ABSTRACT

Kidney stone disease is common with limited treatments and high recurrence. *Spermacoce articularis* is being explored as a safer natural option for its antioxidant and anti-urolithiatic potential. The study aimed to comprehensively evaluate the pharmacognostic, phytochemical, antioxidant, and pharmacological properties of *S. articularis* with a focus on its potential antiurolithiatic activity. Pharmacognostic studies, including organoleptic and fluorescence analysis, revealed distinct characteristics among leaf, stem, and root samples. The leaf and stem extracts exhibited a richer phytochemical profile using methanol, ethanol, acetone, and aqueous solvents than the root extract. The quantitative analysis exhibited a significant amount of both primary (proteins and carbohydrates) and secondary metabolites (alkaloids, tannins, and terpenoids), indicating a rich profile of biologically active constituents. Among all the solvent extracts, the stem methanol and leaf ethanol extracts of *S. articularis* demonstrated the highest antioxidant potential in all enzymatic, non-enzymatic, and radical scavenging assays. The *S. articularis* stem methanol extract (SASM) was found to have the highest dissolution of calcium oxalate crystals through nucleation and aggregation assays, outperforming the leaf ethanol extract. Consequently, further *in vivo* studies were conducted using the SASM at two doses (250 mg/kg and 500 mg/kg) on renal calculi-induced Wistar albino rats, and the results confirmed positive efficacy, with a significant reduction in calcium oxalate crystal deposition and prevention of renal tissue damage, compared to the standard cystone group. To identify the active compounds responsible for the anti-urolithiasis activity, chromatographic methods such as TLC, HPTLC, and GC-MS were employed. TLC and HPTLC analyses confirmed the presence of terpenoids and phenols in the stem methanol extract. GC-MS profiling detected 40 bioactive compounds, and 25 organic compounds from various functional groups were selected for molecular docking. *In silico* analysis showed D-mannitol had high binding affinities to Tamm-Horsfall Protein, Calcitonin, and Calcium oxidoreductase. Molecular dynamics simulations suggested D-mannitol may inhibit calcitonin hormone, supporting its potential in kidney stone treatment. The top 10 hit compounds obtained from docking also showed favorable pharmacokinetic properties. Overall, the study highlights that *S. articularis* is a valuable natural resource that warrants further investigation for the development of anti-urolithiasis treatments.