**Isolation of Potent Inhibitors of Drug Resistant *Plasmodium* from *Cassia nigricans***

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**ABSTRACT**

Malaria is a global health challenge that causes significant morbidity and mortality resulting from diminished efficiency in the available antimalarial drugs. In addition drug resistance, affordability and compliance to drug therapy have contributed to the challenge. Medicinal plants are being screened for development of novel antimalarial. In the present work, the antimalarial activity of *Cassia nigricans* was studied using the *in vivo* Peter 4 day suppression test on mice infected with *Plasmodium berghei* NK-65 strain. The result showed that ethylacetate, hexane and methanol extracts inhibited the growth of the parasite by values that were non-significantly (P > 0.05) different from the activity of artesunate. The aqueous, methanol and chloroform extracts exhibited *in vivo* median inhibitory concentration (IC\(_{50}\)) of 77, 32, 24 mg/kg bw respectively. Six (6) fractions (A-E) from the chloroform extract on column chromatography demonstrated IC\(_{50}\) in the range of 80 – 200 µg/mg bw. Five (5) compounds isolated from fraction B possess significant antiplasmodial effects at IC\(_{50}\) ≤ 12 µg/mg bw. GCMS analysis indicated that the compounds were all unsaturated fatty acids. One of the fatty acid (F042) inhibited *P. berghei* *in vivo* (IC\(_{50}\) of 3 µg/ml). Fatty acids are nontoxic and good inhibitors of plasmodium enoyl –ACP reductase (FabI). The compounds may act in a way different from inhibitors of bc\(_{1}\) complex or interrupters of hematin detoxification and may therefore be potent against chloroquine and atovaquone resistant parasite.