Chemical investigations for antimalarial, antitrypanosomal and other chemical constituents of uvaria lucida ssp. Lucida and enantia kummeriae

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Master of Science (chemistry)

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This Thesis reports on phytochemical investigations of two Tanzanian plants of the family Annonaceae, namely, Uvaria lucida ssp. lucida Benth. and Enantia kummeriae Engl. & Diels. The crude chloroform extract of the stem bark of U. lucida ssp. lucida, showed activity against the brine shrimp larvae in the brine shrimp test and in vitro activity against the multidrug resistant K] strain of Plasmodium falciparum malaria parasite. The medium and the most polar fractions of this extract yielded five C-benzylated flavanones chamanetin, isochamanetin, dichamanetin, uvarinol and isouvarinol, the carotenoid lutein and two hitherto unknown oxygenated pyrenes 2.7-dihydroxy-3,6-dimethoxypyrene and2-hydroxy-3,6,7-trimethoxypyrene. 2.7-Dihydroxy-3,6-dimethoxypyrene was also simultaneously isolated at the University of Erlangen, Germany from a West Africa Uvaria species, U. doeringii. This is the first time that both isomeric tribenzylated flavanones uvarinol and isouvarinol have been isolated together from a Uvaria species. Uvarinol was first isolated from U. chamae but the compound and its positional isomer, isouvarinol are also reported to occur in a non- Uvaria species, viz. in Xylopia africana. Since so far C-benzylated flavonoids are not known to occur in plants other than Uvaria species, it is quite possible that X. africana might have been wrongly identified, and therefore the plant may in fact be an Uvaria species. Of the compounds isolated from U. lucida ssp. lucida chamanetin is known to be active against P. falciparum malaria parasites and therefore this compound is concluded to be among the active principles of the crude extract. The chloroform and methanol extracts of Enantia kummeriae showed in vitro activity against Trypanosoma brucei rhodesiense, the parasite that causes sleeping sickness. The plant is, however, not used locally for the treatment of sleeping sickness. The ethanol extracts of the root and stem barks yielded the protoberberine alkaloids palmatine , jairorrhizine and dchydroscoulcrine. Palmatine and jatrorrhizinc were found to be non-toxic to brine shrimp larvae in the brine shrimp test, but exhibited a very significant in vitro activity against both the multidrug resistant K| and the chloroquine sensitive NF 54 strain of P. falciparum, the activity being in the same range as that of the standard antimalarial drug, quinine. This potent antimalarial activity and the fact that palmatine and jatrorrhizine showed no toxicity to brine

shrimp larvae may suggest that the two compounds are potential candidates for the development of antimalarial drugs. However, previous investigations showed that these protoberberine alkaloids do not posses any significant antimalarial activities in mice. The two alkaloids, palmatine and jatrorrhizine, have been submitted for trypanocidal assays at the Swiss Tropical Institute. The medium polar chloroform extract of E. kummeriae yielded a mixture of |3-sitosieroI and stigmasterol, which are common plant constituents.