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Identification of antitrypanosomal constituents of some meliaceae species and screening of selected structural variants by *in vitro* and *in vivo* assays

ABSTRACT

African human trypanosomiasis (sleeping sickness) and animal trypanosomiasis (nagana) are vector-borne parasitic diseases, which are causing major health and economic problems in rural sub-Saharan Africa. The current chemotherapeutic options are very limited and far from ideal. There are serious social, economical and environmental repercussions associated with their usage and this has prompted researchers to improve on the existing methods of controlling the disease vectors and to discover new compounds for treating the diseases. Some of the major problems encountered in the treatment of trypanosomiasis include high cost of the few old drugs, high toxicity, low efficacy and increasing resistance of trypanosomes to these drugs, as well as general lack of research and development aimed at developing new drugs. The use of natural products derived from metabolic activities of plants is one of the strategies being explored to address some of the problems encountered with allopathic chemical drugs. This is because natural products are renewable, readily available, more selective and much less toxic. Some Meliaceae species have been found to contain such metabolic components with antiprotozoal, insecticidal, antifungal and antimicrobial activities. This has prompted the screening of more Meliaceae species with the hope of identifying candidates that can be developed into new efficient trypanocidal drugs that are safer and more affordable compared with existing synthetic drugs. The current research sought: to undertake *in vitro* screening of some Meliaceae species growing in Kenya; to isolate and structurally characterize trypanocidal constituents of the screened species; to evaluate *in vivo* activities of all compounds that demonstrate *in vitro* activities; to compare the structural details of active compounds, and to identify candidate natural products that show promise for downstream development into drugs for treating both human African trypanosomiasis (HAT) and animal African trypanosomiasis (AAT).