African Network for Drugs and Diagnostics Innovation (ANDI)

“Creating a sustainable platform for R&D innovation in Africa”

PART 1: HEALTH PRODUCT R&D LANDSCAPE IN AFRICA

PART 2: COLLECTION OF MEETING ABSTRACTS

Founding meeting in Abuja, Nigeria, 6-8 October 2008
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PREFACE

Recent international and regional intergovernmental fora have highlighted the link between health, innovation and economic development. Expenditure on health and health research and development, by both the public and private sector, is now increasingly seen as an investment in economic prosperity. The proposed African Network for Drugs and Diagnostics Discovery and Innovation (ANDI) combines these two elements. It would provide a platform for health-related research and development that both addresses the health needs of the continent and helps lay a foundation for innovation driven economic development.

African governments have contributed greatly to the development of a Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property that was approved through a World Health Assembly resolution in May 2008 (WHA61.21). This has paved the way for a greater focus on supporting developing countries to participate in the discovery, development and delivery of the products they need the most. This resolution builds upon other commitments by African governments such as the NEPAD health targets, the Abuja declaration of March 2006, the Accra declaration on Health Research adopted in June 2006 and the Algerian declaration on Research for Health in the African Region adopted in June 2008. ANDI comes at a time when various stakeholders are seeking concrete ways to meet these commitments and to promote sustainable product R&D and capacity development in developing countries, especially in Africa.

The draft African R&D landscape and the list of abstracts presented in this document demonstrate that health research innovation is already taking place in Africa, but greater efforts are needed to add to this effort and to link existing activities and energies together through appropriate partnerships that can further enhance the output and impact of this work. We believe that the ANDI initiative provides a significant way forward in achieving this objective and we anticipate that the ANDI meeting will result in concrete next steps for implementation.

Scientists must demonstrate that they have the commitment to direct their research in a way that will address practical needs and so give governments and industry confidence to invest in the development of these new ideas. Sustained support and commitment of African Governments to academic infrastructure in general and the practical work of ANDI in particular, would similarly give African scientists the confidence and incentive to engage in research directed towards practical outcomes. The enthusiasm and effort from many African scientists that has gone into this meeting is already clearly a testament to this fact.

We wish you all a successful meeting and look forward to generating a platform and network through which all interested parties, from within and outside the continent, can actively contribute to innovation for health in Africa, by Africans for Africa.

Uford Inyang
Director General, National Institute for Pharmaceutical Research and Development, Nigeria
Chair, Local Organising Committee for the ANDI Meeting.

Robert Ridley
Director, Special Programme for Research and Training in Tropical Diseases (TDR)
PART 1: HEALTH PRODUCT R&D LANDSCAPE IN AFRICA (DRAFT)

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Regional contact persons for data collection for the mapping:

Persons who participated in the compilation of data and preparation of draft report:
Solomon Nwaka, Bernadette Ramirez, Foluke Fakorede (Special Programme for Research and Training in Tropical Diseases, World Health Organization), and John Amuasi (Research and Development Unit, Komfo Anokye Teaching Hospital, Kumasi, Ghana).

Thanks to the many people who provided data for this mapping including those who sub-mitted abstracts for the ANDI meeting.
EXECUTIVE SUMMARY

Africa bears the greatest burden of disease in the world today but it has little control over the source and supply of medicines most needed by its citizens. The establishment of the African Network for Drugs and Diagnostics Innovation (ANDI) has been initiated to promote and sustain an African-led R&D innovation through the discovery, development and delivery of affordable new tools for the treatment of diseases in Africa, including those based on traditional medicines and natural products. It is envisaged that ANDI will establish a secretariat in Africa with a strong element of public-private partnership to support capacity and infrastructure development. ANDI’s creation follows numerous calls by international health and policy experts for increased investment in health R&D in Africa. The WHO Commission on Macroeconomics and Health (2001), the UN Millennium Project (2005), the G8 Gleneagles report on Africa, the Noordwijk Medicines Agenda (2007) and most recently the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (WHA 61.21), all stress the need to promote R&D and economic development in developing countries. Declarations from recent ministerial meetings on health research have also emphasized the need for more investment and commitment from African governments. The African Union have developed a pharmaceutical manufacturing plan for Africa and is pro-actively reviewing progress made in the implementation of the plan of action on the African Union decade of traditional medicines.

Many international and philanthropic agencies have invested in, and continue to support, research and capacity building in Africa. Yet available capacity in Africa has not been systematically harnessed to promote local health innovation efforts. A continent-wide effort such as ANDI requires not only greater funding, accountability, and coordination but also a better understanding of the existing R&D environment on the continent. This is especially important in the area of health product discovery, development, evaluation and delivery, which requires significant expertise, financing and management. Some country-specific analyses of the R&D landscape exist, but often times these studies are not focused on health products R&D and the results of such studies are not widely disseminated. The mapping exercise presented here, therefore, is intended to support the first phases of development of an R&D strategy for ANDI. It provides an initial description of available human and infrastructural capacity, gaps and challenges, and highlights new opportunities for product R&D innovation in Africa. Indeed, it will also help to inform donors, policy-makers and others on the landscape for R&D in Africa.

The mapping exercise involved consultation with many African researchers and scientists, interviews and discussions with scientists and policy makers, and literature as well as internet searches.

Our results show that significant, but isolated, product discovery and development activities are ongoing in Africa. To achieve coherent and sustainable product innovation, greater effort is needed to bring groups working in this area together so they may join forces, share lessons, and explore a more coordinated approach to health R&D and innovation. In the specific area of drugs, our study shows that no one African country or institution has demonstrated the capacity to move from basic research to discovery of a new chemical entity to registration and commercialization of a single new drug product. However, consultations with many experts suggest that this can be achieved.
through a strategic mechanism to support relevant, continent-wide activities in a coordinated and structured manner. Although the study mainly focused on activities related to drug R&D and traditional medicines, it should be noted that African institutions also have an untapped potential to expand their work in diagnostics development and vaccine research, especially through genomics. Indeed, several African institutions have already been able to discover and commercialize new diagnostic tools.

Significant capacity also exists in the areas of basic research, lead identification, clinical trial and marketing. However, the challenge is the lack of sustainable mechanisms to translate findings from basic research into concrete products and to further optimize and commercialize such findings. African hospitals and institutions also have capacity to undertake clinical trials, however it is not clear whether most of the clinical centres can yet carry out studies to international Good Clinical Practice (GCP) standards. Major gaps identified were in the areas of: lead optimization, pre-clinical Good Laboratory Practice (GLP) safety assessment, and raw material processing. In the area of manufacturing, several companies were identified, but it was not clear whether these firms can manufacture products to international Good Manufacturer Practice (GMP) standards. In all cases, there is a need for better management and coordination of research and procedures. Several experts interviewed expressed the strong desire for greater emphasis in research to support the use of traditional medicines and better management of local knowledge, including intellectual property.

In summary, initial data from the mapping exercise suggest that: 1) significant gaps in capacity, financing and infrastructure remain. At the same time, ongoing activities and available capacity and infrastructure can be leveraged to support expanded health product R&D innovation work in Africa; 2) in the area of traditional medicines, there remains a need for more systematic research evaluation and validation of the biological activities of traditional medicines; 3) concerted coordination of fragmented R&D in Africa activities is urgently needed; and 4) mechanisms to support the management of intellectual property need to be put in place.

ANDI, as one of its first priorities, intends to finalize the findings contained in this draft mapping study and integrate them into its business and implementation plan.
### List of Abbreviations

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<td>AU</td>
<td>African Union</td>
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<td>ANDI</td>
<td>African Network for Drugs and Diagnostics Innovation</td>
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<tr>
<td>CIPIH</td>
<td>Commission on Intellectual Property Rights, Innovation and Public Health</td>
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<tr>
<td>DMPK</td>
<td>Drug Metabolism and Pharmacokinetics</td>
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<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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<tr>
<td>GLP</td>
<td>Good Laboratory Practice</td>
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<tr>
<td>GMP</td>
<td>Good Manufacturing Practice</td>
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<tr>
<td>HLM</td>
<td>High Level Ministerial</td>
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<td>IGWG</td>
<td>Intergovernmental Working Group on Public Health, Innovation and Intellectual Property</td>
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<td>MDGs</td>
<td>Millennium Development Goals</td>
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<td>NEPAD</td>
<td>New Partnership for Africa’s Development</td>
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<td>OECD</td>
<td>Organization for Economic Cooperation and Development</td>
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<td>R&amp;D</td>
<td>Research and Development</td>
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<td>WHA</td>
<td>World Health Assembly</td>
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1. BACKGROUND AND RATIONALE FOR ANDI

The burden of disease in Africa

The burden of communicable and non-communicable diseases in Africa is well documented.\textsuperscript{1-4,23} The last century has seen unprecedented benefits of modern science to health and economic development. Despite advances in the prevention, diagnosis and treatment of disease, Africa is still struggling to overcome the daily impact of some of the controllable and preventable diseases that afflict its people in large numbers. This burden is evidenced by the shortening life expectancies and economic declines of many African countries. This disparity is well-illustrated by the contrasting prospects of baby girls born at the same time in Japan and Sierra Leone. “While the baby born in Japan can expect to live for about 85 years, life expectancy for the child in one of Africa’s poorest countries is just 36 years. The Japanese girl will receive some of the world’s best health care whenever she needs it, but the girl in Sierra Leone may never see a doctor, nurse or health worker”. Life expectancy has always been shorter in Africa than in any other continent and this is even dwindling further.\textsuperscript{1} The gap between developed and developing countries is made more evident by the deplorable statistics on HIV/AIDS, malaria, tuberculosis and some of the more neglected diseases. Owing to HIV/AIDS and other communicable diseases (which still present as the major causes of child deaths), millions of children born in African countries today are at greater risk of dying before their fifth birthday than they were a decade ago.\textsuperscript{2}

Although communicable diseases, exemplified by diarrhoeal diseases, tuberculosis, HIV, malaria, trypanosomiasis, leishmaniasis, helminths and soil-transmitted infections; account for over 60% of the mortality and morbidity in Africa,\textsuperscript{1} the global increase in non-communicable diseases is adding to the intimidating health and economic challenges facing many African countries. The growing burden of heart disease, stroke, diabetes, cancer and other chronic diseases, have further compounded already high mortality and morbidity, and premature death.\textsuperscript{5} Although WHO’s World Health Report is global in scope, these findings unavoidably draw the main focus to the increasingly failing health situation in Africa,\textsuperscript{2} where trends may hamper attainment of the health-related Millennium Development Goals (MDGs).

It is estimated that only 10% of the resources spent on global health research are directed towards health conditions that affect the people with the greatest disease burden. Much of this disease burden is in sub-Saharan Africa. The continent accounts for barely 1.1% of the total value of the global pharmaceuticals market. Many people do not have regular access to essential medicines, and there are as yet no effective diagnostic, preventive or therapeutic options for many of the health challenges Africa is facing. The lack of market incentives to support health innovation, product Research and Development (R&D) and access to essential medicines are factors in the crippling burden of these diseases along with the fragile health research and health services infrastructure.\textsuperscript{6,7}

The Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) describes the concept of innovation as a cycle consisting of three major phases that feed into each other from discovery, development and delivery. The Commission indicates that within the innovation cycle, public health need is expected to create a demand for products of a particular kind, suited for the particular medical or social context, and which supports efforts to develop new or improved
Health research\textsuperscript{4} and economic development

The direct link between health and development has been established and accepted within medical, public health and other scientific circles.\textsuperscript{5} The creation of knowledge through research and its translation into products and processes appropriate to socioeconomic conditions is a major factor in overall development.\textsuperscript{6,10,13,13a} The importance of research to development is underscored by the fact that every year, the Organization for Economic Cooperation and Development (OECD) member countries together spend about 1.5 times more on research and development than the value of the entire economic output of sub-Saharan Africa.\textsuperscript{11} Increasing research and development skills and capacities in a variety of science and technology disciplines have supported the advancement of emerging economies such as China, India, Malaysia, Singapore and South Korea, and South Africa. In addition, macroeconomic evidence suggests that countries with the weakest conditions of health and education have a much harder time achieving sustained growth than those countries with better conditions of health and education.\textsuperscript{9}

Some suggested mechanisms through which health R&D contributes to health improvement and economic development are depicted in Figure 1 (see next page).\textsuperscript{10}

The global strategy and plan of action

The increasing global awareness about the need for increased health R&D innovation has resulted in the availability of new funding from governments and philanthropic agencies such as the Bill and Melinda Gates Foundation, the Wellcome Trust and the Rockefeller Foundation in support of a wave of R&D efforts targeting diseases that disproportionally affect the developing world.\textsuperscript{6} One immediate effect of the new investments made over the past 10 years has been increased product development activities through public-private partnerships (PPPs).\textsuperscript{13,13a} Some of these partnerships have scaled up the search for cures for diseases such as those caused by kinetoplastids (The Drugs for Neglected Diseases Initiative), HIV/AIDS (The GAVI Alliance),\textsuperscript{14} tuberculosis (The Global Alliance for TB drug development),\textsuperscript{15} and malaria (The Medicines for Malaria Venture).\textsuperscript{16} However, many analysts and policymakers in developing countries believe that the only way the availability of new affordable drugs,
diagnostics, and vaccines for such diseases can be sustained in the long term, is through committed investments in R&D, manufacturing and distribution within African countries themselves.\textsuperscript{10,17,18,6}

The challenge of better access to healthcare products for poor populations has been the subject of many World Health Assembly (WHA) resolutions. At the Fifty-ninth World Health Assembly in 2006, Member States established an Intergovernmental Working Group on Public Health, Innovation and Intellectual Property (IGWG) with the mandate to prepare a global strategy and plan of action aimed at fostering innovation, building capacity and improving access to health products to achieve better health outcomes in developing countries. The eight specific elements that comprise the Global strategy and plan of action on public health, innovation and intellectual property include: prioritizing R&D needs, promoting R&D, building and improving innovative capacity, technology transfer, management of IP, improving delivery and access, ensuring sustainable financing mechanisms, and establishing monitoring and reporting systems. Following extensive deliberations; including regional consultations and other multilateral meetings linked to the IGWG, the Sixty-first World Health Assembly in May 2008 adopted the Global strategy and plan of action through Resolution WHA 61.21.\textsuperscript{19}

\textbf{Figure 1B: Mechanism by which health R&D leads to health improvement and economic growth.}\textsuperscript{16}
This Global strategy and plan of action lends unanimous support to the need for increased investments in basic and applied scientific research in the biomedical and health sciences as well as health product discovery, development delivery for diseases that affect development countries. The concept of the African Network for Drugs and Diagnostics Innovation (ANDI) comes at an opportune moment following renewed interest to support developing countries for R&D innovation.

2. THE CONCEPT OF ANDI

The concept of an African health product research collaboration

Over the past 5 years or more, the concept of an indigenous African institution focused on health product research and innovation has been raised and discussed. Several reports have highlighted the need for African governments and international agencies to support the transition of African science from fragmented and isolated activities to more coordinated and integrated R&D efforts across the continent. The CIPIH report quotes a Science and Technology Adviser of the Africa's New Partnership for Africa's Development (NEPAD) as saying: “Scientific and technological capacity for health cannot, thus, be reduced to equipment, funding and number of health scientists and technicians. It is the configuration of skills, policies, organizations, non-human resources, and overall context to generate, procure and apply scientific knowledge and related technological innovation to identify and solve specific health problems. The capacity is built through interactive processes of creating, mobilizing, using, enhancing or upgrading, and converting skills/expertise, institutions and contexts. It is not about isolated activities and products.”

High Level Ministerial (HLM) meetings to develop an African perspective on health research for achieving sustainable health MDGs in Africa were held in Abuja, and Accra in 2006. On 23-26 June 2008 there was another high-level meeting in Algiers, in preparation for the Bamako 2008, Global Ministerial Forum on Research for Health to be held in Mali 17-19 November. At these meetings, African Ministers of Health and other stakeholders concluded that it is important for the African continent to increase its stake in shaping research agenda and in undertaking research. The meetings also recognized the need for Africa to take advantage of existing research institutions in achieving agreed health targets, and also to foster collaboration and leadership to promote essential national health research in Africa.

In a 2007 TDRNews article, Solomon Nwaka (Head, Drug Discovery for Infectious Tropical Diseases, WHO/TDR) underscored the importance of empowering developing countries to actively participate in product R&D: “Developing countries need to participate in discovering, developing and manufacturing their own drugs, and in establishing functional market mechanisms that suit their own needs.”

Initial WHO/TDR analyses have shown that basic capacity and infrastructure to support R&D innovation activities, ranging from basic research, product discovery, and development do exist in different parts of Africa. However, these activities, available expertise and infrastructure are not coordinated and interlinked. Greater efforts are needed to bring groups working in this area together to join forces, share lessons, identify challenges and explore a more coordinated approach to product R&D and innovation in Africa. WHO/TDR is working with a number of institutions in Africa as part of an
Innovative Drug Discovery effort for Infectious Tropical Diseases that is based on networks of partners from academia and industry in developed and developing countries. The success stories from several African centres participating in these and other drug discovery networks has provided the impetus for broader participation of other African institutions and investigators in a coordinated initiative. Ongoing activities in Africa are now being leveraged to establish an “African Network for Drug Discovery and Product Innovation (ANDI)” through the Abuja meeting in October 6-8, 2008. Although ANDI is not a panacea, it is certainly a concrete response to the Global Strategy and Plan of Action and some of the earlier calls for more investment and support for health innovation in Africa.

**Response from African scientists and other supporters**

No one African country or institution has demonstrated the capacity to move from basic research to discovery of a new chemical entity to registration and commercialization of a single new drug product. However, consultations with many African scientists and experts both at home and in the diaspora suggest that this can be achieved through a strategic mechanism to support relevant continent-wide activities in a coordinated and structured manner. This has led to the conceptualization of the African Network for Drugs and Diagnostics Innovation (ANDI) as a platform to help support African institutions to participate in discovering, developing and manufacturing the health products they need the most. ANDI can also contribute to a sustainable African-led R&D innovation by strengthening and utilizing existing capacity and infrastructure to promote collaborative efforts directed towards sustained delivery of affordable health products including those based on natural products and traditional medicines.

The initial concept for ANDI led to an electronic consultation with many African scientists at home and abroad through an e-mail dated 15th February 2008 (see Box 1). An indication of the level of support and appreciation for the ANDI concept is captured in selected quotes from the significant number of e-mail responses from African scientists, including those in the diaspora, and other supporters (Box 2).
Box 1.
E-mail from Solomon Nwaka sent to colleagues in Africa and those in the Diaspora

Dear Colleagues,

It has become clear that several drug discovery activities are ongoing in African but more efforts are needed to bring groups working in this area together to share lessons, identify challenges and explore a more coordinated approach to product R&D and innovation in Africa. WHO/TDR is working with a number of institutions in Africa as part of our Innovative Drug Discovery efforts for Infectious Tropical Diseases. This effort is based on networks of partners from academia and industry in developed and developing countries, and based on success stories from several participating centres in Africa, it has become important to explore a broader participation of African investigators and institutions in this initiative. This of-course includes natural products and traditional medicines based R&D.

The TDR drug discovery team is considering a meeting in Africa to discuss ongoing activities supported by TDR and how these can be leveraged to establish an ‘African Network for Drug Discovery and Product Innovation’. I am proposing that the meeting be held in the week of October 6, 2008. I will be visiting the National Institute for Pharmaceutical Research and Development (NIPRD) at Abuja next week and will discuss the possibility of holding the meeting in Abuja with the Director General of NIPRD.

I welcome any suggestions you may have and hope that you would like to participate. We might be able to involve some Africans leaving abroad and other international organizations if the level of interest for this meeting is high.

Best regards,

Solomon Nwaka

Head, Drug Discovery for Infectious Tropical Diseases,
TDR, World Health Organization,
Geneva, Switzerland
BOX 2.
Enthusiastic support for the establishment of ANDI

“…the idea to bring African scientists together in an initiative is a timely and marvelous one…brilliant idea…can contribute to help improve the generally poor health care services in the continent. The widespread enthusiasm expressed since the first mail on 15 February 2008 is equally encouraging and demonstrates a shared keen interest by all in tackling the long-standing problems connected with healthcare issues in the African continent…It should be understood that the ultimate target of this whole initiative is to get essential and life-saving medicines which are effective against the plethora of diseases ravaging Africa to our drug stores and also at affordable prices to the masses of suffering Africans. Anything short of achieving this ultimate goal definitely fails to meet the expectation of the African masses and thus the initiative would be viewed merely as another mental exercise and exhibition of academic/scientific excellence!!…I wish us all loads of success in this noble initiative.”

Alexander Ochem, International Center for Genetic Engineering and Biotechnology (ICGEB), Trieste Italy

“Laudable initiative which when fully implemented will reveal the amount of work that African Scientists in African Institutions have done in the area of drug discovery and innovation. The network will enable us identify African Scientists and Institutions that are involved in meaningful product R&D within and outside of the continent.”

Ulford S. Inyang, Director General, National Institute for Pharmaceutical Research and Development, Abuja, Nigeria

“The idea to bring African scientists together in a network for drug discovery and innovation is a wonderful proposition. ANDI may open new vistas …the right forum for addressing health problems by providing expected drugs. Good take off for ANDI! …for connecting people and giving African scientists the opportunity to share experiences and vision towards a common vision: design and development of drugs by African experts for Africa.”

Barthelemy Nyasse, University of Yaounde, Cameroon

“I am excited that the successful drug discovery network paradigm of WHO/TDR will be applied to an African Network.”

Carmelle T. Norice, Columbia University, New York, USA

“We look forward to working together on this important journey.”

John C. Afele, African Diaspora Mobilization Initiative, Capacity Development Management Action Plan Unit & World Bank Institute, Africa Region, The World Bank, Washington DC, USA
“…this meeting comes at a very appropriate time, considering, in particular, the mandates approved by the Sixty-First WHA on May 24 in relation to the IGWG and WIPO’s International Bureau's commitment to extend all possible cooperation to the Secretariat in this important process.”

Carlos Mazal, Senior Counsellor, World Intellectual Property Organization, Geneva, Switzerland

“Many thanks for the information and details about the Abuja conference which looks most interesting. I wish to forward the information to my colleagues and fellow-volunteers on the Biotics Exploration Fund of the International Organization for the Chemical Sciences in Development who I know will share my interest and enthusiasm about your program. I feel that multidisciplinary international collaboration is the only way to make progress in these areas.”

Gordon Cragg, former Chief of the Natural Products Branch of the Developmental Therapeutics Program at the National Cancer Institute

“Excellent initiative.”

Richard Somiari, President and CEO, ITSI - Biosciences, Philadelphia, USA

“Thanks for this exciting initiative.”

Abdoulaye Djimdé, Head, Molecular Epidemiology and Drug Resistance Unit Malaria Research and Training Center, Department of Epidemiology of Parasitic Diseases Faculty of Medicine, Pharmacy and Odonto-Stomatology, University of Bamako, Bamako, Mali

“This ought to be an unstoppable TSUNAMI! This is really exciting. I am more than willing to participate.”

Norman Nyazema, School of Health Sciences, University of Limpopo, South Africa

“This is a great opportunity for African scientists to come together in this network.”

Geoffrey M. Rukunga, Kenya Medical Research Institute, Centre for Traditional Medicine and Drug Research, Nairobi, Kenya

“… really exciting to participate.”

Fathia Gawish, Theodor Bilharz Research Institute, Cairo, Egypt

“… ready to give a hand in the work, hoping for the success of this network.”

Ahmed Elhawary, Theodor Bilharz Research Institute, Imbaba, Egypt
“Without a blink or any reservation I think this is exactly the way to go with product R&D in Africa. “Let us cry our die!” More grease to your elbows.”

Fidelis Cho-Ngwa, University of Buea, Cameroon

“We are very interested in the drug discovery network.”

Chioli Pascal Chijioke, Dept of Pharmacology & Therapeutics, College of Medicine, University of Nigeria Teaching Hospital, Enugu State, Nigeria

“I am really happy that this proposal is gaining widespread support. There has already been some important inputs and I think its time to start working on an ‘innovative’ concept.”

Collen Masimirembwa, AiBST, Harare, Zimbabwe

“Quite an interesting initiative… my excitement knows no bounds. It is also timely, as the ECA and AU are currently focusing on developing IP and Patent laws for Africa.”

Ifeoma Okoye, University of Nigeria, Nigeria

“I would be happy to help out with the efforts in any way that I can. I know that there are a number of collaborative research efforts ongoing between the NIH and various African researchers, but to my knowledge there is no larger network under which these efforts are coordinated and monitored. An organization like the proposed ANDI could be very necessary and useful in this regard, and I would be glad to contribute to getting it started.”

Tshaka Cunningham, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Laboratory of Viral Diseases, Cell Biology and Viral Immunology Sections, Bethesda, MD, USA

“I think this is a wonderful idea. Please let me know where I can help.”

Lyndon J., Merck Company

“This is indeed a very exciting opportunity and one that can firmly put Africa on the map. I am looking forward to getting involved.”

Richard Gordon, BioFocus DPI, Chesterford Research Park, Saffron Walden, Essex

“This is an excellent initiative. Thanks for the giant stride. I look forward to hearing from you regarding further development in this great initiative.”

Chuk’ Okereke, Department of Clinical Pharmacology and Translational Medicine, Eisai Medical Research Inc/ Eisai Global Clinical Research Inc, Ridgefield Park, NJ, USA
"I must commend you for proposing this brilliant initiative. I absolutely support the proposition. And your timing is optimal, in my view. I feel that this initiative will go a long way and reduce our mutual isolation from each other."

**Echeazu Ogu**, Regulatory Affairs Certification - US FD&C Regs, Independent Consultant - Pharmaceutical & Biotech BonScience, Inc, Newark, Delaware, USA

"I am glad to receive information about the Network. My joy is that the dream of stimulating product research and development in Africa is still very much alive. I am also excited that the Network has captured many African biomedical scientists. I look forward to participating in the Network."

**Charles Wambebe**, International Biomedical Research in Africa, Abuja, Nigeria

"As an African researcher I am truly happy about it and I would be pleased to participate."

**Sanaa Botros Theodor**, Bilharz Research Institute, Imbaba, Egypt

"I have full support for this landmark initiative and will contribute my very best where I can."

**Sungano Mharakurwa**

"A great idea. I would like to be an active participant in such drug discovery R&D efforts. I look forward to the proposed meeting."

**Joshua Odingo**

"…… a great idea, which I believe will facilitate some success stories in drug discovery, which our continent so desperately needs. We need to earn respect. We need to show the world what we can do in drug discovery when we are united based on complimentary scientific expertise."

**Kelly Chibale**, University of Cape Town, South Africa
3. THE PRODUCT R&D LANDSCAPE IN AFRICA

Rationale for mapping

In order to lay a solid foundation for a viable African Network for product innovation, it is important that the capacity of African scientists and institutions to carry out various aspects/stages of the desired R&D are measured and discussed. This will invariably help identify various gaps – including infrastructural, areas where expertise is needed, and appropriate methods to be applied in filling these gaps. The data gathered from the mapping exercise will inform the development of a framework and structure for ANDI.

Recently some attempts have been made to provide information on on-going R&D activities in Africa, however, there exists no comprehensive source of information on drugs, diagnostic or vaccine R&D capacity across Africa. This mapping exercise is expected to contribute in filling this gap and in providing vital information that will help to strategically position ANDI to achieve its objectives, including:

- to support product R&D in Africa;
- to provide ongoing review and analysis to better understand the health product R&D landscape and capacity across Africa;
- to support and advocate for investment in indigenous human resources and funding for health research;
- to promote the utilization of existing technologies and research capacity to advance increased access to health interventions;
- to contribute to strengthening the weak link between research and health policy;
- to promote the integration, and coordination of health product R&D.

Methods

The mapping exercise commenced in May 2008. The data collection tools employed include: electronic communications, survey/questionnaire in blank tabular form which were filled in by respondents (responses were collated in a spreadsheet presented here in the results section), key informant interviews, literature and internet searches.

The initial electronic exchanges with African scientists generated data and information that led to the creation of a spreadsheet with the different R&D components and extent of capacity across Africa. The data was obtained using various non-probability sampling methods. This was further strengthened through a focused set of about 20 African researchers (at institutions and/or relevant ministries in various African regions including, West, Central, North, East and Southern Africa. This activity was carried out via email. Snowball sampling was also employed. In this case those individuals and institutions who were directly contacted to fill out the table were encouraged to circulate the table and/or provide contact details of others within or outside of their countries who could do the same.

Key informant interviews were also conducted including through personal visits. These interviews were aimed at providing new information, as well as to offer further insight into the information that
was obtained via the questionnaire (Table 1). The interviews helped to further consolidate all data gathered (Table 1, Figure 2) on R&D activities but more importantly capacities in drugs and diagnostics R&D ranging from early stage discovery work (including targets, tools, screening, chemistry, drug metabolism and pharmacokinetics (DMPK), natural products, traditional medicines); preclinical development-toxicology; and clinical development, right up to manufacturing, marketing and regulatory bodies. Although the focus was on infectious tropical diseases, the provision of information on research capacity into other diseases was encouraged. Indeed many respondents highlighted the need to consider non-communicable diseases as well as support for management of intellectual property as additional activities for ANDI.

The literature review conducted involved searching of various databases for articles in peer reviewed journals, patent literature, reports, presentations, transcriptions of interviews and news articles, internet and websites of various institutions/organizations. Input of the keywords: Drugs, Diagnostics, vaccine Research and Development in Africa, Innovation in Africa, R&D in Africa, Developing Countries, in various combinations with no limits resulted in a number of hits.

**Results of mapping**

Capabilities within Africa in the various health product R&D Stages and commercialization are presented in Table 1 (additional details are presented in Annexes 1, 2 and 3), for the following areas: basic and exploratory discovery research relevant to drugs, diagnostics, vaccines and insecticides; hit identification; hit to lead identification; lead optimization; natural products and traditional medicines; management of intellectual property; pre-clinical toxicology and safety pharmacology; clinical studies; regulatory expertise; process chemistry/raw materials; manufacturing/formulation; marketing; phase iv/pharmacovigilance. The extent of capacity in the afore-mentioned specific R&D areas was grouped into two – to illustrate widely available capacity and limited capacity or gaps. Selected examples of countries/centres with these capacities were also provided. One of the expected outcomes of this mapping exercise is the identification of priority areas in drug and diagnostic R&D in which African countries could collaborate by building on expertise and resources that already exist in key areas.
Table 1. Capabilities within Africa in the various product R&D stages & commercialization

<table>
<thead>
<tr>
<th>R&amp;D stage</th>
<th>Capacity and gaps in health product R&amp;D</th>
<th>Examples of centres/countries with capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic exploratory research relevant to Health Products</td>
<td><strong>Examples of available capacity</strong></td>
<td><strong>Examples of gaps</strong></td>
</tr>
<tr>
<td></td>
<td>• Identification of different protein targets for the development of drugs, diagnostics and vaccines.</td>
<td>Data management including protection</td>
</tr>
<tr>
<td></td>
<td>• Use of molecular methods such as regular Polymerase Chain reaction (PCR), quantitative PCR (Q-PCR), genomic sequence and analysis using different software, genetic engineering, probe hybridization techniques, biological and molecular cloning, evaluation of immune markers for laboratory diagnosis of infections, serological assays involving the use of rapid tests, ELISA-based evaluations and immuno-fluorescent assay techniques.</td>
<td>Ethical challenges</td>
</tr>
<tr>
<td></td>
<td>• Reference laboratories designed for diagnosis as well as clinical and vaccine research.</td>
<td>Translation of basic research into innovative products (translational research)</td>
</tr>
<tr>
<td></td>
<td>• Screening, lymphocyte phenotyping, cytokine activation and production, epitope tracking and HLA typing, etc.</td>
<td>See Annex 1</td>
</tr>
<tr>
<td></td>
<td>• Bio techniques: DNA sequencing flux cytometrics, Elispot, ELISA, Western Blot, cell cultivation, etc.</td>
<td></td>
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<tr>
<td></td>
<td>• Virology: viral load calculation, study of genetic resistance to ARV, and viral subtype sequencing.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Biological profiles for the follow-up of PVVS, and vaccine and clinical research.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Analysis of data obtained from sequences and subtypes of viral origin, immune polymorphism, the clinical progression of the diseases, and the most relevant social determinants.</td>
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<tr>
<td></td>
<td>• Epidemiological baseline studies and evaluation of in vivo, in vitro activities of antimalarial compounds.</td>
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<tr>
<td></td>
<td>• Ligation-mediated PCR genotyping.</td>
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<tr>
<td></td>
<td>• Epidemiology and immunodiagnosis of schistosomiasis hematobium.</td>
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<tr>
<td></td>
<td>• Studies on circulating adhesion molecules in schistosomiasis.</td>
<td></td>
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<tr>
<td></td>
<td>• Synthetic chemistry.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Computational modelling.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Systems Biology.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Biomarkers of Mycobacterium tuberculosis and others pathogens.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Functional annotation of reconstructed genome transcripts.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Host-parasite relationships: induction of regulatory immune mechanisms.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Molecular epidemiology and prognostic markers.</td>
<td></td>
</tr>
</tbody>
</table>
## Hit Identification and Hit to Lead Identification

- Synthesis and evaluation of compounds as antiparasitic and antineoplastic agents
- Centres have the capacity to screen plant medicines as sources of lead compounds for treatment of infectious diseases such as malaria and Buruli ulcer, as well as non-communicable diseases like diabetes mellitus, cardiovascular and renal disease.
- In-vitro Efficacy Assays: HIV, TB, Protozoan and helminth parasites, Cancer and bio-safety level 3 (BSL 3) environments available.
- Synthetic chemistry
- Parallel and robotic synthesis capability

## Lead Optimization

- Computational modelling
- Parallel and robotic synthesis capability
- Spectroscopic characterization of secondary metabolites
- Chromatography

### Access to chemical libraries
- Throughput of primary assays. High throughput screening, in silico screens. Analysis and prioritization of hits
- Choice of in-vitro efficacy assays
- Medicinal chemistry, in vivo ADME/PK testing, construction of SAR. Proactive coordination and management of projects.
- Data and project management including protection

### Pharmacognosy
- Departments at Faculty of Pharmacy- Helwan and Cairo Universities, Chemistry of Natural Products-National Research Center – Egypt
- University of Cape-Town (UCT) – South Africa
- Council for Scientific and Industrial Research (CSIR) – South Africa
- African Institute of Biomedical Science and Technology (AIBST) - Zimbabwe

### Lead optimization chemistry and QSAR
- CaCo2 testing, Cytotoxicity
- Microsome stability, PAMPA, Metabolite Identification
- PK, Toxicokinetic animal models, efficacy animal models
- Detailed medicinal chemistry, ADME, construction of SAR, Toxicology. Proactive coordination and management of projects, candidate selection.
<table>
<thead>
<tr>
<th>Natural Products and Traditional Medicines</th>
<th>Management of Intellectual Property</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Significant capacity in this area. Centres have the capacity to screen plant medicines as sources of lead compounds for treatment of infectious diseases such as malaria, TB, Buruli ulcer, as well as non-communicable diseases like diabetes mellitus, cardiovascular and renal disease.</td>
<td>• Mainly administered by Ministries of Industry and Ministries of Justice</td>
</tr>
<tr>
<td>• Evaluation of plant drugs using medicinal phytochemistry, pharmacology and toxicology. Including isolation of active ingredients, structure elucidation using NMR and MS, Chemical profiling of botanical extracts using HPLC MS/MS</td>
<td>• Available IPR laws</td>
</tr>
<tr>
<td>• Pharmacology, physiology and biochemistry equipment including laboratories.</td>
<td>• Various private law-firms in West-Africa offer IP services</td>
</tr>
<tr>
<td>• NEPRD have developed natural product-based formulation called Nipresan for the treatment of sickle cell anemia.</td>
<td>• Some African countries, e.g., Cameroon, are members of WIPO and are party to the Paris Convention for the Protection of Industrial Property</td>
</tr>
<tr>
<td>• Experience and facilities to study medicinal plants with antimalarial activity, immunology and HIV/AIDS.</td>
<td></td>
</tr>
<tr>
<td>• IMPM developing anti-HIV tests kits from its spin off called Cam Diagnostics.</td>
<td></td>
</tr>
<tr>
<td>• Labothera laboratories developed HEPASOR, a Hepatoprotective and hepatocurative drug made up of Protoberbine extracted from Enantia Chlorantha (Annonaceae).</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation and identification of active components. Proactive coordination and management of projects, aligning extracts to classical drug discovery pathway</td>
<td>Limited practical capacity in this area</td>
</tr>
<tr>
<td>Lack of knowledge in IP issues. Toxicology and teratogenicity studies</td>
<td>Existing IP laws are generally not appreciated by researchers and the general populace and therefore not enforced</td>
</tr>
<tr>
<td>Data protection. Scaling up production and marketing</td>
<td>Preparation and filing of patents. Management of intellectual property; licensing principles</td>
</tr>
<tr>
<td>Quality assurance of drugs: quality control and surveillance</td>
<td>Many African Countries</td>
</tr>
<tr>
<td>Development of standard documentation</td>
<td></td>
</tr>
<tr>
<td>See Annex 2</td>
<td></td>
</tr>
</tbody>
</table>
### Pre-clinical Toxicology and Safety Pharmacology

<table>
<thead>
<tr>
<th>Facility</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic toxicological studies including drug/chemical-induced toxic injury, drug metabolism and drug-drug and drug-herbal interactions. Reproductive and genotox testing.</td>
<td></td>
</tr>
<tr>
<td>NMIMR conducts research into biomonitoring and prevention of poisoning from mycotoxins and toxic heavy metals.</td>
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<tr>
<td>NMIMR has the VICAM Afla Test equipment capable of analyzing aflatoxins in foods to meet international standards.</td>
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</tr>
<tr>
<td>NMIMR has the LUMEX mercury analyzer capable of measuring mercury in both biological and environmental samples.</td>
<td></td>
</tr>
<tr>
<td>NMIMR is also equipped with a spectrofluorometer, clinical chemistry and haematology autoanalyzers, HPLC, analgesimeter and a plethysmometer.</td>
<td></td>
</tr>
<tr>
<td>General gap in the area of safety pharmacology.</td>
<td></td>
</tr>
<tr>
<td>Microsome stability, PAMPA, Metabolite Identification</td>
<td></td>
</tr>
<tr>
<td>PK, Toxicokinetic animal models, binding panels, hERG, mutagenicity and carcinogenicity studies, GLP facilities</td>
<td></td>
</tr>
</tbody>
</table>

### Clinical Studies

<table>
<thead>
<tr>
<th>Facility</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many African research institutions possess facilities and expertise for Phases I &amp; II and III clinical trials according to GCP.</td>
<td></td>
</tr>
<tr>
<td>Observation wards, resuscitation equipment, medical and paramedical staff etc. available.</td>
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<tr>
<td>Many collaborate in multi-centre drug, vaccine and diagnostic clinical trials.</td>
<td></td>
</tr>
<tr>
<td>Protocols used in these trials are not locally developed although might contain some input from local investigators.</td>
<td></td>
</tr>
<tr>
<td>High end scientific work is carried out in the West or North, with the African centres supporting by facilitating the collection of biological samples or information.</td>
<td></td>
</tr>
<tr>
<td>See Annex 3</td>
<td></td>
</tr>
<tr>
<td>Regulatory Expertise</td>
<td>Raw Material processing, and active pharmaceutical ingredients</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------------------------------------------------</td>
</tr>
<tr>
<td>• Most possess drug regulatory agencies in the form of Food and Drugs Boards (FDBs). • Levels of expertise and powers vary from country to country.</td>
<td>Ability to process raw material is limited. Most import purified forms to use in manufacturing.</td>
</tr>
<tr>
<td>Most rely heavily on prior approval from regulatory agencies in the West and North such as the European Medicines Agency (EMEA) and the U.S. Food and Drug Administration (FDA)</td>
<td></td>
</tr>
<tr>
<td>Food and Drugs Boards of many African countries Ministries of Health</td>
<td>Several Pharmaceutical Companies in North, South Africa, few in sub-Saharan Africa. LaGray Chemical Company-Ghana.</td>
</tr>
</tbody>
</table>
Spontaneous reporting and other pharmaco-epidemiological methods available to systematically collect and analyze adverse events associated with the use of drugs, identify signals or emerging problems, and communicate how to minimize or prevent harm.

Parallel structures and lack of empowerment.

Difficulty in collecting data remotely. Most initial reports have to be manually transmitted.

Four West African countries (Togo, Benin, Nigeria, and Ghana) appear to be full members of the WHO programme for international drug monitoring at the Uppsala Monitoring Centre programme.

No Central African country is a full member of the WHO Uppsala Monitoring Centre. Only two Central African countries are associate members; Cameroon and the Democratic Republic of the Congo.

Uganda and Tanzania are the only East Africa countries that are full members of the WHO Uppsala Monitoring Centre. Kenya, Ethiopia and Zanzibar are associate members.

Only two Central African countries are associate members; Cameroon and the Democratic Republic of the Congo.

Translation of PV information into policy.

Food and Drugs Board (FDB) and the Centre for Tropical Clinical Pharmacology and Therapeutics (CTCP) of the University of Ghana Medical School (UGMS) collaborate in carrying out pharmacovigilance in Ghana.

Two parallel structures controlling pharmacovigilance in Cameroon, the Directorate of Pharmacy and Drugs (DPM) and the National Drugs Committee.

University of Cape Town - National Adverse Drug Event Monitoring Centre – South Africa.
Discussion

In the course of this work, it became clear that core assets, particularly scientific expertise and capacity are available in various institutions on the African continent (Table 1, Annexes 1, 2 and 3). Figure 2 further groups these core assets into three categories: 1) widely available capacity in many countries, 2) available capacity in a few countries and 3) limited capacity across the continent. Basic exploratory research, natural products/traditional medicine, clinical studies and marketing top the list of capabilities that are available in many African countries. In the specific area of basic research, the challenge is to translate these research findings into product leads. Many institutions lack the mechanism and resources to perform this translational activity. Many investigators interviewed expressed the desire for increased emphasis in area of natural products and traditional medicines, necessary intellectual property management support, as well as support for programme management and generation of sustainable funding for product R&D.

A few countries have notable expertise for hit to lead and lead optimization, management of intellectual property, regulation, and Phase IV/Pharmacovigilance, however several individual institutions have relevant capacity. Least available in the African continent is the capacity for preclinical toxicology/safety pharmacology as well as capacity for raw material processing including process chemistry and active pharmaceutical ingredients production to GMP standards. In the area of clinical trials, significant capacity exists but infrastructural and management support for Good Clinical trials Practices (GCP) are still limited.

Understandably, there are also several gaps in different areas which should not be overlooked in the process of finding solutions. However, to address the innovation gap at large it is important to urgently

Figure 2. Capacity in Health Product R&D in the African Continent
recognize the unique characteristics and strengths of the various African institutions and use these as strong enablers and value drivers. The link between technology, science, and innovation in achieving MDG targets in Africa is increasingly being recognised by policy makers. What is needed is a continent wide or regional coordination strategy for product R&D rather than individual stand alone activities. Also, since the domestic financial resources are limited, convergence, coordination and accountability are critical for success. Creating a coordinated network of African scientists (both within the continent and among Africans in Diaspora) and other relevant partners through the African Network for Drugs and Diagnostics Innovation (ANDI) may contribute in making existing and future investments in health products R&D more effective.

Although the study generated more information on drug R&D in Africa, it also became clear in the process that capacity for diagnostics and vaccine research, especially with the use of genomics tools, is available. Indeed, several African institutions have been able to discover and commercialize diagnostics. Furthermore, this analysis does not fully investigate the available capacity for implementation research in Africa (although it can be said that there are some areas of overlap that have been included in the assessment of capacities for Pharmacovigilance and Phase IV studies).

A number of African-based research initiatives have been established in recent years e.g. INDEPTH network (Ghana), AMANET (Tanzania), MIM (Tanzania) etc. In addition, regional network initiatives, such as the African Biosciences Initiative, spearheaded by NEPAD, have sought to create "centres of excellence" with the objective of bringing together researchers and institutions from common regions to pool their resources. Examples include SANBio, based in South Africa, whose focus is on cutting-edge research relating to agriculture, human and animal health, the environment and industry. However, the primary focus for some of these initiatives is either downstream research to support health policy setting or capacity building for basic research. In addition, some of these initiatives focus on specific diseases. ANDI is unique and different from these initiatives as follows: 1) it will identify mechanisms for translating research findings into innovative health interventions (initially targeting neglected diseases, but the disease scope may expand as capacity becomes available). 2) It will also devise a mechanism for evaluation and validation of natural products and traditional medicines. 3) It will manage intellectual property and promote innovation in Africa. All these point to the primary focus of ANDI in product R&D. It is envisaged that ANDI will synergize with and complement existing activities and perhaps facilitate the translation of the outputs from these initiatives into products that meet target product profiles for relevant diseases. The proposed work of ANDI fits with the EU health and pharmaceutical manufacturing strategy, as well as the global strategy.

In the area of health R&D funding in Africa, most investigators who contributed to this mapping expressed disappointment with the dearth of, or limited funding support, from African countries themselves, and called for more local investment in research. Although this work is still ongoing, it appears that a significant part of the funding being used by investigators for R&D are coming from outside the continent and managed externally. Several African Universities and research institutions do not have sustainable local or external sources of funding. Indeed, the study found that availability of, and access to, sustainable funding for product R&D is a major impediment to health innovation in Africa. Having said this, investments in health research through international and local support in past years have already brought modest successes; these demonstrate that increased investment in innovation allows African countries to grow economically and develop the capacity to take control of their own destiny.
In conclusion, the initial findings from this mapping exercise suggest that: 1) ongoing activities, available capacity and infrastructure can be leveraged to support serious health product R&D innovation work in Africa; 2) focused efforts and significant resources both human and financial are needed to fill existing gaps in the product R&D process and to support sustainable product R&D work in Africa; 3) in the area of traditional medicines, there is a need for more systematic research evaluation and validation of the biological activities of traditional medicines; 4) coordination of what are now fragmented R&D activities in Africa is urgently needed; 5) institutional mechanisms for management of intellectual property are lacking in most institutions and countries; 6) lack of sustainable financing, together with the fragmentation of efforts, pose barriers to sustained and rigorous product R&D in Africa. What is now needed is a forceful expression of political will and a coordinated and collaborative mindset among all actors to foster a sustainable R&D innovation effort in Africa.
REFERENCES


### ANNEX 1. EXAMPLES OF CENTRES/COUNTRIES WITH CAPACITY TO CARRY OUT BASIC EXPLORATORY RESEARCH RELEVANT TO HEALTH PRODUCTS

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>INSTITUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkina Faso</td>
<td>Institut de Recherche pour le Développement</td>
</tr>
<tr>
<td>Cameroon</td>
<td>- Centre de Recherche pour la Santé des Armées (CRESAR)</td>
</tr>
<tr>
<td></td>
<td>- Centre International de Référence Chantal Biya, Centre Hospitalier</td>
</tr>
<tr>
<td></td>
<td>Universitaire (CIRCB/CHU)</td>
</tr>
<tr>
<td></td>
<td>- Organisation de Coordination pour la lutte contre les Endémies en</td>
</tr>
<tr>
<td></td>
<td>Afrique Centrale (OCEAC)</td>
</tr>
<tr>
<td>Congo</td>
<td>- Centre d’Etudes des Ressources Végétales / Groupe de Recherches Biomédicales</td>
</tr>
<tr>
<td>Egypt</td>
<td>- Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Cairo University</td>
</tr>
<tr>
<td></td>
<td>- Genetic Engineering and Biotechnology Research Institute, Minofiya University</td>
</tr>
<tr>
<td></td>
<td>- Theodor Bihar Research Institute, Giza</td>
</tr>
<tr>
<td></td>
<td>- Zoology Department, Faculty of Science, Cairo University</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Jimma University</td>
</tr>
<tr>
<td>Gabon</td>
<td>Centre de Primatologie, Centre International de Recherches Médicales (CIRMF)</td>
</tr>
<tr>
<td>Ghana</td>
<td>Noguchi Memorial Institute for Medical Research (NMIMR)</td>
</tr>
<tr>
<td>Kenya</td>
<td>- Kenya Medical Research Institute (KEMRI)</td>
</tr>
<tr>
<td></td>
<td>- Department of Biochemistry, Kenyatta University</td>
</tr>
<tr>
<td>Madagascar</td>
<td>Institut Malgache de Recherches Appliquées (IMRA)</td>
</tr>
<tr>
<td>Mali</td>
<td>- Malaria Research and Training Centre (MRTC)</td>
</tr>
<tr>
<td></td>
<td>- Department of Traditional Medicine of the National Institute for Research in Public Health (INRSP)</td>
</tr>
<tr>
<td>Morocco</td>
<td>Laboratory of Immunology, Biochemistry and Molecular Biology,</td>
</tr>
<tr>
<td></td>
<td>Faculty of Sciences and Technologies, Cadi-Ayyad University, Béni-Mellal</td>
</tr>
<tr>
<td>Nigeria</td>
<td>- Nigerian Institute of Medical Research (NIMR)</td>
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<tr>
<td></td>
<td>- University of Nigeria</td>
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<tr>
<td></td>
<td>- Nsukka, Federal University of Technology Owerri,</td>
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<td></td>
<td>- University of Benin,</td>
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<td></td>
<td>- University of Ibadan,</td>
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<td></td>
<td>- University of Maiduguri,</td>
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<tr>
<td></td>
<td>- University of Calabar, University of Jos and others</td>
</tr>
<tr>
<td>South Africa</td>
<td>- Council for Scientific and Industrial Research (CSIR)</td>
</tr>
<tr>
<td></td>
<td>- South African National Bioinformatics Institute (SANBI)</td>
</tr>
<tr>
<td></td>
<td>- University of Cape-Town (UCT), many South African Universities</td>
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</tbody>
</table>
## ANNEX 2. EXAMPLES OF CENTRES/COUNTRIES WITH CAPACITY TO CARRY OUT NATURAL PRODUCTS RESEARCH

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>INSTITUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudan</td>
<td>University of Khartoum, Institut de Endemic Diseases</td>
</tr>
<tr>
<td>Tunisia</td>
<td>- Laboratoire des Mycobactéries, Institut Pasteur de Tunis</td>
</tr>
<tr>
<td></td>
<td>- Laboratoire d’immuno-oncologie moléculaire, faculté de médecine de Monastir,</td>
</tr>
<tr>
<td></td>
<td>Avenue Avicenne</td>
</tr>
<tr>
<td>Zambia</td>
<td>The Malaria Institute at Macha</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>African Institute of Biomedical Science and Technology (AiBST)</td>
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<td><strong>ANNEX 2. EXAMPLES OF CENTRES/COUNTRIES WITH CAPACITY TO CARRY OUT</strong></td>
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<td><strong>NATURAL PRODUCTS RESEARCH</strong></td>
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<tr>
<td></td>
<td><strong>COUNTRY</strong></td>
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<tr>
<td></td>
<td><strong>INSTITUTION</strong></td>
</tr>
<tr>
<td>Cameroon</td>
<td>- University of Buea</td>
</tr>
<tr>
<td></td>
<td>- Institut medical et d’etudes des plantes medicinales (IMPM)</td>
</tr>
<tr>
<td></td>
<td>- Laboratory of Medicinal Chemistry at the Faculty of Science</td>
</tr>
<tr>
<td>Egypt</td>
<td>- Schistosome Biological Supply Center (SBSC), Theodor Bilharz Research Institute</td>
</tr>
<tr>
<td></td>
<td>- Department of Pharmacology, Faculty of Pharmacy, University of Alexandria</td>
</tr>
<tr>
<td>Ghana</td>
<td>- Centre for Scientific Research into Plant Medicine (CSRPM)</td>
</tr>
<tr>
<td></td>
<td>- Kwame Nkrumah University of Science &amp; Technology, School of Pharmacy</td>
</tr>
<tr>
<td>Kenya</td>
<td>Kenya Medical Research Institute</td>
</tr>
<tr>
<td>Madagascar</td>
<td>Institut Malgache de Recherches Appliquées (IMRA)</td>
</tr>
<tr>
<td>Mali</td>
<td>- Department of Traditional Medicine of the National Institute for Research</td>
</tr>
<tr>
<td></td>
<td>in Public Health (INRSP)</td>
</tr>
<tr>
<td>Morocco</td>
<td>- Laboratory of Endocrinian Physiology and Pharmacology</td>
</tr>
<tr>
<td>Nigeria</td>
<td>- National Institute of Pharmaceutical Research and Development,</td>
</tr>
<tr>
<td></td>
<td>University of Ibadan, University of Nigeria Nssuka, University of Lagos,</td>
</tr>
<tr>
<td></td>
<td>Federal University of Technology Owerri,</td>
</tr>
<tr>
<td></td>
<td>University of Ife, Imo State</td>
</tr>
<tr>
<td></td>
<td>University Owerri</td>
</tr>
<tr>
<td>South Africa</td>
<td>- University of Cape Town (UCT)</td>
</tr>
<tr>
<td></td>
<td>- Medical Research Council</td>
</tr>
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<td></td>
<td>- University of Pretoria</td>
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<tr>
<td>Sudan</td>
<td>University of Khartoum</td>
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African network for drugs and diagnostics innovation • Abuja, 6-8 October 2008

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# ANNEX 3. EXAMPLES OF CENTRES/COUNTRIES WITH CAPACITY TO CARRY OUT CLINICAL TRIALS

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<td>- Faculdade de Medecina, Agostinho Neto University, Faculty of Medicine</td>
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<tr>
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<td>- Regional Center for Entomological Researches of Cotonou (CREC)</td>
</tr>
<tr>
<td></td>
<td>- Réseau Béninois de Recherche et de Communication sur le SIDA</td>
</tr>
<tr>
<td></td>
<td>- Université Nationale du Benin, Faculte des Sciences de Santé</td>
</tr>
<tr>
<td><strong>Burkina Faso</strong></td>
<td>- African Malaria Vaccine Testing Network (AMVTN),</td>
</tr>
<tr>
<td></td>
<td>- Muraz Center (MC)</td>
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<tr>
<td></td>
<td>- African Malaria Vaccine Testing Network (AMVTN),</td>
</tr>
<tr>
<td></td>
<td>- Centre National de Lutte contre</td>
</tr>
<tr>
<td></td>
<td>- le Paludisme (CNLP)</td>
</tr>
<tr>
<td></td>
<td>- Ecole Supérieure des Sciences de la Santé</td>
</tr>
<tr>
<td></td>
<td>- Ouagadougou University Hospital</td>
</tr>
<tr>
<td></td>
<td>- Yalgado Ouedraogo Hospital</td>
</tr>
<tr>
<td><strong>Burundi</strong></td>
<td>- ANSS – Burundi</td>
</tr>
<tr>
<td></td>
<td>- Programme National de Lutte contre la Lèpre et la Tuberculose (PNLT)</td>
</tr>
<tr>
<td></td>
<td>- University of Burundi, Faculty of Medicine</td>
</tr>
<tr>
<td><strong>Cameroon</strong></td>
<td>- Ministry of Public Health</td>
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<tr>
<td></td>
<td>- Organization de Coordination pour la Lutte contre les Endemies en Afrique</td>
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<td></td>
<td>- Centrale (OCEAC)</td>
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<tr>
<td></td>
<td>- University of Yaounde, Faculty of Medicine</td>
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<tr>
<td></td>
<td>- Central African Republic Centre National de Reference des MST et du SIDA</td>
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<td></td>
<td>- National University Hospital</td>
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<td><strong>Chad</strong></td>
<td>- Faculté Des Sciences de la Sante</td>
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<td><strong>Côte d’Ivoire</strong></td>
<td>- OCCGE Institut Pierre Michet</td>
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<td></td>
<td>- Université d’Abidjan-Cocody, UFR Sciences Médicales</td>
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<tr>
<td></td>
<td>- Université de Bouake, Faculty of Medicine</td>
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<tr>
<td><strong>Democratic Republic of the Congo</strong></td>
<td>- Université Catholique de Bukavu, Faculté de Medicine</td>
</tr>
<tr>
<td></td>
<td>- University of Kinshasa, The Faculty of Medicine: Ecole de Santé Publique</td>
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<td></td>
<td>- University of Kisangani, Faculty of Medicine</td>
</tr>
<tr>
<td></td>
<td>- University of Lumumbashi, Faculty of Medicine</td>
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<tr>
<td><strong>Ethiopia</strong></td>
<td>- Armauer Hansen Research Institute (AHRI)</td>
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<tr>
<td></td>
<td>- Ethiopian Health and Nutrition Research Institute, Vaccine Research</td>
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<td></td>
<td>- and Development Task Force</td>
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<tr>
<td></td>
<td>- Jimma University, Institute of Health Sciences</td>
</tr>
<tr>
<td></td>
<td>- Medical School of Gonder</td>
</tr>
<tr>
<td></td>
<td>- University of Addis Ababa, Department of Medicine; School of Pharmacy</td>
</tr>
</tbody>
</table>
Gabon - International Center for Medical Research (CIRMF)
- The Albert Schweitzer Hospital, Medical Research Unit
- Université Omar Bongo, Faculté de Médecine et des Sciences de la Santé (FMSS)

Gambia - Medical Research Council (MRC) Laboratories
- University of The Gambia Medical School

Ghana - Centre for Tropical Clinical Pharmacology and Therapeutics
- Komfo Anokye Teaching Hospital
- Korle-bu Teaching Hospital
- Navrongo Health Research Center
- Noguchi Memorial Institute for Medical Research
- Severe Malaria in African Children (SMAC) site
- Kintampoh Health Research Centre

Guinea - University of Conakry, Faculty of Medical Sciences

Kenya - International Center for Insect Physiology and Ecology (ICIPE)
- Kenya Medical Research Institute (KEMRI)
- Kenyan AIDS Vaccine Initiative (KAVI)
- Moi University, College of Health Sciences
- The African Medical and Research Foundation (AMREF)
- United States Army Medical Research Unit - Kenya (USAMRU-K)
- University of Nairobi

Lesotho - Lesotho National Malaria Program
- Lesotho National TB Program

Liberia - University of Liberia, A.M. Dogliotti College of Medicine
- The Liberian Institute for Biomedical Research

Madagascar - Institut Pasteur de Madagascar
- Université d'Antananarivo, Faculté de Médecine
- Université de Madagascar (Mahajanga), Faculté de Médecine

Malawi - Malawi College of Medicine
- Ministry of Health,
- Malaria Control Programme
- National Tuberculosis Control Program,
- Community Health Sciences,
- Ministry of Health and Population
- Severe Malaria in African Children (SMAC) site
- Wellcome Trust Research Laboratories

Mali - University of Mali, Malaria Research and Training Center

Morocco - Ibn Rochd Hospital

Mozambique - Centro de Investigacao em Saude Manhica (CISM)
- Universidade Catolica-Beira, Medical School
- Universidade Eduardo Mondlane, Faculdade de Medicine

Namibia - University of Namibia, Faculty of Medical and Health Sciences.
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<tr>
<th>Country</th>
<th>Institutions</th>
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<tbody>
<tr>
<td><strong>Nigeria</strong></td>
<td>- Ahmadu Bello University Teaching Hospital</td>
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<tr>
<td></td>
<td>- Federal Medical Center</td>
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<tr>
<td></td>
<td>- Nigerian Institute of Medical Research</td>
</tr>
<tr>
<td></td>
<td>- Nnamdi Azikiwe University</td>
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<tr>
<td></td>
<td>- Obafemi Awolowo College of Health Sciences</td>
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<tr>
<td></td>
<td>- University of Calabar, University of Calabar Teaching Hospital</td>
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<td></td>
<td>- University of Ibadan, College of Medical Sciences</td>
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<td></td>
<td>- University of Ilorin Teaching Hospital</td>
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<td></td>
<td>- University of Jos, Jos University Teaching Hospital</td>
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<tr>
<td></td>
<td>- University of Nigeria, College of Medicine</td>
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<td></td>
<td>- University of Port Harcourt Teaching Hospital</td>
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<td><strong>Republic of Congo</strong></td>
<td>Laboratoire National de Santé Publique</td>
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<td><strong>Rwanda</strong></td>
<td>- National University of Rwanda, School of Public Health</td>
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<td>- National University of Rwanda, Faculty of Medicine</td>
</tr>
<tr>
<td></td>
<td>- Treatment and Research AIDS Center (TRAC)</td>
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<td><strong>Senegal</strong></td>
<td>- Research and Development Institute</td>
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<td></td>
<td>- University of Dakar (Université Cheikh Anta Diop)</td>
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<td><strong>Sierra Leone</strong></td>
<td>University of Sierra Leone, Faculty of Medicine and Pharmacy</td>
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<tr>
<td><strong>Somalia</strong></td>
<td>Amoud University, College of Medicine and Allied Health</td>
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<tr>
<td></td>
<td>(<em>Amoud University is not truly a research facility—indeed none exists in the</em></td>
</tr>
<tr>
<td></td>
<td>(<em>country today. The University is included here because its College of</em></td>
</tr>
<tr>
<td></td>
<td>(<em>Medicine and Medical Sciences is offers the best hope for a research</em></td>
</tr>
<tr>
<td></td>
<td>(<em>institution in the country).</em></td>
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<td><strong>South Africa</strong></td>
<td>- Aurum Research Unit, Aurum Health Research</td>
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<td>- Global Alliance for TB Drug Development, South Africa c/o Medical</td>
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<td></td>
<td>- Research Council</td>
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<td></td>
<td>- Medical Research Council, South Africa (MRC)</td>
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<td>- Global Alliance for TB Drug Development, South Africa c/o Medical Research Council</td>
</tr>
<tr>
<td></td>
<td>- Medical University of Southern Africa (MEDUNSA) Santa Cape Town</td>
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<td></td>
<td>- South African HIV Vaccine Action Campaign (SA HIVAC)</td>
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<td></td>
<td>- The South African National Institute for Virology (NIV)</td>
</tr>
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<td></td>
<td>- University of Cape Town, Faculty of Medicine</td>
</tr>
<tr>
<td></td>
<td>- University of Natal, Faculty of Medicine</td>
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<td></td>
<td>- University of Pretoria, Centre for the Study of AIDS</td>
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<td>- University of Stellenbosch, Faculty of Health Sciences - School of Medicine</td>
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<td>- University of the Free State, Faculty of Health Sciences</td>
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<td>- University of Transkei (UNITRA), Faculty of Medicine and Health Sciences</td>
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<td>- University of Witwatersrand</td>
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<tr>
<td><strong>Sudan</strong></td>
<td>- Juba Teaching Hospital</td>
</tr>
<tr>
<td></td>
<td>- Tropical Medicine Research Institute (TMRI)</td>
</tr>
<tr>
<td></td>
<td>- University of Khartoum, Institute of Endemic Diseases</td>
</tr>
<tr>
<td><strong>Swaziland</strong></td>
<td>Ministry of Health and Social Welfare</td>
</tr>
<tr>
<td>Country</td>
<td>Institutions</td>
</tr>
<tr>
<td>---------</td>
<td>--------------</td>
</tr>
</tbody>
</table>
| **Tanzania** | - African Malaria Vaccine Testing Network  
- Hubert Kairuki Memorial University (HKMU), Faculty of Medicine  
- Muhimbili University College of Medical Research  
- National Institute for Medical Research  
- Tanzanian Essential Health Interventions Project (TEHIP)  
- The African Medical and Research Foundation (AMREF)  
- The Ifakara Health Research and Development Center  
- The Kilimanjaro Christian Medical College (KCMC)  
- Vignan’s International Medical & Technological University, Faculty of Medicine |
| **Togo** | - National HIV/STD Center, CHU-Tokoin  
- Université du Bénin au Togo, Faculté de Médecine de Lomé |
| **Uganda** | - AIDS Information Center  
- AMREF Uganda  
- Joint Clinical Research Center (JCRC)  
- Makerere Institute of Social Research  
- Makerere University, Institute of Public Health  
- Mbarara University of Science and Technology  
- Med Biotech Laboratory  
- Mildmay Palliative Care Center  
- National Chemotherapeutics Laboratory (NCTL)  
- The AIDS Support Organisation (TASO)  
- Uganda AIDS Commission  
- Uganda Virus Research Institute |
| **Zambia** | - Chainama Hills College Hospital  
- Tropical Disease Research Centre  
- University of Zambia, School of Medicine  
- Uganda Virus Research Institute |
| **Zimbabwe** | - Bastirai Group  
- Biomedical Research and Training Research Institute  
- Blair Research Institute, TVBU  
- Chitungwiza Hospital  
- The Medical Research Council of Zimbabwe  
- Training and Research Support Center (TARSC)  
- University of Zimbabwe-Bulawayo College of Health Sciences  
- University of Zimbabwe, Faculty of Medicine  
- University of Zimbabwe-Bulawayo College of Health Sciences |

Note: Several other centres, including institutions in North Africa, have capacity for basic research, pre-clinical clinical research but are not included in this list.
PART 2: COLLECTION OF ABSTRACTS FOR ABUJA MEETING

INTRODUCTION

The African Network for Drugs and Diagnostics Innovation - A concept paper

Nwaka S
Special Programme for Research and Training in Tropical Diseases, World Health Organization, Geneva, Switzerland
nwakas@who.int

Several factors, including the lack of market incentives to support health innovation, fragile health services infrastructure, and weak socio-economic conditions, are believed to be responsible for the unacceptable burden of infectious tropical diseases in developing countries especially in the African continent. In the past ten years, new funding from governments and philanthropic agencies has resulted in increased product R&D activities for some of these diseases through public-private partnerships operating largely from developed countries. However, many in developing countries now argue that the only way the availability of new affordable drugs, diagnostics, and vaccines for these diseases can be ensured and sustained in the long term, is through committed investments in R&D, manufacturing and distribution within these countries. Therefore, developing countries need to participate in discovering, developing and manufacturing the health products they need, and in establishing functional market mechanisms that suit their needs.


Several isolated product discovery and development activities are ongoing in Africa, but greater effort is needed to bring groups working in this area together to join forces, share lessons, and explore a more coordinated approach to health R&D and innovation in Africa. The success stories from several African centres participating in the innovative network model for drug discovery for tropical diseases (Nwaka and Hudson, Nature Reviews Drug Discovery, 5:941, 2006; Hopkins, Witty and Nwaka, Nature, 449:166, 2007) have provided the impetus for a broader participation of other institutions and investigators in such a coordinated initiative. This has resulted in the concept of ANDI – the African Network for Drugs and Diagnostics Innovation. Consultation with many African researchers and scientists (including those at home and in Diaspora) as well as institutions (universities, R&D agencies, Ministries of Health and Science & Technology), has further strengthened the case for the urgent establishment of ANDI, through the meeting at Abuja. The objective of ANDI is to promote and sustain African-led R&D innovation through the discovery, development and delivery of affordable new tools for the treatment of diseases in Africa including those based on traditional medicines and natural products. It is envisaged that ANDI will have a secretariat in Africa with a strong element of public private partnerships. ANDI will also support capacity and infrastructural development in Africa. This meeting will discuss the R&D landscape and the operational framework for ANDI.

On behalf of the Organizing Committee for the ANDI meeting, we thank all the participants and supporters, and look forward to a fruitful outcome of the meeting.
## ORAL PRESENTATIONS

*(Arranged alphabetically by last name of principal author)*

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<tr>
<th>PROGRAMME NUMBER</th>
<th>AUTHOR/S</th>
<th>TITLE</th>
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<tbody>
<tr>
<td>1.</td>
<td>Botros S</td>
<td>The need for an African Centre of Excellence to develop novel antischistosomal drugs and drugs for food borne trematodiasis. Theodor Bilharz Research Institute (TBRI)-Egypt is a role model</td>
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<tr>
<td>2.</td>
<td>Chibale K</td>
<td>Discovery of an orally active antimalarial drug lead through a WHO/TDR network of partnerships</td>
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<td>3.</td>
<td>Inyang US</td>
<td>Research and development of phytopharmaceuticals at NIPRD: Challenges, opportunities and achievements</td>
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<td>Masimirembwa C</td>
<td>Biobank and pharmacogenetics database of African populations – tools to support drug/diagnostics discovery, development and optimal use of medicines</td>
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<td>Meoni P</td>
<td>Developing herbal medicines and new chemical entities from African traditional medicines: applying new technologies to ancient knowledge</td>
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<td>Ntie Kang F, Dali B, Owono LC,</td>
<td>3D QSAR studies of Gossypol-like inhibitors of <em>Plasmodium falciparum</em> lactate dehydrogenase as potential antimalarial drugs</td>
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<tr>
<td>7.</td>
<td>Rasoanaivo P</td>
<td>Plants-based drug discovery in Madagascar: lessons and opportunities</td>
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<td>8.</td>
<td>Ronoh W and Rukunga G</td>
<td>Research, development and innovation in East Africa: The case of Kenya Medical Research Institute</td>
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</table>
# POSTERS

*(Arranged alphabetically by last name of principal author)*

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<th>PROGRAMME NUMBER</th>
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<td>Abdel Khalik SMA, Yousif F, Melek FR, Abdalla W</td>
<td>Health problems in rural communities; exploring application of traditional medicine</td>
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<td>Antitrypanosomal potential of <em>Tridax procumbens</em> in <em>T.b. brucei</em> infection in mice</td>
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<td>Abdulrahim ME, Ibrahим K, Muazzam I, Ibrahim J, Onigbanjo HO and Idris HS</td>
<td>Antihelmintic screening of Nigerian plants traditionally used for the treatment of schistosomiasis</td>
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<td>Abia W, Arojo O, Nmeka I, Mingel D and Aliyu A</td>
<td>Influence of sex on subchronic toxicity of <em>Erythrophleum suaveolens</em> plant extracts in rabbits</td>
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<td>Adaramoye OA and Medeiros IA</td>
<td>Endothelium-independent vasodilation induced by kolaviron, a biflavonoid complex from <em>Garcinia kola</em> seeds, in isolated rat superior mesenteric arteries</td>
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<td>Ademowo OG, Okeola V, Nneji CM, Falade CO, Farombi OE</td>
<td>Evaluation of the antimalarial and antioxidant effects of methanolic extract of <em>Nigella sativa</em> in mice infected with <em>Plasmodium yoelii nigeriensis</em></td>
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<td>8.</td>
<td>Akanji O</td>
<td>Building capacity for drug discovery, development and manufacturing under cGMP in West Africa</td>
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<td>Akoutey R</td>
<td>Ending resistance in modern medicine</td>
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<td>Akumba DD, Babayi H, Ogbadoyi EO, Okogun J, Onigbajo HO, Oladosu P, Adamuc I, Salaud Z and Casmir P</td>
<td>Antimicrobial activity of leaf extract of <em>Detarium senegalensis</em></td>
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<td>11.</td>
<td>Alio I, Kappes B and Bormann S</td>
<td>Lowered activity of the human erythrocytic pyridoxal kinase - a possible genetic trait offering protection against malaria</td>
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<td>12.</td>
<td>Amlabu E, Okogun JI</td>
<td>Bulk (pilot scale) extraction of an anti-diabetic agent (AD1)</td>
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<td>13.</td>
<td>Amuasi JH, Boakye I, Sevcsik A</td>
<td>Artesunate plus amodiaquine combination therapy in Ghana: Albatross or lifeline?</td>
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<td>Atadja P</td>
<td>Discovery and development of deacetylase inhibitors as anti-cancer therapeutics – from target discovery to bedside</td>
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<td>Attah SK</td>
<td>The viability of <em>Onchocerca volvulus</em> isolated from high-dose ivermectin treated patients: comparing histology and <em>in vitro</em> methods</td>
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<td>16.</td>
<td>Bah S, Paulsen BS, Diallo D and Johansen HT</td>
<td>Purification and characterization of cystatins from medicinal plants used in the treatment of schistosomiasis</td>
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<td>Current research on antimalarial medicinal plants used in Cameroonian folk medicine</td>
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1. The need for an African center of excellence to develop novel antischistosomals and drugs for food borne trematodiasis: Theodor Bilharz Research Institute (TBRI)-Egypt is a role model

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For schistosomiasis and food borne trematodiasis, 779 and 75 million individuals are at risk of infection with >200 and 40 millions infected respectively. So far, no vaccines are available; with operational challenges and resource constraints for implementation of preventive measures, the key strategy remains the use of safe and efficacious drugs. The proposed center of excellence at TBRI aims to promote that African discoveries, focusing on drugs for the above mentioned diseases, become medicines for the improvement of the health and well being of Africans. For the past 20 years, the Pharmacology Laboratory at TBRI, has utilized the basic technical skills and facilities required for the discovery of antischistosomal drugs and drugs for food borne trematodiasis and in R&D efficacy/resistance studies of antischistosomal drugs, conventional toxicity studies and pharmacokinetic studies. The Biological material essential to conduct such experiments are available at the Schistosome Biological Supply Centre (SBSC). Since 2003, the SBSC has been a WHO/TDR Screening Centre for Schistosomiasis and is a part of WHO/TDR’s global drug discovery network. The Medicinal Chemistry laboratory, through bio-guided fractionation of natural Egyptian plants, has succeeded in the isolation of compounds with anticancer, antioxidants, and molluscicidal properties. TBRI also has a 300-bed hospital facility that is connected to its research departments and which has the essential diagnostic laboratories and available qualified clinicians for clinical drug trials. It is anticipated that ANDI will offer the proper structure that will scale up available resources, mobilize common scientific disciplines from various African academia, establish proper protocols for the systematic evaluation and validation of products reducing the risk of failure in subsequent development efforts, target more resources to priority areas of national interest and also facilitate links to for successful commercialization of products. Establishment of centers of excellence under the umbrella of ANDI will not only support health product innovation but will also produce highly-skilled workers that can drive the therapeutic innovation pipeline and safeguard the community from counterfeit products.
2. Discovery of an orally active antimalarial drug lead through a WHO/TDR network of partnerships

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Clinically available drugs are rarely discovered. What is often discovered are hits which are then developed into leads for subsequent optimization before selection of a pre-clinical drug candidate. Whereas hits simply give a positive result in a primary screen, leads give confidence that a pre-clinical drug candidate may be found. A lead compound must meet a certain minimum criteria including evidence of in vivo activity, a favorable pharmacokinetic profile, evidence of an emerging structure-activity relationship (SAR), chemical tractability and favorable physical properties including those based on the Lipinski criteria. The ability to deliver lead drug candidates in an academic environment is limited by a general lack of the necessary competence and coordination in the key areas for iterative medicinal chemistry. These areas include a partnership of competencies of screening, medicinal chemistry and drug metabolism/pharmacokinetics. This network of partnership is critical to delivering optimized leads in an efficient and cost effective manner. This presentation will highlight activities in hit to lead and early stage lead optimization in the discovery of an orally active antimalarial lead within a network of partnership model involving academia and industry and facilitated by the WHO/TDR.

3. Research & development of phytopharmaceuticals at niprd: challenges, opportunities and achievements.

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NO ABSTRACT
4. Biobank and pharmacogenetics database of African populations – tools to support drug/diagnostic discovery, development and optimal use of medicines

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Background: Biobanking of human material in the form of organs, tissues, sub-cellular fractions and DNA holds the promise to better understand human disease and how to treat them. The influence of genetics on response to therapeutics, pharmacogenetics, is influencing the process of discovery, development and clinical use of medicines such that drugs will be given only to those they are predicted to be efficacious and at doses predicted to be safe. Aims: (a) To establish a Biobank and pharmacogenetics database of African populations that will be used to support drug discovery and development initiatives, (b) To design and deploy pharmaco-diagnostic tools towards disease diagnosis and optimal clinical use of some medicines, and (c) to explore the inter-ethnic genetic diversity of African populations and how they compare to other major populations (Oriental and Caucasian). Methods: A Consortium of 6 countries, Nigeria, Kenya, Tanzania, Uganda, Zimbabwe and South Africa was formed with the aim of establishing a Biobank and Pharmacogenetics database of African populations in 2003. Ethical approvals for the study in various countries were obtained. Over the past 3 years, 2004-2007, at least 100 blood samples from health volunteers were collected from 3-4 major ethnic groups from each of the consortium member countries. The blood was shipped to AiBST and each sample processed and stored as frozen blood, dried blood spots on filter paper and genomic DNA. The samples were analysed by PCR-RFLP for genetic variability of genes coding for drug metabolizing enzymes. 16 SNPs of 7 genes were evaluated. An electronic database for the tracking of samples and processing of genetic data was developed. Results: A Biobank of 1500 samples from 9 major African ethnic groups (Yoruba, Ibo, Hausa, Kikuyu, Masai, Luo, Shona, San, Venda and mixed Bantu) from 5 African countries. The samples cover the major regional and linguistic classes that have been historically used to categorise the continent’s populations. The genetic polymorphism of genes (CYP2B6, 2C9, 2C19, 2D6, NAT-2, GSTM, GSTT) important in the metabolism of over 50% of drugs in current use, showed frequency distribution patterns that significantly differed from Caucasian and Oriental populations. Cluster analysis by principle component analysis, however, did not show any major difference among the African populations. The frequencies of CYP2B6 and CYP2D6 variants are predictive of major clinical effects on the use of ARVs and antipsychotics. PK modeling indicated that the over 20% patients homozygous for the CYP2B6*6 might require lower doses of efavirenz. The CYP2D6*17 variant could also be used to revised doses of anti-psychotics downwards. Discussion: The establishment of this Biobank and Pharmacogenetics database of represents a major advance that strategically positions Africa in the genomics era. Important interfaces with the pharmaceutical industry will be made towards the validation of drug targets, with biotechnology companies towards the design and validation of pharmaco-diagnostic tools, with academic research institution, towards the discovery of important biomarkers for diseases and response of to medicines.
5. Developing herbal medicines and new chemical entities from African traditional medicines: applying new technologies to ancient knowledge

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Recent years have seen a continuous rise in the interest of the general public for herbal remedies, but this attention has not been paralleled by adequate resources to provide an international regulatory and scientific backbone to the development of herbal medicines for serious and life threatening conditions. This is particularly evident in African countries, where a very significant proportion of the population still uses botanical preparations with sometimes potent pharmacological effects under the recommendation of traditional healers and outside the control of scientific or regulatory agencies. Materials used often include dried plant material of variable quality and content and unsuitable for modern, effective therapy of chronic and life-threatening diseases. Similarly to the great discoveries of new therapies from plants in the early 20th century in Europe, Indigenous Knowledge and African Traditional Medicine could provide the key to the discovery of New Chemical Entities (NCE) or be developed into well defined Herbal Medicines that could be adequately formulated to address many of Africa’s endemic diseases. Within the Biosciences Unit of the Council for Scientific and Industrial Research of South Africa, we have established a competency area building the necessary expertise to identify plants currently used by traditional healers and covering the information gap between their traditional use and the necessary requirements to initiate properly controlled clinical studies according to international regulatory guidelines. Plants with high potential for HIV, Malaria or Tuberculosis are extracted with methods mimicking the traditional use and the resulting extract is subject to our research protocols. Through the selection of relevant bioassays and subsequent bioassay-guided fractionation, we determine the simplest possible fraction of the plant extract still maintaining the full biological activity. Active compounds within this fraction are chemically characterised by HPLC-MS and tested for potency and possible synergistic effects. Poorly active compounds with interesting structures or pharmacological profile can be used to initiate medicinal chemistry and lead optimisation programs. Based on this information, we determine the best development path (NCE, Herbal Medicine) for the given product. In order to optimise the pre-clinical development in a resource-poor context, we have developed a stage-gate process capable of effectively managing projects in the pre-clinical stage thus avoiding unnecessary studies and activities. Specific case studies will illustrate how Indigenous Knowledge and African Traditional Medicine can be used to build a pipeline of drug candidates for infectious diseases complying with international regulatory standards.
6. 3D QSAR Studies of Gossypol-like Inhibitors of *Plasmodium falciparum* Lactate Dehydrogenase as Potential Antimalarial Drugs.

Ntie Kang F1,2, Dali B1,3, Owono Owono LC1,2,4, Megnassan E.1,3, Braiuca P5, Frecer V5, Miertus S1

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Gossypol [2,2-bis-(Formyl-1,6,7-trihydroxy-5-isopropyl-3-methylnaphthalene)], a polyphenolic, binaphthyl disesquiterpene extracted from seeds of the cotton plant, Gossypium hirsutum, was shown to be lethal to the parasite *Plasmodium falciparum* by inhibiting the lactate dehydrogenase (pfLDH) responsible for the oxidation of NADH to NAD+. This is a vital process for the survival of this parasitic protozoan, largely responsible for the endemic malaria disease in most parts of the world. Unlike hemigossypol structures, no crystal structure exists for gossypol or its closest derivatives in the protein databank (pdb). The work presented here is the second stage of our investigation of the gossypol structures as potent inhibitors of the pfLDH. In this study, we investigated gossypol derivatives from two series of experimental data that have been proven to bind effectively at the active site of the pfLDH near the Arginine 171. We first performed docking simulations using different software to obtain superimposed poses which form interesting interactions with catalytic residues in the active site of this enzyme. Using the 3D QSAR CoMFA approach, as implemented in the ALMOND and MOE 2007.09 software, we have established a good correlation between the structure and the desired activity. Calculation of Quantum Chemical Molecular descriptors leading to the LUMO-HOMO investigations of the hydrogen transfer processes are also performed with Gaussian 03W and are in line with experimental data. This proved that the structures being investigated could serve as leads in our search for new anti-malarial drugs.

7. Plants-based drug discovery in Madagascar: lessons and opportunities

Rasoanaivo P

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The Institut Malgache de Recherches Appliquées (IMRA) has been involved in drug discovery for the last fifteen years. Disease of focus was first malaria, but it has been extended to diabetes and neurodegenerative diseases, and recently to Chikungunya which is seriously affecting the Indian Ocean region. The programme has resulted in the discovery of several bioactive compounds, some of which being in the advanced pharmacological investigations. Lessons learned for these activi-
ties are in the areas of both techniques and policy. Drug discovery is more and more a dialogue between chemists and biologists. The promiscuity of chemistry and biology infrastructure is one key-factor for a successful bioassay-guided fractionation. Other technical aspects include the mode of extraction, the test concentrations, and the choice of the appropriate in vitro or in vivo tests. All these had led us to propose the reverse pharmacology approach as to explore the potential of medicinal plants. This scheme is driven by the cross-pollination and recombination of ideas and experiences to generate new possibilities. In rational drug discovery, compounds are first computer designed, then synthesized, and finally tested. In the reverse drug discovery, biological activities are first assessed, and then the structure of active compounds elucidated, and finally structures are submitted to computer-based investigations. In the policy matter, problems have arisen around success and conflicts in networking, IPR and patent issues, and contract negotiating. Due to the unique Madagascar biodiversity and the operational biological tests, opportunities for a successful drug discovery exist at IMRA. It is necessary to share knowledge with other African scientists, and also learn from other experiences.

8. Research, Development and Innovation in East Africa: The case of Kenya Medical Research Institute

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The Kenya Medical Research Institute (KEMRI) headquarters is based in Nairobi, Kenya. The Institute has an annual operational budget of US$ 27 million and a critical mass of health research scientists. Research and Development activities are organized into four programmes: Infectious Diseases; Parasitic Diseases; Epidemiology, Public Health and Health Systems Research; and Biotechnology and Non-Communicable Diseases. The Institute has collaborated with various organizations in trying to achieve its research and development objectives. Notably the Centres for Disease Control (CDC), The Wellcome Trust, The Walter Reed Army Project and Japan International Cooperation Agency (JICA) have been instrumental to KEMRI in putting up the research infrastructure. A production facility has been put up with the assistance of JICA that manufactures diagnostic kits on a large scale. These kits comprise rapid test kits for screening HIV 1 & 2, Hepatitis B and C among others. The key challenge facing the Institute is inadequate budgetary support from government for R&D activities. There is also a low appreciation of the role of R&D in national socio economic development at all levels including public and private sectors as well among the citizens. In conclusion there is the necessary Research and Development capacity at KEMRI in the form of infrastructure, expertise, experience and global networks to contribute substantially to solving the Africa’s most challenging public health issues.

Sia S

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In this talk, I will address the scientific and commercial opportunities for developing portable diagnostic devices, with a focus on diagnostics for use in developing countries. I will provide a landscape of current diagnostic technologies, and how they must be re-designed or adapted for the diseases prevalent in developing countries and for low-resource environments. In addition, I will discuss the route in the United States for commercializing new diagnostic devices, and compare and contrast the commercialization pathway with that for Africa, in terms of fundraising, market need and size, clinical evaluation, regulatory approval, manufacturing, and marketing and distribution.
POSTERS

1. HEALTH PROBLEMS IN RURAL COMMUNITIES: EXPLORING APPLICATION OF TRADITIONAL MEDICINE

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Relevance of the Action. Medicinal plants play a vital role in the maintenance of human health. The proposed research project is based on collaborative work between laboratories at Helwan University and other research institutions. The project works on solving some health problems of poor communities in Africa by utilizing the potential of Egypt’s biodiverse medicinal plants. The proposal seeks to identify and document selected medicinal plants used for the treatment of major human diseases with emphasis on the following five, namely schistosomiasis, cancer, liver diseases, diabetes and cardiovascular diseases. Description of the action and its effectiveness. Crude extracts, selected fractions, as well as pure compounds have been subjected to screening in a wide variety of bioassay techniques in order to confirm the bioactivity and determine the therapeutic value and toxicity profiles. Those fractions and compounds with interesting biological activity will undergo secondary bioassays and, wherever possible, their molecular structure will be determined. Fractions and compounds with biological activity will be further investigated for the presence of synergy involving multiple compounds/fractions from single plants or from complex mixtures of plants. Only those natural ingredients shown to have significant biological activity will remain candidates for further investigation. The project activities are 1) Document published and unpublished literature on the medicinal plants selected for the above medicinal areas, 2) Identify and prioritize promising natural materials, which can be systematically screened, extracted and characterized, 3) Perform different bioassay techniques (in vivo and in vitro on animal model) to evaluate the bioactivity and toxicity profiles of the natural ingredients. 4) Assess resources and needs required for the establishment of a comprehensive centre for research on medicinal plants. 4) Develop a national medicinal plants database used for the selected diseases.

2. ANTITRYPAenosomal POTENTIAL Of TRIDAX PROCUMBENS IN T. B. BRUCEI INFECTION IN MICE

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Chemotherapy of Human African trypanosomiasis remains problematic and ineffective because of the problems of poor efficacy, parasite resistance, high toxicity, high cost, and unavailability. There is therefore an urgent need for drugs that are more efficacious, affordable, nontoxic, and readily available. The therapeutic potential of aqueous extract of the leaves of Tridax procumbens was investigated in Trypanosoma brucei brucei infection in mice. Animals were grouped into 5 of 5 mice each. The prophylaxis and the curative groups were each treated at 250 and 500mg/kg body weight respectively. The treatment was through intraperitoneal (ip) administration for 5 consecutive days. Parasitaemia was monitored daily which showed a fluctuating pattern and the mice treated at 500mg/kg body weight recorded highest survival days of 33 beyond 23 days for the untreated control group (P<0.05). The body weight was determined at intervals and the loss in weight of treated animals was significantly lower compared to untreated control (P<0.05). Post mortem examination following death revealed pale carcass, hepatomegaly and splenomegaly in prophylaxis and untreated control groups but was however less pronounced in the
treated (curative) groups. Therefore hepatomegaly and splenomegaly were significantly alleviated with the curative treated groups (P<0.05). Thus *Tridax procumbens* has some antitypansomal property, capable of reducing weight loss, and alleviate hepatomegaly and splenomegaly in *T. b. brucei* infection.

### 3. ANTIHELMINTIC SCREENING OF NIGERIAN PLANTS TRADITIONALLY USED FOR THE TREATMENT OF SCHISTOSOMIASIS

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Urinary schistosomiasis is treated traditionally by means of herbal remedies in the rural areas of Nigeria. Fifteen Nigerian plants were identified as being used locally for this purpose. Nine of these plants were investigated for their anti-schistosomal properties. Crude extracts of the plant material were screened against the schistosomula of the species *Schistosoma haematobium*. Cercariae were obtained from *Bulinus africanus* snails through an *in vitro* technique. By subjecting the cercariae to a sheering stress they were transformed into schistosomula. The schistosomula were placed into culture medium to which the plant extract had been added. The best results were obtained from stem and root extract of *Abras precatorius*; *Pterocarpus angolensis*; *Striga senegalensis* and *Phyllantus muellerianus*, with activities at 6.5mg/ml except for *Pterocarpus angolensis* which exhibit activity at 12.5mg/ml.

### 4. INFLUENCE OF SEX ON SUBCHRONIC TOXICITY OF *ERYTHROPHLEUM SUAVEOLES* PLANT EXTRACTS IN RABBITS

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*Erythrophleum suaveolens* is an expensive medicinal plant of African origin. It is known to be toxic to humans and other animals. Nonetheless, knowledge on its sub-chronic toxicity is limited. Objectives The research sought to investigate sub chronic toxicity of *Erythrophleum suaveolens* plant extract in rabbits at 2.5 and 5.0 mg/kg body weight/day dose levels, and find out the influence of gender on the toxicity. Methods The extracts were daily administered orally by gavage to male and female rabbits for 8 weeks at dose levels of 2.5 and 5.0 mg/kg, while control male and female groups took water. During the test period, mortality, clinical signs and changes in body weight were recorded. Hematological and serum biochemical parameters were determined. Finally, necropsy and histopathological examinations were done. Results Neither mortality nor clinical signs were observed. A general significant (P < 0.05) increase in body weight was noted in all groups. Hematological parameters reported significant differences (P < 0.05) in rabbits in high-dose groups, irrespective of sex. Biochemical parameters showed no significant differences (P > 0.05). However, both hematological and biochemical parameters prior and post experiment, were within reference ranges. Necropsy revealed lesions in lung, liver, kidney and brain. Histopathological examination confirmed the observed lesions and further revealed mild cellular hepatocyte infiltration in both control and test rabbits, suggesting that the lesions are probably not-extract-related. Conclusions: Based on the aforementioned findings, it is probable that 5.0 mg/kg body weight/day of aqueous extract of fresh leaves of *Erythrophleum suaveolens* has no observable toxicity effect in rabbits irrespective of sex.
5. EVALUATION OF PHARMACOLOGICAL ACTIVITIES OF PLANTS USED IN TRADITIONAL MEDICINE FOR THE TREATMENT OF MALARIA/FEVER IN BURKINA FASO

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With support of WHO/TDR/RCS funding, we conducted an ethnopharmacological survey in a humid area of South West in Burkina Faso, where traditional medicine practices are very developed. Interviews conducted with 17 practitioners allowed for the identification of 30 plants commonly used to treat malaria or fever. To avoid confusion, the identification of the plants quoted by healers was confirmed on direct observation by two botanists who verified the authenticity of the information. From literature based on screening, the seven most cited and less studied plants species were selected for pharmacological studies. These plants were: Cassia sieberiana, Entada africana, Entada sudanica, Zanthoxylum zanthoxyloides, Vitex doniana, Combretum molle and Anogeissus leiocarpus. Following plant desiccation and pulverization, 65 extracts were prepared using solvents with different polarity (chloroform, methanol, hydromethanol and water solvents). We are now in the process of establishing parasites culture for in vitro tests and results will be available for the meeting.

6. ENDOTHELium-INdePeNdeNt vasodilatioN iNduced bY KolaviRoN, a BIFlavoNoid complex FRom GARCINia kola SEEDS, IN ISOLATED RAT SUPERIOR MESEntERic ARTERIES

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Previous studies have established the hepatoprotective, gastroprotective, hypolipidemic and hypoglycemic effects of kolaviron (KV), a biflavonoid complex from Garcinia kola seeds. In this study, we investigated the mechanisms involved in the vasorelaxant effects of KV in isolated rat mesenteric arteries. KV (1-1000 μg/mL) concentration-dependently inhibited the contractions induced by phenylephrine (PHE) (10 μM) and KCl (80 mM) in both endothelium-intact and –denuded rings. Also, KV reduced CaCl2-induced contraction in denuded rings, thus acting as a Ca2+-antagonist. In addition, KV inhibited the transient contraction by PHE in Ca2+-free medium containing EGTA, suggesting a possible action on the release of intracellular Ca2+. KV is not a specific α-adrenoceptor blocker, since it caused a concentration-dependent inhibition of contractile responses to KCl, suggesting that KV blocks the L-type Ca2+-channel. The relaxation induced by KV was significantly inhibited after pre-treatment of the denuded rings with 4-aminopyridine (4-AP) 1 mM and Charybdoxotoxin (ChTX) 0.1 μM, blockers of voltage-dependent K+ (Kv) and large conductance Ca2+-activated K+ (BKCa) channels respectively. In contrast, neither glibenclamide (10 μM), BaCl2 (1 mM) norapamin (0.1μM), blockers of KATP, KIR and SKCa channels, respectively affected the KV-induced vasorelaxation. In conclusion, our results provide evidence that the vasorelaxant effects by KV involves extracellular Ca2+ influx blockade, inhibition of intracellular Ca2+ release and the opening of K+ channels sensitive to 4-AP and ChTX. KV may be a new class of drug for the treatment of hypertension or related vascular disorder.
7. EVALUATION OF THE ANTIMALARIAL AND ANTIOXIDANT EFFECTS OF METHANOLIC EXTRACT OF NIGELLA SATIVA IN MICE INFECTED WITH PLASMODIUM YEOLLI NIGERIENSIS

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Antimalarial activity and effect of methanolic extract of \textit{Nigella sativa} (black seed) on oxidative stress and antioxidant defense system were investigated in mice infected with \textit{Pyeloll nigeriensis}. Thirty adult albino mice were divided into five treatment groups. Three groups were inoculated by intraperitoneal injection with $1 \times 10^7$ infected erythrocytes on day 0. After 72 hours of inoculation, group 1 were administered 1.25g/Kg body weight \textit{N. sativa} extract orally for 5 days, group 2 received chloroquine 10mg/Kg for 3 days and group 3 received normal saline. Groups 5 and 6 consisted uninfected mice but treated with extract alone and normal saline respectively. The Rane test procedure was used to evaluate antimalarial activity. Oxidative status was evaluated by estimating malondialdehyde (MDA), reduced glutathione (GSH) and glutathione-S-transferase (GST) activity in the liver as well as catalase (CAT) and superoxide dismutase (SOD) in blood. The extract produced 99.2% and chloroquine 94.6% chemosuppression relative to untreated control. \textit{P. yeolli} infection caused a significant ($P<0.05$) elevation of MDA level and reduction in GST and GSH. \textit{N. sativa} significantly decreased the elevation of MDA and also inhibited the depression in GST activity and GSH level in infected mice. The extract unlike chloroquine caused a significant increase in SOD and CAT activities in both infected and uninfected mice. \textit{N. sativa} has appreciable antimalarial activity in \textit{P. yeolli} infected mice and causes an alteration in the antioxidant defense system in mice.

8. BUILDING CAPACITY FOR DRUG DISCOVERY, DEVELOPMENT AND MANUFACTURING UNDER CGMP IN WEST AFRICA

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In the quest to reduce dependence on drug importation to address the healthcare needs of Africa, a major capacity gap that needs to be bridged is the ability to develop and manufacture high quality pharmaceuticals in a self-sufficient manner. The objective of our company, LaGray Chemical Company, is to bridge this gap. We have built the first fully vertically integrated pharmaceutical manufacturing company in West Africa, with capabilities in the manufacture of active pharmaceutical ingredients as well as finished dosage forms. As such, we are self-sufficient and have the capacity in drug development and commercialization needed to assist in the reduction of dependence on importation and in bringing drugs, discovered in Africa, from the laboratory to the clinic. Our facility has been built from concept to implementation and being operated in conformance with international standards of current Good Manufacturing Practices. Our goal is to install capacity for seamlessly discovering novel drugs, developing and commercializing them to address regional needs.

9. ENDING RESISTANCE IN MODERN MEDICINE

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Modern drugs, including current ACTs (Artemisinin-based Combination Therapies) used in the treatment of malaria, are manufactured on the basis of the concept of “Actives Principles” whereby the identified “active” molecule/s helping overcome a disease is/are isolated and administered to the patient. The
problem with that approach to disease management is that it limits the range of chemical substances that come into play in eliminating the germ generating the disease. On the contrary, no chemical extraction whatsoever is conducted in Traditional Medicine where medicinal plants are used whole through herbal teas and other methods of administration. For instance, in the case of malaria, in Modern Medicine, the active principle artemisinin (or its derivatives) is extracted from the *Artemisia annua* plant and then concentrated and sold in the form of ACTs that we have in drugstores all over. Traditionally, however, that plant would have been used in an herbal tea or decoction that would deliver to the patient all of the chemical compounds that the herb naturally contains. This, i.e. the decoction or tea, therefore increases remarkably the amount and/or variety of chemical species involved in the fight against the disease and is opposed to the approach consisting in extracting and using just one or two chemical molecules synthesized or taken from fractionated extracts. This shift in paradigm seems to explain the formidable problem, now widespread, that drug resistance to modern drugs against infectious diseases is.

The dire consequences of resistance development are well known: ineffectiveness of formerly effective drugs, wasted time and financial resources invested in long and painstaking research and development of drugs, renewed vulnerability of the people, increases in death rates, etc. Shifting paradigm adequately back to where it ought to be will effectively contain resistance in modern medicine and stop those consequences.

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### 10. ANTIMICROBIAL ACTIVITY OF LEAF EXTRACT OF *DETARIUM SENEGALENSIS*

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Aqueous leaf extract of *Detarium senegalensis* was evaluated for antimicrobial activity against some pathogenic microorganisms of public health significance, namely *Bacillus subtilis* (clinical strains A and B), *Salmonella paratyphi* (clinical strain), *Staphylococcus aureus* (clinical strain and ATCC 13709) and *Candida albicans* (clinical strain and ATCC 10231) using the agar dilution method. At 4000μg/ml, the crude extract had bacteriostatic effects on all the bacteria used in the assay and exhibited similar effect on *C. albicans*. Except for PCV and haemoglobin levels which increased on administration of the extract, the extract at doses of 200, 400 and 1000mg/kg bw had no effect on differential counts and levels of the hematological parameters. Toxicity study in rats showed that exposure of animals to 400 and 1000mg/kg bw led to significant reduction (P<0.05) of the relative weight of the spleen and levels of plasma urea and creatinine. Significant increase (P<0.05) in the levels of AST and ALT were also observed. Administration of 1000mg/kg bw resulted in marked reduction in ALP and Cl levels. Na and K levels significantly increased. The minimum inhibitory concentrations are 2250μg/ml (*Bacillus subtilis* and *Staphylococcus spp*) and 3750μg/ml (*Staphylococcus aureus* ATCC13709). Preliminary phytochemical analysis showed the presence of carbohydrates, flavonoids, phlobatanins, saponins and tannins. We conclude that the crude extract of *D. senegalensis* has the potential to be used as phytomedicine in the treatment of diseases caused by the organisms used in the study when adequately standardized.

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### 11. LOWERED ACTIVITY OF THE HUMAN ERYTHROCYTIC PYRIDOXAL KINASE - A POSSIBLE GENETIC TRAIT OFFERING PROTECTION AGAINST MALARIA

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In regions highly endemic for *Plasmodium falciparum* malaria, red blood cell polymorphism that confer
protection against severe disease are widespread. Common examples are the sickle cell trait, thalassemia, and glucose-6-phosphate dehydrogenase deficiency. Pyridoxal kinase (PdxK) is one of the key players in vitamin B6 metabolism converting the B6 vitamers pyridoxine, pyridoxal and pyridoxine into their respective phosphate esters upon uptake into the cell. The metabolic active form of vitamin B6 is pyridoxal-5 phosphate (PLP) being one of the most frequently used cofactors. PLP is required for a variety of metabolic reactions; however, it has its major function in amino acid metabolism. More recently its involvement in oxidative defense was uncovered with a potency equivalent to that of vitamins C and E (Fitzpatrick et al., 2007). It has been shown that the PdxK activity in erythrocytes of American blacks is approximately 50 percent lower than that of American whites, whereas the Pdx kinase activity in lymphocytes, granulocytes and skin cultured fibroblasts was identical. Recently, it has been proposed that this lowered erythrocytic activity of PdxK is due to a deletion event of 8 bp in the promoter region of its gene. To investigate the effect of lowered erythrocytic PdxK activity on the growth of *P. falciparum* in vitro, individuals were screened for the 8 bp deletion event via PCR. *P. falciparum* was then cultivated in erythrocytes from individuals being homozygous (-/-) or heterozygous (+/-) for the deletion or having no deletion (+/+). Our preliminary data suggest that the growth of *P. falciparum* is impaired in erythrocytes from individuals homozygous for the deletion (-/-) when compared to the growth in erythrocytes of our +/+ and +/+ controls implying that the lowered activity of erythrocytic PdxK is a genetic trait, which could effect the development of the disease.

### 12. BULK (PILOT SCALE) EXTRACTION OF AN ANTI-DIABETIC AGENT (AD1)

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Nigeria is endowed with great natural resources especially medicinal plants. Technology has made it easy to add values to them to manage/cure some ailments. This work tends to increase production output from benchscale to semi-industrial scale via the use of a UNIDO multi-purpose pilot plant facility. Results achieved from bulk extraction of plant materials for drug production and essential oils for fragrance are discussed.

### 13. ARTESUNATE PLUS AMODIAQUINE COMBINATION THERAPY IN GHANA, ALBATROSS OR LIFELINE?

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In 2005, due to concerns about the declining efficacy of chloroquine (CQ) monotherapy, policy makers in Ghana announced a change from CQ as first-line treatment for uncomplicated falciparum malaria to artesunate plus amodiaquine (AS+AQ), an artemisinin combination therapy (ACT). Soon after, reports about adverse events following the use of AS+AQ began to circulate in health circles, and eventually were picked up by the public/mass media. As a result, the Ministry of Health withdrew the locally manufactured single doses of artemesunate (200mg) plus amodiaquine (600mg) from the market and decided to re-examine the new policy. This article examines the factors behind and challenges faced by these policy decisions.
14. DISCOVERY AND DEVELOPMENT OF DEACETYLASE INHIBITORS AS ANTI-CANCER THERAPEUTICS – FROM TARGET DISCOVERY TO BEDSIDE

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Modern drug discovery and development involves a multi-stage process that incorporates diverse technologies and skill sets that start with elucidation and understanding of the disease mechanisms, target identification, generation and optimization of modulators of the disease target and finally culminating in preclinical and clinical trials to alter the course of the disease process. I will present an overview that illustrates how understanding of mechanisms of tumorigenesis led to the identification of histone deacetylases as cancer target, what assays and chemical design strategies were utilized in lead identification and optimization that finally led to the discovery of histone deacetylase inhibitors Dacinostat (LAQ824) and Panobinostat (LBH589), and their development as anticancer agents. Cancer is typified by inappropriate gene expression – both over-expression of genes associated with cellular proliferation and survival (e.g., oncogenes), and underexpression of genes that control these processes (e.g., tumor suppressor genes). Therefore, mechanisms that control gene expression have become attractive targets for new anti-cancer therapeutics. Histone deacetylases (HDACs), are a family of enzymes that posttranslationally modifies the structure of chromatin, leading to differential gene expression. Recent studies have also identified many tumor relevant non-chromatin proteins to be post-translationally and functionally modified by acetylation. In a search for activators of the gene encoding p21, a protein which inhibits cell cycle progression and tumor cell proliferation, the natural products, trichostatin A, trapoxin A, and psammaplin A, all subsequently shown as HDAC inhibitors were identified as hits. Based upon an analysis of their pharmacophores and a structure-activity study of straight chain hydroxamates, a new class of small molecule HDAC inhibitors resulted in LAQ824 and LBH589. They potently inhibit class I and II HDACs, transcriptionally activate the p21 promoter, inhibit tumor cell growth and induce either tumor stasis or regression in tumor-bearing animal models. In clinical trials, Panobinostat has demonstrated very encouraging anti-tumor efficacy in several hematological and solid tumors including Cutaneous T-cell Lymphomas, Hodgkins Lymphoma, Multiple Myeloma, Acute Myeloid Leukemia and Hormone Refractory Prostate Cancer. This drug is currently being investigated worldwide in multiple late-stage clinical trials, both as single agent and in combination with standard therapy.

15. THE VIABILITY OF ONCHOCERCA VOLVULUS ISOLATED FROM HIGH-DOSE IVERMECTIN TREATED PATIENTS: COMPARING HISTOLOGY AND IN VITRO METHODS

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Hitherto, histology has been one of the methods used to evaluate drug efficacy in onchocerciasis subjects. In preclinical drug studies, efficacy has been determined using in vitro methods: motility, XTT or MTT bio-reducible tetrazolium reduction tests and lactate. In a double-blind placebo-controlled study, ivermectin doses of 150-1600 μg/kg body weight were administered to 100 adult onchocerciasis subjects. Nodules were extirpated at day 180 and 48% of them examined by histopathology. Male worms, intact female and female anterior ends were retrieved from the remaining nodules by dissection or collagenase digestion. When the viability of the worms was assessed, a total of 262 male worms were retrieved of which 91.6% were found to be alive. About 82% of female worms from the 150 μg/kg group were alive, whilst, altogether 74% were alive among the higher dose groups. The histology results also showed that 92% of male worms and 62% of female worms belonging to the 150 μg/kg group and 90% of males and 69% of female worms belonging to the higher treatment groups were alive on examination. For both sexes of worms, no significant difference was found between the 150 μg/kg group and the other treatment groups. The results obtained from both methods were comparable and showed that higher doses of ivermectin up to 1600 μg/kg were not more effective than the 150 μg/kg standard dose. Hence, it is suggested that the in vitro methods be used as alternative methods or in combination with histology to evaluate drug efficacy.
16. PURIFICATION AND CHARACTERIZATION OF CYSTATINS FROM MEDICINAL PLANTS USED IN THE TREATMENT OF SCHISTOSOMIASIS

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Cysteine proteases (CP) expressed by Schistosoma mansoni participate in the hydrolysis of host hemoglobin. Cystatins are CP inhibitors present in humans as well as in plants. Malian medicinal plants used against schistosomiasis, Securidaca longipedunculata (SL) and Stylosanthes erecta (SE), were investigated for presence of cystatins. Two different four-step procedures are described for the purification of cystatins from the plants. The purity of the purified cystatins was monitored by SDS-PAGE. The protease inhibitory assay was performed in 96-well microtiter plates using the fluorogenic peptide substrates Z-Arg-Arg-NHMec and Z-Phe-Arg-NHMec. High papain inhibitory activity observed in crude extracts of the plants suggested the presence of CPIs. The papain inhibitory activity in the three extracts eluted into one single protein peak for each extract after affinity chromatography on CM-papain agarose column. After gel filtration the three extracts exhibited one papain inhibitory activity with different molecular weights. Two different cystatins with Mr of 13 and 28 kDa were purified from SR respectively named CtSR-13 and CtSR-28. CtSR-13 inhibited 99% of human cathepsin B and 58% of Sm papain-like cysteine protease activity, while only 25% of legumain-like activity in Sm extract was inhibited. SE and SL showed the same papain inhibitory profiles and molecular entities as SR, although the highest inhibitor yield was observed with SR. The phytocystatins hereby isolated and purified could participate in the regulation of endogenous protease activities of the plants and defensive mechanism against insects and plant pathogens. They also could more importantly support the traditional use of the plants against schistosomiasis.

17. EVALUATION OF ANTIMALARIAL ACTIVITY OF MORINDA LUCIDA LEAF EXTRACT AND ALSTONIA BOONEI STEM BARK

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NO ABSTRACT

18. IN-VITRO ANTIMICROBIAL ACTIVITY OF TWO MEDICINAL PLANTS: TABERNAEMONTANA CRASSA AND SENNA ALATA

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With the aim to produce better antimicrobial traditional drugs, this study investigated two medicinal plants, Tabernaemontana crassa (Apocynaceae) and Senna alata (Cesalpinaceae) in order to evaluate their antimicrobial properties. These plants are currently used in traditional medicine of Cameroon to treat wounds and fungal diseases. The activities of ethanol extract of the stem bark of T. crassa and leaves of S. alata were tested, in disc-diffusion assays, against 30 reference or laboratory strains of Gram-positive cocci (Staphylococcus spp., Enterococcus spp.), Gram-negative bacilli (Escherichia coli,
Klebsiella spp., Enterobacter spp., Serratia marcescens, Acinetobacter baumannii and Pseudomonas aeruginosa), Yeast (Candida spp., Cryptococcus neoformans) and filamentous fungi (Aspergillus spp., Trichophyton spp.). The minimal inhibitory concentration (MIC) of each extract were then estimated, against each of more susceptible microorganism (i.e those given an inhibition zone measuring at least 14 mm in diameter in the disc-diffusion assays), by agar dilution. The extract of T. crassa exhibited good activity against bacteria and fungi (inhibition zone diameter = 14 mm). This activity was very high against gram-positive cocci (MIC < 0.625 mg/ml). Senna alata extract showed good activity on Gram-positive cocci (inhibition zone diameter = 17 mm; MIC > 10 mg/ml) and weak activity against Gram-negative bacilli (0 = inhibition zone diameter =16 mm) and fungi (0 = inhibition zone diameter =20 mm). The bark of T. crassa showed a high antimicrobial activity and will be a good candidate for better antimicrobial traditional drug.

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19. TRYPLASM-NANOCRYSTALS AND DIMINAZENE IN COMBINATION WITH CHLOROQUINE AND DIMINAZENE IN COMBINATION WITH ARTESTUNATE

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Background: Leishmania is a parasitic protozoa with a worldwide distribution and results in high morbidity and mortality affecting millions in the areas where it occurs. There are demands for new antileishmanial drugs due to the demonstration of acquired resistance and unresponsiveness to pentavalent antimonials in recent years. The aim of this study is to develop a multi-drug combination based on the formulation of TRYPLASM encapsulated in liposomes which have been more effective and less toxic as other drugs used for the treatment of the Human African Trypanosomiasis (HAT) and Leishmaniasis. Furthermore, in cooperation with the research team from Prof. Dr Rainer H. Mueller from the Department of Pharmaceutical Technology, Biotechnology & Quality Management. Objectives: This study sought to explore the potential of Trypan®, a diminazene based drug for treatment of leishmaniasis and HAT. Methods: Cultures of both Leishmania major and L. donovani promastigotes in M199 medium and Trypan® at various concentrations were tested. The cultures were incubated at 25 °C and parasite counted at 48 hour interval. In vivo, a total of 40 BALB/c mice divided into 5 groups of 8 mice each were infected with 2x10⁶ promastigotes on the left footpad. The first two groups were treated with 70µg/ml of Trypan®, a total of 500µl used immediately after infection, one group by topical application and the other administered intraperitoneally. The two other groups were subjected to the same treatments but treatment commenced 10 weeks post infection. Mice that were not treated formed the control groups. Footpad sizes were measured every 2 weeks for 21 weeks. Results: Trypan® showed growth inhibition against either L. major or L. donovani promastigotes in all the concentrations tested. Secondly, Trypan® had effect on L. major infected lesions when applied topically immediately after infection. Conclusion: This study demonstrates efficacy of Trypan® in vitro against both L. major and L. donovani. We have also demonstrated that Trypan® is curative for cutaneous leishmaniasis when applied topically.

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20. GIBEX-AFRICA: A UNIQUE MODEL FOR COLLABORATIVE RESEARCH IN AFRICAN NATURAL PRODUCTS

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Natural products research in Africa has been going on for sometime now. At this juncture the challenge for the African scientist working in the area of natural products with the aim of discovering drug candidates
is to depart from the traditional culture of isolation-structural elucidation of plant and/or animal products lacking meaningful bioassay, chemosystematics, taxonomy and medicinal chemistry. There must be a total paradigm shift to a truly multidisciplinary approach in African natural products research. In fact one of the immediate things required by the African natural products community is to realize the potential for collaboration in lead identification and optimization through synthetic medicinal chemistry with attendant interfaces with biological function and processes. This should be done within the network of partnerships model. Such a paradigm shift is likely to contribute immensely to the training of students and future scientists, capable of competing internationally, in multi-disciplinary research and more importantly, increase the chances of delivering drug candidates. The poster will highlight the activities of the Global Institute for Bioexploration network in Africa (GIBEX-Africa) as a unique continental (African) model for collaborative network and partnership in the area of natural product-based drug discovery.

21. THE SOUTH AFRICAN MALARIA INITIATIVE: A UNIQUE DISEASE-BASED MODEL FOR COLLABORATIVE DRUG/DIAGNOSTIC DISCOVERY IN AFRICA
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Malaria mainly affects sub-Saharan African people who remain among the poorest in the world. By and large Africa as a continent does not have a history of successfully discovering and developing modern pharmaceutical products. This unfortunate status quo can be attributed in part due to a lack of capacity and competency in several key areas especially within the drug discovery and development value chain. Decades of biomedical research in the field of malaria in Africa have had very little impact in translational terms partly due to a lack of appropriate multidisciplinary scientific frameworks essential to building a critical mass in order to ensure maximal impact. Coupled with limited resources, this has necessitated the need to consolidate drug/diagnostic efforts based on networks of scientists with complimentary expertise. These considerations led to the formation in 2005 of the South African Malaria Initiative (SAMI), which has three main research programmes including drug discovery and diagnostics. The main objective of the SAMI drug discovery programme is to utilize existing expertise and infrastructure to discover and develop an antimalarial drug candidate, which can then be taken through clinical development stages with international Public Private Partnerships e.g. Medicines for Malaria Venture and/or industry partners. On the other hand the diagnostics programme is aimed at developing new and novel reliable and affordable diagnostic screens for malaria. The poster will describe the activities of the SAMI drug and diagnostic discovery programmes.

22. STRUCTURE-BASED DESIGN AND DEVELOPMENT OF SELECTIVE ACE INHIBITORS AS POTENTIAL DRUGS AGAINST CARDIOVASCULAR DISEASE AND HYPERTENSION
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Inhibitors of angiotensin-converting enzyme, ACE, have proven to be effective in the treatment of hypertension, heart failure, myocardial infarction and diabetes. Somatic ACE is a member of the M2 Gluzincin family of metalloproteases and is an essential component of the Renin Angiotensin System, RAS. All the first generation ACE inhibitors were designed without the benefit of a three-dimensional structure of the protein and are associated with numerous side effects. Although historically ACE inhibition has been the main focus for treating hypertension, it is now known that a number of peptidases in the RAS are involved in blood pressure and fluid homeostasis. The poster will highlight our general approaches to structure-based design of the next generation domain-selective ACE inhibitors using recently solved crystal structures of ACE.
23. DEVELOPMENT AND USE OF AN EFFICIENT AND LOW COST IN VITRO ASSAY FOR MULTIPARASITE STAGE DRUG SCREENS IN ONCHOCERCIASIS


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Current treatment of human onchocerciasis relies on the use of ivermectin which is only microfilaricidal and for which resistant parasite strains are increasingly being detected. Herein we report the development and use of an efficient and low cost in vitro culture assay for onchocerciasis drug screens based on the closest relative to *Onchocerca volvulus*, *O. ochengi*, which is easily obtained from cows. Embryos, microfilariae and adult worm killings are assayed in the same culture, and the assays are allowed to run for 6 days (standard) without use of any epithelial feeder cell layer. A huge amount of cells recovered with the worms from the nodule following dissection was sufficient. Both microfilariae and adult worms in control cultures without drug maintain viabilities (based on motility and MTT- or XTT-Formazan tests) of 85-100% within these periods. By contrast, microfilariae were all dead 24-48 hours after, in cultures that had amocarzine (CGP6140) at a concentration of 10 ug/ml, or an extract of *Morinda lucida* at a concentration of 250 ug/ml. When cultured in RPMI-1640 medium in the presence of HEPES the need for change of medium during the 6 days culture was not necessary, while microfilariae could still maintain full viability in cultures that had gone down to pH 6.6. The strategies used in the maintenance of sterility, scalability of the assay, analysis of cheaper bovine serum variety, the best culture medium and other assay parameters will be discussed.

24. ANTIINOCICEPTIVE AND ANTIBACTERIAL EFFECTS OF THE METHANOLIC STEM BARK EXTRACT OF STEMONOLOCUS MICRANTHUS

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The methanolic stem bark extract of *Stemonolocus micranthus* was investigated for antinociceptive and antibacterial activities using standard procedures. The extract was evaluated for antibacterial activity against 35 multi-resistant Gram negative clinical isolates. Results of phytochemical analysis showed the presence of carbohydrates, proteins and steroids at high concentrations while reducing sugars, tannins, and terpenoids were present at moderate concentrations. The extract contained glycosides, saponins and resins at low concentration while it was devoid of alkaloids, flavonoids, oils and acidic compounds. Preliminary acute toxicity study of the extract in mice at dose rate ranging from 100 to 2000 mg/kg, po showed no death throughout the period of observation. Brine shrimps lethality test showed that *S. micranthus* extract was significantly (p<0.05) toxic with LC50 of 387.14 ppm. The extract (100, 200 mg/kg) significantly (p<0.05) increased the pentobarbitone-induced sleeping time in mice. Oral administration of the extract (100, 200 and 400 mg/kg) and indomethacin (10 mg/kg) significantly decreased the number of writhings induced by acetic acid. Also, *S. micranthus* extract (100, 200 mg/kg) decreased the paw licking activity of both the early (0-5 min) and late (20-30 min) phases in formalin test and increased the percentage analgesia in tail flick test. However, these effects were not observed in mice that received 400 mg/kg extract. *S. micranthus* extract showed very potent local anaesthetic property in a concentration-dependent manner, which was about one third of that of lignocaine. The extract was active against 31 of the 35 bacterial isolates with Inhibition Zone Diameter ranging from 10mm to 14mm and Minimum Inhibition Concentration ranging from < 2.5mg/ml to 10 mg/ml. The results of this study have shown that *S. micranthus* has promising medicinal properties; thus, the plant can be exploited in the development of phytomedicines or as a source of lead compounds for drug development.
Background. Pancreatic islet transplantation is a promising treatment for type I diabetes mellitus, but current immunosuppressive strategies do not consistently provide long-term survival of transplanted islets, and there is an inadequate supply of donor human islets. We are therefore investigating the use of adeno-associated viruses (AAVs) as gene therapy vectors to transduce pancreatic islets with immunosuppressive genes prior to transplantation. Methods. We compared the transduction efficiency of AAV2 vectors with an AAV2 capsid (AAV2/2) to AAV2 vectors pseudotyped with AAV5 (AAV2/5), AAV8 (AAV2/8) or bovine adeno-associated virus (BAAV) capsids, or an AAV2 capsid with an insertion of the low density lipoprotein receptor ligand from apolipoprotein E (AAV2apoE) on cultured islets, in the presence of helper adenovirus infection, which can increase the kinetics of transduction. Results. The AAV2/5 vector was superior to AAV2/2 and AAV2/8 in mouse or rat islets. Flow cytometry indicated AAV2/5-mediated gene expression in approximately 9% of rat islet cells and almost 12% of insulin-positive cells. Comparing an adenovirus MOI of 1 to an MOI of 10, the AAV2/8 vector had a higher dependence on the helper virus multiplicity of infection than the AAV 2/5 vector. At an adenovirus MOI of 10, transduction of human islets was also easily detected with the AAV2/8 vector. Rat islets transduced with an AAV2/5 vector harboring the immunosuppressive transgene, tgfβ1, retain the ability to correct hyperglycemia when transplanted into immune-deficient mice. Conclusions. AAV2/5 and AAV2/8 are able to transduce pancreatic islets. AAV2/5 is able to transduce pancreatic islets at a low concentration of helper virus, while AAV2/8 requires a high helper virus concentration. Furthermore, islets transduced with an AAV2/5 vector harboring an immunosuppressive gene retain the ability to secrete insulin and regulate blood glucose levels. Therefore, AAV 2/5 vectors may be useful for transferring immunosuppressive genes to donor pancreatic islets prior to transplantation.
26. *IN VITRO ANTIFUNGAL PROPERTIES OF METHANOLIC EXTRACT AND PLUMBAGIN FROM *Diospyros canaliculata*

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Plants have been used as a traditional medicine for the treatment of fungi diseases. Plants may provide drugs directly or template molecules on which to base further new structures by organic synthesis. In our search for an anti-fungal agent from natural plants with potential for the treatment of opportunistic fungal infections, we investigate the antifungal activity of plumbagin and raw extract from *Diospyros canaliculata* on human pathogenic fungi. Clinical isolates of human pathogenic fungi including molds (*Aspergillus flavus*, *Penicillium*, *Cladosporium*, *Alternaria*, *Helminthosporum*, *Fusarium*, *Trichophyton rubrum*) and yeasts (*Candida albicans*, *Candida glabrata*, *Candida kefyr*, *Geotrichum candidum*) were tested in vitro by cup-plate agar diffusion and broth macrodilution methods. The growth of all dermatophytes tested was inhibited by the extract and plumbagin. The diameter of inhibition zones varied from 9-13 mm and from 10-18 mm for the extract and plumbagin respectively. MIC’s (Minimal inhibitory concentration) values ranged from 6.25-12.5 mg/ml for the extract and 3.12-6.25 μg/ml for plumbagin. Extract showed fungicidal effect at a concentration of 12.5 mg/ml on *T. rubrum*. Plumbagin was fungicidal on all dermatophytes tested at 12.5 μg/ml except *T. rubrum* (6.25 μg/ml). Both extract and plumbagin from the stem bark of *Diospyros canaliculata* possess antifungal activity. Compared to ketoconazole used as standard antifungal plumbagin could be considered as a promising antifungal drug. Toxicological studies need be carried out in order to insure the safety of extract and plumbagin which can be used traditionally in the treatment of fungi ailments.

27. MIRAZID DID NOT EXHIBIT ACTIVITY AGAINST *Fasciola hepatica/gigantica* IN EGYPTIAN SHEEP

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This study investigates the efficacy of mirazid against *Fasciola hepatica/gigantica* in sheep and the reflection of treatment on host histopathological changes and biochemical enzyme markers. Sheep were infected with 150 metacercariae and classified, 3 months after infection, into three groups. Group I was treated with mirazid in a dose of 600 mg/kg (2 tablets/day) for six consecutive days on an empty stomach. Group II was treated with triclabendazole in single doses of 10 mg/kg/day for two consecutive days after overnight fast. Group III was left without treatment as infected untreated control. Comparable groups of normal sheep were subjected to the same treatments and killed one month post treatment in parallel with the infected groups. Results revealed that mirazid failed to reduce the total number of worms significantly when compared with the infected untreated group. The percentage of worm reduction was very low (6 %) with evident presence of eggs in liver, gall bladder, bile ductules and solutions in a comparable way to that in infected untreated sheep. This was associated with insignificant improvements in the serum levels of total protein, albumin, alanine aminotransferase and ?-glutamyl transferase that was recorded in the infected untreated sheep. On the other hand, triclabendazole resulted in complete disappearance of worms and eggs with remarkable improvements in the serum liver enzyme markers. Histopathologically; chronic cholangitis, portal tract exudation and fibrosis concomitant with bile stasis (cholestasis) were markedly controlled or regressed after triclabendazole treatment, but unremarkably changed by mirazid. In conclusion, triclabendazole resulted in complete eradication of *Fasciola* infection (100 % worm and eggs eradication) with improvement of liver function tests and healing of histopathological changes compared to mirazid where worm reduction was trivial (6 %) with unremarkable changes in the serum enzyme markers and still presence of cholangitis and bile stasis.
28. NATURAL PRODUCTS-DIRECTED DRUG DISCOVERY:  
THE UNIVERSITY OF BUEA EXPERIENCE.

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Parasitic diseases, such as malaria, trypanosomiasis, leishmaniasis and tuberculosis, account for a large percentage of disease burden in developing countries. Treatments for these diseases are for the most part either inadequate, too costly or under considerable pressure due to the steady increase in drug resistance. Therefore, new and affordable treatments are needed to combat these diseases. Many disease-endemic countries are also home to vast repositories of the world’s forests, which harbor potentially useful treatments for these diseases. Therefore, natural products-driven drug discovery represents a potentially useful approach to the search for novel therapies for these diseases. The Pharmacochemistry Research Group (PRG) at the University of Buea, in collaboration with other teams around the world, seeks to discover novel treatments for parasitic diseases, by combining natural products research with synthetic medicinal chemistry in standard drug discovery paradigms that include: biological screening (random and ethnomedically-directed) of plant extracts or single molecules; secondary metabolite isolation and identification, and chemical modification of selected active molecules for optimization of pharmacological and/or pharmaceutical properties. Accordingly, screening of medicinal spices identified Scleria striatonux de Wild (Cyperaceae), as having moderate antiplasmodial activity against chloroquine-sensitive and –resistant strains of P. falciparum. Phytochemical investigation resulted in the isolation of several compounds, four of which were identified as novel sesquiterpenes, including a bicyclic cyclofarnesyl endoperoxide, which displays moderate antiplasmodial activity and provides a platform for subsequent chemical modification.

29. TWO NEW SESQUITERPENES FROM THE ROOT OF CISSAMPELOS OWARIENSIS

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The isolation and identification of two new sesquiterpenes, owarienone 1 and cissampelone,2 from the root of Cissampelos owariensis are described. Spectroscopic data and comparison of their retention indices and their mass spectra with the stored laboratory mass spectral library showed 1 and 2 to be 2H-cyclopropa(a)naphthalene-2-one,1,1a,4,5,6,7,7a,7b-octahydro-1,1,7,7a-tetramethyl, and 5(1H)-azulenone-2,4,6,7,8,8a-hexahydro-3,8-dimethyl-4-(1-methylethylidene), respectively. The antimicrobial activities of 1 and 2 against some human pathogens and the antiviral activity of the ethanol extract against the measles virus (enveloped) are also reported.
30. OVERVIEW ON SCREENING ACTIVITIES OF COMPOUNDS AND MEDICINAL PLANTS AGAINST SCHISTOSOMIASIS IN AFRICAN COUNTRIES

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Treatment of schistosomiasis is based mainly on chemotherapy with praziquantel, which is the drug of choice used in a single dose. However, more information are still needed on optimization of praziquantel; its use in cases of pregnancy and lactation and for children; formulation to prevent cercaria penetration; rapid and good test to detect reinfection; marker of morbidity. Improvement of the treatment of schistosomiasis may be developed by: combination of praziquantel with other drugs, repetition of the treatment with Praziquantel or if new drugs could be discovered. The possible critical situation: Praziquantel is a single drug available and recent reports suggest that resistance to praziquantel may be developing in African countries such as Egypt due to the aggressive use of the drug for more than 10 years. While herbal medicine has produced some very effective treatment for malaria, e.g. quinine and artemisinin, some attempts have also been made to screen plants against schistosomiasis. New antischistosome active compounds were investigated in some African countries. This review article is an attempt to focus on the African scientific screening of new compounds for schistosomicidal activity trying to present promising schistosomicidal drugs and help the future cooperation of African scientists in these research studies.

31. ORAL SUSTAINED RELEASE TABLETS OF ZIDOVUDINE USING BINARY BLENDS OF NATURAL AND SYNTHETIC POLYMERS

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AIDS is considered to be an epidemic and about 38.0 million adults and 2.3 million children are living with human immunodeficiency virus. The annual number of AIDS deaths can be expected to increase for many years to come, unless more effective and patient compliant antiretroviral medications are available at affordable prices. The major drawbacks of antiretroviral drugs for the treatment of AIDS are their adverse side effects during long-term therapy, poor patient compliance and huge cost of the therapy. Zidovudine (AZT) is a potent antiviral agent used in the treatment of AIDS. Its oral bioavailability is reduced to as low as 63% due to first pass hepatic glucuronidation and a high clearance. It has a short biologic half-life (0.5 to 3 h) necessitating frequent administration of large doses (200 mg every 4-6 h or 300 mg twice daily) to maintain therapeutic drug levels. Treatment of AIDS using conventional formulations of AZT is found to have many drawbacks such as frequent development of anemia, leucopenia and accumulation of the drug in multi-dose therapy. These side effects are dose- dependent and a reduction of the total administered dose reduces the severity of the toxicity. Poor patient compliance and high cost are also common drawbacks. Sustained release formulations of AZT can overcome some of these problems. Oral sustained release matrix tablets of zidovudine were prepared using two different types of polymers at different proportions and blends. The effect of polymer type, proportion, and pH of the dissolution medium on the in vitro release of the drug was studied using the half change technique. Release kinetics were analysed using Zero-order, Higuchi’s square-root and Ritger–Peppas’ empirical equations. Compatibility of drug with the matrix formers used was also studied. In vitro release performance as revealed by t70% (time taken for 70% of drug to be released) showed that the release rate decreased with increase in polymer proportion. Matrix tablets containing 10 and 20% Ae were found to exhibit immediate-release characteristics releasing 100% in the first hour, those containing 30% Ae showed a first hour release of about 26% and extended the release up to 5h, while those containing 30% carbopol showed a first hour release of about 25% and extended the release up to 8h. Of the five different blends of Ae and carbopol, 1:2, 2:1 and 1:3 showed a first hour release of about 39, 30 and 24% respectively and extended the release up to 8 h. Release kinetics was predominantly anomalous. No incompatibility was observed between the drug and the two polymers used in the formulations. Overall, the drug release
from matrix tablets of zidovudine containing blends of Ae and carbopol 71G demonstrates the advantage of polymer blending over single polymer use and this can overcome the disadvantages of conventional tablets of zidovudine, while reducing the cost of importation of excipients.

32. HEMATOLOGICAL, ANTI-INFLAMMATORY AND ANTIOXIDANT PROPERTIES OF A COMMERCIAL HERBAL PREPARATION, JOBELYN®

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Jobelyn® is a herbal preparation whose primary active ingredient is from the leaves of Sorghum bicolor plant that has been used for over a century to treat several diseases. Phytochemical screening revealed the presence of oligomeric and polymeric proanthocyanidins, anthocyanins, monomeric catechins, carbohydrates, protein, saponins, apigenidin and proapigenidin. In rabbits and rats with trypanosome-induced anemia, in vitro studies demonstrated that Jobelyn® rapidly increases haemoglobin and packed cell volume levels. Investigation of antioxidant capabilities revealed that Jobelyn® has oxidative radical absorbance capacity (ORAC) of 3,123.0 per mg and antioxidant capacity which is more than 13 well-known antioxidant-rich fruits combined. Animal and in vitro studies, supplemented by epidemiological evidence and human studies, indicate numerous health benefits (including protection from various ailments), associated with the antioxidant effects. Studies on the effects on lipopolysaccharide-induced cytokine and PGE2 release in human monocytes of healthy human blood donors using enzyme-linked immunosorbent assay (ELISA) indicate that Jobelyn® significantly inhibits lipopolysaccharide-induced release of cytokines (IL-1beta, TNFalpha, IL-6, IL-8) and PGE2. Its selective effect on COX-2 activity makes it a very promising anti-inflammatory medicine with minimal side effects. Results of acute toxicity studies using laboratory animals revealed LD50 values of 215.1mg/kg and 193.4mg/kg for oral and intraperitoneal routes, respectively. It is concluded that Jobelyn® is safe and useful for the management of anemia-related diseases such as aplastic anemia, sickle-cell anemia and HIV/AIDS, and is a promising medicine for protection against many diseases. The product is likely to be a suitable alternative to most currently used anti-inflammatory medicines.

33. DISCOVERY OF NEW ANTI-TUBERCULOSIS AGENTS FROM NATURAL AND SYNTHETIC SOURCES

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New drugs for tuberculosis are urgently needed to shorten the duration of therapy, to more effectively treat drug-resistant TB and to eliminate the latent state. At the Institute for Tuberculosis Research we are taking both target and ligand-based approaches to the identification of new lead compounds. The development of high throughput compatible assays to identify activity against both replicating and non-replicating cultures is a key component since the key to shortening treatment may depend upon identifying compounds which can more effectively kill the latter phenotype. Equally important is the early profiling of active compounds with respect to mammalian cell toxicity, effect of serum, activity against drug-resistant strains of M. tuberculosis as well as other microorganisms. Promising compounds are also assessed for CYP450 inhibition, microsome stability and pK profile in mice. Demonstration of efficacy in a low dose aerosol infection model by the reduction of lung colony forming units leads to an intensive analoging effort to optimize the compound class. A fifty thousand compound parallel synthetic library has been screened and the above assays used to prioritize 3 scaffolds for lead ID/optimization studies. Over 60,000 actinomycete extracts and 15,000 fungal extracts have been screened with hit rates of 0.5-1%, hits profiled and scale up fermentations completed. Newly developed techniques for fractionation
and characterization of active extracts include high speed countercurrent chromatography coupled with GC-MS profiling of fractions. This facilitates the identification of active, minor components and the determination of synergy as well as enabling the identification of active principles prior to isolation. The combination of HTS-compatible assays, early profiling and efficient isolation of active principles should facilitate the identification of lead compounds for TB drug development.

34. PRE-CLINICAL AND CLINICAL STUDIES OF NIPRD AM 1, AN HERBAL ANTI-MALARIAL PHYTOMEDICINE

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NIPRD AM 1 is a single plant preparation developed from the aqueous extract of a plant that is used extensively as food and as medicine in many parts of Africa. Often, the bark, roots and leaves are used to treat sores, gonorrhoea, stomach disorder, cough and malaria, but the root extracts are usually preferred for the treatment of malaria. The antispasmodic and anti-plasmodial activities have been reported. We carried out the non-clinical efficacy and safety evaluation of NIPRD AM 1 before mounting a pilot comparative randomized clinical trial of the product against symptomatic but uncomplicated Malaria in human volunteers at the two district hospitals located in Gwagwalada and Wuse, both in the Federal Capital Territory, Abuja, Nigeria. The aim of the study was to determine the non-clinical safety and efficacy of the product before a pilot human study so as to provide scientific data that would support further development of the product. Phytochemical studies, acute (LD_{50}) and sub-acute toxicity studies were done in our laboratory. The product was studied in vivo against the rodent malaria Plasmodium berghei in mice. Randomised comparative clinical trial of NIPRD AM 1, Chloroquine and Sulphadoxine /Pyrimethamine (SP) were also carried out at Gwagwalada Specialist (GSH) and Wuse General (WGH) Hospitals Abuja based on an approved study protocol prepared in line with the ICH GCP guidelines. Patients with history of fever, generalised body pain, headache, bitterness in the mouth, vomiting, dizziness, poor appetite and age above 18 years were recruited and screened for presence of malaria parasites. Both physical examination and laboratory investigations were carried out.

Patients attending out-patient department of Gwagwalada Specialist Hospital who met the inclusion criteria were given either NIPRD AM 1 or chloroquine. Those attending Wuse General Hospital were placed either on NIPRD AM1 or SP. Efficacy was determined by the time taken to achieve negative blood slide at day 7 and for patients to be asymptomatic. Safety was assessed by comparing the baseline haematological, serum chemistry and vital/physical signs with those done at subsequent follow up visits. Two-way analysis of variance (ANOVA) with 95% level of significance was used for the statistical analysis. Dunnett's Post hoc analysis was applied. The product had an LD_{50} above 2000mg/kg p.o. in rats and mice and did not show any significant toxic activity on the organs or systems in the 28 day sub-acute toxicity study. However, there was evidence of sedation, decrease in food consumption and weight loss associated with the product. The crude extract showed 50% suppressive activity in vivo against the rodent malaria parasites. NIPRD AM 1 was efficacious against uncomplicated malaria in humans, with its activity superior to those of CQ and SP. The parasite clearance was better than chloroquine and there were no threats of serious side effects affecting the organs or tissues. Data has been obtained which would enable a randomized double blind multicentre clinical trial of NIPRD AM 1.
35. MOLECULAR TRACKING OF LABORATORY-BASED MULTI-DRUG RESISTANCE AMONG NIGERIANS INFECTED WITH MYCOBACTERIUM TUBERCULOSIS: A PRELIMINARY STUDY IN THE IDENTIFICATION OF POSSIBLE DRUG TARGET SITES

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Ninety-six Mycobacterium tuberculosis isolates from Lagos, Abuja and Kano states of Nigeria were subjected to drug susceptibility testing. Thirteen of the 26 (50%) observed multi-drug resistant strains (as determined by minimum inhibitory concentrations above 0.2ug/ml and 1 μg/ml) for Isoniazid (katG) and Rifampicin (rpoB) genes, were sequenced by Nonsynonymous single nucleotide polymorphism analysis, nsSNPs. DNA sequencing data revealed a series of 6 deletions and 5 point mutations in the rpoB gene. Three strains demonstrated no differences when compared to wild type sequence of the gene. Only one Isolate Y33, from a patient residing in Mushin, Lagos who self-treated herself with native as well as orthodox (septrin antibiotic) medicine, demonstrated a major nsSNP within codon 516 of the rpoB gene and codon 336 of the katG gene. Six deletions and 5 point mutations were observed from sequence data of the katG gene. Three isolates demonstrated no difference when compared to the wild type gene sequence. Non-synonymous polymorphism at codon 516 of the rpoB gene has been associated with low-level resistance to Rifampicin. In this preliminary study, the finding that most of these Nigerian M. tuberculosis isolates failed to demonstrate major mutations in the katG and rpoB genes sites which usually act as resistance determining regions and mainly pose as targets for most anti-Tuberculosis (First and Second-line) drugs emphasize the need for the development of newer drugs tailored to meet the Nigerian indigenous needs.

36. SETTING UP DRUG DISCOVERY PROGRAMS: DO’S AND DONT’S

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Setting up alliances comes in many forms. These may take the form of academic - academic, academic -industry and industry - industry. Each of these has different start and end points and objectives. Having completed his PhD at the University of Cape Town in 1999, Richard completed a post doc at the University of Cambridge during 2000 and 2001. After this, he joined BioFocus DPI a contract research organisation conducting pre-clinical services for pharmaceutical and biotech companies. In 2004, Richard moved to a commercial role at BioFocus DPI - today he is responsible for all commercial activities in the European market covering target discovery, HTS, natural product discovery and medicinal chemistry. Over the last few years, the preclinical market has changed significantly with much of the drug discovery taking place in Academia. This is reflected in the nature of work conducted through his company and the types of deal structures available. This poster is about the good the bad and the ugly on what has worked (and what hasn’t) and things that ANDI need to consider to make this initiative successful.
The Department of Pharmacology and Pharmacognosy is one of the three departments within the School of Pharmacy of the University of Nairobi. The vision of the Department is to be a centre of excellence in teaching and basic and applied biomedical research. The objectives of the Department are to build capacity in traditional medicine and biomedical research through post-graduate training; to provide specialized medical services; and to carry out basic and applied medical research. The Department is made of 13 members of academic staff with diverse areas of specialization such as traditional medicine research, clinical trials design, bioethics, pharmacogenetics, pharmacokinetics and in vitro and in vivo animal experimentation. All the members including the technical staff have been trained in Good Laboratory Practices (GLP) and some have undertaken Good Clinical Practice Training (GCP). They have also spearheaded product formulation and development and carried out clinical trial research on herbal products for management of HIV/AIDS and peptic ulcer disease. The Department is currently offering a Masters program in Pharmacognosy and Complementary Medicine. Three additional postgraduate programs offering specialization in Clinical Pharmacology, Molecular Pharmacology and Pharmacocoe epidemiology and Pharmacovigilance have been developed and are awaiting approval by the University senate. Through collaborative links, the Department has established two research laboratories: African Institute of Biomedical Science and Technology/University of Nairobi (AiBST/UON) research laboratory and Multilateral Initiative for Malaria Studies (MIMS) Pharmacognosy Laboratory. In the past, the Department has focused on screening herbal products for analgesic, in vitro and in vivo antimalarial, antipyretic and antidiabetic activity. Building on this strong base in research the department is now focused on embarking on: preclinical safety testing; in vivo and in vitro pharmacokinetic studies; pharmacogenetic studies; clinical genetics; therapeutic drug monitoring in the use of antiretrovirals, anti-tuberculosis drugs; development of pharmacoinformatic tools for disease diagnosis and pharmacotherapeutics; natural product research and product development including clinical trials. A binding memorandum of understanding was signed between the chief executives of University of Nairobi and AiBST on the 10th of August, 2006. Challenges to the current and future growth of the Department include understaffing and lack of access to state of the art equipment. It is hoped that these challenges will be overcome by strengthening links with local and international partners. The Department looks forward to collaborative arrangements with all interested parties.

The discovery and development of new drugs is a very costly and long process requiring capacity and competency in several key areas within the drug discovery and development value chain. While South Africa has capacity and competency in basic science and clinical studies of various diseases, the challenge has always been how to translate this into new medicines. One of the missing key areas is a platform for preclinical drug development, which is critical in efforts to discover and develop new life-saving medicines. South African government’s support of health biotechnology has been growing, and in 2000 it began focusing its research support to biotechnology. This led to the adoption of the 2001 National Biotechnology Strategy. This strategy seeks to capitalize on the high quality of research carried out in public research institutions and universities, but is hampered somewhat by the lack of entrepreneurial culture among South African researchers.
The three key bottlenecks in the drug development process that will be addressed by this strategy are human capital development for academic and industry needs, infrastructure for development and manufacturing and the regulatory approval process. This comprehensive strategy with a detailed roadmap will lead to the establishment of the Pre-clinical Drug Development platform in South Africa. This Platform will deliver added value to the drug discovery and development process and to individual stakeholders by providing a more effective, vibrant and dynamic scientific environment and will create a significant tool to accelerate drug candidates through to clinical evaluation. The national Pre-clinical Drug Development Platform (PDDP) will be a centre of competence that services the needs of the broad biotechnology and pharmaceutical community in SA. The proposed facility will not be a standard laboratory or animal facility, but rather a facility with all the required regulatory controls, and in this case GLP and GMP, required by national and international regulatory bodies.

39. PLANT AUTHENTICATION, A MANDATORY STEP IN THE PROCESS OF DRUG DISCOVERY: A CASE STUDY OF THE MISTLETOES FAMILY (LORANTHACEAE) IN NIGERIA

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Accurate plant identification is the foundation of research into phytomedicines. Without proper identification as a starting point, the safe use of quality products cannot be guaranteed. The use of mistletoes in treatment of various ailments in Nigeria and in fact in most part of the world is well documented\textsuperscript{1, 2}. But this group of plants which is immensely important medicinally is mostly wrongly identified in Nigeria due to the overlapping characters found in the different species in the family\textsuperscript{1, 3}. Most of the names available for the plants at specific and generic levels are uncertain\textsuperscript{4}. To generate a reliable taxonomic key for easy identification of the mistletoes in Nigeria, field studies were undertaken to ascertain how many species can be found and to study their macro-morphology, micro-morphology and phytochemical profile for diagnostic characters. Ten different species in six different genera were identified from field studies and herbarium specimens. The leaf shapes are elliptic, ovate-elliptic or ovate in \textit{Agelanthus brunneus}, \textit{Tapinanthus bangwensis}, \textit{Phragmanthera capitata}, \textit{Globimetula braunnii} and \textit{Engleria gabonensis}. It is linear, linear-lanceolate to ovate-lanceolate in \textit{Agelanthus dodoneifolius}. \textit{T. cordifolius} has sessile leaves. Open corolla is reflex in the genus \textit{Tapinanthus}; erect in \textit{Phragmanthera}, \textit{Engleria} and \textit{Agelanthus}; coiled in \textit{Globimetula}. Flowers are in spikelets in Helixanthera. Epidermal cell shape is isodiametric to elongate in all the species. Striations are found on subsidiary cells of \textit{A. dodoneifolius} and \textit{T. bangwensis} and also on the lower epidermal cells of \textit{P. capitata} and \textit{P. nigritana}. Trichomes and trichome bases are seen on lower surfaces of \textit{Phragmanthera} spp. All the specimens accessed have pericytic type of stomata. Phytochemical profile showed presence of various secondary metabolites in the mistletoes and these varied from host to host. From this study, it was found that the flowers of the mistletoes and in some cases in combination with the leaf characters are the most stable and reliable when identifying the mistletoes. Chemical variation exists within the same species on different hosts. Therefore, chemical profile might not be useful in delineating parasitic taxa in isolation of the host. A reliable taxonomic key has been generated for easy identification of the mistletoes found in Nigeria.

40. TRANSFUSION MALARIA: INFECTIVITY AND MULTIPLICATION OF \textit{PLASMODIUM BERGHEI} STORED AT 4°C FOR VARIOUS TIME INTERVALS

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Blood transfusion is a life-saving venture; it also poses problems if not well managed as there is the risk of transmission of blood-borne pathogens such as malaria parasite. This study examined the prevalence of malaria parasite in blood stored in blood bank Infectivity and multiplication of \textit{Plasmodium berghei}
stored at 4°C was also assessed in albino mice. Malaria parasite prevalence of 34% was observed with parasite density ranging from $1 \times 10^3$ to $2.5 \times 10^3$ parasites per microlitre of blood. Infected blood samples from donor albino mice were stored at 4°C for different time durations and new infections were initiated with mice using high and low inoculum of parasites. The refrigerated and unrefrigerated infected blood samples were found to be infective to mice though with varying prepatencies. Longer prepatencies were observed in blood samples stored for 28 days and mice inoculated with low inoculum. There was no significant difference in the multiplication rate of \textit{Plasmodium berghei} in low and high inoculum of the parasite. This study revealed that \textit{Plasmodium berghei} retains its infectivity despite storage at 4°C for up to 28 days. The high prevalence of malaria parasite observed in stored donor-blood samples from the blood bank indicates a high risk of transfusing malaria infected blood to susceptible recipients. Therefore in a bid to save lives, there is the need to improve the blood screening and transfusion policy in Nigeria in order to prevent transfusing malaria parasite.

41. CYTOTOXIC STILBENOIDS IN GNETACEAE

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Gnetaceae is a family of tropical gymnosperm. It consists of one genus (\textit{Gnetum}) with about forty species distributed in the tropical rain forest of South East Asia, South America and some parts of Africa. Many species in the family are used as food, medicine and are known to contain stilbenoids. We present in this report the isolation and structure determination of several stilbenoids from five species of \textit{Gnetum}. The compounds were purified using ODS and Sephadex LH-20 open column chromatography. The structures of the compounds were determined by 2D NMR spectroscopy (HMQC, COLOC, HMBC and NOESY etc). The compounds were screened for growth inhibitory activity against HL-60 cell line, and two of the compounds; gnemonol G and gnetin C exhibited strong activity with of IC50 10uM and 12uM respectively.

42. ANTIMALARIAL AND ANTI PYRETIC EFFECTS OF ESSENTIAL OILS FROM SIX NIGERIAN MEDICINAL PLANTS ON \textit{PLASMODIUM YOELII NIGERIENSIS} (IN VIVO) AND \textit{P. FALCIPARUM} (IN VITRO)

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Essential oils from leaves or fruit peel of six medicinal plants of Nigeria namely: \textit{Citrus aurantifolia} (CA), \textit{Citrus sinensis} (CS), \textit{Citrus medica} (CM), Callistemon rigidus (CR), Syzygium malaccense (SM) and Dennettia tripetala (DT) were examined for their antimalarial property \textit{in vivo} and \textit{in-vitro}. More than 80% of the asexual erythrocytic stages of chloroquine resistant- \textit{Plasmodium yoelii nigeriensis} were inhibited with 400 mg/kg (s.c.) after the 4-day schizontocidal test (94-97.7% chemosuppression) by \textit{Citrus medica}, \textit{Syzygium malaccense} and \textit{Dennettia tripetala}. In vitro antiplasmodial action of \textit{Citrus medica} and \textit{Citrus aurantifolia} with reference to IC50 surpassed that of the standard antimalarial drugs, chloroquine and artemether, while \textit{Dennettia tripetala} showed comparable activity. In-vitro activity of various oil suspensions against \textit{P. falciparum} also produced significant inhibition in parasites growth. IC50 confirmed remarkable antimalarial activity of \textit{Citrus medica} and \textit{Citrus aurantifolia}. Our results
suggest essential oils of *Citrus medica*, *Citrus aurantifolia* and *Dennettia tripetala* as promising new antimalarial agents. Based on the outstanding antimalarial profile of *Citrus medica* essential oil, the plant represents natural product with potential for further development as an antimalarial drug.

**43. TOXICITY ASSESSMENT OF THE AQUEOUS EXTRACT OF *CALOTROPIS PROCERA* IN RABBITS**

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*Calotropis procera* has been reported to possess medicinal properties but equally pose deleterious effect on animals. To investigate the extent of damage, a toxicological evaluation of the aqueous extract of fresh leaves of the plant was conducted. Phytochemical screening revealed the presence of alkaloids, saponins, tannins, cardiac glycosides, and flavonoids while elemental analysis showed traces of iron, lead, sodium, and potassium in concentrations of 0.23, 0.03, 0.82 and 9.5 mg/g respectively. Acute toxicity study was carried out with oral administration of 200, 400, 800, and 1600mg/kg of the extract once to groups I, II, III and IV respectively within a 24 hours observation period. Four rabbits died within 24 hours and LD₅₀ was estimated (940mg/kg). 80, 40 and 20mg/kg of the extract were administered daily to groups I, II, and III respectively during subacute toxicity study for 14 days. Statistical analysis of Aspartate Amino Transferase (AST), Alanine Amino Transferase (ALT), Alkaline Phosphatase (ALP), Albumin and protein showed no significant changes at P<0.05. Changes in Packed Cell Volume (PCV), White Blood Cells (WBC), Haemoglobin (Hb), Platelets, and Differential Leucocyte Count (Lymphocytes, Monocytes, Eosinophils, Heterophils/Neutrophils and Basophils) were equally statistically insignificant at P<0.05. However, gross and histopathological examination of some organs and tissues (heart, liver, kidney, brain, small intestine and lungs) revealed lesions. It was concluded that the extract had no significant effect on blood parameters when administered orally at tolerable doses since controls were also affected but have lethal effects at higher doses since the effect was found to be dose-dependent.

**44. CURRENT EFFORTS AND CHALLENGES TOWARDS PRODUCTION OF ARTEMISININ BASED COMBINATION THERAPIES (ACTs) TO COMBAT MALARIA IN NIGERIA**

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Malaria is one of the highest major causes of morbidity in Nigeria (1,858 per 100,000), thus constituting a serious public health problem. It is responsible for 60% of out patient visits to health facilities, 30% childhood death in children under one year and 11% maternal deaths (4,500 per year). In Nigeria, a child will be sick of malaria between 2 and 4 times in one year and 70% of pregnant women suffer from malaria; leading to pregnancy-related complications. The financial loss due to malaria annually is estimated to be about 132billion Naira in form of treatment cost, prevention, loss of man-hours etc. The search for an effective antimalarial drug became more urgent when it was realised that variations of the malaria parasite were developing resistance to chloroquine and other antimalarial drugs of choice. The WHO therefore recommended to all countries to shift to Artemisinin - based Combination Therapies (ACTs) for the treatment of malaria. Various plantations of *Artemisia annua* (medicinal plant from which Artemisinin is obtained) have been established in different zones of the country under the co ordination of the Artemisinin Development Company, Abuja confirming that Nigeria’s vegetation is favourable to the cultivation of the plant. The challenge for NIPRD was to develop research activities leading to standardised scientific data required for the production of the ACTs in the country. In October 2005, dried leafy biomass collected from field cultivations in Calabar were subjected to a modified extraction method and with the available facilities in NIPRD, white spindle shaped Artemisinin crystals with a melting point of 155°C were isolated for the first time in the country. Coupled with collaboration, NMR and HPLC analyses were further carried out to determine the identity, purity and quality of the Artemisinin obtained.
and the results indicated a high degree of these parameters. *In vitro* antiplasmodial activity of the isolated Artemisinin against chloroquine resistant *Plasmodium falciparum* (strain K1) was assessed using the parasite lactate dehydrogenase (pLDH) assay according to Makler et al. The result yielded an antimalarial activity comparable to the reference drug obtained from Aldrich in England. Efforts are currently on to determine the artemisinin contents in the different *A. annua* biomass obtained from different pilot farms in Nigeria as guide to further cultivation expansion, while the derivatization of Artemisinin into Artesunate, dihydro artemisinin, etc is ongoing. These results along with others being compiled are aimed at local production of ACTs in the country as Nigeria strives to meet the Millennium Development Goals (MDGs). Current challenges include the sourcing of viable *A. annua* seeds, acquisition of a 2-5 tonne /annum extraction plant, scaling up of the extraction, isolation, crystallisation, formulation and standardization processes, necessary up to date equipments and capacity building on the new technology.

45. EVALUATION OF THE TRYPANOCIDAL POTENTIAL OF EUCALYPTUS CAMALDULENSIS

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Chemotherapy of African trypanosomiasis in both the human and animal forms has been confronted with multidimensional problems that include unavailability of drugs, resistance, high cost, prolonged treatment protocol and adverse side effects. To explore alternatives, the leaves, stem and root barks of *Eucalyptus camaldulensis* were sequentially extracted with hexane, ethylacetate, methanol and water and the extracts tested for antitrypanosomal activity. Mice infected with *Trypanosoma brucei brucei* were treated intraperitoneally with 200, 400 and 600mg/Kg body weight per day of the extracts for three weeks. Only the methanol extract of the leaves produced complete cure for all the mice in the different dose groups. Subinoculation of healthy mice with the blood and cerebrospinal fluid (CSF) of the cured mice did not result in infection. Acute toxicity studies confirmed the safety of the extract because no mortality was recorded even at 5000mg/Kg body weight. The extract had no prophylactic activity. When tested for antibacterial activity, it inhibited the growth of *Klebsiella pneumonia* and *Staphylococcus aureus*. We conclude that the leaf extract of *E. camaldulensis* has immense potential for the development of drugs against trypanosomiasis and diseases caused by *K. pneumonia* and *Staphylococcus aureus*.

46. LABORATORY DIAGNOSIS OF CHILDHOOD TUBERCULOSIS IN IBADAN, NIGERIA: A FIVE YEAR RETROSPECTIVE REVIEW

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Rationale: Establishing a definitive diagnosis of childhood tuberculosis (TB) has remained a big challenge worldwide more especially in developing countries of Africa and Asia where there is high endemicity of the disease (1, 2).Objective: To determine the yield of *Mycobacterium tuberculosis* from specimens collected from children with diagnosis of TB in Ibadan, Nigeria Design: The TB laboratory records of the University College Hospital, Ibadan were reviewed for results of specimens submitted for all children aged 10 years and below with clinical diagnosis of TB between June 2003 and May 2007. Results: A total of 630 specimens were processed; out of which sputum and gastric washings accounted for 72% and 55.9% were males. Fifty-six (8.9%) were positive for acid fast- bacilli while 26 (4.1%) were positive for culture on Lowenstein-Jensen medium. Overall detecting of *M. tuberculosis* was in 70 (11.1%) as 14 (2.2%) were positive for both microscopy and culture. Specimens from the 5-10 year age group accounted for majority of the positive cases, 69.6% for microscopy and 73.1% for culture. Further analysis showed that
there were no statistically significant differences between the yield in different age groups (p= 0.45; p= 0.54) and also in the yield from different specimens (p= 0.28; p= 0.75). Conclusion: The low yield of *M. tuberculosis* calls for an urgent need for a more sensitive tool to meet up the challenges of diagnosing childhood TB especially in endemic countries with limited resources.

**47. BENEFIT-SHARING, A VITAL TOOL IN SALVAGING OUR INDIGENOUS KNOWLEDGE:
A CASE STUDY OF THE FEDERAL CAPITAL TERRITORY, ABUJA, NIGERIA**

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Indigenous or Traditional Knowledge is that information or knowledge that has been developed by indigenous people in various regions of the world. Such knowledge generally relies exclusively on past experiences and observations and has been transmitted orally or in some form of script across generations of groups or communities of indigenous people. Therefore, this knowledge often has a cultural context, a collective ownership and is constantly evolving. More often than not, this indigenous knowledge is the only source of livelihood for the practitioners; as a result, most of them are not willing to divulge the knowledge without any form of benefit. In order to further develop this knowledge for the benefit of the general populace, promote and improve traditional medicine practice, guard against misappropriation, prevent extinction, and ensure documentation and conservation, it is necessary to promote equitable rewards and invariably protection for the originators of the knowledge. This study was to determine reciprocal benefits based on the requests of the local people through the use of questionnaires. As envisaged, majority of the practitioners wanted immediate and monetary form of compensation. However this was superseded by the desire for traditional medicine clinic/hospital. It was discovered that further training was desired by only a handful of the practitioners and these were practitioners from a particular geopolitical zone of the country. Other needs included basic equipment to make the practice easier, cars and infrastructure for the practitioners’ communities.

**48. INDUSTRIAL PRECLINICAL DRUG ABSORPTION, DISTRIBUTION, METABOLISM & EXCRETION (ADME) AND PHARMACOKINETICS (PK) FOR LEAD DISCOVERY AND LEAD OPTIMISATION**

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Background: The discovery and development of medicines is a complex and costly process involving many failures at various stages. In the pre- 990 era, poor pharmacokinetics was associated with the failure of about 40% of new chemical entities (NCE). The pharmaceutical industry responded by front-loading drug ADME and PK evaluation in lead discovery and lead optimisation. This has resulted in PK accounting for less that 10% of NCE failures in the post-2000 era. Over the past decade, WHO-TDR and a number of research groups in Africa have initiated drug discovery campaigns to combat infectious diseases. The DMPK & BAC Unit at the African Institute of Biomedical Science and Technology was established to support these drug discovery and development efforts. A number of in silico, in vitro and in vivo DMPK methods are at various levels of development at AiBST and are being applied to WHO-TDR drug discovery projects and other collaborative projects with a view to select good lead compounds and integrate drug ADMET knowledge in lead optimization chemistry. Methods: Important drug ADMET properties in the discovery of leads and optimisation of compound series include; solubility, protein binding, permeability, metabolic stability, enzyme inhibition & induction, and bio-activation. Software such as Metasite and Volsurf are being used to predict these properties based on physicochemical properties. In vitro systems being used include permeability studies using Caco2 cells lines and vesicles expressing various drug transporters. Metabolic stability, enzyme identification, metabolite identification and enzyme inhibition studies using various cellular, sub-cellular fractions, and recombinant enzymes. PK studies are being setup using rat and mice which sometimes double as PK and disease model animals. Software
such as Simcyp and Winonlin are being used to evaluate and/or predict likely in vivo PK properties in humans of compounds from in vitro data. Bioanalytical platforms for the in vitro and in vivo studies are mainly HTS plate reader, HPLC-UV/FLUO and LC-MS based. Results: We have evaluated over 25 compounds from WHO-TDR representing diverse chemistries of the various drug discovery projects it co-ordinates. We have also evaluated over 30 anti-parasitic drugs in current use towards optimising their clinical use in light of the fact that when they were discovered, not much DMPK work was done on them and also towards addressing the challenge of potential drug-drug interactions due to poly-pharmacy in the use of these drugs in combating co-infections. We have also developed software for the prediction of metabolically based drug-drug interactions. Discussion: With funding support from WHO-TDR, the AntiMal Project, IPICS and institutional resources from contract research work, the DMPK & BAC Unit at AiBST offers many drug discovery and development initiatives in Africa a world class platform for industrial DMPK towards lead discovery and lead optimisation. Results from these preclinical DMPK studies should be interpreted in context of the pharmacological effects of compounds being evaluated and the medicinal chemistry being explored. This is because the compounds that ultimately make it through the discovery and development process represent global average properties that ensure clinical safety and efficacy.

49. TRADITIONAL MEDICINES RESEARCH AND DEVELOPMENT:
CAN AFRICA DISCOVER, DEVELOP AND COMMERCIALIZE ITS RESEARCH OUTPUTS

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Traditional medicines play a critical role in the healthcare systems of many African countries and there is also an increasing use of medicinal plants and herbs for a variety of conditions. The majority of people in many African countries use traditional medicines for their healthcare needs whether at primary healthcare level or even for chronic disease conditions. There are numerous reasons for the resurgence of interest in herbal and traditional medicines use. This could mainly be because traditional medicines are natural and are thought to be safe, traditional medicines do not have many side effects and hence have found favour with patients on chronic medication and in geriatric medicine. The other reason for the continued use of traditional medicines is the intrinsic cultural beliefs in traditional medicine. A lot of excellent research has been conducted by individuals and individual institutions but none has yielded any intellectual property that has found practical medical commercial application. Why? Africa has a rich biodiversity and intellectual human capital but lacks the infrastructure and the technology to drive innovation. The many academics who conduct science research are in many cases shunning traditional medicines research for reasons that there is no science in traditional medicine. This has resulted in lack of support and policy development towards the ownership and development of traditional medicines research. Those who have persevered and continued to conduct scientific research in traditional medicines have either continued research using inappropriate and not relevant methodologies. Most scientists have not researched African Traditional Medicines (ATM) but have looked at traditional medicinal plants. This research has further progressed using reductionist methods of isolating and characterizing pharmacologically active components of medicinal plants. This approach has thus far yielded very few success commercial products from African Traditional Medicines contrary to the increased interest in traditional medicines. Most of this work has not gone beyond preclinical research because most of these candidates failed the scrutiny and rigorous scientific research and lack of funding and interest to fund clinical trials on African Traditional Medicines. What would be the appropriate research methodologies to evaluate the claims for use of traditional medicines? What endpoints should be use in these assessments? Are there markets for African Traditional Medicinal products? Can Africans create its own market for these products? These issues will be discussed in this presentation. Research in traditional medicines has become individualistic and scientists are reluctant to share information on their research and seek other partners to support and complement their work. This could be because of the wrong assumptions that there are huge commercial benefits that shall be derived from the eventual commercialization of traditional medicines. This problem has also moved to be an institutional problem where academic and science councils or ministries do not collaborate with each other but would rather compete for the very limited to non-existent financial resources. All this has left the indigenous knowledge holders outside as scientist hope to enrich their
individual self. Drug discovery and drug development cannot be an individual or institutional exercise but needs concerted efforts from scientists of all spheres, communities, policy makers, business persons and government. Can Africa then stimulate a South – South research collaboration for drug discovery and development from African Traditional Medicines? What are the pitfalls of this initiative? Are the success stories and what could be learnt from them? Can Africa drive its own research agenda based on African Traditional Medicines? The presentation will attempt to answer some of these questions with case studies of failure and success for establishment of a South – South research initiatives and analyse the reasons for such failures and lessons learnt from these failures. The presentation will conclude by outlining some of the success stories and initiative that are put forward through South African government and the Department of Science and Technology. These initiatives aim at overcoming problems encountered in previous efforts, and attempt to set an African Research agenda for African Traditional Medicines. At the end of this presentation its is hoped that from these case studies, African Network for Drugs/Diagnostics Discovery & Innovation (ANDI) see how to improve these efforts and possibly support such initiative.

50. NO TITLE

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Background: Direct Ziehl-Neelsen (ZN) sputum smear microscopy for diagnosis of tuberculosis (TB) has low sensitivity. Concentration of sputum using bleach with sedimentation has been shown to increase sensitivity in many settings. Objective: To determine whether bleach plus centrifugation has a significant effect on ZN smear negative sputum specimens for diagnosis of TB. Methods: Three hundred and seventy sputum specimens were collected from new TB suspects attending a referral district hospital in Nairobi and processed for direct microscopy and culture. All smear negative specimens were treated with 3.5% bleach and left to stand for 30 minutes before centrifugation. Both direct and bleach treated smears were processed and examined using ZN staining method. Results: Of the 370 specimens, 200(54%) were culture positive. The number of smear positive by direct ZN was 138 (37.2%) with a sensitivity of 66% which increased to 171 (46.2%) with a sensitivity of 81% after treatment of direct ZN smear negative specimens with 3.5% bleach. There was a significant increase in sensitivity from 66% to 81.1% (p<0.05) Conclusion: Use of 3.5% bleach with centrifugation could be recommended for use to enhance case detection with ZN microscopy in TB control programmes especially in settings with high burden of dual TB/HIV infection.

51. POTENTIAL OF KENYAN PLANTS FOR DEVELOPMENT OF ANTI-PLASMODIAL PRINCIPLES

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Malaria is the most difficult problem afflicting people in the Southern hemisphere. In Africa, more than 100 million people are infected with malaria parasites every year, out of a global figure of 300-500 million, ending up with a mortality rate of 1-1.5m a year. Control measures against malaria are designed to eradicate the parasite, or by vector eradication intervention methods such as application of larvicides in breeding ponds or mosquito adulticides in households. High rate of resistance development to drugs and chemicals by the parasite and the vector respectively makes the necessity of malaria control research virtually a continuous one. A source of these principles is the rich tropical flora. From our work with the plant families, Polygonaceae, Myrsinaceae, Asteraceae, Sapindaceae, Leguminosae, Guttiferae, and Rutaceae, among others, we have found principles that are anti-plasmodial and mosquito larvicidal. The acetone extract of the roots of *E. abyssinica* showed potent anti-plasmodial activities against W2 (chloroquine-resistant) and D6 (chloroquine-sensitive) strains of *P. falciparum* g/ml respectively. Amongst the µ0.06 ± 0.07 and 0.64 ± with IC50 values of 0.49 compounds tested were abyssinine – IV with LC50 of 7.7 and 9.0 µg/ml and erythrabyssin-II with 6.5 and 8.1µg/ml against W2 and D6 plasmodium strains respectively were quite promising. *Millettia usaramensis* stem bark extract showed several flavonoids
with anti-plasmodial activities. The geranylated chalcone, 4, 2'-dihydroxy-4'-0-geranylchalcone gave the best activity for W2 M respectively. Rotenoids in the µ and D6 with IC50 values of 8.7 and 10.6 mixture showed significant but less activity. Polygonum senegalense chalcones and flavanones also showed similar activities.

52. THE ROLE OF IGE ANTIBODIES IN PROTECTION AGAINST P. FALCIPARUM

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Malaria occurs in over 100 countries and territories. More than 40% of the people in the world are at risk of getting malaria. There are approximately 200 million to 500 million new cases each year in the world, and the disease is the direct cause of 1 million to 2.5 million deaths per year. Immunity to malaria is complex partly due to the complicated life cycle of the parasite with different antigens expressed at different times. In endemic malaria areas, infection with malaria is associated with elevation of strong specific and non-specific antibody responses with the humoral immune responses involving production of predominately IgM and IgG comparing both total IgE and ant malarial antibodies has been reported in a several studies carried out in a number of different malarial endemic areas review by Perlman P. et al 1999. Further, studies have suggested that IgE may play a role in the pathogenicity of malaria. On the other hand, it is well known that IgE mediates activation of various effectors cells such as monocytes/macrophages, also many studies suggested that. This data may suggest that IgE may also play a role in protection against malaria. The main objective of my research project is to determine the role of IgE in protection against acute P. falciparum malaria in an area characterized by highly seasonal but stable malaria transmission in Sudan. To archive this goal Total and specific IgE had been measured and number of cytokines had been determined in the samples collected from my study subjects with different clinical presentations.

53. ANTIPLASMODIAL ACTIVITY AND TOXICITY OF SELECTED CAMEROONIAN ANTIMALARIAL MEDICINAL PLANT EXTRACTS AND PURE PRODUCTS

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The emergence and spread of drug resistant malaria has stimulated the search for new drug leads from medicinal plants. We investigated extracts from twenty-six plants and seven pure products for antiplasmodial activity against P. falciparum F 32 (chloroquine-sensitive) and field (patient) isolates by in vitro inhibition of erythrocyte invasion and also for toxicity. Thirty–five out of 41 crude extracts (85%) demonstrated a wide ranging activity against F 32 trophozoites. Two methanol extracts from Odyendyea gabonensis (Simaroubaceae) and Bersama engleriana (Meliaceae) were highly active with IC₅₀s of 1.8 and 2.7µg/ml respectively and were also highly active on schizonts. Phytochemical analysis revealed the presence of sterols, flavones and alkaloids in B. engleriana leaves. One fraction and one pure product from B. engleriana leaves were highly active on the field parasites with IC₅₀s of < 2.5 and 4.3 µg/ml respectively. Five highly active extracts (IC₅₀ < 30 µg/ml) were not cytotoxic on lymphocytes and 3 from Scoparia dulcis, Terminalia superba and Ficus exasperata significantly inhibited lymphocyte proliferation (P<0.05). B. engleriana was the least toxic with lower cytotoxicity than chloroquine. No acute toxicity was observed in 6N C57 BL mice for the pure products and highly active extracts. In conclusion, the plants with high antiplasmodial activity with apparent lack of toxicity can be exploited in the development of traditional herbal medicine and in the search for suitable leads for pharmaceutical medicines for effective treatment of malaria.
54. IDENTIFICATION OF A PUTATIVE ANTI FUNGAL DRUG TARGET—CANDIDA ALBICANS

CANDIDA ALBICANS.

SUN41

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Candida albicans is a fungus that colonizes human skin and oral, digestive and vaginal tracts. In hosts made susceptible by HIV/AIDS, pharmacological, or device-related factors, it causes a wide range of infections. Here, we investigated the roles of surface proteins in C. albicans pathogenesis and treatment. We disrupted 21 surface protein genes using targeted insertional mutagenesis. Mutants were screened for changes in biofilm formation and tolerance to the cell wall-perturbing agent caspofungin. Insertion mutations in SUN41, Orf19.5412, Orf19.1277, MSB2, Orf19.3869, and WSC1 resulted in increased sensitivity to caspofungin, while ECM33 insertions caused mild resistance. Insertions in SUN41 and Orf19.5412 caused defects in biofilm formation. Through more focused analyses of sun41Δ null, sun41Δ+pSUN41 reconstituted, and wild-type strains, we confirmed that SUN41 is required for caspofungin tolerance and biofilm formation. Moreover, RT-PCR revealed altered expression of genes responsive to cell wall damage in the sun41Δ mutant, underscoring a role for Sun41 in cell wall integrity. To investigate the role of Sun41 in pathogenesis, we studied our strains in murine disease models. We discovered that Sun41 is critical for disseminated and oropharyngeal candidiasis in mice. Sun41, therefore, has features that make it a putative antifungal drug target: it is required for C. albicans cell wall integrity, biofilm formation and pathogenesis; it is a surface protein accessible to the extracellular milieu; it contains a fungal-specific SUN domain. As Sun41 homologs are present in Candida glabrata, Aspergillus fumigatus, and Coccidiodes immitis, drugs that target Sun41 might prove useful for treating a variety of fungal diseases.

55. AN ANTI-MYCOBACTERIUM PRINCIPLE FROM THE EXTRACT OF CUSSONIA ARBOREA HOCHST. EX A. RICH. (SYN. C. BARTERI SEEM)

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As part of our search for drugs/leads from plants, a preliminary investigation of an aqueous methanol extract of the stem bark of C. arborea used in indigenous tradition recipes for the treatment of the symptoms of tuberculosis, showed activity on Mycobacterium bovis BCG (BCG) with an MIC of 931ug/ml by broth dilution technique. Based on this promising result serial extracts were prepared of the stem bark with hexane, ethyl acetate and methanol. The extracts from hexane, ethyl acetate and methanol had MIC values 400ug/ml, 200ug/ml, 400ug/ml on BCG and 200ug/ml, 100ug/ml, 200ug/ml on Mycobacterium tuberculosis (M.tb) respectively. Bioassay-guided fractionation of the ethyl acetate extract of the stem bark by HPLC, gave a fraction which was found to be active against BCG with an MIC of 7.80ug/ml and against Mycobacterium tuberculosis (M.tb) with an MIC of 6.20ug/ml. The chemical structure of the active compound as derived from its spectra is discussed.
The parasitic protozoa *Trypanosoma* and *Leishmania* are the causative agents of the highly disabling and often fatal diseases, such as African sleeping sickness, Chagas’ disease and leishmaniasis. Millions of people are at risk in the areas of Africa, South America and Asia where these diseases are endemic. Unfortunately, current drugs are far from satisfactory as they often possess toxic side effects, are ineffective against certain disease forms and may require expensive administration procedures; in addition, resistance to these drugs is becoming an increasingly common problem. Glycolysis appears to provide an excellent therapeutic target because it is essential to bloodstream form Trypanosomatidae as the only catabolic source of ATP. Furthermore, due to the evolutionary distance between Trypanosomatidae and humans, the parasite enzymes within the pathway possess distinct properties that differentiate them from their mammalian counterparts, and which could be exploited in the design of parasite specific drugs. The unique organization of the glycolytic pathway in trypanosomatids, with most of the enzymes present in peroxisome-like organelles called glycosomes, is correlated with exploitable differences. Thus, the compartmentalization has resulted in different kinetic properties and activity regulation mechanisms that correspond to differences in enzyme structure. Here, we report the design and the synthesis of inhibitors targeted against *Trypanosoma brucei* phosphofructokinase (PFK) and Glyceraldehyde-3-phosphate dehydrogenase (GAPDH). For the first enzyme, a stepwise synthesis and inhibitor design from a rational starting point identified furanose sugar amino amides as a novel class of inhibitors for this enzyme. The synthesis of GAPDH Inhibitors was inspired by both substrate structure and pharmacophoric moieties present in two known naturally occurring GAPDH inhibitors. Trypanocidal activity showed potency in the low micromolar range and confirms these inhibitors as promising candidates for the development towards the design of anti-trypanosomal drugs.
scientists believe that early studies in human are of more value than extended tests on animals whose metabolism is quite different from Homo sapiens. In practice, what happens today is that as toxicity testing in animals progresses through the various phases, sufficient data emerge to permit experiments to be safely conducted on healthy human volunteers and permission must first be obtained from the regulatory authority. The objective of the volunteer studies is to obtain an idea of how the human body deals with the new drug which after all, is a foreign compound. The decision to test any new drug on patients presents an ethical problem since neither its absolute safety nor its efficacy can ever be guaranteed. The decision requires a properly constituted drug regulatory body to make an informed decision. The regulatory body has to be familiar with CIOMS and WHO guidelines for biomedical research involving human subjects and for research and evaluation of traditional medicine. Lastly, clinical trials are not enough during drug development. Pharmacopoeiology is an essential tool for proper drug development.

58. DEVELOPMENT OF QUALITY CONTROL SPECIFICATIONS FOR THE RAW MATERIALS OF AN ANTISICKLING PHYTOMEDICINE, NIPRISAN®

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Niprisan, an antisickling phytomedicine, developed in Nigeria, is a freeze dried preparation of *Piper guineense* seeds, *Eugenia caryophyllata* flower buds, *Pterocarpus osun* stem, and *Sorghum bicolor* leaf stalk. In addition to the botanicals, the preparation contains a mineral, trona. All the five components are locally sourced. The data presented cover attempts at developing quality specifications for the components. For the botanicals, the methods employed were of the World Health Organization (WHO, 1998). For trona, the methods were of the British Pharmacopoeia (BP 2003). For the botanicals, the results of loss on drying [w/w], total ash [w/w] and water extractable matter [w/w] were: *Piper guineense* seeds, 6-10%, 8-18% and 13-27%; *Eugenia caryophyllata* fruit buds, 7-9%, 3-7% and 26-36%; *Pterocarpus osun* stem, 5-7%, 0.9-6% and 2-4%; and *Sorghum bicolor* leaf stalk, 7-9%, 4-13% and 8-14%. For trona, the loss on drying was 21-36%, while the concentrations of anions were: bicarbonate, 7-18mg/kg; carbonate, 27-36mg/kg; sulfate, 0.6-2.1%w/w; and chloride, 6-8%w/w; and cations [w/w] were: lead, 0.0000-0.0004%; zinc, 0.0003-0.0015%; manganese, 0.004-0.008%; copper, 0.0006-0.0017%; magnesium, 0.012-0.017%. The results are discussed in the context of standards to be adopted in approving the components. Recommendations on procurement and pretreatment of the materials prior to manufacturing are also proffered.

59. THE ICGEB AND CAPACITY BUILDING IN BIOTECHNOLOGY

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The International Centre for Genetic Engineering and Biotechnology (ICGEB) is an intergovernmental organization originally created as a special programme of the United Nations Industrial Development Organization (UNIDO) to provide a Centre of excellence for research and training in genetic engineering and biotechnology with special focus on the needs of the Developing Countries. Located in two sites: at the AREA Science park in Trieste, Italy and New Delhi, India, and with a network of Affiliated Centres in 37 Member States, the Centre is dedicated to advanced research and training in molecular biology and biotechnology and holds out the prospect of advancing knowledge and applying the latest techniques in the fields of public health, energy production, industrial production of high added-value commodities, agriculture, nutrition and environmental protection/remediation. ICGEB provides a scientific and educational environment of the highest standard; it brings biotechnology to developing countries by strengthening their research capabilities and develops state-of-the-art research of importance for bioindustries in Member States. Specific research programmes of high scientific content are in progress.
in the laboratories located in Trieste, Italy and New Delhi, India, addressing both basic and applied research problems, with particular attention to those pertinent to the developing world, among which are the production of novel malaria and hepatitis vaccines, the study of human pathogenic viruses, the study of human genetic diseases and the genetic improvement of plants. ICGEB’s training programmes have a far-reaching impact on its Member States, encompassing not only individual junior and senior scientists but also involving established research laboratories in ICGEB Affiliated Centres.

60. THERAPEUTIC EFFECTS OF EXTRACTS OF SOME AFRICAN MEDICINAL PLANTS IN EXPERIMENTAL AFRICAN TRYANOSOMIASIS

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Human African trypanosomiasis (Sleeping sickness), caused by Trypanosoma brucei, is 100% fatal if untreated. Prevention remains a mirage due to antigenic variation and a variety of socio-economic factors. Chemotherapy therefore remains a major control measure. The available drugs at the moment are severely limited by a variety of problems, which render current therapies grossly inadequate. Therefore there is an urgent need for new drugs. In our preliminary studies, leaves, stem, and root barks of Annona senegalensis and Eucalyptus camaldulensis were extracted in hexane, ethylacetate, methanol, and water. Garcinia kola fruits were extracted in 50% methanol. Aqueous extracts of A. senegalensis leaves at a dose of 200mg/kgBW cured experimental Trypanosoma brucei infection in mice as blood and cerebrospinal fluid (CSF) infectivity tests failed to produce infection. Hexane and aqueous extracts of the stem bark of A. senegalensis also cured experimental T. brucei infection in mice and blood and CSF infectivity tests failed to produce any infection. A combination of methanolic extracts of the leaves of A. senegalensis and E. camaldulensis cured experimental T. brucei infection in mice. Although very preliminary, these findings are indicative of the enormous potential of obtaining antityranosomal drugs that may be capable of overcoming the drug resistance problems in sleeping sickness chemotherapy. Methanolic extract of Garcinia kola fruits kept parasitemia in mice as low as between 9 cells per microscope field for about 5 months after stoppage of treatment. The implication of this finding in cell cycle progression in Trypanosoma brucei is currently being investigated.

61. IS QUALITY THE KEY TO SUSTAINABLE, CREDIBLE AND PRODUCTIVE DRUG/DIAGNOSTICS PRODUCT R&D AND INNOVATION PROGRAMS IN AFRICAN INSTITUTIONS?

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At first glance, the answer to the question “Is Quality the Key to Sustainable, Credible and Productive Drug/Diagnostics Product R&D and Innovation Programs in African Institutions?” would seem to be “maybe”, “not entirely”, or “I am not so sure”. Is Quality really “the key” to making Solomon Nwaka’s call: «Developing countries need to participate in discovering, developing and manufacturing their own drugs» a reality in African Institutions? Is money not the real key? This presentation hopes to make the case that “Quality” is the lone imperative for creating sustainable, credible, and productive drug or diagnostics product R&D and innovation programs in African Institutions. By adapting definitions of “Quality” and “Quality Assurance” from the ICH Guidelines, the argument is made that “Quality” and “Quality Assurance” are not mere down stream activities, but in fact are the essence of every phase of sustainable, credible and productive drug/diagnostics product research, development and innovation. In resource poor, infrastructure limited, and potentially isolated product research programs, such as may exist in some African Institutions, Quality emerges as the “sine qua non” for productivity and sustainability.
Some component elements of Quality, their impact, and the potential implications of ineffective scientific QA/QC processes in drug/diagnostics product R&D and innovation programs in African Institutions will be highlighted. Possible ways to address the issues raised will be suggested.

62. RESEARCH ACTIVITIES OF AFRICAN INSTITUTE OF BIOMEDICAL SCIENCE AND TECHNOLOGY RESEARCH LABORATORY (AiBST/UON)

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AiBST/UON laboratory is housed within the Department of Pharmacology and Pharmacognosy, University of Nairobi, Kenya. It is part of the AiBST network which is a collaborative effort between biomedical researchers drawn from Zimbabwe and Nigeria. The vision of the AiBST/UON laboratory is to be a centre of excellence in biomedical research. The objectives of the laboratory are: to build capacity in biomedical research through post-graduate training; to provide specialized medical services such as bioequivalence studies and therapeutic drug monitoring; and to carry out basic and applied medical. The research areas of interest are in vitro drug metabolism studies, pharmacogenetics, in vitro and in vivo screening for antimalarial activity, in vivo pharmacokinetic and drug toxicity studies. Currently one postgraduate student is pursuing her postgraduate studies in pharmacogenetics. Two proposals have been developed for funding in vivo antimalarial investigations of investigational antimalarial agents and for a bioequivalence study. The establishment of the laboratory has faced a number of challenges such as understaffing and under funding. The AiBST/UON looks forward to collaborative arrangements with all interested parties.

63. NOVEL ANTIMALARIAL OXIDATION PRODUCT OF GEDUNIN

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Gedunin is a tetrnortriterpenoid and a limonoid derivative. Gedunin was isolated from the petroleum ether (40-60) extract of the sawdust of the heartwood of 

*Entandrophragma angolense* (Welw.) CDC of the family Meliaceae as previously reported. The results of spectroscopic analyses of the gedunin crystals obtained were consistent with published work. Gedunin potassium salt was synthesized from the reaction of the gedunin with aqueous methanolic potassium hydroxide. The Gedunin potassium salt obtained was oxidized with 1% w/v potassium permanganate solution at pH 8.0 to give three products one of which is gedunic acid. This is the first time H-nmr and C-nmr of gedunic acid is reported. Another of the three products was found to be more hydrophilic than gedunin and exhibited improved in vivo antimalarial activity in mice producing 91% clearance of parasitaemia at 50mg per kg per day for four days compared to that previously reported for gedunin and 7 methoxygedunin. INTRODUCTION Gedunin, has been reported to be the antimalarial principle in *Azadirachta indica* (neem) and many other plants of the Meliaceae family. The lipophilic nature of gedunin has been shown to limit its antimalarial activity. The present work aim to improve the hydrophilic nature of gedunin and investigate the antimalarial activity of the new products obtained through structure activity relationship studies (SARS). MATERIALS AND METHODS To obtain gedunin the sawdust of the heartwood of *Entandrophragma angolense* (Welw.) CDC of the family Meliaceae was extracted with petroleum ether (40-60) by soxhlet extraction as previously reported. Spectroscopic analyses of the gedunin crystals obtained was carried out. Gedunin potassium salt was synthesized from the reaction of the gedunin with aqueous methanolic potassium hydroxide. The Gedunin potassium salt obtained was oxidized with 1% w/v potassium permanganate solution at pH 8.0 to give three products. The three products were purified by column chromatography on silica gel and prep. tlc. The structures were determined using spectroscopic techniques and their antimalarial activities determined in vivo in mice against *Plasmodium berghei*. RESULTS AND DISCUSSION The structure of gedunin crystals obtained was consistent with published data. One of the oxidation products of gedunin...
potassium salt was found to be gedunic acid. This is the first time the Hnmr and C-nmr of gedunic acid is reported. Another of the three products was more hydrophilic than gedunin and exhibited improved in vivo antimalarial activity in mice producing 91% clearance of parasitaemia at 50mg per kg per day for four days compared to that previously reported for gedunin. CONCLUSION This result demonstrates the potential value of antimalarial drugs and phytomedicines based on gedunin and its derivatives.

64. GEDUNIN, A POTENTIAL DRUG AND DRUG LEAD FOR MALARIA AND OTHER DISEASES WITH A STATEMENT ON THE ANTIMALARIAL HYPOESTOXIDE

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Gedunin 1 has exhibited a number of biological activities. The most significant being its antimalarial activities. Limited structure-activity antimalarial studies have been carried out in vitro. The recent finding that gedunin is destroyed in the liver by cytochrome P450 and that the use of dillapiol allows the hitherto in vivo inactivity in mice to be reversed signifies the need for further antimalarial medicinal chemistry investigation of gedunin derivatives. Its complex structure and multiple functional groups make it a good compound for isolation in large quantities, a starting material for many conversion products and hence structure-activity studies in various screening models. Over thirty different conversion products can be made from gedunin for biological investigations. Old and unpublished chemistries of gedunin which include reduction, oxidation, electrophilic substitution, and rearrangement reactions are discussed. Gedunin is thus suitable for training and practice in the area of synthetic medicinal chemistry for drug discovery projects. To exemplify problems at the highest level faced in drug development efforts in Africa, a statement is made on hypoestoxide – a relatively non-toxic antimalarial that is much more potent than artemisinin, chloroquine and mefloquine.

65. IDENTIFICATION OF A NOVEL PROTEIN, SAGLIN, AS A POTENTIAL SALIVARY GLAND MEDIATOR FOR PLASMODIUM SPORozoITE INVASION

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We are interested in understanding the molecular mechanisms involved in the interaction between malarial sporozoites and putative receptor(s) on the salivary glands of A. gambiae. In previous studies, a protein of ~100 kDa recognized by monoclonal antibody 2A3, capable of reducing the number of sporozoites in P. yoelii infected mosquitoes fed 2A3 mAb displayed a = 70% reduction in the average number of sporozoites per infected salivary gland. Biochemical characterization of the 100 kDa protein was undertaken and it was found to exist as a disulfide bonded homodimer of 50 kDa subunits. By mass spectrometric analysis, we obtained several peptide sequences which when blasted against A. gambiae genomic sequence database identified a gene encoding a novel protein of 412 amino acids. The deduced amino acid sequence revealed the presence of a signal peptide sequence, suggesting it to be a secreted protein. We have designated this protein as SAGLIN. The gene encoding SAGLIN was cloned into a mammalian expression vector and HA-tagged recombinant SAGLIN expressed in 293T cells was affinity purified and characterized biochemically. His tagged recombinant SAGLIN was also expressed in E. coli for immunizing BALB/C mice for antisera production.
**66. IN VITRO ANTIPROTOZOAL ACTIVITY OF ETHNOMEDICALLY SELECTED PLANTS FROM WEST AND CENTRAL AFRICA**

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In our continuing efforts to search for novel anti-infective agents from plants implicated in traditional medicine, we have selected and screened plants traditionally used in West and Central Africa to treat a wide range of protozoal diseases including malaria, African sleeping sickness, leishmaniasis and trichomoniasis. A total of 1200 plant extracts derived from 253 plant species from 80 plant families were tested for *in vitro* antiplasmodial activity against chloroquine-sensitive (D6) and chloroquine-resistant (W2) strains of *Plasmodium falciparum*. The antileishmanial activity of 113 extracts were evaluated using two test systems namely Radiorespirometry technique and Cytosensor Microphysiometer while the 61 extracts were tested *in vitro* for their antitrypanosomal activity using *Trypanosoma b. brucei*, EATRO 110, *Trypanosoma rhodesiense* KETRI 243, *T. rhodesiense* 243 As 10-3 bloodstream forms (strains). The activity against Trichomonads was determined with strains of *Trichomonas vaginalis* C1-NIH (ATTC 30001) and a metronidazole-resistant strain, CDC-085 (ATCC 50143). In each assay, the IC50 value for each sample was derived by the drug concentration-response curves. Our recent efforts in the identification of new antiprotozoal pharmacophores from West and Central African plants have yielded promising results. New ‘leads’ from plants used in traditional medicine for malaria, trypanosomiasis, leishmaniasis and Trichomoniasis were discovered. The results indicate that several medicinal plants used in traditional medicine against protozoa revealed strong antiprotozoal activity in *vivo*. Of the 1200 plant extract samples tested for antiplasmodial activity, 53% showed remarkable activity The most active antiplasmodial extracts were those from 17 plant species with IC50 < or = 3 micrograms/mL. Among the 113 tested extracts, 52(39%) showed antileishmanial activity; 47 out of 61 samples were active against *Trypanosoma spp* and 26(63%) out of 41 samples were active against *Trichomonas vaginalis*. The diverse antiprotozoal compounds isolated from the following plants: *Aframomum meleguata*, *A. auricocarpus*, *Araliopsis tabouensi*, *Chasmanthera dependens*, *Picralima nitida*, *Enantia chlorantha*, *Glossocalyx brevipes*, *Hypitis suaveolens*, *Milletia griffoniana*, *Morinda lucida*, *Odyendeya gabonensis*, *Penianthus longifolius*, *Picralima nitida*, *Gomgronema latifolia*, *Spathodea campanulata* and *Xymalos monospora*, will be discussed. African traditional medicine is a rich source of natural compounds and a powerful tool for the development new anti-protozoan agents.

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**67. LARGE-SCALE ISOLATION AND PURIFICATION OF ANTIPROTOZOAL COMPOUNDS FROM NIGERIAN MEDICINAL PLANTS BY COUNTERCURRENT CHROMATOGRAPHY**

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Using the conventional adsorption chromatography, several attempts to isolate large quantities of pharmacologically active natural products required for clinical trial and chemical optimization have failed; due to irreversible adsorption of these compounds onto the solid stationary phase. As part of our continuing research aimed at identifying new antiprotozoal leads from African medicinal plants, we have been highly...
successful in employing counter-current chromatography (CCC) to separate and isolate natural product compounds in multi-gram quantities in several hours. Counter-current chromatography is a support-free liquid–liquid partition chromatographic technique. It relies simply on the partition of a sample between the two phases of an immiscible solvent system. CCC technique provides various special features such as yielding highly concentrated fractions, concentrating minor impurities for detection, and allowing the separation to be monitored by the pH of the effluent in the absence of chromophores. Improvement of the CCC methods in recent years has resulted in high speed counter-current chromatography (HSCCC), pH-zone-refining CCC, and a new kind of support free all-liquid partition chromatography–Spiral Tube High Speed–CCC. The present paper describes large scale isolation and purification of antimalarial monoterpen indole alkaloids (alstonine, akuammigine, akuammine, picraline, akuammine, akuammicine, picratidine) from the fruit pulp of *Picralima nitida* and antileishmanial pennoigenin saponin from *Dracaena mannii* by HSCCC. It also covers the recent application of pH-zone-refining on Spiral Tube assembly that yielded more antiplasmodial biflavonoids GB-1, GB-2 and kolaflavonone from *Garcinia kola* seeds than normal phase CCC.

68. NEW ANTIMALARIAL CANDIDATES FROM WEST AND CENTRAL AFRICAN PLANTS: AN IN VITRO APPROACH USING *PLASMODIUM FALCIPARUM*

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In 1990, Bioresources Development and Conservation Programme (BDCP) initiated a collaborative *in vitro* antimalarial screening programme with Walter Reed Army Institute of Research (WRAIR) to discover both plant extracts and new natural products as potential antimalarial agents. Plant materials used in African ethnomedicine in the treatment of malaria and/or fever were identified and collected from 1992 to 2004 and stored at the BDCP plant database. A total of 1200 plant extracts derived from 253 plant species from 80 plant families were tested for *in vitro* antimalarial activity against chloroquine-sensitive (D6) and chloroquine-resistant (W2) strains of *Plasmodium falciparum*. The technique measures the ability of the extracts/compound to inhibit the incorporation of [G-3H] hypoxanthine into the malaria parasites. The active plants extracts were subjected to bioassay-directed fractionations leading to the isolation of the antimalarial compounds. Isolated antimalarial pure compounds were identified by spectroscopic methods (UV, IR, MS, LS-MS, 1H-NMR and 13C-NMR). The antimalarial data are stored in our computerized. Database of African Medicinal Plants, AfricMed at BDCP. Our results indicate that several medicinal plants used in traditional medicine against malaria/fever revealed strong antiplasmodial activity in vitro. Out of the 1200 plant samples belonging to 80 plant families and 253 species tested for antiplasmodial activity, a hit rate of 53% was achieved. The assays indicate that extracts from members of the families Annonaceae, Apocynaceae, Asteraceae, Fabaceae, Simaroubaceae, Zingiberaceae, Monimiaceae, Euphorbiaceae, Combretaceae Menispermaceae, Meliaceae and Lepidobotryaceae, were among those that strongly inhibited the growth of CQ-sensitive (D6) and CQ–resistant (W2) clones of *P. falciparum*. The most active extracts were those from 17 plant species with IC50 ≤ 3 micrograms/mL. Bioassay-directed chromatographic fractionation of the above active extracts using modern chromatographic techniques (HPLC, GC-MS, Lobar, DCCC) led to the isolation and characterization of many classes of anti-plasmodial compounds including alkaloids, limonoids, polyphenolic compounds, diterpenes, sesquiterpene lactones, lignans, quassinoids, saponins, flavonoids, and anthraquinone derivatives. A total of 100 compounds and their semi-synthetic analogs have confirmed in vitro antimalarial activity against *P. falciparum*. The results confirm the antimalarial potentials of these plants and thus justify their use in traditional medicine in Africa. The diverse antimalarial structures isolated from the 17 active plant species will be discussed.
69. DISCOVERY OF SMALL SOLID SUBSTANCES (TERMED MAGGOTS) EGESTED BY HIV POSITIVE PATIENTS DURING HERBAL TREATMENT

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Issues: Discovery of small solid substances (termed Maggots) egested by HIV positive patients upon commencement of curative therapy for HIV 1 & 2, AIDS and other terminal diseases such as cancer, hypertension, diabetes. Description: A recommended dose of two herbal formula [brand named Staphvo 1 & 2 liquid combined with Staphvo powder produced purely from herbs] was administered on 250 HIV positive patients for curative treatment of HIV/AIDS. 80% of patients reported that they egested small solid substances (i.e. Maggots) eight hours post administration of the starting dose. Egestion in patients lasted varying number of days due to different level of infection. Lessons learned: A thorough study of the maggots without the aid of any microscope revealed three different shapes of maggots as: Guinea corn shape maggots, short worm like shape (termed semi-maggots) and the real maggot shape (termed full maggot). The semi and full maggots have a pointed anterior, brown in colour in the full maggot. The full maggot is prominently distinguished from the semi by a pair of four tiny suckers attached to reach side of its body and its cream colour. The guinea corn shape maggot is distinguished by shape and white colour. During monitoring of responses to complete treatment (a period of six months) it was observed that the period of time for complete egestion of maggots is directly related to the level of HIV infection. Most patients experienced a relief of symptoms associated with HIV infection on completing the egestion of maggots, and cure of opportunistic infections few months later. The monitoring revealed that most female patients egested the guinea corn shaped maggots while the full blown AIDS patients (CD4 <150) egested the full maggots. Next steps: Clinical assessment of HIV/AIDS positive patients currently placed on the curative herbal therapy is on-going in order to confirm claims of cure.

70. HIV DIAGNOSTICS (DNA PCR & SEROLOGY), VIRAL LOAD (HIV, HBV, HCV), HOST-PATHOGEN INTER-RELATIONSHIPS, GENOTOXICITY OF ARVS

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NO ABSTRACT

71. ASSESSING THE CHALLENGES AND REMEDIES TO THE RISING CASES OF ANTIBiotic RESISTANCE

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MOTIVATION: It is pertinent to note that since the dawn of the antibiotic drug era, resistance has shadowed the success of infectious disease therapy. Illegal, illicit and over-the-counter administration of these antibiotic drugs have been a major concern in the health scheme as it has given rise to substantial increase in resistant but curable diseases. PROBLEM STATEMENT: The illicit and immoral use of these antibiotic drugs have led to the medical challenge on major diseases such as major microbial diseases, some viral diseases, malaria, tuberculosis, etc. The resistance to chemotherapy of these diseases has been so tasking, and it is necessary that the importance of the appropriate use of antibiotic drugs as well as the difficulty of enforcement including public knowledge and lecture should be put in place. APPROACH: Adopting a community and hospital-based survey of a person-to-person type amongst health care givers and consumers alike. This was to assess the challenges and risks involved in self medication and to profer solutions to the immoral use of these antibiotic drugs. RESULTS: It was found
out that most people purchase these drugs from road-side chemists on a hear-say basis that these drugs can actually relieve them of their present complaints without having to see a doctor, where the services and health care delivery are so unsatisfactory. Government health policies also haven’t done enough to enforce the law on these illicit practices knowing fully well its complications. CONCLUSIONS: In the words of Alexander Fleming, «It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body... Moral: If you use penicillin, use enough». Infection control, prudent use of antibiotic drugs, and new drug development hold solution to antibiotic resistance.

72. EXPLORING BIOINFORMATICS, MOLECULAR DYNAMICS AND COMBINATORIAL CHEMISTRY APPROACHES IN DRUG DEVELOPMENT

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On a daily basis, technology evolve with the aim of widening the horizons of innovation in the field of drug development and computer technology has become domineering in the field of current trends of in-silico drug discovery. Data analysis is the act and manner of transforming data with the aim of extracting useful information and facilitating the ability to draw wise conclusions. To this end, algorithms are designed and coded for computer, followed by Bioinformatics for analysis of biological data. Malaria is the second largest killer disease after AIDS especially in sub-Saharan Africa. More worrisome is the issue of resistance to the antimalarial drugs chloroquine and sulfadoxine-pyrimethamine which is now so high in parts of Africa that both drugs are virtually useless. While Combinatorial Chemistry has achieved little successes in some disease like AIDS, more is desired for antimalarials. In this work, we explore the convergence of Bioinformatics and Molecular dynamics tools development. We also identify the yawning gaps among Bioinformatics, Molecular Dynamics and Combinatorial Chemistry in archiving drug development and proffer possible remedies. With the knowledge of the complexity of biological systems and the difficulty to follow in detail the bioactivity of a drug and it’s interaction within an organism, modeling approaches becomes more relevant with QSAR (Quality Structure-Activity Relationship) in focus. This war against diseases of poverty is surmountable in-silico for onward application in vitro and finally in vivo.

73. A PROPOSAL FOR AN OPERATIONAL DATABASE STRUCTURE FOR THE AFRICAN NETWORK FOR DRUG/DIAGNOSTICS DISCOVERY AND INNOVATION (ANDI) PROJECT

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A workable, robust and flexible relational database structure for the acquisition, archiving and retrieval, manipulation and utilization of data and documents (ODBS) derivable from and related to the development process for drug and diagnostic products discovery and innovation project (ANDI) is presented. The establishment and management of this ODBS will involve highly technical knowledgebase for decision making mostly because the objectives and modus operandi of the ANDI project requires presentation of a modest advancement over existing international phytodrug development database. Inclusion of diagnostics development methods and products represents advancement over many available global records. In this proposal, original development data of organic, inorganic and biological origin acquired from participants in the ANDI project, transformed into database variables and records, created and formatted consistent with ANDI objectives and expected outcomes. Records of data and documents generated from ANDI project participants from around the world will be developed using contemporary database software (for example, “DataBase Professional” by MySoftware/Avanquest, Elk Grove, California, USA or Microsoft Access®). The flexible records structure will be internet-based and regularly
backed up on digital high density storage facilities. Data and documents in the proposed structure of
the records will be available to stakeholders and may provide new opportunities for public and private
scientists and institutions interested in product R&D in Africa.

74. IN VITRO ANTIBACTERIAL ACTIVITY AND ACUTE TOXICITY
OF AQUEOUS-METHANOL EXTRACT OF SIDA RHOMBIFOLIA LINN. (MALVACEAE)

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The aim of this research was to investigate the in vitro antidiarrhoeal, antibacterial and acute toxicity
effects of the aqueous-methanol extract from Sida rhombifolia Linn (Malvaceae). Methanol and other
aqueous methanol extracts of S. rhombifolia were screened for their antibacterial activities against
seven pathogenic bacteria involved in diarrhoea. The results indicated that: 1) the inhibition zone
produced by the test ranged from 8 to 23 mm, 2) the aqueous-methanol extract (1v:4v) was the most
active while Salmonella dysenteriae was the most sensitive to all the extracts tested for antibacterial
activities. No death of rats was recorded for the acute toxicity. However, significant increasing of some
biochemical parameters such as aspartate aminotransferase (AST), alanine aminotransferase (ALT),
alkaline phosphatase (ALP) and creatinine (CRT) were revealed. Moreover the phytochemical analysis
of the aqueous methanol extract indicated the presence of tannins, polyphenols, steroids, glycosides,
flavonoids and saponins. The overall results suggested that the aqueous–methanol extract of S.
rhombifolia exhibited in vitro anti-diarrhoea antibacterial activity

75. THE ROLE OF THE UNIVERSITY IN DRUG DISCOVERY FOR NEGLECTED DISEASES

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There is mounting interest in R&D for neglected diseases globally, highlighted by a recent $350 million
pledge towards research and control efforts. However, African and American universities that perform
high risk, upstream research continue to have difficulty translating their drug discoveries into therapeutics.
Challenges include a tortuous and contentious technology transfer system and lack of coordination
of likeminded researchers across the Atlantic. Universities Allied for Essential Medicines (UAEM) is a
start up NGO that seeks (i) to facilitate socially responsible licensing of university discoveries to enable
development of medicinal compounds by partners in resource-poor settings and (ii) to develop a global
platform for neglected disease research by targeting young scientists and trainees. UAEM is building
the first online, open access curriculum on neglected diseases and is in consultation with the Bill &
Melinda Gates Foundation for a university-sponsored alliance on neglected diseases. Our proposals
are supported by ten Nobel Laureates and over 2300 people at over150 institutions globally (www.
essentialmedicine.org/cs), but our presence has been limited to industrialized countries. We now seek a
presence in African universities.
76. SBSC/TBRI, CAIRO AS A SCREENING CENTER FOR FASCIOLIASIS IN AFRICA

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Fascioliasis is a well known veterinary problem which is to date an emerging human disease: the World Health Organization (WHO) has estimated that 2.4 million people are infected with *Fasciola*, and a further 180 million are at risk of infection. In Africa, the highest prevalence was recorded in Egypt especially in communities living in the Nile Delta. The drug used for treatment of this disease is Triclabendazole which needs further studies of its safety and efficacy. Meanwhile resistance of *F. hepatica* to this drug has already been recorded in Australia. This necessitates the discovery of other drugs against this important disease. Successful trials for maintaining the life cycle of the common species in Egypt *Fasciola gigantica* in the laboratory utilizing *Lymnaea natalensis* snails and clean sheep produced in the Animal Production Research Institute, Giza Egypt, have been carried out in the SBSC. Therefore, this facility can offer a suitable place for drug discovery research on fascioliasis by testing chemical compounds and natural plant extracts for their potential antifascioliasis effect both *in vitro* and *in vivo*. It can also participate in studies for discovery of immunodiagnostics.

77. CHALLENGES AND OPPORTUNITIES IN IDENTIFYING A LEAD COMPOUND FROM PLANTS FOR DEVELOPMENT AS ANTI-MALARIAL DRUG

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The treatment of malaria in Africa is becoming increasingly difficult due to the rising resistance of *Plasmodium falciparum* to antimalarial drugs. The discovery of quinine and artemisinin from plants stimulated interest in the search for new antimalarials from plants. Africa is rich in natural resources with wide variety of medicinal plants, some which are used in traditional medicine for the treatment of malaria and other diseases. Some studies in search of new antimalarials from plants have been going ongoing. However there are many challenges encountered. These challenges makes it difficult to identify many candidate compounds. First most African scientists do not get access to finances and equipment required to do the research. Even where finances are available, many a times the funds are not sufficient to carry all the necessary preclinical studies. Human resource may also be a limiting factor. To overcome some of these limitations opportunities exist such as establishing a coordinated network for drug discovery so that different laboratories in Africa are working in harmony rather than singly and in isolation. Such a network would have screening centres whose capacity will be facilitated and enhanced to serve African Scientists and probably the rest of the world. This way the individual strain and frustration in search for funds and qualified manpower will be reduced. WHO/TDR has in the recent years made efforts in an attempt to establish such centres in Africa to function as anti-malarial and phytochemical screening Centres. Kenya is one the proposed screening Centres in the network and already carrying on the screening work. In this meeting details of how the anti-malarial screening Centres are expected to operate will be discussed.
78. Evaluation of Hypoglycemic Properties of Some Selected Herbs Using Alloxan-Induced Diabetic Rats

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Diabetes is a metabolic disorder where the pancreas does not produce enough insulin to process glucose or the insulin receptors are not working properly. It is the fourth leading deadly disease worldwide. In 1995, about 84 million people were affected and by 2025, the number will increase to 228 million worldwide. Currently, the orthodox drugs in use have serious side effects hence the need for alternative or tradomedical means of managing the disease. In this study, the antidiabetic effects of aqueous extracts of some selected plants namely: Zyzzipus spinachristi (900 mg/kg bwt), Blighia sapida (400mg/kg bwt) Anacardium occidentale (300mg/kg bwt). Moringa oleifera (500mg/kg bwt), Terminalia glaucescens (550mg/kg bwt) and Artemisia herba-alba (525mg/kg bwt) were investigated using Alloxan-induced diabetic rats. At the end of 6 weeks, the aqueous extract of Anacardium occidentale at 300mg/kg bwt had the highest hypoglycemic effect (74.2%) compared to the other plants investigated. The sequential extraction of the same plant was carried out and also investigated. The investigation revealed that the ethanolic extract of Anacardium at 200mg and 300mg/kg bwt had the highest hypoglycemic effect (31.1% and 20.2%) compared to hexane, ethylacetate and ethylacetate/ethanol (1:1) ratio. The ethylacetate extract of partially purified ethanolic extract also had the best hypoglycemic effect when compared with other extracts and the standard hypoglycemic drug, metformin. The ethylacetate/ethanol (1:1) ratio and ethanolic extracts were also found to have antibacterial activities when tested on Salmonella, Staphylococcus and Klebsella species.

79. In Vitro Pharmacological Study of Natural Products From Medicinal Plants Within the Framework of Antimalarial Drugs Research and Development

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Following the resistance phenomenon of parasites the development of new, effective and affordable antimalarial molecules becomes an urgent challenge. Among the natural substances isolated from medicinal plants, those which have been reported to have an antiplasmodial activity in vitro constitute a potential source of new antimalaria drugs. Our ethno-pharmacological study aims to seek plants with great antimalaria potential. The extracts and molecules have been obtained by analytical and preparative chromatography and described by Resonance Magnetic Nuclear and Mass Spectrometry. Antiplasmodial tests have been done with Plasmodium falciparum chloroquine-resistant W2 strain. Parasite culture was carried out according to Tragger (1976) protocol and the IC50 was determined. Toxicity effect of natural product has been determined by THP1 cells and DNA methyl-Green Tests in vitro. Two plants, Pavetta crassipes and Mitragyna inermis were studied. In vitro antiplasmodial tests on P. falciparum chloroquine-resistant W2 strain, showed an antiplasmodial activity of total alkaloids with IC50 between 1,23 μG/mL and 14 μG/mL. In vitro cytotoxicity tests showed a viability of humans monocytes (cells THP1) with CAR (Cytotoxicity Antiplasmodial Ratio)>50μG/mL. The in vitro genotoxicity tests on DNA Methyl-Green showed that two extracts do not have any mutagen effect. The molecules isolated from Pavetta crassipes, Elaeocarpidine, OH-Elaeocarpidine, Rutin, Acanthospermol-β-galactosidopyranoside, showed an antiplasmodial activity with IC50 varying from 0.5 to 10μGg/mL. In conclusion, total alkaloids of Pavetta crassipes, as well as OH-Elaeocarpidine, one of molecules isolated from these total alkaloids presented a potential antimalarial activity. These natural substances could lead to antimalarial products if the in vivo tests are successful.
There remains a great inequality in development of and access to health technologies around the world, leading to big differences in the health and wealth of nations. Vaccines, diagnostics and therapeutics are in general developed in the West for Western populations and are either too expensive for developing countries to afford or not relevant to their needs. In response, a number of developing nations – such as India, China, Brazil and South Africa – have begun to invest in their own biotechnology industries to supply relevant, affordable health products. India, for example, has developed vaccines such as Hepatitis B at a fraction of the usual cost, driving prices down globally. But what about countries that are less developed still? In Africa, research and commercialization are on completely separate tracks. How might they best forge a path for locally-relevant health innovation? Based on background research and preliminary analysis of over one hundred in-depth interviews and stakeholder workshops conducted by our team in Ghana, Tanzania, and Rwanda, this presentation will lay out an ambitious yet achievable plan for a network of «convergence centres» in Africa- facilities which will bring together local scientists, entrepreneurs, business people, and investors to develop affordable health products and services focused on local health needs. In combination with an associated venture fund and larger virtual network, these centres can tackle the gap in moving ideas from lab to marketplace, and build on growing economic strengths in several African nations. By linking with each other and with similar networks regionally and globally, a relatively modest investment into creating this critical infrastructure will help translate indigenous talent, capital, and know-how into positive health and economic impacts in a sustainable way, moving innovation from lab to marketplace.

Background: \textit{P. falciparum} gametocytes may persist after treatment with sulphadoxinepyrimethamine (SP) plus artemesunate (AS) and contribute considerably to malaria transmission. We determined the efficacy of SP+AS plus a single dose of primaquine (PQ, 0.75 mg/kg) on clearing gametocytaemia measured by molecular methods. Methodology: The study was conducted in Mnyuzi, an area of hyperendemic malaria in north-eastern Tanzania. Children aged 3–15 years with uncomplicated \textit{P. falciparum} malaria with an asexual parasite density between 500–100,000 parasites/μL were randomized to receive treatment with either SP+AS or SP+AS+PQ. \textit{P. falciparum} gametocyte prevalence and density during the 42-day follow-up period were determined by real-time nucleic acid sequence-based amplification (QT-NASBA). Haemoglobin levels (Hb) were determined to address concerns about haemolysis in G6PD deficient individuals. Results: 108 individuals were randomized. Pfs25 QT-NASBA gametocyte prevalence was 88–91% at enrolment and decreased afterwards for both treatment arms. Gametocyte prevalence and density were significantly lower in children treated with SP+AS+PQ. On day 14 after treatment 3.9% (2/51) of the SP+AS+PQ treated children harboured gametocytes compared to 62.7% (32/51) of those treated with SP+AS (p<0.001). Hb levels were reduced in the week following treatment with SP+AS+PQ.
and this reduction was related to G6PD deficiency. The Hb levels of all patients recovered to pretreatment levels or greater within one month after treatment. Conclusions: PQ clears submicroscopic gametocytes after treatment with SP+AS and the persisting gametocytes circulated at densities that are unlikely to contribute to malaria transmission. For individuals without severe anaemia, addition of a single dose of PQ to an efficacious antimalarial drug combination is a safe approach to reduce malaria transmission following treatment.

82. UTILITY OF FINE-NEEDLE ASPIRATION IN THE DIAGNOSIS OF TUBERCULAR LYMPHADENOPATHY IN HIV/AIDS

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Background: Tuberculous lymphadenopathy is a common manifestation of HIV/AIDS patients. This is due to the fact that tuberculosis is the most common coinfection in HIV/AIDS patients. It is estimated that 50% of HIV/AIDS patients are coinfected with tuberculosis in many African countries. It is this coinfection with TB that leads to the increased mortality in HIV/AIDS patients. Currently there is global commitment to make antiretroviral drugs universally available to HIV/AIDS patients. The consequence of this may probably be increased lifespan of these patients. The most important threat to such drug-aided increased lifespan is coinfection with tuberculosis. Although the World Health Organization has made TB drugs available throughout the world, many institutions involved in the treatment of TB require confirmatory detection of tubercle bacilli before initiation of treatment, hence the referral of these patients for such confirmatory detection of tubercle bacilli. Methodology: Specimens from clinically tuberculous lymphadenopathy of 200 patients were obtained by fine-needle aspiration technique. Thin smears of the cellular aspirates were fixed in 95% ethanol. The smears were stained by two methods: the Papanicolaou and Ziehl Neelsen (ZN) stains. The Papanicolaou stain was to allow for cytologic evaluation and the ZN stain was for demonstration of tubercle bacilli. The preparations were evaluated on a light microscope. Results: Two hundred specimens were evaluated. 80 (40%) of the 200 cases had cytologic features of reactive nodes; 72 (36%) of the 200 cases were ZN stain negative; and 48 (24%) of the 200 cases were ZN stain positive for tubercle bacilli. Conclusions: 60% of the 200 cases showed typical cytologic presentations of reactive nodes; 36% of the 200 cases were ZN stain negative in spite of having typical cytologic features of tuberculosis; 24% of the 200 cases were ZN positive and this allowed the patients to be put on TB treatment immediately. Fine-needle aspiration cytology made an important contribution to the management of these cases of HIV/AIDS–associated tuberculous lymphadenopathy.

83. IN-VITRO ANTIMICROBIAL ACTIVITY OF TWO MEDICINAL PLANTS: TABERNAEMONTANA CRASSA AND SENNA ALATA


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In view of the research and development of traditional medicine in Cameroon, this study investigated two medicinal plants, Tabernaemontana crassa (Apocynaceae) and Senna alata (Cesalpinaceae) in order to evaluate their antimicrobial properties. Previous studies have revealed that their antimicrobial activity is of great medicinal importance. These plants are currently being used traditionally in Cameroon to treat wounds and fungal diseases. The activities of ethanol extract of the stem bark of T. crassa and leaves of S. alata were tested, in disc-diffusion assays, against thirty references or laboratory strains of Gram-positive cocci (Staphylococcus spp., Enterococcus spp.), Gram-negative bacilli (Escherichia coli, Klebsiella spp., Enterobacter spp., Serratia marcescens, Acinetobacter baumannii and Pseudomonas aeruginosa), Yeast (Candida spp., Cryptococcus neoformans) and filamentous fungi (Aspergillus spp., Trichophyton spp.). The minimal inhibitory concentration (MIC) of each extract were then estimated,
against a more susceptible microorganism (i.e. those giving an inhibition zone measuring at least 14 mm in diameter in the disc-diffusion assays), by agar dilution. The extract of *T. crassa* exhibited good activity against bacteria and fungi (inhibition zone diameter ≥ 14 mm). This activity was very high against Gram-positive cocci (MIC < 0.625 mg/ml). *Senna alata* extract showed good activity on Gram-positive cocci (inhibition zone diameter ≥ 17 mm; MIC > 10 mg/ml) and weak activity against Gram-negative bacilli (0 ≤ inhibition zone diameter ≤16 mm) and fungi (0 ≤ inhibition zone diameter ≤20 mm). The bark of *T. crassa* showed better antimicrobial activity and will therefore be a good choice for the production of a traditionally improved antimicrobial.

84. ANTI-EMETIC ACTIVITY OF *GREWIA LASIODISCUS* ROOT EXTRACT AND FRACTIONS

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Preparation of *Grewia lasiodiscus* root bark is used in African traditional medicine to treat fever, pains and emesis. The extraction and fractionation of the methanolic extract of *Grewia lasiodiscus* root bark using solvents of varying polarities yielded active fractions designated GLF1-F3. The effect of the extract at 25,50 and 100mg/kg on pentobarbitone-induced hypnosis was evaluated in mice while the antiemetic activities of the methanolic extract and its active fractions were studied on anhydrous copper sulphate-induced emesis in a day old chicks. The oral median lethal dose (LD50) of the extract was studied and estimated to be 774mg/kg. The extract at 25, 50 and 100mg/kg produced a significant (p>0.05) decrease in onset and duration of sleep when compared with the control groups. The extract at 50,100 and 200mg/kg produced a significant (p>0.05) decrease in copper sulphate induced emesis in a dose-dependent manner. Fraction GLF1, at 50mg/kg produced a 61.51% increase in emesis, while fractions GLF2 and GLF3 produced a 39.0% and 56.50% reduction in frequency of emesis. Our results suggest that the methanolic extracts of *Grewia lasiodiscus* root bark and its most active fraction GLF3 have antiemetic properties, which provide for the first time the rationale for its application in traditional medicine especially in the management of emesis.

85. THE STUDY OF THE QUALITY OF ANTI-HYPERTENSIVE DRUGS MARKETED SUB-SAHARAN AFRICA: CASE STUDY OF MEDICINES MARKETED IN RWANDA

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Objective: The quality of 17 formulations of antihypertensive drugs, all tablets (atenolol, captopril, hydrochlorothiazide, Enalapril, Methyldopa and propranolol) sampled on market in Rwanda and was assessed and the influence of tropical storage conditions on drug content and *in vitro* dissolution investigated. Materials and methods: Drug content and in vitro dissolution were determined immediately after purchase (t0) at 3-months (t3) and during 6-months (t6) storage under room temperatures versus simulated tropical conditions (75% relative humidity, 40 °C) using the methods described in the USP 24 monographs on the drugs concerned. All formulations sampled had a remaining shelf life of at least 2 years at the time of purchase. For each drug, a formulation having market authorization in Europe was purchased from the University Hospital Gent pharmacy and included as reference formulation materials; all drug standards were obtained from Sigma Aldrich (Steinheim, Germany). All reagents used during drug assay were of HPLC grade, the other reagents were of analytical grade. Results: At the time of purchase, the drug content of all the formulations was within the limits recommended by the USP 24 except Cetopril 25mg which content was 154.5 +/- 2.2 % and Cetopril 25mg 53.0 +/- 1.8%. Those two
drugs remained with this behavioral not only in stability tests but also in dissolution test. It seems that the packaging was done in reverse way; tablets of 50 mg were packed in 25mg’s blisters and vice versa. This was verified from other tablets of the same lot. The dissolution test performed revealed that only 75% of Aldomet Kenya was realized after 20 minutes whereas the USP 24 recommended value is 80%. At 3 months (t3): At room temperature, drug content was still in the limits except again Cetopril 25mg which content was 154.6 +/- 3.0 % and Cetopril 25mg 51.0 +/- 3.6%. Also the Aldomet from Kenya was substandard with 89.4 +/- 7.3%. At tropical conditions the Aldomet from Kenya and Aldomet from Pakistan were substandard with 70.9 +/- 4.6% and 82.0 +/- 0.6% respectively. Macroscopically the Aldomet from Kenya was denatured. At 6-months (t6), beside the Cetopril case the drug content was substandard in 4 formulations: Catenol 100 under tropical condition storage (86.7 +/- 0.4), Hydrochlorothiazide from India under tropical condition storage (87.4 +/- 1.2), Aldomet Kenya under room temperature and tropical condition storage (89.1 +/- 3.6 and 69.1 +/- 4.9 respectively) and Cepanolol 40 under tropical condition storage (81.3 +/- 15.7). Dissolution tests at 6-months (t6) revealed that the amount of drug realized was substandard for following drugs under tropical condition storage: Catenol 100 (65%), betanorm (75%), Aldomet (66%), Aldomet Pakistan (74%), Cepanolol (70%). Conclusion: A general view show that the drug content was always less on tropical condition storage compared to the room temperature storage. This is also the case with dissolution results: always the amount of drug released after the due time was less under tropical condition storage. Beside this influence of tropical condition storage, some formulations had a poor in vitro drug release profiles.

86. BRINGING ENTREPRENEURSHIP TO AFRICAN DRUG DISCOVERY AND DEVELOPMENT: CHALLENGES AND OPPORTUNITIES

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Africa represents an important market currently estimated at $429 billion, with a growing population set to reach 1.5 to 2 billion inhabitants before 2050. This potential market for drug innovation and commercialization can effectively be harnessed with a Pan-African scale view of this business equation. Growing businesses with the investments and alliances with public sector researchers needed for drug discovery will be challenging in one country alone to become sustainable. Efforts will have to reach the whole continent to benefit from economies of scale. Mo Ibrahim, Africa’s first billionaire entrepreneur states “Whenever there is a gap between perception and reality, there is a business opportunity”. African Drug Discovery is a viable business opportunity and a way to harness the public and private research capacity of the continent. It will be the business of African focused entrepreneurship to fill this gap and make sustainable growth possible. There is an abiding responsibility and currently a good opportunity for the global community to assist Africa in harnessing its vast bio-resources and network of traditional and cutting edge knowledge to build healthy, prosperous, diversified and sustainable economies. Building linkages between public research capacity and private enterprise to create value in underserved market will be necessary catalysts to improve livelihood strategies for the continent. Accessibility of locally-produced safe and effective drugs to consumers, supply-chain support that ensures their affordability and availability, and education and promotion that reinforces local innovation are worthy of prompt attention. Research and integrated development activities focused on the value of entrepreneurship, mentorship programs and networks with African executives from the Diaspora, committed global partners in international health management can lead to a transformative process in advancing African based drug discovery while directly improving the GNP, health and livelihoods across the continent. Identification of gaps, collaboration particularly with public institutions, engagement, sector and performance issues crucial to developing African Drug Discovery entrepreneurs can establish best practices to move such an initiative forward particularly. What will be the critical support system to move it forward? Who is and will fund Health Venture Capital for Africa? What are the creative funding and partnership opportunities that can be tapped into towards building excellence in Africa’s Drug discovery leaders while strengthening local community based innovation? How can this be done while simultaneously contributing to the advancement, quality assurance of drugs derived from traditional medicine of most benefit to local
communities. How will we grow our entrepreneurs to sustain local innovation? Addressing these issues will help inform all stakeholders interested in building the African Network for Drugs/Diagnostics Discovery & Innovation initiative.

87. PHYTOCHEMICAL AND ANTIMICROBIAL ANALYSES OF THE LEAVES OF NIGERIAN BIGNONIACEAE JUSS

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The phytochemical and antimicrobial analyses of the leaves of ten species of the Nigerian Bignoniaceae were carried out. The species are Crescentia cujete Linn, Jacaranda mimosifolia D. Don., Kigelia africana (Lam.) Benth, Markhamia tomentosa (Benth.) K. Schum., Newbouldia laevis Seem., Spathodea campanulata P. Beauv., Stereospermum acuminatissimum K. Schum., Stereospermum kunthianum Cham., Tabebuia rosea (Berthol.)DC. and Tecoma stans (Linn.) H.B.& K. Crescentia cujete, Jacaranda mimosifolia, Tabebuia rosea and Tecoma stans are introduced species while the rest are indigenous to Nigeria. The phytochemical analysis included the screening of leaf extracts of the species for secondary metabolites like carbohydrates, tannins, phlobatannins, anthraquinone, saponin, flavonoids, alkaloids, sterols, resins, and phenolic nucleus. This screening shows the presence of sterols, flavonoids, terpenes, tannins, resins and phenolic nucleus in all the species; carbohydrate was present in all the species except T. rosea. Phlobatanins and Alkaloids are absent in all the species. Antimicrobial screening was carried out using 2.0mg/ml of successive extracts (using hexane, ethyl acetate, methanol and water) of each species. The test organisms were Klebsiella, Pseudomonas aeruginosa, Escherichia coli, Candida albicans, Bacillus subtilis, Staphylococcus aureus and Salmonella spp. Readings were taken after 24hrs. to see if there were growth (i.e. no activity) or no growth (i.e. activity) on each of the extracts.

88. EFFECTS OF AFRAMOMUM MELEGUETA ON CHRONIC INFLAMMATION AND ON PHENYLHYDRAZINE-INDUCED CELLULAR INJURY

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Chronic inflammation is characterized by formation of exudative fluid, which contained large number of white blood cells (WBCs), recruited to the site of injury. The extract of the seed of Aframomum melegueta (AM), is widely used as an herbal remedy, against chronic inflammation in several countries of the world. This study was carried out to assess the effects of an aqueous seed extract of AM on chronic inflammation and phenylhydrazine-induced cellular injury. The effect of the extract on chronic inflammation was studied utilizing the granuloma air pouch model of carrageenan-induced exudative fluid formation and the ability of AM to reduce the number of WBCs in the fluid was also assessed. The ability of the extract to protect against cellular damage was assessed by using phenylhydrazine-induced rat red blood cells (RBCs) haemolysis and lipid peroxidation. The extract (50-200 mg/kg, i.p) was found to significantly (p < 0.05) reduce the volume of inflammatory fluid and the number of WBCs in the fluid was also assessed. The ability of the extract to protect against cellular damage was assessed by using phenylhydrazine-induced rat red blood cells (RBCs) haemolysis and lipid peroxidation. The extract (50-200 mg/kg, i.p) was found to significantly (p < 0.05) reduce the volume of inflammatory fluid and the number of WBCs in the fluid was also assessed. The results of the study provide some experimental evidences that may support the use of the seed of Aframomum melegueta, in the treatment of chronic inflammation in traditional medicine.
A bioinformatics/chemoinformatics journal club has been established at Nnamdi Azikiwe University (UNIZIK), Awka, Nigeria. The journal club founded in June 2007 aims at building capacity in bioinformatics and chemoinformatics as well as sensitizing and motivating the research communities in Nigeria of the comparative advantages inherent in computational research. Its programs are targeted at the application of bioinformatics and chemoinformatics in confronting unique regional and national problems in highly relevant areas particularly health. Member scientists are drawn from the pharmaceutical sciences, botany, chemistry and computer science of the University. Further expansion of membership into other disciplines is currently being pursued. Obvious challenges include the development of computational, bioinformatics and chemoinformatics skills essential for data analysis as well as enhancement of capacity in pattern recognition and identification of biomarkers. The journal club holds its formal business meeting once a month. Informal meetings among members are also encouraged. Current research projects of the journal club include docking experiments, drug design, plant DNA barcoding, phylogenetic analysis and virtual screening. Capacity building in bioinformatics and chemoinformatics in a developing country such as Nigeria is a new window of opportunity for solving unique regional and national problems especially in health.

90. SCREENING FOR POTENTIAL INTERACTIONS OF SIX HERBAL PRODUCTS IN DEVELOPMENT WITH THE MAJOR DRUG METABOLISING CYTOCHROME P450 ISOFORMS

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The growing use of traditional medicines by patients on conventional medicines has led to a rise in the incidence of herbal-drug interactions. It is therefore appropriate for anyone contemplating to develop traditional remedies to explore their potential interactions with the Western medicines. Currently, the MRC’s Lead Programme of Indigenous Knowledge Systems has a number of promising products from traditional-herbal medicines which hold hope for human use in the treatment of malaria and HIV. Therefore, the aim of this study was to screen these herbal extracts/compounds for possible interaction with the major drug metabolising cytochrome P450 isoforms, i.e., CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6 and CYP3A4. The effect of each of the ‘herbal products’ on the activity of a specific P450-isoform was tested by observing for changes in the rate of metabolism after addition to the reaction mixture of increasing amount of the ‘herbal products’. This was done separately for each of the P450-isoforms (Baculosomes) tested. Results were expressed as percentage activity of the control. Except for product E which inhibited activity of CYP2C19 by 25%, the other herbal products had no effect on any of the P450-isoforms. Peak interference was ruled out by running UV spectrum and use of three dimensional illustrations. In conclusion, the screening tests indicated that there was no significant interaction of the herbal products with the isoforms tested, which implies that these herbal products may be used safely with drugs that are metabolised by these isoforms, but the observations on product E and CYP2C19 need further evaluation.
91. CLINICAL EVALUATION OF AFRICAN HERBAL MEDICINES

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The criteria for clinical evaluation of African herbal medicines are exactly the same as those for assessing orthodox medicines (i.e. quality, safety and efficacy). The African herbal medicine may be a standardized freeze dried extract formulated into suitable dosage forms. The quality of the herbal medicine is determined by various factors which may influence the chemistry of the plant, pharmacology, toxicology and pharmaceutical formulation indicating the significance of establishing phytochemical and biological fingerprints. Generation of robust pre-clinical data on safety and efficacy based on standard methodologies using the principles of WHO Good Laboratory Practice is a prerequisite to consideration of clinical trials. The design of the protocol for the clinical evaluation of herbal medicine should take cognizance of the ethnomedical use, clinical observational study data, national drug regulatory authority guidelines, ICH and WHO Good Clinical Practice principles. The principles indicated above were applied in the clinical evaluation of an herbal medicine called NIPRISAN/NICOSAN for the management of Sickle Cell Disorder (SCD). Patenting of the process technology and potential therapeutic use of NIPRISAN was undertaken. In Africa where about 70% of SCD patients reside, the prevalence is about 2% (SS genes) and 25% (AS genes) among the general population while infant mortality is about 8%. Furthermore, survival rate in rural areas of SCD children by age 5 years is about 20%. Since there is no standard therapy in Africa for SCD patients, most patients use traditional herbal medicines. NIPRISAN is a standardized extract from four medicinal/food plants. Pre-clinical data of NIPRISAN using both in vitro and in vivo methodologies indicated profound efficacy and safety profiles . SCD (Hb SS) patients confirmed by hemoglobin electrophoresis in alkaline/acid media with moderate-to-severe recurrent episodes who had experienced at least 3 painful or vaso-occlusive crises in the previous year were recruited for the study. Double-blind, placebo-controlled, randomized cross-over clinical trial of NIPRISAN was undertaken at the National Institute for Pharmaceutical Research and Development (NIPRD) clinic, Abuja in 1997. Health diaries were used by all study participants. Clinical monitors visited patients at home every week. 100 patients were recruited but 82 satisfied inclusion criteria at 3 months pre-trial period. Summary of phase IIB pivot clinical trial data confirms its safety and efficacy in the management of SCD patients . NIPRISAN has been licensed to XECHEM Inc (an American company) and it is currently being commercially produced at Abuja for the global market.

92. A PROGRAM FOR ESTABLISHING SCREENING CENTRES FOR SCHISTOSOMIASIS IN SUB-SAHARAN AFRICA

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To meet the requirements of the African Network for Drug and Diagnostics Innovation (ANDI) in the field of schistosomiasis, one or more screening facilities may be established in sub Saharan Africa. Each facility has to produce schist material needed for hit identification and lead optimization by maintaining the life cycles of various species/strains of Schistosoma (S. haematobium, S. mansoni and S. intercalatum). These facilities have to maintain, on a large scale, breeding colonies of hamsters and mice and parasite compatible vector snails. In present, a facility (Schistosome Biological Supply Centre, SBSC) located at Theodor Bilharz Research Institute (TBRI) in Cairo. It is formed of laboratories for snails breeding, snail infection, experimental parasitology, animal husbandry and antigen preparation. This facility has been acting since 2003 as a WHO Screening Centre for Schistosomiasis. This facility is willing to collaborate and help in establishing similar other centres with the objective to exchange experience, technology transfer, training of professional scientific staff (biologists & veterinarians) and technical staff on standard techniques and advice on maintaining optimal biological and physical conditions which should be given high priority. In such new centres collection of adult worms for in vitro screening should depend on methods suitable with large numbers and producing of infected experimental animals should be suitable for in vivo evaluation of effective compounds. SBSC can help also in planning, designing, choosing
suitable equipment, establishing routine laboratory tasks, laboratory safety practice and records, as well as receiving African trainees. Such proposed sub-Saharan African schistosomiasis screening centres should build sustainable R&D capacities and infrastructure that allow fruitful collaboration and comparison of critical results.

93. CURRENT RESEARCH ON ANTIMALARIAL MEDICINAL PLANTS USED IN CAMEROONIAN FOLK MEDICINE

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Malaria remains one of the leading public health problems in Cameroon as in other parts of Sub-Saharan Africa. In the past decades, this situation has been aggravated by the increasing spread of drug-resistant Plasmodium falciparum strains. New antimalarial drug leads are therefore urgently needed. Traditional healers have long used plants to prevent or cure infections. This article reviews the current status of botanical screening efforts in Cameroon as well as experimental studies done on antimalarial plants. Data collected from 54 references from various research groups in the literature up to June 2007 shows that 217 different species have been cited for their use as antimalarials in folk medicine in Cameroon. About a hundred phytochemicals have been isolated from 26 species some among which are potential leads for development of new antimalarials. Crude extracts and or essential oils prepared from 54 other species showed a wide range of activity on Plasmodium spp. Moreover, some 137 plants from 48 families that are employed by traditional healers remain uninvestigated for their presumed antimalarial properties. The present study shows that Cameroonian flora represents a high potential for new antimalarial compounds. Further ethnobotanical surveys and laboratory investigations are needed to fully exploit the potential of the identified species in the control of malaria.
**APPENDIX 1. PROVISIONAL LIST OF PARTICIPANTS TO THE ANDI MEETING**

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