PHARMACOLOGICAL AND TOXICOLOGICAL EFFECTS OF SELECTED MEDICINAL PLANTS TRADITIONALLY USED TO TREAT MALARIA IN MSAMBWENI SUB-COUNTY, KENYA.

By

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF REQUIREMENTS FOR MASTER OF SCIENCE DEGREE IN NATURAL PRODUCTS AND BIOPROSPECTING OF THE UNIVERSITY OF NAIROBI.

DEPARTMENT OF PUBLIC HEALTH, PHARMACOLOGY & TOXICOLOGY (PHPT)

2015
DECLARATION

This is my original work and has not been presented in any other University for award of a degree.

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ABSTRACT

Malaria is a major public health problem and continues to kill a million people each year, with more than 90% of these cases found in sub-Saharan Africa. In Kenya, more than half of the population is exposed to malaria with minimal opportunities for treatment. The management of malaria is complicated because the parasites that cause the disease are resistant to most of the safest and cheapest first line treatments developed so far. There is therefore an urgent need for discovery of new antimalarial agents.

This study was conducted to investigate pharmacological and toxicological effects of some selected plants from Msambweni district that have been claimed to possess antimalarial properties. The antimalarial and hematological activities of aqueous and organic plant extracts were determined using a mouse model infected with Plasmodium berghei (ANKA). Cytotoxicity and oral acute toxicity was evaluated using brine shrimp and the mouse models respectively. The phytochemical compounds were screened using standard methodologies for possible active compounds.

Crude extracts were prepared from three plant species; Zanthoxylum chalybeum Engl.[(Rutaceae) (Root bark)], Ocimum suave willd [(Lamiaceae) (Leaves)] and Plectranthus barbatus Andr.[(Lamiaceae) (Root bark)]. Plants depending on the part traditionally used to treat malaria were collected from Shimoni in Msambweni Sub-County, Kenya.

Adult healthy swiss albino mice (Mus musculus L.) were infected intraperitoneally with Plasmodium berghei (ANKA) to induce malaria and then treated orally with a dose of 100 mg/kg body weight of each crude extract according to standard procedures. The negative control was treated with distilled water and the positive with chloroquine (CQ).

Brine shrimp lethality assay was used to test for cytotoxicity while healthy female swiss albino mice were used for oral acute toxicity as per Organization for Economic Co-operation and Development (OECD 420-2001) guidelines. The chemosuppression means obtained from the 4 - days suppressive test were analyzed using one way ANOVA and Dunnett test for multiple
comparisons. Aqueous extracts of Z. chalybeum, O. suave and P. barbatus had percentage chemosuppression of 81.45, 55.23 and 67.70% respectively. The organic extracts on the other hand exhibited percentage chemosuppression of 78.39, 54.78 and 78.69% respectively. Chloroquine, which was the positive control, had a chemosuppression of 97.76%. There was no significant difference between the chemosuppression of the aqueous extracts of Z. chalybeum and the organic extract of P. barbatus and that of chloroquine (p<0.05).

Oral administration of Z. chalybeum extracts in mice caused an increase in the red blood cell count, packed cell volume (PCV), hemoglobin and the neutrophils while extracts from O. suave and Plectranthus barbatus only caused an increase on neutrophils and monocytes respectively. Organic extract of Z. chalybeum had an LD<sub>50</sub> lower than 50 µg/ml (42.73) and hence considered highly toxic to brine shrimp while those of O. suave, P. barbatus and the aqueous extracts of Z. chalybeum and P. barbatus were moderately toxic to the brine shrimp (LD<sub>50</sub> >100<500). Aqueous leaf extract of O. suave was weakly toxic to brine shrimp (LD<sub>50</sub> >500<1000).

Acute oral toxicity studies showed that the aqueous and the organic extracts of the three plants investigated were not toxic to mice at a concentration of 2000 mg/kg body weight. Alkaloids, flavonoids, sesquiterpene lactones and tannins were found present in all extracts while glycosides were only present in P. barbatus. Saponins were found present in extracts of O. suave and P. barbatus but found absent in Z. chalybeum.

The findings suggest that folkloric medicinal application of the three plants by Msambweni Community has a pharmacological basis and to some extent safe. Alkaloids, flavonoids, saponins, sesquiterpenes and tannins found present in the three plant extracts upon phytochemical screening are perhaps compounds responsible for the antimalarial activity. It is also evident that the three screened plant extracts has ability to increase RBCs and WBCs. Bioactivity guided fractionation and isolation of bioactive molecules from the two most active species could lead to new hits against P. falciparum malaria.