



INDIGENOUS KNOWLEDGE SYSTEMS (HEALTH) LEAD PROGRAMME

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The Medical Research Council of South Africa established the Indigenous Knowledge Systems of Health Lead Programme to address historical research priorities and neglected research priorities as they relate to traditional medical knowledge.

The Indigenous Knowledge Systems Lead Programme, abbreviated, IKS Lead Programme's mission and vision are to promote and advance indigenous knowledge systems through research and development by making it a valued health model in the global environment and to redress health traditions, which until now have neglected health research priorities and issues. The vision of the IKS Lead Programme is to be a centre of excellence in traditional medicines research regionally and to be competitive globally.

The objectives of the IKS Lead Programme are:

- Coordination and development of health research in indigenous knowledge
- Development of institutional and community networks
- Development of an enabling clinical trials environment
- Innovations and commercialization in traditional health systems.
- Policies governing intellectual property and benefit-sharing
- Development of Research programmes that are appropriate & relevant
- Support academic research
- Funding

To achieve its mission and vision of excellence in traditional medicines research and to stimulate research interest in this field, the IKS has as one of its core research activities, Knowledge Development and Knowledge Management for training of students, Traditional Health Practitioners and scientists in this field of science and further to retain and utilize those skills and technologies that the country has developed.

The IKS Lead Programme therefore runs an internship program for attracting young prominent scientist into science research and traditional medicines research. These students each one of them is answering on particular research question relating to traditional medicines.

The IKS Lead Programme is grateful to the support and financial assistance from the Department of Science and Technology (DST), through its Professional Development Programme and the support and financial assistance obtained from the National IKS Office (NIKSO) of DST for the internship program. The Programme further extends its appreciation of support from the National Department of Health and also special thanks to all the Indigenous Knowledge holders who work with the Programme and the students within this Programme. The program has been supported to attract postdoctoral fellows, PhD and special

skills in pharmaceutical chemistry and other disciplines in health research. The following are current the interns mentored and under this DST / NIKSO program.

POSTDOCTORAL FELLOWS:



Dr Duduzile Molefe

Background: PhD in Organic Chemistry, Rhodes University

Support: DST Professional Development Program

Mentor and supervisor: Dr MG Matsabisa

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Research Question: Develop synthesis and upscaling methodologies for the antiplasmodially active sesquiterpene dimmers. To also develop analytical HPLC method for the qualitative analysis and chromatographic differentiation of plant parts of plants and different plant species

Project summary: Traditional medicinal plants are used in traditional medicine for management and prevention of different disease conditions. For those medicinal plants and traditional medicines that have a potential for exploitation, these would be required in large commercial scales and stress would be put on those wild harvested plants. Isolation of “lead” molecules from plant would not support the industrial scale needs for the supply of these molecules. There is therefore a need for the synthesis of these “lead” molecules for clinical and industrial research. The other aspect is traditional medicines use in most cases bark or underground parts of plants. This has a conservation impact and new methods are required that can show that there are differences between plant parts as there may be marked differences for substitute plants. Dr Molefe project is looking at the 5 medicinal plants that compose the traditional medicines used for HIV and AIDS and against malaria to answer these research questions.

Currently Dr Molefe is at Emory University, in Atlanta as an exchange program student between Emory University and IKS Lead Programme through the support of NRF and DST. At Emory University she is being trained in protein engineering as part of drug discovery. Her work involves enzyme kinetics using monoamine oxidases of human and rat origin. The project is looking at designing drugs or lead molecules that would mimic substrates that inhibit these enzymes. The work would be very valuable to find molecules

of plant origin that can be used to develop drugs for Alzheimer's disease, depression and Parkinson's disease.



Dr Nchinya Benedict Bapela

Background: PhD Pharmacology, University of Pretoria

Support: NIKSO

Mentor and supervisor: Dr MG Matsabisa

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Research Question: There are numerous claims on traditional medicines used in the treatment of chronic and life threatening disease conditions, such as tuberculosis. However the current research methods are geared to isolating and identifying a single chemically characterized molecule effective against *Mycobacterium tuberculosis*. However, in most claims traditional medicines used for TB are a combination of different plants and these plants need to be evaluated as a single product.

Project Summary: Use of *Mycobacterium marinum* as a model for development of High throughput (HTS) assays for identifying and screening of compounds and extracts from traditional medicines which would be inhibitors of virulence and the assay to be a test model for *Mycobacterium tuberculosis* has not been commonly used in pharmacological bioassays.

Mycobacterium marinum, causes disease in both human and fish. In humans it causes superficial lesions called swimmers granuloma and in fish it causes tuberculosis-like granulomas on the skin. *Mycobacterium marinum* is a close relative of *mycobacterium tuberculosis* as judged by its DNA sequence analysis. The histopathology of *mycobacterium marinum* resembles that of *mycobacterium tuberculosis*. *Mycobacterium marinum* has a generation time of 4 hours as

compared to 20 hours of *mycobacterium tuberculosis*. Compounds that inhibit *mycobacterium marinum* are more likely to have the same effect against *mycobacterium tuberculosis*.

The development of this assay system will speed up the screening process for identification of active extracts and “lead” molecules against the tuberculosis causing bacterium. Once the method is standardized and validated, for using it in a High Throughput Screening (HTS) procedure, thousands of compounds and extracts will be tested in a short period of time. Dr Bapela has also a further interest in using other techniques such as the intramacrophage model for activity, using *Mycobacterium marinum* strain that has a Green Fluorescent Protein plasmid incorporated in it. He will also develop a mouse and fish model for testing compounds and whole extracts that can be developed as drugs for treating tuberculosis.



Dr Tobias Ntuli

Background: PhD Cell Biology, University of KwaZulu-Natal

Support: DST Professional Development

Mentor and supervisor: Dr MG Matsabisa

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Research Question: The alcoholic and water extracts of some plant extracts have been reported to be effective against malaria. However numerous researches done both *in vitro* and *in vivo*, including our own research has failed to show any antiplasmodial and antimalarial activities of any of the part of this plant. The plant is also know to have both male and female plants and both showed no activity against the *Plasmodium falciparum*, the causative agent for malaria

However, previous work done at the MRC IKS Lead Programme and UCT, Pharmacology has shown that some non-organic plant extracts reverse resistance and of the plasmodium parasite to chloroquine and this activity is caused by a high molecular weight protenaceous fraction.

Project Summary: *In vitro* evaluations of the aqueous extracts of the plant have been evaluated for their chloroquine potentiation and chloroquine resistance reversal effects. The HPLC methods and Solid phase methods for the separation and identification of the active extracts have been achieved. The amino acid analysis of the extracts has been completed and amino acid content of the barked described.

The task is to purify the protein and therefore plant protein or tannin-associated protein extract methods are being developed. The identification and eventual characterization of these proteins will enable us to test them for other conditions such as in cancer chemotherapy, antiretroviral resistance in HIV and AIDS and other infectious diseases such as in extreme tuberculosis resistant strains.

PhD INTERNS



Ms Carmen Lategan

Background: PhD student: Department of Medicine, Division of Pharmacology, University of Cape Town

Support: NIKSO, DST

Supervisor: Professor PJ Smith.

Mentor: Dr MG Matsabisa

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Project Title: The Investigation of 5 South African Medicinal Plants for Antiplasmodial activity and the Isolation and Characterization of Novel Antiplasmodial compounds.

Research question: Medicinal plants are commonly used and document in the treatment, prevention and management of malarial infections. Malaria is a health threat in many tropical countries and worse so in Africa with a handful of available drugs in the market. These available

drugs the majority of them have been rendered useless due to the resistance the plasmodium parasite has developed against them. There is an urgent need for the discovery and development of new safe and effective drugs against malaria based on lead from traditional medicinal plants.

Project Summary: Three novel compounds have been isolated from were evaluated for *in vivo* antiplasmodial activity using a mouse-model. Both plants have an effect on parasite growth while treated. The *in vivo* bioavailability of the most promising novel compound was determined and a preliminary pharmacokinetic profile obtained. The *in vitro* and *in vivo* results suggest that the two investigated plants have antimalarial properties.



Mr Percival Legoale

Background: PhD student: Department of Pharmacology, University of the Western Cape

Support: DST Professional Development, DST

Supervisors: Professor P Mugabo (University of the Western Cape), Professor A Walubo (University of the Free State), Dr MG Matsabisa (MRC).

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Project title: The effect of cytochrome P450 on the pharmacological activity of Phela, a traditional herbal medicine used as a putative immune booster in HIV and AIDS disease conditions.

Research question: Traditional medicines are very popularly used because they are thought to be safe and effective for chronic conditions. The second reason is that traditional medicine's popularity for chronic conditions is that there is no satisfactory treatment for these conditions and because of desperation and in most instances deep cultural beliefs, patients tend to oscillate between using prescription and traditional medicines. The effect of traditional medicines on cytochrome P450 metabolizing enzymes is not fully known and there existence of any drug-herb

interactions that might affect treatment management is not fully studied. This research can also help us understand why traditional medicine water extract are in most cases never have any pharmacological efficacy in *in vitro* and our hypothesis is that the products need to be metabolized first so that they can produce active metabolites.

Project Summary: Percival has just graduated for his MSc degree and has enrolled for a PhD program which is co supervised at UWC and University of the Free State. He has been involved in the chemical isolation and characterization of pharmacologically active compounds from traditional medicinal plants. His current research now will entail developing and HPLC analytical method for finger printing a medicinal product Phela, isolate the major components of this product, characterize these chemically and expose these compounds and the complete extracts of the product to human P450 metabolizing enzymes. He will then collect the metabolites with the aim of chemically characterizing these and testing them for pharmacological activities. He will once having determined these metabolites perform pharmacokinetic studies o Phela over 3 day using a non-human primate model. This will be the first such experiment which aims a developing a platform for determine how traditional medicinal products are metabolized in a living system.



Ms Mamello Sekhoacha

Background: PhD student. Department of Medicine, Division of Pharmacology, University of Cape Town

Support: DST Professional Development

Supervisors: Prof PJ Smith

Mentor: Dr MG Matsabisa

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Project Title: *In vitro* and *in vivo* antimalarial activity of South African medicinal plants and isolation and characterization of active constituents

Research question: Much research in Africa has been on *in vitro* bioassay and the results obtained whether they be new molecules has very rarely been taken into clinical research. The

development of traditional medicines which have shown very strong activity have not be taken further. The project therefore seeks to develop these molecules and extract into both higher animal preclinical and clinical research.

Project summary: The use of medicinal plants still plays a vital role to cover the basic health needs in developing countries where pharmaceuticals are not available or are unaffordable. Herbal remedies used in the traditional medicine provide an interesting and largely unexplored source for the discovery of potentially new drugs for chemotherapy. South Africa has a remarkably diversity of flora that has not been satisfactorily explored. It is on this basis that medicinal plants with a reputation of use in treatment of malaria are being investigated.

Mamello is integrally involved in the development of clinical trial protocols for evaluation of traditional medicines and also the development of protocols for the evaluation of safety and efficacy of “lead” molecules with antimalarial activity in *in vivo* animal models.



Ms Renée Street

Background: PhD student, Research Centre for Plant Growth and Development, School of Biological and Conservation Sciences University of KwaZulu-Natal

Support: DST Professional Development

Supervisors: Prof J van Staden

Mentor: Dr MG Matsabisa

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Project Title: Heavy Metals and pesticides contaminants in South African Medicinal Plants

Research Question: Most medicinal plants are wild harvested and their quality and authenticity cannot be guaranteed and this poses a problem for the research and development of traditional

medicines. This not only threatens medicinal plant biodiversity but also leads to speculation with regard to safety as industrial encroachment has led to contamination of water sources and natural habitats. This possible contamination of medicinal plant by heavy metals and pesticides is rarely taken into consideration. The toxicity of these plants could be due to their possible contaminants such as heavy metal for those plants collected along the road side and pesticide for those plant collected in agricultural land. Evaluating and monitoring potentially harmful substances is an essential step in improving the overall safety and quality of medicinal plants which will in turn result in safeguarding the consumer.

Project summary: With the experience that Renée has brought to the IKS Lead Programme, she is now setting up a methodological process and system, to develop procedures for analysis of all plants that the Programme researches to be evaluated for heavy metal analysis and possible pesticide contamination through SABS laboratories.



Ms Nomathibane Petronella Mangisa

Background: PhD Student, School of Anatomical Sciences, University of the Witwatersrand

Support: DST Professional Development

Supervisors: Dr Z Dlamini and Dr MG Matsabisa

E-mail: npmangisa@yahoo.com

Project title: Screening for anti-cancer “splicing activity” from plant extracts of South African indigenous plants.

Research Question: There are many claims that are received from traditional health practitioners and also health benefit claims that patients give testimonies of from the use of traditional medicines for cancer. There has been many in vitro bioassay research done based on cytotoxicity testing of medicinal plants. The mechanisms of action of some of these compounds/extracts are unknown and also the scientific verification of these claims, for traditional medicines cannot be easily verified

using the current research methodologies. There is a need therefore to develop appropriate systems for researching traditional medicines used traditionally for the treatment of cancer.

Project Summary: The proposed research will exploit natural product research methodology to identify natural products with targets that regulate splicing to switch from pro-carcinogenic to anti-carcinogenic using specific examples of such splicing. Indigenous South African plants will be screened for anti-cancer 'splicing' activity. Cytotoxic and cell viability assays have been used extensively in the past to screen and identify biologically active compounds. However, splicing assays, while used extensively to identify biological pathways have not, to our knowledge been exposed to similar screens.

Research aims and objectives

To screen indigenous South African medicinal plants and traditional medicines used for cancer treatment using splicing arrays

To ascertain if these plant extracts also induce other/numerous splicing pathways

To isolate and chemically characterize active secondary metabolites using bioactivity guided fractionation.

To further scrutinize the metabolites if they serve as novel drug or lead to development of a novel drug



Ms Sejabaledi Agnes Rankoana

Background: PhD Student, School of Social Sciences, Public Health, University of Limpopo

Support: DST Professional Development, MRC

Supervisors: Prof N Nyezama and Dr MG Matsabisa

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Project title: A Pilot Evaluation of the use of Indigenous Knowledge in Primary Health Care among the Northern Sotho in the Limpopo Province

Research Question: Most scientific research studies conducted on traditional medicines rarely look at the use of indigenous knowledge in primary health care. The project aims at assessing the

use of IKS at primary health care and documenting this use so as to identify the systems, methods, and plants used in management of conditions at primary health levels.

Project Summary: The study is designed according to the framework of Medical Ethnobotany to explain the indigenous systems and approaches to primary health care. The study is planned to describe the cultural belief systems and values which are observed and employed for preventive and curative purposes of primary health care to determine instances of self-diagnosis, self-medication and consultation. The results of the study show that primary health care is an intangible cultural heritage of the researched communities-the people have a long history of the use of indigenous health care practices that have preventive and curative purposes. The study offers information about medical ethnobotanical knowledge employed for sustainable primary health care. A list of herbal medicines prepared and administered for health care is drawn to determine knowledge of medicinal plant application for primary health care.

MSc INTERNS:



Ms Makhotso Rose Lekhooa

Background: MSc student, Department of Pharmacology, University of the Free State

Support: NIKSO, DST

Supervisors: Professor A Walubo and Dr. M.G. Matsabisa

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Project title: The effect of a traditional medicine Phela on the immune system

Research question: Traditional medicines are popularly used in HIV and AIDS as immune modulators. The effect of these plants is often mistaken and compared to those of antiretrovirals and assumptions made that they have the same mechanism of action of ARVs to be targeting the

virus. The project aims at looking at the effect of plant based immune modulators on the immune system both acute and chronic immune responses.

Project Summary: Since immune cells are regulated by cytokine signals, cytokines will be measured and analyzed to study the effect of Phela on the immune system. It is known that TH-1 cytokines enhance cell mediated immunity, while TH -2 cytokines enhance a humoral response. Therefore, understanding the mechanism of action via this loop will help in designing immune booster therapy and isolation of pure substances that can be incorporated together with HIV treatment to boost the immune system. Makhotso has obtained ethical approval to conduct this project after developing a proposal.

1. Research proposal has been completed.
2. Also the proposal was submitted to the ethics committee of the University of the Free State.
3. Proposal has obtained ethical approval from the University.
4. In process: Registration of the proposal with the University for study purposes. This involves defence before an independent committee (evaluation committee).



Mr Brian Sehume

Background: MSc student, School of Pharmacy, University of the Western Cape

Support: DST Professional Development

Supervisors: Professor J Syce and Dr MG Matsabisa

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Project Title: Pharmaceutical Evaluation of Phela Capsules used as Traditional Medicine for Immune Modulation

Research question: Herbs used in traditional medicine are nowadays frequently manufactured as conventional pharmaceutical dosage forms i.e. tablets, capsules and solutions such as tinctures,

syrops etc. , and in most cases preservatives, flavourants, colourants and tablet coatings are used, but these are generally not properly evaluated for their pharmaceutical properties. The Indigenous Knowledge Systems Lead Programme (IKS) of the Medical Research Council (MRC) works in partnership with Traditional Health Practitioners (THP) to manufacture pharmaceutical dosage forms of traditional medicines for the THPs and for its clinical trial stocks. Little is however known about the pharmaceutical quality of these preparations, behaviour of constituent plant materials and how it will react with other excipients or adulterants. There is a need therefore to evaluate and validate the pharmaceutical quality of these products as they shall eventually end up being prescribed to patients.

Project Summary: The project entails the formulation of the product, Phela, for dissolution studies and other pharmaceutical testing to determine the integrity of this product. Brian has already looked at the formulation of Phela capsules and how they dissolve at different pH to simulate the behaviour of this product in the gut. This, compared to the traditional formulation, would enable us to determine the bioavailability of Phela capsules. The objectives of this study are to (i) pharmaceutically evaluate (i.e. for organoleptic characteristics, mass uniformity, release characteristics and stability or shelf-life) the capsules of the traditional medicine called Phela and to (ii) evaluate the suitability of the powder form of the plant materials that constitute the contents of the Phela capsules (in terms of organoleptic features, flow properties, hygroscopicity, ash values, contaminants, particle size, chemical uniformity and stability). Standard pharmaceutical methods and procedures will be used to determine the organoleptic properties, dissolution and stability, and HPLC assay for the content uniformity of the capsules. From the results a certificate of analysis should ensue, any pharmaceutical problems associated with the capsules identified and criteria for the formulation, manufacture and evaluation of future established.

Undergraduate Studies



Ms Miranda Thobela Javu

Background: B.A. degree (Anthropology) University of the Western Cape and a Traditional Health Practitioner

Support: NIKSO, DST, IKS Lead Programme MRC

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Degree: B.A (Anthropology), University of the Western Cape

Progress to Date:

Miranda is a qualified Traditional Health Practitioner and with a specialization as a Diviner since 1992 to date and also a third year B.A Degree in anthropology part time student at the University of Western Cape focusing on Anthropology as her major subject. Miranda is currently employed by Medical Research Council at IKS [Health] Lead Programme employed as a project coordinator and is based at MRC-IKS Delft Laboratories. She is an integral part of the IKS Lead Programme School and Traditional Health Practitioner outreach programs. She has been a member of Table Mountain National Park Steering Committee since 2004; a chairperson of Indibano Healers Organization and nominated as a Western Cape Traditional Health Practitioners Forum Representative in partnership with the Provincial Dept. of Health against HIV and AIDS since 2006, and a member of National Coordinating Committee for African Traditional Health Practitioners of South Africa (NCCATHPSA). Her interest is in Medical Anthropology, where she will be focusing on illnesses and diseases from medical and traditional points of view. Miranda is now in her 3rd year for her studies at the University and with a passion to continue her career into IKS research and bring into the IKS Lead Programme a different perspective on IKS research at the MRC.

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