July-September 2008

Newsletter

Volume 25

Dr David Parirenyatwa : Vice President of WHO Regional Committe for Africa

Dr. David Parirenyatwa elected to be Vice President of the World Health Organisation Regional Committee for Africa

On the 5th of September 2008, Dr. David Parirenyatwa was elected to the post of Vice President of the World Health Organisation Regional Committee for Africa. This was done at the 58th session (1-5th of September) of the WHO regional meeting for Health Ministers, which ended in Yaounde, Cameroon.

Dr. Parirenyatwa

Doctor **David Parirenyatwa** was born in August 1950 in Mashonaland, Zimbabwe. He is the current Minister of Health and Child Welfare. Parirenyatwa served as Deputy Minister of Health and Child Welfare until he was appointed as Minister of Health and Child Welfare in August 2002.

One of the major refereral hospitals, Parirenyatwa Hospital, in Zimbabwe, is named after his father who was a leading revolutionary fighter for the liberation of Zimbabwe. David has therefore continued his father's legacy by spear heading the fight

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University of Cape Town (UCT) and AiBST In Collaboration

The Department of Chemistry and Division of Pharmacology at UCT and AiBST have, amongst them, expertise in medicinal chemistry, pharmacology and drug metabolism and pharmacokinetics ("DMPK").

Thus, UCT and AiBST, by way of an MOU, formalised their wish to work together in order to benefit from and leverage each other's expertise by establishing a partnership that will result in collaborative academic efforts focusing on the establishment of a drug discovery network that integrates medicinal chemistry, pharmacology and DMPK.

The Parties appointed Prof. Kelly Chibale (UCT) and Dr. Collen Masimirembwa (AiBST) as their representatives for purposes of managing this MoU.

The Parties committed to establishing a partnership that will result in collaborative academic efforts focusing on the establishment of a drug discovery network that integrates medicinal chemistry, pharmacology and DMPK.

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Contact details

Visiting Address:
1st Floor LAPF Center
Jason Moyo Av/Chinhoyi St
Harare
Zimbabwe
Postal: P.O. Box 2294
Harare, Zimbabwe
Fax: 263 4 710562
Phone: 263 4 710563/4
Website: www.aibst.com
Editor: Stewart Masimirembwa
Email: stewart.masimirembwa@aibst.com

AiBST Publications

Britta Bonn

Journal: Drug Metab Dispos.

Title: The Molecular Basis of CYP2D6 mediated N dealkylation - Balance between metabolic clearance routes and enzyme inhibition.

Auhtors: Bonn BK, Masimirembwa CM, Aristei Y, Zamora I.

Abstract: N-Dealkylation is a commonly observed metabolic reaction for drugs containing secondary and tertiary amines. On searching the literature, it is obvious that this reaction is far less common among cytochrome P450 2D6 catalyzed reactions compared to other CYP's. The CYP2D6 pharmacophore and characteristic features in

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Rose Hayeshi

Journal: Biopharmaceuticals and Drug Disposition

Title: Lysosomal Trapping of Amodiaquine: Impact on Transport across Intestinal Epithelia Models

Auhtors: Rose Hayeshi, Collen Masimirembwa, Stanley Mukanganyama, Anna-Lena B. Ungell

Abstract: The lipophilic weak base amodiaquine is an antimalarial drug that has been used for over 40 years. Little is known of amodiaquine's mechanism of transport

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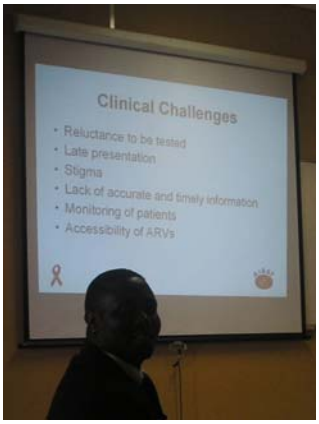
Capacity Building for Private Healthcare Professionals



Dr Mayida

AiBST's Capacity Building for Private Sector Healthcare Professionals went into full swing on Friday 19 September 2008 by the holding its first annual strategic planning workshop. Participants drawn from four stakeholder organisations, three of them being umbrella organisations with healthcare facilities across the country, converged at AiBST. Zimbabwe Business Council on Aids (ZBCA) was represented by DELTA Corporation's HIV/AIDS Coordinator, Ms Sithembiso Maseko. The Evangelical Fellowship of Zimbabwe (EFZ) was represented by its National Health & HIV Programmes Officer, Mr Peter Bare whilst Mr Joseph Munyebvu, the Premier Laboratory Manager represented his Medical Laboratory at the workshop.

Dr Masimirembwa

The project presents a unique opportunity for private-private partnerships to strengthen the capacity of Zimbabwe to collect and use surveillance data for national HIV/AIDS programs by expanding HIV/STI/TB surveillance programs in the ten provinces of the country. Of notable interest was that AiBST, using its distinctive competencies and state-of-the-art technological platforms would strengthen private sector capacity for laboratory support in terms of surveillance through diagnosis, treatment, disease-monitoring and HIV-screening, CD4 count, Viral Load determination and Therapeutic Drug Monitoring.

Also, this project will deepen private sector capacity for healthcare institutions through training 200 healthcare professionals per year on management of HIV/AIDS and on how to deliver ART, according to national and/or international standards. The first course will run from 01 to 03 October 2008 ●

New Laboratory Equipment : CO_2 Incubator

AiBST has recently purchased a CO_2 incubator. This was funded by the International Programme in Chemical Sciences, IPICS, in Sweden. The CO_2 incubator will be used in AiBST cell culture research which include the use of HepG2 cells and hepatocytes for metabolism and Caco2 cells for permeability studies. Strengthening our ADMET platform with cell based systems will hopefully enable us to generate *in vitro* data that are more predictive of *in vivo* DMPK parameters ●

Dr Parirenyatwa

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for better health for Zimbabweans. His notable success has been with his fight against the HIV/AIDS pandemic which has seen Zimbabwe reduce prevalence rates from 20.1 to 18.1% since 2004 and a further drop to just under 15.8% by end of 2007. These remarkable achievements have been made against very difficult economic conditions in Zimbabwe thus attesting to his visionary leadership of the Ministry of Health and Child Welfare, the determination of the health professionals and the continued support of both government and the international community in ensuring that Zimbabweans have access to good healthcare. His nomination to Vice President of the WHO regional office is yet another vote of confidence in his quest for better healthcare facilities and services for the African people at large.

The President of The Regional Committee, WHO's Governing Body in the African Region ((http://www.afro.who.int/), is Dr Luis Sambo. The meeting held in Yaounde, Cameroon addressed issues related to the health of women and curbing the harmful use of alcohol in the Region, strategies for cancer prevention and control and progress reports on HIV prevention. Other items discussed were on the strengthening of laboratories which are key to disease detection. Delegates shared best-practices in reducing maternal mortality; scaling up HIV prevention, treatment and care; improving immunization coverage, and scaling up interventions for malaria prevention and control in the Region.

The nomination of Dr. David Parirenyatwa as Vice President to this influential regional organization is therefore testimony to the achievements made by the Ministry of Health and Child Welfare and places our country, Zimbabwe, favorably to discuss and share experiences in combating disease in the African region.

The African Institute of Biomedical Science and Technology, AiBST, (www.aibst.com) whose headquarters is in Zimbabwe, congratulates Dr. David Parirenyatwa and the Ministry Health of Child Welfare on this nomination. AiBST will continue to work in the framework of the Ministry of Health and Child Welfare, together with the Ministry of Science & Technology Development and Ministry of Higher & Tertiary Education towards its objectives of promoting the sciences and technologies of drug discovery, development and optimal use of medicines in Africa ●

New staff members

Ms Mildred Magara

Mildred joins AiBST as an Office Manager. She is a holder of a Diploma in Secretarial Administration and Public Relations. Currently she is studying for degree in Human Resources with University of South Africa (UNISA).

Tirivanhuwo Nhando

He has worked for the ministry of education as a high school teacher for several years after which he joined the private sector starting at COTCO as an assistant accountant. He gained experience on financial aspects of contract farming and manufacturing. He then moved on to Exor Holdings before joining AiBST.

PROFILE FOR DR. S. MOYO

Dr S studied for a Bachelor's degree in Veterinary Science at the University of Zimbabwe and graduated in 2007. She joined the Faculty of Veterinary Science at the same university as a Resident Veterinary Pathologist: and was a wildlife veterinarian and pathologist with the Zimbabwe Wildlife Group at the same time.

In July this year, Dr Moyo joined AiBST as a Master of Philosophy student in the department of DMPK/PD-Tox. She brings with her a wide range of knowledge encompassing the entire spectrum of medical activities from the molecular system to the entire ecosystem, the role of animal models in biomedical research as well as the impact of animals and disease on human health and well being.

Her MPhil work will be on the integration of *in vivo* pre clinical pharmacokinetics and pharmacodynamics in the discovery of antimalarial drugs.

Mr Lloyd Dziwanyika

Lloyd is a holder of a HEXCO National Certificate in Science Technology and he joins AiBST as a Laboratory Technician. Currently he is studying Applied Biology at the Harare Polytechnic ●

AiBST Publication Rose Hayeshi

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across membranes. Transport experiments of amodiaquine in CsCo-2 cells showed a low recovery of 30% and a rapid disappearance from the apical chamber. Compounds structurally similar to amodiaquine, and those affecting non-specific binding of amodiaquine or the pH of the system, were tested to unravel the mechanism behind these observations. Chloroquine and ammonium chloride increased the transmonolayers permeability of amodiaquine and decreased its accumulation in CaCo-2 cells, whereas BSA had no effect. This suggest that amodiaquine is trapped in acidic cell compartments such as lysosomes. Amodiaquine was also trapped in rat intestinal tissue. In addition, permeability from the apical to basolateral direction was significantly higher, suggesting an active uptake over the apical membrane of the rat tissue. It can be concluded that amodiaquine is trapped in acidic cell amodiaquine is trapped in acidic cell compartments due to its base properties and recovery may be improved by the use of ammonium chloride rather than BSA in transport experiments. Urther studies are required to confirm whether amodiaquine is actively absorbed in the intestines.

Key words: amodiaquine, Caco-2,rat jejunum, lysosomotropy, low recovery ●

AiBST Publication Britta Bonn

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the active site cavity suggest a favored substrate orientation that prevents N dealkylation from occurring. In this study, the literature was searched for N-dealkylated and non N dealkylated CYP2D6 substrates. The hypothesis suggested and confirmed was that N dealkylation occurs by this enzyme when the preferred site of metabolism is blocked towards other oxidative metabolic pathways. An interesting observation was also that addition of stable groups at preferred sites of metabolism generally improved the metabolic stability but also resulted in retained or increased inhibition of the enzyme. In addition, the effect of pH on N- and O-dealkylation of dextromethorphan was shown to be consistent with the hypothesis that an ionized amino function favored substrate dockings resulting in O-dealkylation ●

AiBST & UCT

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The partnership shall have at least the following areas of emphasis:

- the setting up of a joint drug discovery computational modeling laboratory in the Department of Chemistry at the UCT;
- the establishment of research collaboration and joint publication among teaching/research staff;
- the exchange of educational materials and scientific equipment;
- student and/or staff exchanges;

University of Cape Town (UCT) Group

UCT/AiBST Drug Discovery And Computational Modelling Laboratory

The Parties will establish a drug discovery computational modelling laboratory, to be called the AiBST-UCT Computational Modelling Laboratory ("AiBS-UCT C-Lab") to be physically located at UCT's Department of Chemistry.The officers of the AiBST-UCT C-Lab shall be as follows: The Director shall be Prof. Kelly Chibale of UCT. Dr. Collen Masimirembwa of AiBST shall be a Co-Director and Prof. Peter Smith shall be an Associate Director. The primary focus of the AiBST-UCT C-Lab shall be on Computational Modelling methodologies for drug discovery and development.

AiBST Group

The AiBST-UCT C-Lab shall be supported with experimental industrial DMPK expertise from AiBST, preclinical pharmacology from Prof. Peter Smith's laboratory in UCT's Division of Pharmacology, and organic synthesis from Prof. Kelly Chibale's laboratory in UCT's Department of Chemistry.

The Laboratory shall apply for research grants in order for it to acquire state of the art computers and licenses to some of the leading software for modelling in the areas of compound library design, ligand receptor interactions, predictive ADMET, and design of clinical trials.

Outcomes

Outcomes of the collaboration in terms of this MoU shall include the following:

The AiBST-UCT C-Lab shall organise at least one annual course in advanced Computational Modeling for Drug Discovery. The first course is to be organised in 2009 on Predictive Drug Metabolism and Pharmacokinetics.

The creation and strengthening of linkages between AiBST and UCT which will include exchange and sharing of postgraduate students, lectureship visits by senior scientists and sharing of technology platforms. Prof. Kelly and Dr. Collen Masimirembwa already jointly supervise a PhD student, Roslyn Thelingwani.

Joint application of research grants to strengthen the objectives of this MOU. It is noted that a major research grant has already been awarded to Prof. Kelly Chibale (UCT) and Dr. Collen Masimirembwa (AiBST) in this regard ●