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ABSTRACT

Tuberculosis (TB) is one of the leading causes of death globally, and the rise in drug-resistant forms of TB has become a significant threat. Subsequently, it is crucial to explore new, effective and safe anti-TB agents. Several plant species are used in traditional medicine for the treatment of TB in Africa. In Uganda, *Acacia hockii*, *Albizia coriaria*, *Combretum molle*, *Warburgia ugandensis*, and *Zanthoxylum leprieurii* are among the most common plant species used locally to treat tuberculosis. This study aimed at bioprospecting for anti-mycobacterial compounds from selected plant species that could be used as templates for formulation of novel TB drugs. The extracts of each of the selected plant species and the isolated compounds were tested for antimycobacterial activity using Micro-plate Alamar blue assay. The acute toxicity of the aqueous extracts from the selected plants was determined using the OECD guidelines No. 425. Isolation and purification of the compounds from *Z. leprieurii* root/stem bark extracts, which exhibited promising activity, were performed using column chromatography and preparative-HPLC. Structure elucidation of the compounds was carried out using spectroscopic techniques. The aqueous extracts of the selected plant species showed moderate-weak activity (293.00-2344.00 µg/mL) against the susceptible TB strain (H₃₇Rv) and weak activity (1172.00-4688.00 µg/mL) against the multidrug-resistant (MDR) TB strain. On the other hand, the methanol/dichloromethane (DCM) (1:1) extracts showed significant-moderate activity (98.00-586.00 µg/mL) against H₃₇Rv and moderate-weak activity (293.00-1172 µg/mL) against the MDR TB strain. From the acute toxicity tests, one mortality and significant lesions in the examined organs following histopathological analyses were recorded from the *A. coriaria* treated group. The LD₅₀ of each of the extracts was estimated to be above 2000 mg/kg. The extracts of the selected plants except for *A. coriaria* exhibited low acute toxicity levels and could be safe for formulations into herbal products. Three novel compounds: heydenoate, adubamide, and dranzoanol as well as seventeen known compounds were isolated from *Z. leprieurii* root bark and six known compounds were isolated from its stem bark. Seven of the isolated compounds have shown significant activity (0.98-7.81 µg/mL) against the H₃₇Rv TB strain and may present vital templates in pursuit of novel and highly effective TB drugs. The findings of this study could justify the ethnopharmacological use of the plant parts of the selected plant species to treat tuberculosis.