ABSTRACT

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Malaria is the most significant parasitic disease globally especially in Sub-Saharan Africa. The disease kills a child every two minutes. This is coupled with increased malaria parasites resistance to the available drugs. The challenges of parasites resistance call for search of novel antimalarial compounds from plants. Extracts from *Securidaca longipedunculata* Fresen (Polygalaceae) showed antiplasmodial properties. This study led to the isolation and characterization of compounds from roots extracts of *S. longipedunculata,* and antiplasmodial activities of roots, leaves and stems extracts, and each extract combined with standard antimalarial drugs. Cytotoxicity activities of extracts and pure compounds was also determined.

The roots extracts were subjected to a combination of chromatographic separations. Structures of isolated compounds were elucidated by mass spectrometry and Nuclear Magnetic Resonance spectroscopy. Crude roots, stems and leaves extracts, pure compounds and drug-extract combinations were each tested for immediate *ex vivo* and *in vitro* antiplasmodial activities using SYBR Green I method against W2, D6, 3D7 and DD2 reference strains of *Plasmodium falciparum*. Cytotoxicity assays were also done using the antiproliferative assay using drug-sensitive and multidrug-resistant cancer cell lines.

Roots extracts yielded a new benzophenone 2,3,4,5-tetramethoxybenzophenone (**1**), alongside seven known compounds. Both methanol (MeOH) and ethyl acetate (EtOAc) roots extracts were active with IC_{50} values of less than 5 ng/mL against the D6 and 3D7 strains of *P. falciparum*. The MeOH extract showed good antiplasmodial activity against field isolates with IC_{50} value of 9.8±1.3 ng/mL and IC_{50} value of 1.4±0.07 against W2 strain. Compounds **5** and **8** exhibited *in vitro* activity with IC_{50} value of 19.7 μM and 14.5 μM respectively and compounds **1** and **2** displayed *ex vivo* antiplasmodial activities with IC_{50} value of 28.8 μM and 18.6 μM, respectively all against D6 strain. Synergism was displayed across all fixed doses of artemether-roots extract, lumefantrine-stems extract, and lumefantrine-leaves extract combinations against D6, DD2, and W2 strains of *P. falciparum*, respectively. The artemether-roots extract combinations displayed the highest synergism across all fixed doses with an average FIC_{50} value of 0.403±0.068 against D6 strain of *P. falciparum*. For cytotoxicity assay, all the extracts (apart from MeOH leaves extract) and pure compounds were not toxic to the normal BEAS and LO2 cell-lines.

There is potential for isolation of more compounds from *S. longipedunculata*. The observed synergism and high antiplasmodial activities of the plant species indicates its potential use as drug combination in controlling the occurrence of malaria resistance.