Characterisation of antimalarial compounds from plants used in traditional health practices in Lake Victoria basin

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ABSTRACT

Malaria, transmitted by bites of infected female anopheline mosquitoes, is an infectious disease caused by parasitic protozoa of the genus *Plasmodium*. The parasite infects human and insect hosts alternately. It remains a leading cause of morbidity and mortality in Kenya and is responsible for 2% of disease burden world wide with 90% of the cases in Africa. Prevention of malaria encompasses a variety of measures that may protect against infection or the development of the disease in infected individuals (vector control, protective clothing, and use of bed nets, vaccination, and chemotherapy or chemoprophylaxis). Parasite and vector resistance to drugs, and insecticides respectively coupled with ineffective repellants and absence of a vaccine have limited the control of the disease in most of the sub-Saharan Africa. With increasing cases of drug resistant parasites, expensive drugs and poor distribution of modern health facilities, there seems to be resurgence in use of herbal remedies to treat malaria and other infections before seeking conventional western remedies. Four plants: *Maytenus heterophylla* (Celastraceae); *Strychnos henningsii* and *S. usambarensis* (Loganiaceae); and *Periploca linearifolia* (Asclepediaceae), used for the treatment of malaria in the Lake Victoria basin were investigated for efficacy. Different plant parts were sequentially extracted with hexane, chloroform, ethyl acetate and methanol. The extracts were screened for *in vitro* anti-plasmodial activity against two *Plasmodium falciparum* isolates, D6 (chloroquine-sensitive) and W2 (chloroquine-resistant) strains and the activity (IC_{50}) determined. All the fractions were active against D6 and W2 strains (IC_{50} < 50 µg/ml). The activity of the plant extracts was slightly lower (IC_{50} 3.30 - 37.43 µg/ml) against W2 than D6 strain (IC_{50} 1.07- 25.78 µg/ml). The chloroform extracts of all the

plants were the most active (IC_{50} 4.00 - 10.58 µg/ml. The methanol extract of *S. henningsii* had the highest activity (IC_{50} 1.07 ± 0.07 µg/ml) while the ethyl acetate fraction of *P. linearifolia* had the lowest activity (IC_{50} 37.43 ± 0.96 µg/ml) against D6 strain. The extracts were also investigated for toxicity using brine shrimp larvae (*Artemia salina*). All the fractions and the aqueous extracts were not toxic (LC_{50} > 200 µg/ml). The fractions with low IC_{50} and high LC_{50} values may be used as a source of compounds for use in anti-malarial therapy or in combination with standard drugs. The methanol extracts were also tested for anti-oxidant activity using DPPH. The activity of the extracts was found to increase with concentration. The methanol extracts were found to have significant radical scavenging activity implying that the use of these plants as medicines may protect the human body against radicals which cause severe pathological conditions. The plants may therefore serve as a natural source of anti-oxidants. Isolation of three compounds (lupeol ester **(50)**, β-sitosterol **(54)** and β-amyrin **(55)**) from *P. linearifolia* fractions with high *in vitro* anti-plasmodial activity was achieved using chromatographic techniques (VLC, TLC and CC), and their characterization accomplished using spectroscopic techniques (1D and 2D NMR, IR and UV), chemical methods and MS spectrometry.