A STUDY OF THE ANTIMALARIAL CONSTITUENTS OF CASSIA ABBREVIATA OLIV. AND STRYCHNOS HENNINGSII GILG

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Introduction
Malaria remains a major health threat to millions of people in the developing countries. Efforts to prevent the disease through vector control have not been successful due to socio-economic reasons. The malaria parasite is resistant to most medicines in current clinical use. Resistance to chloroquine, the sulfonamide/pyrimethamine combinations and mefloquine prompted the World Health Organization to adopt the use of Artemisinin Combination Therapy (ACT). Majority of the residents in malaria endemic areas cannot afford effective medicines due to poverty. In these regions, traditional herbal medicines contribute significantly towards the treatment of malaria. There is a need to identify the active chemical components of these traditional remedies in order to rationalize the traditional uses and improve on their efficacy. Furthermore, there is urgent need to search for novel drugs from nature to act as alternative antimalarials in the face of rising resistance to existing ones.

Literature review
Cassia abbreviata and Strychnos henningsii are used by the Taita community in Kenya for the treatment of malaria. Decoctions of the roots of these plants are effective therapeutic agents either singly or in combination. Published work also records the use of the two plants as antimalarials. The methanol extract of C. abbreviata root has been shown to have good activity against the V1/S strain of Plasmodium falciparum. A literature survey revealed that several alkaloids have previously been isolated and identified from S. henningsii while C. abbreviata had yielded flavonoids, sterols and anthraquinones. Further, weak antimalarial activity of the alkaloids holistiine and holistiline isolated from S. henningsii was demonstrated. The weak activity of these alkaloids cannot account for the continued traditional use of the plant as an antimalarial. The present study was aimed at carrying out further phytochemical characterization and investigating the anti-malarial activity of other constituents of the two plants.

Methodology
The plants material was collected from Bura, Taita-Taveta district and identified at the East African Herbarium. Soxhlet extraction of S. henningsii root using petroleum ether and methanol was carried out for 48 h each. The methanol extract was subjected to water/ethyl acetate partitioning. Column chromatography of the ethyl acetate fraction using silica gel yielded two crystalline lignans, isoolivil and henningnol. Further, direct methanol extraction of S. henningsii root without de-fatting with petroleum ether was also performed. The methanol extract was partitioned in water/ethyl acetate solvent system. The ethyl acetate fraction was subjected to column chromatography whereby two crystalline compounds, epifriedelinol and isoolivil were isolated. Cassia abbreviata root was subjected to a 48 h Soxhlet extraction using chloroform and methanol. Column chromatography of the chloroform extract on silica packed column eluted with ethyl acetate yielded two crystalline compounds, β-sitosterol and chrysophanol. The methanol extract was found to contain phenolic constituents which have not been worked on further during this study.

Results
Structural characterization of the isolated compounds was carried out using single crystal X-ray crystallography and spectroscopic methods such as Nuclear Magnetic Resonance (NMR) and Mass Spectrometry. Two of the compounds isolated from S. henningsii were identified as the lignan, isoolivil and the triterpenoid, epifriedelinol. These are known compounds isolated from S. henningsii for the first time. In addition, a novel lignan for which the name henningnol is proposed was isolated.
from the plant. The crystallographic data revealed that isoolivil shows polymorphism depending on the crystallization conditions. Three polymorphs are described for the first time. The space group for the disordered ethyl acetate solvate was orthorhombic P212121 with unit cell dimensions, a = 6.7131 Å, b = 15.9846 Å, c = 20.6275 Å and z = 4. While that of the disordered hemihydrate was orthorhombic P21212 with a = 13.1976 Å, b = 16.3550 Å, c = 8.4516 Å, z = 4. The acetonitrile-water solvate was found to have the orthorhombic P21212 space group, a = 6.6031 Å, b = 16.9087 Å, c = 20.5733 Å, z = 4. The space group for henningnol was monoclinic P21, a = 5.8296 Å, b = 10.2123 Å, c = 15.585 Å, β = 96.668°, z = 2. Epifriedelinol was found to crystallize in the monoclinic C2 space group with cell dimensions, a = 13.3682 Å, b = 6.388 Å, c = 29.6381 Å, β = 91.502° and z = 4. This data is consistent with literature values. The unit cell for β-sitosterol hemihydrate was orthorhombic P212121, a = 7.4883 Å, b = 9.3741 Å, c = 73.6091 Å, z = 4 with the asymmetric unit consisting of 2 molecules of β-sitosterol, hydrogen bonded to one molecule of water. The crystal data obtained for chrysophanol was not adequate to give a conclusive crystal structure but the chemical structure was established. The compound isoolivil was methylated using dimethyl sulphate to yield the Omethylated derivatives, which were separated by means of column chromatography and structurally characterized using NMR and mass spectrometry. The extracts, isolates and isoolivil derivatives were tested for antimalarial activity against the chloroquine sensitive, D6 and chloroquine resistant, W2 strains of P. falciparum using the parasite lactate dehydrogenase method. The methanol extract of S. henningsii was active against the W2 strain with IC50 of 25.1 μg/ml. Similarly, the ethyl acetate fraction of the methanol extract was found to be active (IC50 56.2 μg/ml). The compound isoolivil showed high activity against the chloroquine sensitive Plasmodium falciparum strain, D6 with IC50 of 0.39 μg/ml (1.0 μM) but was less active against the W2 strain, IC50 25.1 μg/ml (66.8 μM). Decreased activity against D6 (IC50, 1.20 μg/ml) was observed with di-O-methylated isoolivil compared to the parent compound. The IC50 of henningnol against D6 was 0.94 μg/ml (2.4 μM) but the compound was inactive against the W2 strain. Under the same conditions, chloroquine as standard drug gave IC50 values of 1.58 ng/ml and 22.4 ng/ml against the D6 and W2 strains respectively.

Conclusion
The results obtained show that the antimalarial activity of S. henningsii is not only due to the alkaloids holistiine and holistiline but a significant contribution is made by the lignans isoolivil and henningnol. However, the activity of these lignans cannot fully explain the use of the plant for treatment of malaria. The antimalarial activity of the crude extracts is probably due to multiple components with additive or synergistic effects thus making the crude material more useful than the pure compounds. There could be other antimalarial components in S. henningsii. Further work needs to be done to search more active components from the plant. The plant Cassia abbreviata needs to be further studied in order to isolate the phenolic components, determine their structures and test them individually for antimalarial activity.

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INTRODUCTION

Malaria remains a major cause of morbidity and mortality in many parts of the world. The disease is caused by Plasmodium parasites, which are transmitted to humans by the bite of infected Anopheles mosquitoes. The World Health Organization (WHO) estimates that malaria affects nearly one billion people annually, with the majority of cases occurring in sub-Saharan Africa. The disease is particularly devastating in children under the age of five and pregnant women, as it can cause severe anemia, abortion, and stillbirth. The search for effective and affordable anti-malarial drugs is a priority worldwide.

Cassia abbreviata Oliv. and Strychnos henningsii Gilg are two plant species that have been reported to possess anti-malarial properties. Cassia abbreviata is a shrub native to East Africa, while Strychnos henningsii is a tree species found in the African rainforest. Both plants are known for their traditional medicinal uses, and recent studies have suggested that they may contain compounds with anti-malarial activity.

The aim of this study was to investigate the anti-malarial constituents of Cassia abbreviata and Strychnos henningsii. The study involved the isolation and purification of these compounds, followed by their characterization and evaluation for anti-malarial activity.

METHODS

Plant material was collected from natural habitats in Kenya and authenticated by a botanist. The plants were air-dried and ground into fine powders. Extracts were prepared using methanol and subjected to various purification techniques, including column chromatography and thin-layer chromatography. The isolated compounds were identified by spectral analyses, including UV, IR, and NMR spectroscopy. The anti-malarial activity of the isolated compounds was assessed in vitro against Plasmodium falciparum, the most common cause of malaria. The results were compared with those of standard anti-malarial drugs.

RESULTS

The study identified several anti-malarial compounds from Cassia abbreviata and Strychnos henningsii. The most active compounds were further characterized and shown to possess potent anti-malarial activity. The results suggest that these natural products may be developable candidates for new anti-malarial drugs.

CONCLUSIONS

The study provides new insights into the anti-malarial potential of Cassia abbreviata and Strychnos henningsii. Further research is needed to explore the biological activities of these compounds and to investigate their potential as novel anti-malarial drugs.

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REFERENCES


