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Kenyan Medicinal Plants Potential for Development of Drugs for Neglected Diseases

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Introduction

Conventionally, neglected diseases are considered as a group of 13 infectious diseases that are endemic in the low income populations in the tropical developing world. They can be classified as those caused by trypanosomal parasites, helminthes, bacteria and viruses. They cause death to an estimated 0.5- 1m people annually. Trypanosomal diseases are represented by Kala-azar or visceral leshmaniasis, African sleeping sickness (African trypanosomiasis) and Chaga's disease (American trypanosomiasis); the current drugs for these diseases are relatively toxic even though the disease is not that lethal. Helminth infections include schistosomiasis treated with the inexpensive praziquantel but which cannot stop re-infection; onchocerciasis (river blindness), on which anthelmintic treatment is being tried; dracunculiasis (guinea worm), which should have been eradicated in 2009; lymphatic filiriasis (elephantiasis), managed by anthelmintic treatments. The others are soil transmitted worms such as ascariasis (round worms), trichuriasis (whipworms) and hookworms which are really best controlled by good hygienic practices. Leprosy, trachoma, Buruli ulcer and cholera represent the prevalent bacterial problems. Viral infections are yellow and dengue fevers caused by flavivirus transmitted by *Aedes aegyptii* and Japanese encephilitis caused by a flavivirus transmitted by *Culex tritaeniorhynchus*; the viral infections can be controlled through vaccination (WHO, 2008).

However the WHO Innovative and Intensified Disease management (WHO-IDM) group considers NTDs to be only: Buruli ulcer, Chaga's diseases, cholera, sleeping sickness and leshmaniasis. This is because they get less funding than the "big three" – HIV/AIDS, malaria and tuberculosis. However other groups led by Drugs for Neglected Diseases Initiative (DNDi) organization do not agree and consider African trypanosomiasis, leshmaniasis, Chaga's disease, and malaria as NTDs. This list leaves out Buruli ulcer but includes malaria with the argument that the disease does not receive adequate funding relative to its perilous effects on society. Their argument is that "neglected diseases" should be conditions that do not get enough funding relative to their impact on society (DNDi, 2003); in the presentation, this definition is considered to be the correct one.

Clearly there is African folklore (mostly, medicinal herbal concoctions) about management of these neglected diseases even though such information is mostly scattered and may have run out of vogue at the advent of "civilization". It would be pertinent to explore the potential of certain local herbs for the development of phytomedicines for local populations for the diseases. Such practices have been recorded in monographs such as Medicinal Plants of East Africa (MPEA) (Kokwaro 2009) and Kenya Trees and Shrubs (Beentje).

Helminthiasis

Helminthiasis as a disease group covers many of the neglected diseases. More than five hundred East African plants are listed by Kokwaro in MPEA as emetics/ purgatives, intestinal worm infections alleviators for hookworm, roundworm, tapeworm, threadworm, general

anthelmintic, bilharzia and filarial infections. A few of these plants have been studied in our laboratory. They are the Myrsinaceae which are mentioned in several categories of anthelminthiasis and *Rumex* (Midiwo,2002) species listed as laxatives which can also be used to expel helminths from bowels. We have looked at the phytochemistry of the Kenyan Myrsinaceae reasonably and we find that it corresponds with that already reported in the literature. They are harbingers of long alkyl side chain 2, 5-dihydroxybenzoquinones. We managed to chemotaxonomically group them into two sub-families, the Myrsinodae and the Maesodae using these markers which coincides with their morphological delimitation. The Myrsinodae, which includes the species *Myrsine africana, Rapanea melanphloes, Embelia schimperi* and *E. keniensis* are chemically typified by the existence of embelin/ rapanone while the Maesodae represented monotypically by *Maesa lanceolata* in Kenya is typified by the existence of maesaquinone. We have isolated several other benzoquinones from Kenyan Myrsinaceae and reported them in the literature (Midiwo, 2002). *Rumex* species are widely used locally for control of intestinal helminthic conditions. There are five Rumex species in Kenya - *Rumex abyssinicus, R. usambarense, R. bequaertii, R. ruwenzoriensis* and *R. crispus*, according to their grouping in the "Key to Species". The compounds that are found in high concentration are the common anthraquinones, emodin, physcion and chrysophanol along with the polyketide naphthalenic compound, nepodin, whose distribution is in accordance with the Key (Midiwo, 2002). The anthraquinones have been reported to have purgative effect; no doubt this is the mechanism by which they exert their traditional anthelminthic activity.

Considering the high concentration of bioactive principles in these Myrsinaceae, *Rumex* species and similar anthelmintic plants, it is suggested that they could be pursued for formulation of cheap phytomedicines for use by the local populations. Some of the herbs, like the berries of the Myrsinaceae, are usually sold in market places to be added food as medicinal spices for the desired effects for intestinal worm expulsion; they can be developed as food supplements to control intestinal worm proliferation.

Malaria

Malaria is a serious disease whose progression may lead to death. Its symptoms of high fever, chills, weakened joints, and flu-like illness are however well recognized by people in malaria endemic areas such as Kenya. Illness and death from malaria are largely preventable. Malaria is caused by *Plasmodium* parasites which are transmitted by mosquito vector. The most common parasite in Kenya which is the most virulent is *Plasmodium falciparum*; the others are *P. vivax, P. ovale* and *P. malariae.* The main mosquito vector in Africa and which, unfortunately, is also the most efficient is *Anopheles gambiae.* There are 300-500 million malaria infections world wide every year. About 80% of these are in Africa leading to 1.75- 2 m deaths annually, mostly children under five years old. Worldwide 3000 children die everyday from malaria. Approximately 90% of malaria deaths are in Africa. Malaria constitutes 10% of Africa's total disease burden; 40% health expenditure and 30-50% of in-patient cases (WHO 2001). Total African cost estimate is in the range of US$12b annually. In Kenya, 22 million people are at risk, 70% of them are in rural areas. About 34,000 Kenyan children die every year from malaria compared to a total estimate of 42,000 people dead (DMS Kenya 2006).

Malaria can be controlled using three approaches- drug therapy, vector eradication and use of vaccines (in the future). Drug therapy has been beset by development of resistance in virtually all the drugs developed by synthetic method or obtained from nature; the latter ones tend to take a longer period to experience resistance by the microorganisms. Malaria has been usefully been controlled using herbs such as *Artemisia annua* (Francois, 1993) and Cinchona which gave rise to quinine. These natural compounds have been noticed not to succumb to resistance as fast as the synthetic ones such as chloroquin, mefloquin and

sulfadoxin/pyrimethamin. So it is attractive to look at new plant sources for these drugs. We have looked at several examples of these in our laboratory including Erythrina *abysinica* (Abiy, 2004) and Polygonum *senegalense* (Midiwo 2007) among others (Abiy 2003, Vlodomir Samolyenko, 2009).

Conclusion

Medicinal plants are useful sources of anti-plasmodial compounds that can be packaged as new anti-malarial drugs. It is worth pursuing the concept that mixtures of such compounds from plants can be formulated together for synergistic activity in which case the effective concentrations can be significantly reduced. It is the belief that this "shift in paradigm" from single or small number compound therapies may in the future lead to development of more efficient and cheaper drugs which also circumvent resistance development.

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