing Sue, Professor of Counseling Psychology at Columbia University calls these signals “macroaggressions,” which can have a profound and detrimental effect on the people around us. Is there a way to change unconscious biases that influence who we hire, promote, and most value at work? Which site we choose to work with? There’s certainly no simple approach, but yes our brains can be trained to do that.

24 July 2017

Afternoon Session

Time: 14:25-14:50

### Clinical Research in Children

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Clinical research involving children is essential to increase our understanding of childhood conditions and to improve health care for children. Yet professionals and parents often feel uneasy about asking children to take part in research, for example because of potential risks or burdens. When children are given medicine, often those medicines have only been tested in adults. Without research in children themselves, we have no choice but to treat them that way. Children are a unique population with distinct developmental and physiological differences from adults. Clinical trials in children are essential to develop age-specific, empirically-verified therapies and interventions to determine and improve the best medical treatment available. It also helps us to treat our children like children, rather than as little adults. The objective of the talk is to improve awareness and to make it easier to access accurate, up to date, understandable information relevant to the conduct of clinical trials in children.

24 July 2017

Afternoon Session

Time: 14:50-15:15

## Data Management in Clinical Trials

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Clinical data management (CDM) is a critical phase in clinical research. CDM is involved in all aspect in processing clinical data. CDM is the collection, integration and validation of Clinical data, therefore an effective CDM leads to generation of high-quality, reliable, and statistically good data from clinical trial. CDM is a multidisciplinary activity and all team members should be involved in all phase of clinical research right for the designing to the completion; hence, companies must assure that all staff involved in the clinical research is trained and qualified to perform data management tasks.

24 July 2017

Afternoon Session

Time: 15:15-15:40

## Preclinical Studies of Nanofabricated Methylglyoxal; Combination with Conventional Chemotherapeutic Drugs and Effects on Cancer Stem Cells

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**Background and Purpose:** Extensive studies on toxicity and pharmacokinetics of methylglyoxal approved its use in a clinical trial authorized by the drug controller general India on 105 terminally ill cancer patients. The success of the clinical study instigated further research to understand the underlying molecular mechanism, develop a nanofabricated form, use in combination with conventional chemotherapeutic drugs and its role on drug resistant cancer stem cells. **Methods:** Breast cancer cell lines MDA MB 231, MCF 7, 4T1, and Balb/c and Swiss Albino mouse models were used to study the mechanism of action of methylglyoxal. A chitosan based nanofabricated form of methylglyoxal has been synthesized and its toxicity and efficacy have been studied in carcinoma and sarcoma induced Swiss Albino mouse models. Mammospheres were developed to study the effect on cancer stem cells. **Results:** We deciphered that methylglyoxal triggers reactive oxygen species mediated mitochondrial apoptotic pathway in triple negative breast carcinoma. It can down-regulate phospho-akt and prevent the nuclear translocation of nuclear factor- $\kappa$ B as well. Substantial suppression of tumor size and volume were also observed in 4T1 cell induced tumor in Balb/c mice. We also demonstrate that metronomic doses of methylglyoxal in combination with cisplatin or doxorubicin yields synergistic growth inhibitory and apoptotic effects both *in vitro* and *in vivo*. Methylglyoxal treatments also suppress the mammosphere forming ability and decreases the number of cancer stem cells (CD44+CD24- population). The nanofabricated form of methylglyoxal studied for its toxicity on normal animals and efficacy on cancer cells demonstrated heightened efficiency compared to methylglyoxal *in vitro* and *in vivo* with no adverse toxicity. **Conclusions:** Methylglyoxal and nanomethylglyoxal are promising candidates for a potent, cost-effective therapy with minimum side effects against aggressive malignant tumors.

End of Day 1

## Neuropharmacology in Cerebrovascular Accident (CVA): A Stepwise Preclinical Research Process

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Two pathologies are known to be among the main causes of death worldwide (Lloyd-Jones et al., 2009); first, the cardiovascular diseases and secondly the cerebrovascular accident (CVA) even though in Africa, the HIV/AIDS pandemic has the highest rate of deaths. CVA is a devastating condition with 50% permanent disabilities; out of its three pathological types, ischemic/occlusive, hemorrhagic and subarachnoid hemorrhage, the ischemic/occlusive insult occur more often in old patients ( $\approx 80\%$ ) while hemorrhagic accident is frequent in younger patients (Heiss, 2010; Moskowitz et al., 2010; Donnan et al., 2008). From Adeloje (2014) systemic review, the stroke prevalence was 317.3 (314.0-748.2)/100,000 population in 2009 in Africa, with 1.89 million stroke survivors. This estimates increased to 2.09 million (2.046-4.93) stroke survivors allegedly due to population ageing, excessive fat, sugar and salt consumption, and physical inactivity (ibid). The modifiable risk factors are now well known (i.e., arterial hypertension, Diabetes mellitus, hypercholesterolemia, obesity) as well as the nonmodifiable risks: Race, gender, age, and family history of CVA (Moskowitz et al., 2010; Donnan et al., 2008). Vasospasm, which is triggered by inflammation due to the release of hemoglobin from red cells lysis, reduces cerebral blood flow and leads to penumbra, immediate ischemia, delayed cerebral ischemia, and later on neuronal death (Laskowitz and Kolls, 2010). This seemingly simplistic succession of stages is, however, executed through complex cellular mechanisms (Kaur et al., 2013; Broughton et al., 2010). It is managed with Nimodipine, acting on the one hand on the smooth muscles cells, and on the other hand, on the neurons in the penumbra zone, at the borderline between salvage and death status (Ginberg, 1997), as explained later. This pharmacological agent is the result of extensive preclinical laboratory studies (PCLS).

Preclinical laboratory research can be epitomized by Covey's quote "begin with the end in mind" (Covey, 1989). Drug is developed through the PCLS and the clinical essay.

In PCLS, there are the *in vitro* and the *in vivo* studies. As indicated by Macrae (2011), the former is the design and concept of the research on the drug most often at molecular level and the latter deals with the tests in biological models either with marine/canine species or primate/porcine species. Henceforth, the drug is from its inception, subjected to rigorous testing to insure its nontoxicity and its safe dosage once it is on the market.

*In vitro* studies, rodents, either rats or mice, are the commonly used animals. In the case of ischemic/occlusive studies in CVA, protocols include lencephalic models and according to Stair (1999), it is only when the results are satisfactory at this stage than the gyrencephalic animals such as cat, pig, or non-human primate are involved, choice dictated by the similarity between the gyrencephalic vasculature anatomy and the human anatomy (ibid.). Good laboratory practices guide the next step, from the design to the quality assurance and delivery on the pharmaceutical market (Kaur et al., 2013).

25 July 2017

Morning Session

Time: 11:15-11:40

## The Use of Human Cytolytic Fusion Proteins (HCFPs) for Targeted Immunotherapy

Shivan Chetty, Sandra Jordaan, Neelakshi Mungra, Adebukola Daramola, Stefan Barth

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The ability to selectively target and kill cells of interest while minimizing the adverse effects to healthy cells is a central focus of current biotechnology based therapeutic strategies for a variety of infectious diseases (HIV, parasitic infections) and cancer. Traditionally, cell specific therapeutic approaches have focused on combining antibodies for cell surface receptors to biologically active drugs or bacterial toxins. These immunotoxins and antibody-drug conjugates have been shown to be reasonably effective but are often associated with some level of toxicity due to the presence of a nonhuman effector component. As an improvement, the newer generation of fusion proteins called targeted human cytolytic fusion proteins (hCFPs) incorporate lysis inducing human enzymes. Examples of human enzymes that have been employed as cytolytic effectors to induce apoptosis in disease-specific target cells include granzyme B (initiates proteolytic cascades), microtubule-associated protein tau (modifies microtubule formation), and angiogenin (cleaves tRNA and blocks translation). However, some challenges do exist with using human enzymes as compared to bacterial toxins. Lacking the translocation sequences of bacterial toxins, internalized hCFPs are largely trapped in the endosome, and do not efficiently get into the cytosol. Our research focuses on the use of novel enzymes for disease specific hCFP targeted approaches as well as developing strategies to overcome the mentioned challenges.

25 July 2017

Morning Session

Time: 11:40-12:05

## Morbidity and Mortality Trends for Noncommunicable Diseases in ORTDM-EC-SA

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**Background:** This study sought to illustrate morbidity and mortality trends for noncommunicable diseases (NCDs) in ORTDM-EC-SA. Seemingly and in clinical impressions, NCDs are emerging in low- and middle-income countries and in particular among poor black populations. **Methods:** Retrospective cohort study to present trends for 2008-2014 and quantitative comparative approaches to identify independent socioeconomic associates. **Results:** Morbidity trends are decreasing while mortality trends were increasing during the period 2008-2014. Morbidity rate of hypertension and diabetes mellitus is declining with hypertension having a higher incidence rate compared to diabetes mellitus. More deaths resulted from diabetes mellitus than hypertension but stroke was the leading cause of death ( $423.6 \pm 72$ ). Deaths resulting from hypertension, diabetes mellitus, and stroke are increasing while that of chronic obstructive pulmonary disease (COPD) is declining. Incidence rate of diabetes mellitus and hypertension was associated with high deprivation and human development index (HDI) while mortality rates were associated with poverty and high deprivation. Incidence rate of diabetes mellitus was independently associated with HDI, while that for hypertension was independently associated with high deprivation index. The independent associates of high mortality rates were, drop in poverty rates for diabetes mellitus; high deprivation index for hypertension; and high rate of poverty for COPD. **Conclusion:** Downward trend was observed for morbidity rates, whereas an upward trend was observed for mortality rates. There is, therefore, a need for improved primary health-care approaches specifically around early diagnosis of NCDs and recording, and appropriate treatment and management of these conditions.

**Key words:** Noncommunicable Diseases, Mortality, Morbidity, Trends, Socioeconomic



## Model Based Pharmacokinetic-pharmacogenetic Analysis of Lopinavir and Nevirapine in a Cohort of South African Children Infected with HIV

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**Aims:** A model-based approach was used to characterize both lopinavir and nevirapine steady-state pharmacokinetics, quantifying demographic, and genotypic effects on both drug's disposition. **Methods:** Steady-state population pharmacokinetics of lopinavir and nevirapine were modeled using nonlinear mixed-effects modeling. The models were used to derive individual clearances, area under curves (AUCs), and minimum concentrations ( $C_{\min}$ ). Genome-wide association (GWAS) method was used to explore relationships between genotypes and model derived pharmacokinetic indices. **Results:** Lopinavir and nevirapine pharmacokinetics were both separately best described with a one compartment models with a transit compartment absorption models. GWAS analysis revealed no significant association with lopinavir pharmacokinetics. The CYP2B6 516G>T genotype was associated with nevirapine AUC ( $P = 0.005$ ) and  $C_{\min}$  ( $P = 0.005$ ), respectively. After adjusting for CYP2B6 516G>T, CYP2B6 983T>C was associated, respectively, with AUC (0.0007) and  $C_{\min}$  (0.0008). The rs1922240 in the ABCB1 was associated with nevirapine CL after adjusting for both CYP2B6 516G>T ( $P = 0.008$ ) and CYP2B6 983T>C ( $P = 0.007$ ). **Conclusions:** Genetic polymorphisms were associated with nevirapine CL, AUC, and  $C_{\min}$ . These data will inform continued efforts to translate pharmacogenomic knowledge into optimal nevirapine utilization in routine clinical settings.

## An *In vitro* Model for Drug Accumulation at the Target Site

Lloyd Tanner<sup>1,2</sup>, Gabriel Mashabela<sup>2</sup>, Lubbe Wiesner<sup>1</sup>, Digby Warner<sup>2</sup>, Richard K Haynes<sup>3</sup>

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**Background:** The protracted duration of standard tuberculosis (TB) therapy reveals the inadequacy of current first-line TB drugs to eliminate *Mycobacterium* TB (MTB) in its various host environments<sup>1</sup> (Barry et al., 2009; Russell et al., 2010). This may be a result of poor distribution of anti-TB agents into the pulmonary lesions in which the bacilli reside (Kjellson et al., 2012). To address this possibility, we have investigated the MTB-infected macrophage as a model for TB drug penetration. Here, we present observations supporting the utility of this model in assessing intramacrophage drug concentrations and efficacies of selected anti-TB agents at the target site. **Methods:** THP-1 macrophage-like cells were infected with *Mycobacterium smegmatis*, treated with anti-TB agents (both known drugs and experimental compounds), and sampled at seven different time-points over 24 h. Samples were analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS), and quantitative estimations of drug concentrations were determined with reference to a standard curve. All analytical observations were complemented by flow cytometry and high-resolution fluorescence microscopy. **Results:** The anti-TB compounds showed marked differences in their ability to accumulate within the macrophage, especially following infection with *M. smegmatis*. This differential accumulation correlated with drug activity and, importantly, was consistent with the fluorescence intensity observed for the experimental compound, a phenoxazine derivative. **Conclusions:** These results give insight into drug pharmacokinetics at the target site and support further studies, including investigations of the impact on drug levels of macrophage activation status and/or internalization of MTB. The dynamic system combining mycobacterial reporter strains with the inherently fluorescent phenoxazine offers the unique opportunity to complement LC-MS analyses with live cell imaging of intracellular MTB under drug treatment.

25 July 2017

Afternoon Session

Time: 14:00-14:25

## Antimicrobial Resistance: The Missing Puzzle Piece

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Antimicrobial resistance is one of the most serious health threats. It increases mortality, morbidity, and health expenditures. Inappropriate use of antimicrobials contributes to increasing antimicrobial resistance. Infections from resistant bacteria are now too common, and some pathogens have even become resistant to multiple types or classes of antibiotics. The loss of effective antibiotics will undermine our ability to fight infectious diseases and manage the infectious complications common in vulnerable patients. In 2015, the 68<sup>th</sup> World Health Assembly adopted the global action plan on antimicrobial resistance aimed at combating the increasing health threat posed by antimicrobial resistance. When first-line and then second-line antibiotic treatment options are limited by resistance or are unavailable, health-care providers are forced to use antibiotics that may be more toxic to the patient and frequently more expensive and less effective. Even when alternative treatments exist, research has shown that patients with resistant infections are often much more likely to die, and survivors have significantly longer hospital stays, delayed recuperation, and long-term disability. This presentation is aimed at sharing efforts to prevent the above threats using a combination of proven public health strategies: Immunization, infection control, protecting the food supply, antibiotic stewardship, and reducing person-to-person spread through screening, treatment, and education.

25 July 2017

Afternoon Session

Time: 14:25-14:50

## Human Immunodeficiency Virus and Acquired Immune Deficiency Syndrome Prevention Practices in Correctional Centres in the Eastern Cape, South Africa

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The millions of intermittently incarcerated people, many of whom are illicit drug users, have been among the most difficult people to reach with critical health information, management, and treatment. Usually, inmates in prisons are disproportionately affected by multiple health problems; including human immunodeficiency virus (HIV), other sexually transmitted infections, tuberculosis, and viral hepatitis. An exploration of the availability of policies and guidelines on HIV in prisons and their effective implementation in these correctional centres would inform future HIV programming. A purposeful selection study was conducted on 39 participants (12 staff and 27 inmates) at five correctional centres: Kirkwood (Sentenced offenders Centre), Queenstown (Remand Centre), Idutywa (Remand Centre), Mthatha (Remand Centre) and Cradock (Juvenile Centre) in Eastern Cape. Data were collected using closed-ended self-administered questionnaires and informal discussions. Screening for HIV and other sexually transmitted diseases and infections are carried out on inmates on arrival at the Correctional Centre facilities. All the Correctional Centres, except the Remand Centre at Mthatha, have qualified medical personnel manning the centres, with the provision of programs and education targeting eradication of HIV and other sexually transmitted diseases and infections. No postexposure prophylaxis at any of the centres, even amidst possible act of sodomy. Although the Correctional Centres do not readily have antiretroviral therapy on site, inmates requiring the treatment are treated at public health facility nearest to the center. Inmates on treatment who have completed their jail terms are referred to a public health facility nearest to their place of residence, with a 7-day treatment medication. Although policies and guidelines regarding preventive and treatment of HIV infected inmates are available at the Correctional Centres, their implementation and adherence to treatment are not always administered. There is, therefore, need for capacity building of staff, especially nurses in the area of nurse initiated management of ART, and provision of level playing ground for these policies and guideline to be implemented.

**Key words:** Human Immunodeficiency Virus/AIDS, Prevention, Inmates, Correctional Centres

25 July 2017

Afternoon Session

Time: 14:50-15:15

## Toxic Epidermal Necrolysis Associated with Lamotrigine

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Stevens–Johnson syndrome (SJS), a dermatological emergency, is a rare condition with a reported mortality rate of around 5%. SJS is an immune-mediated hypersensitivity reaction that typically involves skin and mucous membrane. Hypersensitivity has majorly been associated with reaction to certain drugs and infections although rarely caused by cancers.

SJS and toxic epidermal necrolysis (TEN) are very dangerous skin conditions. They destroy cells leading to epidermis to detach from the dermis. TEN is very dangerous and may be linked to high mortality rates. TEN may be categorized by the magnitude of body surface area (BSA) detachment as SJS (a “minor form of TEN” with <10% BSA detachment), overlapping SJS/TEN (10-30% BSA detachment), or TEN (more than 30% BSA detachment). Whereas the pathogenesis of TEN is still not clear; immunological mechanisms, especially T-cell-dependent reactions such as cell-mediated cytotoxicity, have been identified. Change in drug metabolism is another possible mechanism that results in reactions mediated by toxic intermediate metabolites. SJS clinically presents with the following; envelopment of the skin and oral, urethral, vaginal, nasal, eye, gastrointestinal (GI), and lower respiratory tract mucous membranes. Such bullous lesions may rupture and cause other complications. GI and respiratory involvement may develop into necrosis. Some studies show that mucosal involvement presents with erythema, edema, shedding, blistering, and ulceration. Despite the fact that SJS is a serious systemic disorder with mortality rate of 5%, TEN is severe with a mortality rate of 30-35%. Whereas there are variation in SJS’s association with individual antiepileptic drugs, largely all antiepileptic drugs have been reported to cause this syndrome. Lamotrigine, an antiepileptic drug, is an emerging treatment for depression. Although there are not many studies in the Sub Saharan region linking lamotrigine to TEN, there have been some reports associating it with SJS. The patient, we present in our case, developed SJS and later TEN after three weeks of using lamotrigine for management of her depression. The development of side effects however, occurred after the patient had shown great signs of progress in her state of depression.

25 July 2017

Afternoon Session

Time: 15:15-15:40

## Comparative Effect of Three Wound Healing Ethnomedicinal Extracts on Fibroblast Migration and Reactive Oxygen Species Release *In vitro*

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**Background:** A large proportion of the world’s human population relies on medicinal plants for primary health care. Three of the plants commonly used for managing wounds in Ghana and other tropical countries are *Aspilia africana* (AA), *Boerhavia diffusa* (BD), and *Erythrina senegalensis* (ES). This study was aimed at studying the effect of the plants on fibroblast migration and intracellular reactive oxygen species (ROS) release. **Methods:** Water extracts, simulating ethnomedicinal preparations were screened for cytotoxicity in SC-1 fibroblasts using the sulforhodamine B assay and microscopy (live/dead staining, Phase contrast, and PlasDIC). Oxidative stress was induced with 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH), and ROS release measured every minute for 2 h using 2,7-dichlorofluorescein diacetate. Wounds were generated in a mono-layer cell culture and migration assessed at 0, 8 and 24 h using microscopy. **Results:** All extracts exhibited negligible cytotoxicity. AAPH increased ROS release by 72.3% relative to the negative control. Pretreatment with 100 µg/mL of AA, BD, and ES resulted in up to 67.1%, 28.8%, and 69.0% reduction in ROS release, respectively. Treatment with 100 µg/mL of BD and ES reduced fibroblast migration from 64.4% in the untreated cells to 50.4% and 43.5%, respectively, while AA had no observable effect. **Conclusion:** The ethnomedicinal extracts have all demonstrated potential to suppress ROS release, an effect which could facilitate healing of wounds with oxidative stress occurring. All extracts, except AA, negatively affected fibroblast migration which could delay wound healing. Beneficial effects on wound treatment may thus be related to antioxidant activity, and not cellular migration.

### End of Day 2

26 July 2017

Morning Session

Time: 10:55-11:20

## Gastric Ulcer Healing Properties of *Ledebouria Ovatifolia* (Baker) Jessop

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*Ledebouria ovatifolia* is a wild plant widely used for medicinal purposes including diarrhea, stomach ache, and gastric ulcer in Africa rural settings. This study aimed to evaluate the healing effect of *L. ovatifolia* on experimental induced gastric ulcer in rats. Indomethacin (50 mg/kg, po), ethanol (2 ml/rat, po), and stress were used to induce gastric ulcer. The antiulceration lesion index was calculated; also, the macroscopic and histopathologic assessments were made. The results showed that oral administration of *L. ovatifolia* significantly decreases gastric ulcer as compared to control group. Ulceration inhibition was 67% and 87% for indomethacin-induced ulcer, 13% and 33% for ethanol-induced ulcer, and 50% and 70% for stress-induced ulcer, respectively, for 100 mg and 200 mg/kg of *L. ovatifolia*. Macroscopic and histopathologic assessment of ulcerated stomach showed a reduced area of the gastric lesion, with moderate disruption of the gastric epithelium as well as the mucosa stomach cell in *L. ovatifolia* treated groups in both dosages. These results clearly showed that *L. ovatifolia* may possess antiulcerogenic properties which may support evidence for its traditional utilization.

**Key words:** Gastric Ulcer, *Ledebouria ovatifolia*, Indomethacin-induced Ulcer, Stress-induced Ulcer, Ethanol-induced Ulcer

26 July 2017

Morning Session

Time: 11:20-11:45

## The Effect of *Helicobacter pylori* on Gastroesophageal Reflux in a Rural Population of South Africa

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**Background:** There is no available data on the effect of *Helicobacter pylori* on gastroesophageal reflux in black African rural population. **Objective:** To define the role of *H. pylori* infection on gastroesophageal reflux parameters in South African rural population. **Methods:** Healthy volunteers living in Canzibe location, a rural village in the Eastern Cape province of South Africa were recruited for the study. They underwent 24-h ambulatory multichannel intraluminal impedance-pH monitoring. The quantification of *H. pylori* antibodies immunoglobulin G (IgG) was determined in the serum of each participant by enzyme-linked immunosorbent assay and was correlated to the frequency, composition and distribution of gastroesophageal reflux episodes. **Results:** A total of 51 participants were included in the study (20 males, 31 females). Mean age was 37 years (range 18-60). All participants were found with a positive level *H. pylori* IgG concentration in the serum. Our results showed that higher *H. pylori* IgG concentration level in the serum was correlated ( $r = -0.2$ ) with lesser esophageal acidity and a decreased frequency of acidic refluxes. It was also significantly ( $P = 0.04$ ) associated with more weakly acidic reflux. **Conclusion:** In this study, *H. pylori* infection was associated with decreased esophageal acidity.

**Key words:** Gastroesophageal Reflux, Impedance-pH Monitoring, Reflux Pattern, *Helicobacter pylori*

26 July 2017

Morning Session

Time: 11:45-12:10

## Validation of Molecular Diagnosis of Hepatitis B virus and Human Papillomavirus from Clinical Samples at Parirenyatwa Hospital (Harare) using Nested PCR

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**Background and Purpose:** Hepatitis B virus (HBV) and human papillomavirus (Pap) (HPV) are responsible for deadly carcinomas, and they account for millions of global mortalities annually. This study aimed to detect and identify the HBV and HPV from residual clinical samples using molecular methods. In Zimbabwe, routine HBV diagnosis relies on serological assays to detect the HBV S-antigen (HBsAg), while cervical cancer caused by HPV relies on the Pap smear. **Methods:** Immunochromatographic (HBsAg serological) assays were used to detect HBV detection in residual serological samples collected at Parirenyatwa Hospital. Confirmatory tests were done using nested polymerase chain reaction (PCR) to evaluate PCR against the gold standard HBsAg serological assay. Nested PCR of the L-gene was also evaluated in detection of HPV genotypes in preconfirmed HPV case samples. **Results:** About 42.9% of HbsAg positive samples were positively detected by nested PCR of the HBV S-gene implying a low sensitivity. None of the negative samples reported positive upon PCR, implicating a high specificity of the assay. Conventional PCR in HPV preconfirmed cases detected 33.3% of the samples. However, nested PCR of the L-gene detected 100% of the cases. HPV nested amplicons were then sequenced and analyzed using BLAST algorithm and Geneious software. A total 15 HPV genotypes were identified. Of these, 13 were high risk and 2 were low-risk genotypes in terms of cervical cancer risk. **Conclusion:** Contrary to the higher detection rate expected for the PCR assay, immunological assay proved a better detection strategy. This can be attributed to the high mutation rate of HBV. However, PCR using consensus primers proved to be a good diagnostic assay for detection of HPV from samples.

26 July 2017

Morning Session

Time: 12:10-12:35

## The Effect of Vitamin E succinate and Etoposide on MDA-MB-231 Breast Cancer Cell Line Viability

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Among UK women, breast cancer remains the leading cause of death in those aged 35-49 (Office for National Statistics 2012). While advances in diagnosis and therapy have resulted in improved survival, much remains unknown about treating such malignancies. In our laboratory, we investigate therapeutic interventions for breast cancers utilizing the MDA-MB-231 cell line as a model system. In this project, we aimed to (a) determine the effect of two anticancer agents, etoposide (ETO) and vitamin E succinate (VES), on the growth of our cell line when used independently at varying concentrations, and (b) determine the inhibitory concentration at 50% ( $IC_{50}$ ) for each drug so that we could utilize these values to guide the determination of the combined effect of both drugs on cell viability. The MDA-MB-231 cell line was incubated for 48 h with increasing concentrations of each drug independently (the combination experiment was not completed as a result of a technical, laboratory-wide error). Cell viability was quantified utilizing a spectrophotometer and the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay. Although increasing concentrations of each drug resulted in greater cell death, a one-way ANOVA was not significant for the ETO group ( $P > 0.05$ ). For the VES group, the ANOVA was statistically significant ( $P < 0.05$ ), with *post hoc* tests indicating a significant change in cell viability ( $P < 0.01$ ) for the 100  $\mu$ M concentration. Although the  $IC_{50}$  for ETO was determined to be 21.7  $\mu$ M, we were unable to calculate the same for VES, as cell viability never dropped below 50%. Future experiments should test a wider concentration of each drug independently, with a larger number of technical repeats for each concentration. Once the dose response curves for each drug are determined and  $IC_{50}$  are calculated; these concentrations may be used to guide the testing of the combined effect of the drugs on cell survival.

End of Day 3

Closing Ceremony



### Phytochemical and Biological Screening of 36 Vegetable Species for Tuberculosis Use in Lubumbashi

Wa Ilunga EN<sup>1</sup>, Marsi Mbayo K<sup>2</sup>, Kalunga RM<sup>2</sup>, Amuri SB<sup>1</sup>, Nsasi AN<sup>3</sup>, Simbi JBL<sup>2</sup>

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**Context:** One of WHO's goals for 2014-2023 is to promote safe and effective use of traditional medicine, which is also an important source of research for new antituberculosis molecules from plants. The aim of this study is to evaluate the antimycobacterial activity of some Lubumbashi plants and to identify some groups of bioactive substances responsible for this activity. **Materials and Methods:** The antimycobacterial activity of the methanolic extracts was evaluated according to the method of Heifets (1988), with slight modifications. This consists in measuring the minimum bactericidal concentration plant methanolic extracts on *Mycobacterium smegmatis*. The conventional methods of staining, precipitation and foaming proposed by Abisch and Reichstein (1960) and William et al. (1970) as used by Kahumba (2000) were used for chemical screening. **Results:** Chemical screening resulted in 688 tests for chemical bioactive substances. Tannins (93%) and saponins (88.4%) were the most commonly encountered, while quinons (20.9%) and alkaloids (17.4%) were the least represented. As for biological screening, 313 sensitivity tests were carried out whose 20 extracts were found to be active at the concentration of 1 mg/ml, 13 active extracts at 0.1 mg/mL, 8 active extracts at 0.01 mg/mL, 2 active extracts at 0.001mg/mL, and an active extract at 0.0001 mg/mL. The *Pavetta schumanniana* leaves gave the greatest antimycobacterial activity (CMB = 0.0001 mg/mL). Therefore, *Acacia sieberiana* stem bark was also found to be active at (CMB = 0.001 mg/mL). **Conclusion:** The plants in our study were found to be active *in vitro* up to the concentration of 0.1 µg/mL. *Pavetta schumanniana* would be a good candidate for the fight against tuberculosis. The groups of bioactive substances found in these plants would justify their use in traditional medicine.

**Key words:** *Mycobacterium*, Phytochemistry, Katanganian Flora, *Acacia sieberiana*, *Pavetta schumanniana*

### Ethnobotanical Survey of Some Vegetal Species Used Against the Tuberculosis in Lubumbashi and its Surroundings

Wa Ilunga EN<sup>1</sup>, Marsi Mbayo K<sup>2</sup>, Kalunga RM<sup>2</sup>, Amuri SB<sup>1</sup>, Nsasi AN<sup>3</sup>, Simbi JBL<sup>2</sup>

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**Context:** The tuberculosis upsurge and the resistant strains emergence to standard treatment are more than disturbing. Therefore, finding further new compounds more effective than existing is important for achieving WHO objectives. This ethnobotanical study allows to inventory plant used in the traditional medicine against tuberculosis by traditional healers of Lubumbashi and its surroundings. **Methodology:** An ethnobotanical survey was carried out by direct interviews with resource persons to identify the plants used against tuberculosis in Lubumbashi and its surroundings. **Results:** The survey was conducted among 47 persons; their age ranged from 33 to 63 years, with a sex ratio men/women of 6.8. All consulted traditional healers speak Kiswahili (100%), 51% also speak Kiluba, and 27% speak also French. These 47 species are spread in 26 families, including *Fabaceae* (17.2%), *Euphorbiaceae* (10.67%), *Annonaceae* and *Moraceae* (8.51% each). Leaf is the most organ used (44%), while the decoction is the main mode of drug preparation (47%). The main administration route is oral (79%). Respiratory pathologies (cough [61.82%], tuberculosis [32.73%], asthma [3.64%], and bronchitis [1.82%]) are the most frequently treated by these plants with a frequency of 31% compared to other pathologies. **Conclusion:** This ethnobotanical survey showed that traditional medicine of Lubumbashi and its surroundings is treating tuberculosis and other respiratory diseases. Thus, the next step of this research could be concerned with phytochemical and biological screening of those plants surveyed to justify their use in the treatment of tuberculosis.

**Key words:** Ethnobotanical Survey, Medicinal Plant, *Mycobacterium tuberculosis*, Haut-Katanga

### Medicinal Plants Real or Placebo Properties? The Case of *Mimosa pudica* Empirically Used in Cameroon to Treat Anxiety and Depression

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In the columns of one paper of the World Health Organization published on 16<sup>th</sup> May, 2002, it appears that in the developing countries, over 80% of the population lives in rural areas. In general, the content of the exchange of these populations is insufficient to help all the needs of daily life including access to modern medicines already very expensive in large cities. To solve the problems of health, these populations use medicinal plants. Often the therapeutic properties of these plants remain hypothetical or just placebos. Currently, in Cameroon and elsewhere in Africa, Asia and South America, government efforts are growing in the direction of more rational and scientific use of medicinal plants. *Mimosa pudica* Linn. is a plant empirically used in some countries to treat anxiety and depression. In the present study 2 months old mice, *Mus musculus* Swiss were acutely treated by different doses of *M. pudica* (3, 10 and 30 mg/kg) and anxiety related responses evaluated by analyzing stress-induced hyperthermia (SIH), elevated plus maze (EPM), elevated T maze, open field, and hole board parameters. The horizontal wire and rota-rod tests were then used to highlight possible myorelaxant properties of *M. pudica*. Finally, we investigated the effect of aqueous extract of *M. pudica* on regulation of dorsal raphe nucleus (DRN), 5-hydroxytryptamine (5-HT) neuronal activity using an *in vitro* mouse brain slice preparation providing from adult male C57/BL6 mice. The decrease of SIH was observed with *M. pudica* (30 mg/kg) treatment. In the EPM, a significant increase of open arms entries and percentage of time spent in the open arms with *M. pudica* (10 mg/kg) was observed. Neither diazepam (3 mg/kg) nor *M. pudica* (3 and 10 mg/kg) produced changes of motor activity. However, the change of motor activity was observed with *M. pudica* (30 mg/kg). In the hole-board test, *M. pudica* (3 and 10 mg/kg) significantly increased the number and duration of the head-dips, respectively. The anxiolytic properties of *M. pudica* as assessed using the EPM test were abolished by flumazenil (3 mg/kg), by bicuculline (5 mg/kg), and FG 7142 (10 mg/kg). Acute treatment with *M. pudica* extract also had an anxiolytic effect on behavior in the ETM, specifically on inhibitory avoidance behavior. In the horizontal wire test, both *M. pudica* (3 and 10 mg/kg) and distilled water allowed animals to grasp within 30 s. *M. pudica* (3 and 10 mg/kg) did not impair the duration of the time spent on the rota-rod. However at the dose of 30 mg/kg, up to 60 min, the *M. pudica* significantly reduced the time that animals remained on the rota-rod. Acute application of the extract alone had no effect on the activity of DRN 5-HT neurones. However, when coapplied with the GABAA receptor agonist 4,5,6,7-tetrahydroisoxazolo[5,4-c]pyridin-3-ol (THIP), the extract enhanced the inhibitory effect of the THIP on DRN 5-HT neurones. This study indicates that *M. pudica* contains an effective psychotropic agent that acts via the benzodiazepine site of the GABAA receptor complex as an anxiolytic at low doses and as a muscle relaxant at higher doses. These results in part could justify and confirm the use of this plant extract as an anxiolytic agent.

**Key words:** Anxiety, Behavior, Dorsal Raphe Nucleus, GABA-A Receptor, 5-hydroxytryptamine, *Mimosa pudica* (Linn.)

### Effect of Efavirenz on Day 7 Plasma Lumefantrine Concentration During Coinfection of *Plasmodium* sp. and HIV-1 in Cameroonians Adults

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**Background:** The antiretroviral triple therapy containing efavirenz (EFV) and the antimalarial artemisinin-based combination therapy artemether/lumefantrine are commonly coadministered to treat HIV infection and malaria. EFV is a known inducer of cytochrome P450 3A4, and artemether/lumefantrine are metabolized by this enzyme. This predisposes patients to poor treatment response and the risk of developing resistances. We evaluated the effect of EFV on day 7 plasma lumefantrine concentration during co-infection of *Plasmodium* sp. and HIV-1 in Cameroonians adults. **Methods:** It was an open-labeled, parallel, nonrandomized clinical study with two groups. (1) Group 1: HIV positive adults on EFV. (2) Group 2: HIV negative adults not on EFV. Both groups received 80/480 mg AL BID for 3 days and venous blood was sampled 7 days after the start of treatment. We determined plasma lumefantrine concentration with and without the presence of EFV with a high-performance liquid chromatography. **Results:** A total of 60 participants consisting of 30 HIV-1 positive and 30 HIV-1 negative participants all with microscopically confirmed plasmodium species infections were enrolled in the study. Lumefantrine concentration on day 7 was significantly lower in HIV positive participants than in HIV negative participants (31.6% lower) with  $P = 0.0001$ . **Conclusion:** Exposure of lumefantrine was significantly lower during EFV-artemether/lumefantrine coadministration compared to that during administration of artemether/lumefantrine alone.

**Key words:** Efavirenz, Artemether, Lumefantrine, Drug Exposure

### Evaluation of the Acute Toxicity of *Garcinia huillensis* Baker, a Plant Used Against Urogenital Schistosomiasis in Haut-Katanga, Republic Democratic of Congo

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**Context:** This research follows the ethnobotanical survey and evaluation of antischistosomal activity *in vitro* in Haut-Katanga on plant species used against urogenital schistosomiasis. **Objectives:** The aim of this study was to evaluate the acute toxicity of the stem bark total aqueous extracts of *Garcinia huillensis* Baker, a plant used in Congolese traditional medicine against urogenital schistosomiasis which confirmed good antischistosomal activity *in vitro*. **Methods:** Acute toxicity was evaluated in female *Cavia porcellus* L. using the limit test at 5000 mg/kg body weight after the preliminary test at 2000 mg/kg body weight as described by the "OECD Protocol 423." The lethal dose 50 (LD<sub>50</sub>) is determined by linear regression, using the least squares method. Some clinical signs of poisoning were assessed for 14 days. Some hematological parameters (glucose, urea, creatinine, and hemoglobin) and biochemical parameters (alanine amino transferase [ALAT] and aspartate amino transferase [ASAT]) of guinea pigs surviving after 14 days of observations were assayed according to International Federation of Clinical Chemistry. **Results:** Some symptoms of poisoning were noted in subjects treated as decreased body weight and food and locomotion skills. The results obtained at the end of the experiment gave a LD<sub>100</sub> 5000 mg/kg body weight, a LD<sub>50</sub> of 2300 mg/kg body weight and a tolerated maximum dose DMT of 1200 mg/kg of body weight. This DMT was significantly higher than 55.8 mg/kg, the average daily dose recommended by traditional healers. Statistically significant differences were observed between *C. porcellus* treated with *G. huillensis* and those from control groups. Indeed, an increase in blood levels of urea and ASAT and a decrease in glucose, creatinine, hemoglobin, and ALAT were recorded in the treated groups. **Conclusion:** The study shows that the stem bark of *G. huillensis* would not be toxic under the conditions of our experiment, which would justify the nontoxic oral use of the plant in Congolese traditional medicine.

**Key words:** Lethal Dose 50, Hematological and Biochemical Parameters, *Cavia porcellus*, Bilharzia, Lubumbashi

### Evaluation of the Molluscicidal Activity of Some Plants Collected in Lubumbashi and Surroundings (Republic Democratic of Congo)

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**Context and Objective:** The present investigation aimed to the search for a natural product from vegetable origin for the control of molluscs, intermediate hosts of schistosomiasis, the second world global parasitosis in terms of morbidity after malaria. **Materials and Methods:** An ethnobotanical survey, based on a pre-established questionnaire, was conducted in Lubumbashi and surrounding areas from January to May 2015. Methanolic extracts from the leaves and stem and root barks of the most used plants were subjected to an *in vitro* evaluation of the molluscicidal activity on *Biomphalaria glabrata*. **Results:** The ethnobotanical survey identified 45 plant species used in Lubumbashi and its surroundings to control molluscs. Methanol extracts from the eight most frequently used out of the 45 plant species were tested for *in vitro* molluscicidal activity on *Biomphalaria glabrata*. These eight plants are *Cajanus cajan*, *Diplorhynchus condylocarpon*, *Droogmansia munamensis*, *Isoberlinia angolensis*, *Khaya nyasica*, *Kigelia aethiopum*, *Rhynchosia insignis* and *Steganotaenia araliacea*. This assessment showed that *C. cajan* at 0.5 mg/mL, *D. munamensis* (1 mg/mL) and *S. araliacea* (1 mg/mL) are the most active species because they showed 100% molluscicidal activity on *B. glabrata* after 8 h of exposure. **Conclusion:** These three species would be good candidates for further investigation to isolate molluscicidal molecules that can be incorporated into the mollusc eradication arsenal for the control of schistosomiasis.

**Key words:** Molluscicides, *In Vitro*, Medicinal Plants, Schistosomiasis, Democratic Republic of the Congo

### Intramuscular Based Insulin Protocol: A Safe Approach to Hyperglycemic Emergencies in Limited Resources settings

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**Objectives:** We aimed to evaluate the effect on serum potassium (K<sup>+</sup>) of an intramuscular (IM) based insulin diabetic ketoacidosis treatment protocol. **Design:** This was a single arm intervention in patients with Type 2 or with ketosis-prone atypical diabetes (KPD). Patients were eligible if they presented with significant ketosis (ketonemia  $\geq 1.5$  mmol/L or ketonuria  $\geq ++$ ) and/or marked hyperglycemia (random capillary blood glucose  $> 22.2$  mmol/L) were eligible. Type 1 diabetes mellitus and acidosis (HCO<sub>3</sub><sup>-</sup>  $< 14$  mmol/L) were exclusion criteria. The intervention consisted of hourly IM insulin at 10 IU of regular insulin for glycemia  $> 22.2$  mmol/L, 5 IU for glycemia between 13.9 mmol/L and 22.2 mmol/L, and 3 IU for glycemia  $< 13.9$  mmol/L. In all participants, we measured every hour capillary blood glucose, ketonemia, and serum electrolytes. Potassium supplementation was to be started if serum potassium level dropped below 3.2 mmol/L. The primary outcome was the need of exogenous K<sup>+</sup> supplementation before disappearance of ketones or achievement of blood glucose  $< 13.9$  mmol/L. **Results:** We enrolled 15 consecutive patients aged  $46.6 \pm 8.4$  years (9/15 newly diagnosed) of whom 11 had KPD and 4 Types 2 diabetes mellitus. The mean body mass index was  $27.0 \pm 3.9$  kg/m<sup>2</sup>. Baseline blood glucose was  $25.5 \pm 0.47$  mmol/L and 11/15 had significant ketosis. Target blood glucose or ketosis resolution was achieved within 2-4 h using 11-38 units of regular insulin. Mean (range) baseline serum K<sup>+</sup> was 4.1 mmol/L (3.6-4.9 mmol/L). It dropped steadily to 3.7 mmol/L (3.2-4.6 mmol/L) after 1 h, 3.6 mmol/L (3.4-4.0 mmol/L) after 2 h, 3.6 mmol/L (3.5-3.8 mmol/L) after 3 h and 3.6 mmol/L (3.5-3.8 mmol/L) after 4 h. None of the patients dropped below 3.2 mmol/L over the intensive IM insulin treatment period so as to require exogenous K<sup>+</sup>. **Conclusions:** In this cohort of Type 2 or KPD patients with hyperglycemic crises without acidosis, a simple treatment protocol based on IM insulin did not induce significant hypokalemia within the 4-h treatment period.

### An Ethnobotanical Overview of Some Plants Known to be Antimalarial Used in the City of Lubumbashi and its Surroundings, Upper Katanga Province, Republic Democratic of Congo

Mbuyi Kalonji<sup>1</sup>, Kalunga Muya<sup>1</sup>, Numbi wa Ilunga<sup>1</sup>, Bakari Amuri<sup>1</sup>, Kahumba Byanga<sup>1</sup>, Lumbu Simbi<sup>1,2</sup>

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**Introduction:** This work is part of a series of surveys carried out to identify the plants considered antimalarial used in the city of Lubumbashi and its surroundings. **Materials and Methods:** The ethnobotanical survey was conducted in the city of Lubumbashi and its surroundings using a method of open-ended interviews based on a pre-established questionnaire. **Results:** About 39 resource persons, mainly living in the communes of Lubumbashi and Ruashi (40.1%), were interviewed. Their mean age is  $53 \pm 10.69$  years. Men are in the majority (75%). Thus, 96 plants were identified and their ethnobotanical knowledge inventoried. These species belong to 39 families of which Fabaceae are the most represented with 21 species (22.59%). In addition to malaria, the listed species are also used in 75 other indications, including sexually transmitted infections (9.18%). The decoction (65.3%) is the most used method of preparation. Drink (50%) remains the most widely used mode of administration. Leaves (39.7%) are the most widely used part of the plant. **Conclusion:** The use of plant-based recipes for antimalarial control in Upper Katanga is therefore a common practice.

**Key words:** Ethnobotanical Survey, Malaria, *Plasmodium falciparum*, Medicinal Plants



### Phytochemical Study of Some Plants Considered Antimalarial Used in the City of Lubumbashi and its Surroundings

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**Context:** A number of studies have been carried out in the city of Lubumbashi and its surroundings to enhance the use of medicinal plants and to find a strong solution to the many cases of resistance due to antimalarial drugs. **Objectives:** The objective of the study is to identify qualitatively and quantitatively the different chemical compounds in the 35 plants and to look for the presence of cyanogenic heterosides in these plants as a toxicity index. **Statistical Methods and Analyzes:** The coloring, precipitation, and foaming reactions were used as described by Bruneton (2009). Statistical analysis was performed using Microsoft Excel 2013 and SYSTAT 12.02.00 software. **Results:** After analysis, eight bioactive groups were characterized (alkaloids, tannins, flavonoids, saponins, quinones, steroids, terpenoids, and leucoanthocyanins). Tannins (97.9%) and saponins (92.8%) are the most widely used. Chemical screening revealed the presence of cyanogenic heterosides in a single plant (*Stephania abyssinica* Walp.). Some of the chemical groups found contain molecules which have already exhibited antimalarial properties, in particular alkaloids such as quinine, terpenoids such as berberine, artemisinin and derivatives, and quinones. **Conclusion:** These identified chemical groups contain molecules with antimalarial properties. Further studies will enable them to be isolated and characterized.

**Key words:** Chemical Screening, Phytochemical Study, Malaria, Plants, *Plasmodium falciparum*

### Metabolic Effects of Add-on Probiotics Supplementation in Uncontrolled Type 2 Diabetes Mellitus (T2DM) Patients

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**Background and Objective:** The etiology and progression of diabetes mellitus is related to the alteration of gut microbiota. Hence, restoring gut microbiota will improve metabolic profile in Type 2 diabetes mellitus (T2DM) patients. The main objective of the study was to evaluate the effects of add-on probiotics containing *Lactobacillus* spp. and *Bifidobacterium* spp. on metabolic profile in uncontrolled T2DM patients. **Methods:** We undertook a single arm nonrandomized clinical trial. 10 T2DM patients received the allocated treatment. The intervention was a daily intake of add-on probiotics over an 8-week period. We assessed before and after intervention: Insulin sensitivity using the hyperinsulinemic-euglycemic clamp, insulin secretion using a standardized mixed meal tolerance test, glycated hemoglobin, serum lipid profile, and body composition. In addition, clinical tolerance, alanine aminotransferase level, and serum creatinine were assessed at week 0, 4, 8, 10, and 14 for safety purpose. Quantitative variables are compared using the Wilcoxon rank sum test. A  $P < 0.05$  was statistically significant. **Results:** About 10 participants (6 females and 4 males) were included with a median age of 59 (52.5-62.5) years. Plasma glucose reduced significantly; 6.9 (8.1-4.9) mmol/L before versus 5.8 (6.3-4.3) mmol/L after,  $P < 0.05$  at  $t_0$  and 7.6 (9.0-5.9) mmol/L before to 6.2 (7.4-5.3) mmol/L after,  $P = 0.04$  at  $t_{30}$ . There was a significant reduction of 25 units in hemoglobin A1c (HbA1c); 80.9 (86.0-73.5) mmol/mol versus 56.3 (67.2-45.1) mmol/mol,  $P = 0.005$ . Insulin sensitivity showed a trend toward increase; 9.1 (12.6-8.3) mg/kg/min versus 11.3 (15.8-9.7) mg/kg/min,  $P = 0.07$ . Insulin secretion increased significantly at  $t_{90}$ ; 0.54 (0.93-0.41)  $\mu\text{g/L}$  versus 1.59 (2.58-0.53)  $\mu\text{g/L}$ ,  $P = 0.021$  and at  $t_{120}$ ; 0.49 (0.71-0.28)  $\mu\text{g/L}$  versus 1.49 (2.28-0.51)  $\mu\text{g/L}$ ,  $P = 0.038$ . Total and low-density lipoprotein (LDL) cholesterol were also significantly lower,  $P = 0.015$  and  $P = 0.015$ , respectively. **Conclusion:** The use of probiotics induced an improvement in glycemic control with a reduction of 25 units in HbA1c, 25% in total cholesterol, and 26% in LDL cholesterol. Insulin sensitivity and secretion improved by 18% and 23%, respectively. Hence, probiotics are useful as add-on treatment in the management of T2DM.

### Place of Procalcitonin in the Early Diagnosis of Infections in Patients with Chemo-induced Severe Neutropenia at the Yaounde General Hospital

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Procalcitonin (PCT) is an early, sensitive and specific marker of bacterial infection. Its role in predicting chemotherapy-induced infections is still unclear. The purpose of this study was, therefore, to assess the interest of PCT assay in early diagnosis of chemotherapy-induced infections. Patients who went under chemotherapy from July 2015 to January 2016 were followed. PCT level was measured at day 12 of the cure and tolerance data were collected through a standardized questionnaire. The study population consisted of patients aged 20 to 63 years with 77% of women and 23% of men. The proportion of severe neutropenia was 58% with 33% for Grade 3 and 25% for Grade 4. A normal level of PCT was found in 93% of cases. Furthermore, 14/30 patients (47%) having severe neutropenia were infected. Two patients out of two presenting high PCT levels showed an infection versus 12/14 patients with low levels (odds ratio = 0.3; 95% confidence interval:  $P = 0.10$ ). There was no correlation found between the occurrence of infections and the high rate of PCT. This study should be extended to a larger sample.

**Key words:** Chemo-induced Severe Neutropenia, Procalcitonin, Infections

### Incidence and Risk Factors for Postoperative Infections among Neurosurgical Patients in Mthatha, South Africa

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**Background:** Despite progress in hospital care, infections continue to represent one of the major complications among hospitalized patients, particularly following neurosurgical procedures. Expenditures associated with the management of such infections can be avoided if the associated risk factors are identified and specific preventive measures are implemented. **Objectives:** The study sought to determine the incidence of health care acquired infections and their associated risk factors following neurosurgical procedures. **Methods:** Retrospective and prospective observational study designs were conducted from October 2013 to September 2014. A standardized form was used to collect data from patients who had undergone neurosurgical procedures. Data included patients' demographics, duration of stay in the hospital, type of operations, and primary diagnosis. Post-operative infections were defined according to the US Center for Disease Control and Prevention definitions. Infection rates were calculated and risk factors associated with post-operative infections were determined. SPSS version 23 was used for statistical analysis. **Results:** A total of 1688 patients who had undergone neurosurgical operations were studied. The incidence and prevalence were 6.4% and 3.4%, respectively. Surgical site infection was significantly associated with craniotomy ( $p = 0.001$ ), traumatic brain injury ( $p = 0.004$ ), and brain abscess ( $p = 0.001$ ) while central nervous system infection was significantly associated with hydrocephalus ( $p = 0.001$ ), ventriculoperitoneal shunts ( $p = 0.001$ ), and prolonged stay ( $\geq 2$  weeks) in the ward ( $p = 0.025$ ). **Conclusion:** Postsurgical infections remain an important problem in neurosurgery. Mitigation of the identified risk factors is mandatory in improving patient care.

**Key words:** Neurosurgery, Surgical Site Infection, Craniotomy, Ventriculoperitoneal Shunt, Risk Factors



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# Notes

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