The International Symposium on Methods for Studying Drug Metabolism and Transport, and African Traditional Medicines (METHODS2015)

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1. INTRODUCTION

The “International Symposium on Methods for Studying Drug Metabolism and Transport, and African Traditional Medicines (METHODS2015)” was held on 23rd to 25th November 2015 at Saint George Hotel and Conference Centre in Pretoria, South Africa. It was hosted by Department of Pharmacology and its Research Unit on Indigenous Knowledge Systems (IKS), University of the Free State, in partnership with the Department of Science and Technology (DST) of South Africa. The symposium addressed research issues at the helm of the Department of Science and Technology (DST) national research policy, which is also aligned with the research focus of the Department of Pharmacology at the University of the Free State. Furthermore, the symposium created an interface for policy makers and research scientists both local and international, to deliberate on the best practices for research and development of African Traditional Medicines (ATM) and the pharmacokinetic processes of drug metabolism and transport. The theme of the symposium was “Rallying for Safe and Effective Medicines” with the following main objectives:

- To enable researchers to assess the appropriate research methods for production of safe and effective medicines, including the African Traditional Medicines.
- To inform researchers of the current DST strategy and progress in research and development of ATM.
- To appraise participants on the increasing importance of research in the pharmacokinetic processes of drug metabolism and transport in general, and their application to African Traditional Medicines.
- To review the latest developments, particularly new research methods, for research and development of African Traditional Medicines, and the pharmacokinetic processes of drug metabolism and transport.
- To create opportunities for national and international collaboration, new avenues in research and development, planning of more open learning forums, etc.
To give researchers access to a pre-symposium workshop for practical training of students on laboratory methods for drug metabolism and Transport, and ATM research development.

2. PARTICIPANTS
The symposium attracted 117 participants the majority of whom were from the host country, South Africa. There were 61 students (52%) of whom 52 were from South Africa and 13 were from other countries, i.e., Zimbabwe, Namibia, Ethiopia, Nigeria, Jamaica, China, India and Sri Lanka. Forty-six (46) South African students and 9 international students received bursaries from the symposium organizers. Bursaries were awarded according to the need and they included waiver of registration fees for the symposium and pre-conference workshops, accommodation and, for the international students, contribution towards the ticket costs.

The speakers profile was 80% from South Africa. They included; Prof. A Walubo and Dr. GM Matsabisa from the Department of Pharmacology university if the Free State (UFS); Dr. Cecilia Bester from the Agricultural Research Council; Dr. Neil Gower, from the Medicine Control Council (MCC); Prof. Nceba Gqaleni from Durban University of Technology; Prof. Xuesheng Ma from the School of Natural Medicine, University of the Western Cape; Prof. Indries Moodley from the University of Kwazulu-Natal; Prof. Khajamohiddin Syed from the Central University of Technology; Prof. Glen Taylor from the Research Directorate, University of the Free State; Dr. Mboneni Muofhe, the Deputy Director General in the Department of Science and Technology (DST); Dr. Hlupheka Chabalala, Director IKS Based Innovations, DST; Prof N Lall from University of Pretoria; Dr K Alexandre from The Council for Science and Industrial Research (CSIR); Mr. Ben Durham, Chief Director in DST; Prof Anne Grobler, Director of the DST/NWU Preclinical Drug Development Platform and GLP-Laboratory; Mr Robert Longrigg from Afriplex Pty Ltd). The international speakers were: Prof. Collen Masimirembwa, Africa Institute for Biotechnology and Science (AiBST), Harare, Zimbabwe; Prof. Eleni Aklilu, Division of Clinical Pharmacology, Karolinska Institutet, Stockholm, Sweden; Prof. Olavi Pelkonen, emeritus of Professor of Pharmacology, University of Oulu, Finland; Prof/Dr. Matthias Schwab, Head of the Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany; Prof. Tonghua Liu from Beijing University of Chinese Medicine, China; Prof. Farnao Castro Braga, Federal University of Minas Gerais, Brazil; Prof. Tuhinandri Sen from Jadavpur University, Kolkata, India and from University of the West Indies, Jamaica were; Dr. Rupika Delgoda, Dr. David Picking, Dr. Simone Badal, and Dr Lowe the Managing director, Eden Gardens Pharmaceuticals – Jamaica.
3. RELATED ACTIVITIES (WORKSHOPS)

The symposium was preceded on the 22nd November 2015 by two pre-conference workshops that were overprescribed to 60-69 people of whom 31 (45%) were students. Workshop-1 was on ‘the Pharmacogenetics of Drug Metabolism and Transport’ and was facilitated by Prof. Collen Masimirembwa from Zimbabwe, while workshop-2 was on ‘the advances in traditional medicines’ research’ was facilitated by Prof. T. Sen from India and Prof. Braga from Brazil.

4. OPENING CEREMONY

The symposium was opened on the evening of 22nd November 2015, at a Gala dinner honored by the minister of science and technology (DST) who was represented by the director general (DG) Dr Phil Mjwara. It was also attended by officials from the host institution, the University of the Free State, i.e., Prof. Corli Witthuhn, the Deputy Vice Chancellor Research; Prof. GJ van Zyl, the Dean Faculty of Health Sciences and Prof. Alan St Clair Gibson, the Head School of Medicine. Dr. Mboneni Mhoufhe, the Deputy Director General (DDG) for Technology Innovations in the DST was the Master of ceremony.

In the subsequent speeches at the dinner, the university delegation indicated to the Director General that they were grateful for acquiring the DST-funded Indigenous Knowledge Systems (IKS) Unit from the South African Medical Council (SAMRC) and appreciated the continued support the unit gets from the DST. They confirmed that that the IKS unit was well located in the Department of Pharmacology in the Faculty of Health Sciences and that its mission and vision articulate with those of the Department of Pharmacology, the Faculty of Heath Sciences and the university at large. In turn, the DG (guest of honor) indicted that the IKS unit was one of the DST’s flagship projects, in line with the DST grand ‘bio-economy’ strategy. He then reiterated the department’s resolve to support research on African traditional medicines, and this includes support for human capital development and research equipment to advance traditional medicines research locally and internationally.
5. PROCEEDINGS
The proceedings of the symposium went smoothly as planned in the main program. The proceeding can be classified into four categories:

- Strategies for research on Drug Metabolism and Transport (DMT), and research on African Traditional Medicines (ATM)
- Research on African Traditional Medicines (ATM)
- Research on Drug Metabolism and Transport (DMT)
- Integration of research on African Traditional Medicines with research on Drug Metabolism and Transport.

i) Strategies for research on DMT and ATM
In plenary session 1, the symposium was started with an introduction of department of pharmacology’s research strategy on ‘Drug Metabolism and Transport’. Prof. Walubo illustrated the evolution of technological knowledge and advancement in research on CYP450 and drug Transporters since the pre-scientific era (1800 AD), i.e. from the Wöhler synthesis of urea in 1828, through the discovery of atoms in 1800-1830, to the current era (2000) of the fast advancing –Omics technology and personalized medicine. Prof. Walubo concluded by advising that owing to the growing complexity of scientific knowledge, research on CYP450 and drug transporters requires a collaborative approach across several disciplines. Thereafter, Dr. Mboneni Muofhe, the Deputy Director General in DST outlined the national ‘ATM Bioprospecting and Product Development Strategy’. This strategy is to ensure that the wealth of South Africa’s indigenous knowledge (IK) is used for the benefit of the people of South Africa, by focusing on strategic programs in African traditional medicines, cosmeceuticals, nutraceuticals and health beverages. As such, a holistic IKS-based research, development and innovation approach was adopted in order to support community-based technology demonstration, manufacturing and Ubuntu-inspired marketing and commercialization, with a hope of improving the quality of life and sustainable livelihood of the people. This approach articulates with the three sectors or drivers of the government’s ‘Bio-economy Strategy’, i.e., the cultivation and propagation of indigenous plants (Agriculture), the disease-controlling potential of IK-based bioprospecting products (Health) and the industrialization of all IK-based innovative products (Industrial and Environmental Bio-innovation).

In plenary session 3, the presenters addressed other strategic approaches to research. Dr. Hlupheka Chabalala, director of IKS Based Innovations, described the strategy for research and development of African Traditional Medicines, with special reference to the need for balancing the quest for innovation and academic research. Dr. Chabalala intrigued participants with his in-depth description of the traditional health philosophies, implying that it was abandoned for the western philosophy, and still remains unexplored. During the discussions, it was agreed that the potential for discovering new medicines from traditional medicinal products/plant has never been exhausted. This was further illustrated by Dr Glen Taylor, the Director of Research and Development at UFS, in a case presentation of developing a natural medicinal product for HIV. It required balancing the pursuit for academic research, versus innovation, versus preservation of intellectual property and the pressure for commercialization. In the same perspective, Prof O Pelkonen, used the wide inter-individual variations (polymorphisms) observed in the activities cytochrome P450 and drug transporters to highlight the need to tune research results towards the current trends in health practice, i.e., towards personalized medicine, by recognizing that people respond differently to medicines, whether conventional or African Traditional Medicines.

These strategic sessions lay the foundation for a sequence of sessions on progress on research and innovation on ATM and DMT, and on the need for integrated approach for research on ATM and DMT.
A session on progress: one of Prof. Braga presentations on Brazil

A session on progress: Prof. Aklilu presenting

Symposium in progress

Symposium in progress

Symposium in progress
ii) RESEARCH ON AFRICAN TRADITIONAL MEDICINES (ATM)

In session 1, the preclinical ATM research landscape in South Africa was illustrated by members of the South African ATM-Bioprospecting and Product Development Consortium. Prof N Lall reported on their findings on an adjuvant for TB therapy from a South African plant, while Dr K Alexandre, reported on the prevention of HIV-1 infection of cells by a South African medicinal plant coded BP36. Prof I Moodley reported on his group’s progress on the development of Morula (Sclerocarya birrea) derivatives for the treatment of diabetes mellitus. In the same session, Dr MG Matsabisa gave an overview of the milestones in the pre-clinical development of African Traditional Medicines products using PHELA, an immune booster, as an example. This was followed by Dr C Bester’s illustration on how they used ‘Indigenous health beverages’ to enhance community development, economically, socially and healthy wise. Indeed, this session re-affirmed that the ‘ATM-bioprospecting program’ is in unison with the national Bio-economy strategy, i.e., from the farm to products, and to community development.

Session III expounded on the requirement for ‘quality evaluation’ of herbal derived medicines. Using the Brazil experience, Prof Fernao Braga, Brazil, narrated on the use of biological and chemical data to validate claims on medicinal value, while Prof O Pelkonen reviewed the advances on the application of Omics techniques in research and development of herbal derived medicines. The two presentations were capped by Prof. Anne Grobler in her overview on the role of their specialized pre-clinical drug development laboratory at the North West University in assisting the South African researcher to conduct high quality pre-clinical studies. She affirmed that, with their laboratory, South Africa has the technology to conduct high quality pre-clinical studies on African herbal derived medicines. In session V, further challenges in the development and Evaluation of Herbal derived Medicines were discussed. Mr. Ben Durham, Chief Director, DST, outlined the road map, progress and future plans, for research and development of ATM; while Dr. MG Matsabisa, gave an overview on the challenges of conducting clinical trials for herbal derived medicines in South Africa.

In plenary session 5, the national and international perspectives of traditional medicines were presented and the South African perspective was compared with the rest of the world. Prof. Liu from China illustrated the insulin resistance reversal effects by several Chinese and African derived herbal extracts, while Prof. Tuhinadri Sen from India, described their work on targeting bacterial biofilms to combat antibiotic resistance, using quorum sensing inhibitors of natural origin. Thereafter, session 3 provided a comparison on the regulation of herbal derived medicines in the different countries. Here, Prof. Fernao Braga presented on the regulation of herbal derived medicines in Brazil with special reference to the contribution of academic research, while Dr Neil Gower, the chair of MCC-expert committee on Complementary Medicines gave an overview on the Complementary Medicines Regulatory framework in South Africa. Dr Xuesheng Ma from China, currently a visiting professor at the University of the Western Cape in South Africa, described the institutionalization (in-hospital use) and regulation of the Chinese traditional medicines.
iii) RESEARCH ON DRUG METABOLISM AND TRANSPORT

In session II, Prof. Matthias Schwab and Prof. Andrew Walubo deplored the clinical significance of genetic variations in drug metabolizing enzymes and drug transport proteins, respectively. Using tamoxifen as an example, Prof. Matthias Schwab illustrated how knowledge of CYP2D6 polymorphisms can be used to select appropriate breast cancer patients for treatment with tamoxifen as well as to predict response to tamoxifen. Prof. Walubo explained the importance of transporter polymorphisms in the response to anti-retroviral therapy and cholesterol lowering agents; in the toxicity of cyclosporine and tricyclic antidepressants; as well as recognizing drug resistant epilepsy, to mention but a few. Thereafter, in session 4, Prof. Pelkonen imbued participants with the latest methods for studying drug induced hepatotoxicity, specifically the in-vitro methods to predict hepatotoxicity and appropriate extrapolation. Thereafter, Prof. Walubo capped this with a review on combating paracetamol, isoniazid and nevirapine induced hepatotoxicity. He revealed, among others, their recent results on the successful use of grape fruit juice to treat or prevent paracetamol induced hepatotoxicity. Prof. Collen Masimirembwa put this in perspective by describing their experience in unveiling several clinically significant genetic polymorphism in African populations. This was further illustrated by Prof. Eleno Aklilu, in an overview of their studies on enzyme polymorphisms that induce susceptibility to anti-retroviral adverse drug reactions among some African populations. Thereafter, Dr K Syed gave an excellent overview on their work in which they have discovered several mycobacterial and fungal cytochrome P450 enzymes that are being targeted in the development of new drugs against the respective pathogens.
iv) INTEGRATED ATM AND DMT RESEARCH
The interface between Science and African Traditional Medicines was illustrated here in several sessions. In plenary session 2, Prof. Collen Masimirembwa gave an overview on the screening of herbal medicines for interactions with drug metabolizing enzymes of the commonly used drugs in most African populations, specifically the antimalarial drugs. Prof. Nceba Gqaleni illustrated the importance of education and development of traditional health practitioners in hand with public health care workers. In the same perspective, Dr David Picking from Jamaica reviewed the prevalence of medicinal plant use in Jamaica and then illustrated their work in assessing for potential drug-medicinal plant interactions for several of these plants. Dr R Delgoda from Jamaica explained how they utilized the Caribbean biodiversity to harness plant extracts that inhibited or slowed down phase I and II drug metabolizing enzymes with potential adverse effects such as the metabolic activation of chemicals to cancerous free radicals. Thereafter, Mr Danie Nel from Afrilex South Africa and Dr Lowe of Eden Gardens Pharmaceuticals-Jamaica, elaborated on the role of industry in research and development of ATM. Danie described how they have made agreements with relevant researchers and communities to manufacture medicinal products in which the communities are part of the beneficiaries not only in shares but also job opportunities. Dr Lowe presented a case study to illustrate the advance in research and development to commercialization of Jamaican medicinal plants.

6. POSTER PRESENTATIONS
The symposium enabled participants, particularly the students, to share their relevant research results with colleagues in six poster sessions during which 64 posters covering various topics on research on Traditional Medicine (38 posters) and Drug Metabolism and Transport (26 posters) were presented.

7. EXHIBITION
The pictures below shows some of exhibitors/stands who showcased their products, during the set up phase.
8. SPONSORS
We are grateful to the generous donations from our sponsors towards the symposium and workshops that enabled greater participation whereby about 80% of the participants were sponsored by the organizers. The major local sponsors were the national Department Science and Technology (DST), the South African Medical Research Council (SAMRC), the Department of Pharmacology, University of the Free State (UFS), and the National Research Foundation (NRF). The international sponsors were mainly scientific organizations/societies, i.e., the Drug Metabolism and Transport Section of the International Union for Basic and Clinical Pharmacologists (IUPHAR), The American Association of Pharmaceutical Scientists (AAPS), and The International Society for the Study of Xenobiotics (ISSX). The international sponsorship enabled us share the platform with several international students.

We are grateful to the generous sponsorships received from the displayed organizations
9. IMPRESSION

a) Some of the important observations by delegates during this symposium:

- The potential for discovery of new medicines from natural products has never been exhausted
- People respond differently to medicines, whether conventional or traditional medicines
- Integration of research on traditional medicines with relevant scientific disciplines such as ‘drug metabolism and Transport’ will address the core of African population health.
- The traditional medicine philosophy remains under researched, thereby denying us the potential for development of new remedies.
- Owing to fast growing and complex technological advance (knowledge), further research in ‘cytochrome P450 and drug transporters’ requires a collaborative effort across different disciplines
- Forums for research information such as this symposium (METHODS2015) are part and parcel of the strategy for accelerated research and development.

b) Using a questionnaire that allowed participants to rate the symposium, it was confirmed that the whole scientific activity was highly welcomed by the participants as informative and, to some, it opened new research avenues and, hopefully, more collaboration to come.

c) I would like to thank my fellow colleagues on the organizing committee of METHODS2015 and the event management company, ‘Orange Galaxy’ for their untiring effort to ensure success of the event.

Prof. A. Walubo  
Chairman