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NEWSLETTER

KANNA Issue 12

The Editor's Note

The 12th edition of the AAMPS newsletter is once again packed with useful information and contributions from some of Africa's leading "natural product" scientists

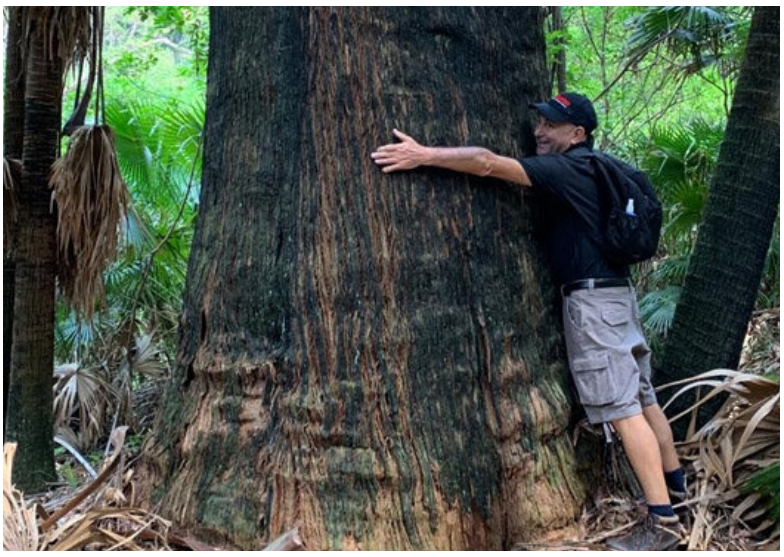
Dr. Nigel Gericke has, during his career, helped in the formulation and commercialisation of some of Africa's most important herbal medicines. HIs work on *Sutherlandia* and more recently *Sceltium* is world renowned. NIgel has been an AAAMPS supporter and contributor to its Herbal Pharmacopiea (AfHP 1) for more than 15 years. We are honoured to have him help prepare three new monographs for the upcoming second edition (AfHP 2). Thank you, Nigel!

No less important is the work of **Dr. Edward Mberu**, a former lead scientist at KEMRI in Kenya. Dr. Mberu is now a technical officer at the WHO Tropical Disease Research unit based in Geneva, where he plays a critical role in assisting tropical disease research units right across Africa.

During this first quarter of 2023, three excellent webinars were organised under our Connect Conversations banner. In one of the webinars, **Dr. Hellen Oketch** talked about the work of the USP, particularly in Africa. This was followed by a fascinating lecture by **Dr. Anjanette de Carlo** on the science of Frankincense, and the work of GFA/Save Frankincense. The third talk was by **Dr. Anthony Richards and myself** on the role of slavery as a platform for bringing African foods and medicinal plants to the New world.

Before closing I would like to thank our new coordinator, **Yvonne Shonhe Kunatsa**, who has done a great job in making the newsletter and related activities such a success.

Enjoy,



Highlights

Meet The Monograph Author

Dr Nigel Gericke

Q: What Monograph are you working on?

A: I worked as a contributor to three AfHP monographs: *Mesembryanthemum tortuosum* (synonym *Sceletium tortuosum*) commonly known as kanna; *Myrothamnus flabellifolius*, commonly known as the resurrection plant; and *Afromomum melegueta*, commonly known as alligator pepper or grains of paradise.

Q: Who did you work with and what was the best thing about working with that person?

A: I worked solo on my contributions, reviewing the literature on these plants in order to abstract and adapt published information to the monograph template. Of course, this literature was published by many researchers, and it was a great pleasure to study their work and appreciate the growing scientific research on each of the three plants.

I appreciated the anonymous AfHP reviewers' comments, queries and suggestions on earlier drafts of my contributions, which certainly strengthened the final versions.

Q: Tell us one fun fact about the species that you chose.

A: *M. tortuosum*

The lower, older leaves of the plant become skeletonized in the dry season, revealing the beautiful leaf veins, and accounting for the genus' synonym, *Sceletium*. An early painting of the plant from a 1685 expedition to Namaqualand, South Africa illustrates this characteristic feature.

M. flabellifolius

During the dry season the vivid green pleated leaves of the plant fold, and become thoroughly dry, brown, and brittle, yet they will revive to their original state in a few hours of soaking in water. This explains why the plant is called the resurrection plant. The plant has a number of mechanisms for its extreme drought tolerance, including light-reflecting leaf scales, pleating and folding of leaves, metabolic adjustments, and stabilization of the membranes by sucrose and trehalose.

A. melegueta

As far back as the 13th century, traders from West Africa carried the spice across the Sahara to sell it in Tripoli, with the final destination to what is now Italy. The Italians called it "grains of paradise"

because of the unknown country of origin, and high value of the product. Trade continued, and in 1871 the Gold Coast (present day Ghana) exported 39,000 kg of seeds to the United Kingdom, 13,000 kg to Germany, 12,000 kg to France, 7 000 kg to Holland and 16,000 kg to the United States. Recently, there has been a resurgence of interest in the seeds for extracts for the dietary supplement market in the USA.

Q: Why do you have such interest in this Species?

A: *M. tortuosum*

M. tortuosum in flower

In 1986, I first read about this South African plant in William Emdoden's book *Narcotic Plants*. There was very little information on the plant, and I decided to look into it. Upon chewing a traditionally fermented sample of the plant in 1992, it was clear that it had rapidly acting central nervous system activity – initially stimulating, and after some twenty minutes this changed to a calming activity. I embarked on a quest to investigate the plant's chemistry and mechanisms of action responsible for this,

and undertook ethnobotanical research of the plant in Namaqualand to understand potential for abuse liability, use in infants and pregnancy, as well as the therapeutic potential.

M. flabellifolius

I was doing a plant collection on a hilltop in Thaba'Nchu, not for from the South African city of Bloemfontein, in 1977. One of the unusual-looking plants I collected there was *Myrothamnus flabellifolius*, and I did not know it had traditional medicinal uses. Many years later, in the early 1990's, I recognized the plant on traditional medicine markets in South Africa, and set out to understand why it was a popular indigenous medicine.

A. melegueta

I became acquainted with the plant when I attended Professor Maurice Iwu's Bioresources Development and Conservation Programme (BDCP) workshop in Nsukka, Nigeria, in 1997. The seed pods were on sale on local markets, so I enquired about the uses and was intrigued by the pungency, food use as a spice, and the very diverse medicinal uses.

Q: What uses does it have and have you used it yourself?

A: *M. tortuosum*

Traditionally, in Namaqualand, South Africa, the plant is typically chewed as a quid. It has been used for endurance, pain relief, as a tonic, for elevating mood, as well as reducing the stress

of thirst and hunger while walking long distances in arid areas. The plant is also used to enhance a sense of calm and wellbeing. *M. tortuosum* is commonly used to treat colic in infants. It is also used for treating asthma, headache, abdominal cramps, and constipation. The plant is sometimes used on social occasions as an intoxicant, and is used by traditional healers to wean alcoholics off alcohol. Colonists in the Cape of Good Hope used tinctures of the plant as a sedative.

I have personally used the plant for three decades, initially in the form of capsules of milled plant material, and later in the form of commercially-available tablets or capsules of standardized plant extracts of the plant, which I have taken daily for the last decade. I primarily use these products to reduce stress and give a sense of general well-being. Based on my observations of lucid elderly chewers of the plant in Namaqualand, I hope that regular consumption of these supplements may be neuroprotective and/or cognitive enhancing.

M. flabellifolius

Traditionally in southern Africa infusions are widely used as a health tea and tonic. The medicinal uses include for colds, 'flu, asthma, pain, backache, kidney problems, haemorrhoids, hypertension, painful menstruation, and mastitis, depression, epilepsy and insanity, diabetes, and stroke, erectile dysfunction and shingles. Powdered leaves mixed with fat are used to moisturize skin and to treat burns and wounds.

M. flabellifolius leaves

I have used infusions of the plant at home simply as a pleasant-tasting health tea.

A. melegueta

The seeds are extensively used in West Africa as a culinary spice due to the pungent ginger-cardamom flavour, and for making spiced beer, peppery alcoholic spirits, pungent cordials and lemonades, and spiced vinegar and sauces. An Ewe common name for *A. melegueta* in Ghana is megbe-dogboe meaning "never found lacking by the sick". Some of the uses of the seeds are as a tonic, a stimulant, and for enhancing endurance; the seeds are chewed to treat coughs, colds and sore throat, abdominal pain, dysentery, rheumatism, and to treat hypertension and hypertension. Seeds mixed with salt and applied to the interior of the mouth as a treatment for sleeping sickness. The seeds are widely added to other traditional medicines to enhance the activity of the other medicinal plants.

I have used the seeds at home, inspired by the traditional uses.

This includes use as a spice, grinding the seed in an ordinary pepper grinder, and adding to cooked food to give another dimension of flavour and pungency. Regularly chewing a few whole seeds during the day is my favourite home remedy for the common cold and for sore throat.

Q: What kind of research have you done into it?

M. tortuosum

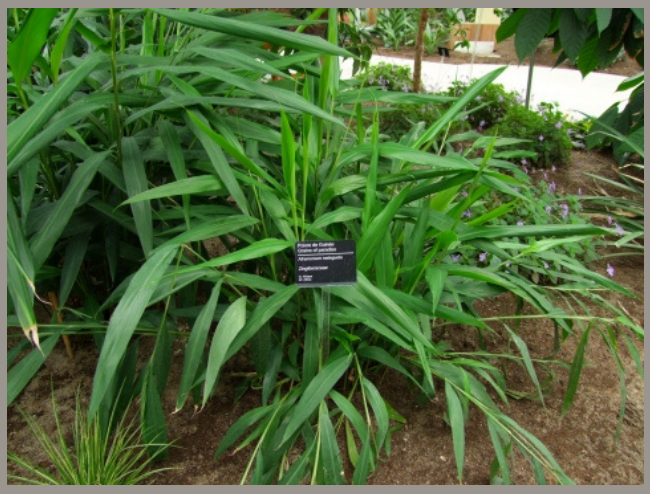
From 1995 to 1999, I conducted ethnobotanical research on the plant in Namaqualand to understand the local uses, methods of preparation, use in pregnancy, safety and tolerability, abuse liability, and sustainability of the wild plant resource. During this time, I discovered the serotonin reuptake inhibition activity of extracts of the plant, and isolated alkaloids. Subsequently, through my work with HG&H Pharmaceuticals, the dual SRI and PDE4 inhibition activity for extracts of the plant and an isolated compound was discovered. I led randomized placebo-controlled clinical studies on the safety, tolerability, anxiolytic and cognitive-enhancing potential of a commercialized, standardized extract of the plant.

M. flabellifolius

Apart from informal enquiries on the plant uses at traditional medicine markets, I have not conducted phytochemical or pharmacological research on this plant.

A. melegueta

On behalf of Nektium Pharma, I worked with the Nektium R&D team on developing extracts of the plant and then studying their commercial potential of the plant through pharmacological studies. The details of this research are proprietary, and not yet published.



A. melegueta

Q: What are your thoughts on the AfHP?

A: The African Herbal Pharmacopoeia (AfHP) is an important initiative to promote a greater awareness and quality assurance of the best known and most researched traditional African herbal medicines. The AfHP will contribute to health and well-being, and provide scientific and economic benefits to the African continent, as well as the rest of the world.

The foundation for the safe use of any herbal medicine are standardized methods for evaluating the identity and quality of the source raw material. The comprehensive quality assurance section of the AfHP provides these methods for each featured botanical plant. The AfHP preserves and promotes traditional knowledge, and provides supporting evidence for ownership of

this knowledge; makes it easier for local authorities to identify and utilize local plant resources for healthcare; promotes safe plant use in self-care, including more standardized approaches to dosing; aids the appreciation of side-effects and contraindications; provides a reference for local researchers to encourage further research into the chemistry, pharmacology and toxicology of important African medicinal plants; provides an invaluable resource for local and international product developers, particularly in the food, beverage, nutraceutical, and personal care industries where African bioresources are underutilized.

Q: In five years' time, what advances do you think this species would have made commercially and in research?

A: *M. tortuosum*

There is a clear trajectory of increasing commercial plant production activities, and increasing numbers of commercial extracts of the plant on local and international markets. There are increasing numbers of nutraceuticals / dietary supplements containing extracts of the plant, particularly on the United States market. This trend is likely to continue over the next five years, including market penetration to new territories for standardized, clinically studied extracts for companies that invest in addressing the diverse regulatory hurdles.

Standardized extracts of the plant, made to Pharma GMP, and clinically studied for safety and efficacy have FDA-approved botanical drug potential for the USA, and EMEA-approved Herbal Medicinal Product potential for the USA market. It is not clear if this will be achieved within the next five years, but with adequate investment, it is possible.

New biotech startups, including Kanna Health Ltd. in London, and Sensorium Therapeutics in Boston, are researching the therapeutic potential of isolated compounds and derivatives inspired by compounds found in Kanna and also related compounds found in some in members of the Amaryllidaceae family. The first Phase 1 clinical study (safety and tolerability in healthy subjects) on an isolated pure compound will likely have been completed within the next 12 months, and a Phase 2 clinical study (safety, tolerability and efficacy in a group of patients) may well have been completed within five years.

M. tortuosum leaves and flower

M. flabellifolius

The growth of the commercialization of resurrection plants over the next five years will likely be constrained unless commercial-scale plant production is achieved, rather than reliance on sustained-yield wild harvesting.

Commercial plant material will more likely be utilized in growing numbers of tea and tea blend products than in nutraceuticals. Extracts of the plant, if commercial production is achieved, will be incorporated into a growing range of cosmetic or other topical preparations. It is expected that the plant will continue to be of mainly academic research from a pharmacological point of view over the next five years. The interesting finding of cognitive-enhancing potential by Gadaga *et al,* 2019 may be the start of further research into the CNS potential of the plant, which may lead to greater interest in extracts of the plant for the development of branded, evidence-based nutraceuticals.

A. melegueta

It has been encouraging to see branded extracts of alligator pepper appear on the nutraceutical market in the USA in recent years. There is also a growing number of papers on the pharmacology of the extract, and a small number of human clinical studies. The trend of increasing academic research is likely to continue over the next five years, into weight-management, immune health and inflammation, and effect on the microbiota. It is anticipated that there will be increased investment in clinical studies in the development of new, branded, standardized alligator pepper nutraceutical ingredients.

Our Scientist Profile

Dr. Edward Mberu

Can you give us a short introduction about yourself and your professional background?

1987-2023

I'm a Technical Officer at Tropical Diseases Research (TDR), a Special Programme for Research and Training in Tropical Diseases based at WHO office in Geneva. My primary responsibilities are to provide technical and managerial support for research and capacity strengthening and project management, with a focus on infectious diseases of poverty in low and middle-income countries. Prior to joining TDR, I worked as a research scientist at the KEMRI-Wellcome Trust Research Laboratories where I managed the malaria parasite *in vitro* and antimalarial pharmacokinetics labs. I later worked as a Diagnosis Officer in the Malaria Unit, WHO/AFRO, Harare, Zimbabwe and as a research Associate and Laboratory Specialist at Family Health International (FHI360), Africa Regional Office, Nairobi, Kenya. Before joining WHO/AFRO, I held a two-year TDR Career Development Fellowship on Project Management of Tropical Diseases Research in Africa and used malaria operational research as an entry point to strengthen malaria treatment and diagnosis at community level in collaboration with National Malaria Control Programs. In addition, I held a one-year postdoctoral fellowship with the Department of Pathobiology at the

University of Washington, Seattle, USA, focusing on the molecular basis for antifolate *in vitro* resistance in *Plasmodium falciparum*.

At which institutions did you study and in which fields?

I studied at Kenyatta University and University of Nairobi, both based in Nairobi, Kenya and then the University of Washington, Seattle USA.

Can you share a brief overview of what your field of expertise is about?

My field of expertise span the fields of parasitology, pharmaceutics, and molecular biology.

In what way can your profession aid in the development of the African herbal pharmacopoeia?

By providing skills for tracking drug resistance, understanding of the molecular basis for resistance, and screening for novel agents for countering resistance.

What drove you to pursue a career in your profession?

The curiosity to experiment again and again, despite discouraging results.

What kind of research are you currently doing?

My current focus is on strengthening implementation/operational research https://adphealth.org/irtoolkit/

Using a reverse Lamina Flow hood at the KEMRI-WTRL, Nairobi, Kenya.

Which successes in your field are you most proud of?

Research Output (patented intellectual property)

- Diaminopterin derivatives as antifolate agents against *P. falciparum* and all organisms that have a complete endogenous folate pathway. Patent P407594 GB, May 2002. W.P. Thompson & Co., Liverpool, UK.
- Reversing antimalarial resistance and potentiation of antifolate activity by probenecid in *P. falciparum*. Patent P407595 GB, May 2002. W.P. Thompson & Co., Liverpool, UK

What changes or developments would you like to see in your field?

More national resources devoted for medicinal plants research and their conservation.

What are some of the challenges that you have faced as a black scientist?

All black scientists despite their gender are disregarded when it comes to career and funding opportunities. They have to work double or more to be recognized globally.

What opportunities are available to young people who would like to follow the path to your profession?

The entire spectrum of career paths spanning from lab and botany experts, community liaison, teachers and specialist phytochemical and medicinal chemists, drug target engineers/designers.

What advice can you offer to young aspiring scientists in the pharmaceutical industry?

Strive for enhanced understanding of commonly used medicinal plants among diverse communities. Undertake detailed phytochemical screening and biological *in vitro* and *in vivo* activities. Seek collaborations for rational design, synthesis and lead optimization of potent novel agents and their cytotoxicity.

Connect Conversations

The focus on this month's conversations was on "Global Excellence in African Ethnopharmacology."

Dr Hellen Oketch-Rabah
Senior Manager, Dietary Supplements & Herbal Medicines at U.S. Pharmacopeia

Dr. Oketch-Rabah emphasized on the need to give scientists across the African continent visibility so that their work is appreciated. She also highlighted the need to document information that emanates from the traditional use of plants, as well as science. Documented work yields great potential for the development of new medicines like digoxin., in addition to aiding collaboration. Dr. Oketch highlighted some of the plants that have been recognized for their medicinal and pharmacological effects. For example, the Madagascar periwinkle has had various alkaloids being developed for the treatment of acute lymphocytic leukemia, small cell lung cancer, and Hodjkin's diseases. The Calabar beans have been used to treat glaucoma. After all, we could have more products like the Umckaloabo products from South Africa, that are on the market. These products are made from Pelargonium sidoides.

Catharanthus roseus
(Madagascar periwinkle)

Dr. Anjanette DeCarlo

Dr. DeCarlo's talk was on frankincense. She highlighted that they have developed an app that will assist tree growers. This app will be given to the farmers for free. However, grants are needed to fund the trainings for the farmers, as well as for buying and disseminating phones that have the app already installed in them.

Dr. Anthony Richards and Denzil Phillips

This conversation that was led by Dr. Richards and Mr. Phillips was on the migration of plants from Africa to the Caribbean and America.

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The duo mentioned that many plants migrated during the slave trade era. Such plants include the *Aloe vera*. H*ibiscus sabdariffa* also had its origins in Africa where its leaves are eaten. In the Caribbean, this plant is used as a drink.

Okra, which is also another migrated plant, is known for its anticancer, anti-inflammatory, antifatigue, antidiabetic, antioxidant, and antibacterial properties. *Oryza glaberrima*, which is also known as the African rice, is commonly used for hair nourishment.

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