Title of the research: *In Silico*, *In Vivo* Studies and Identification of Potentially Bioactive Compounds from Three Selected Medicinal Plants against Urolithiasis

Name: FAYEHUN, Opeyemi Oseyemi
Matric Number: CHE/21/3499
Department: Chemistry
Area of Specialization: Medicinal and Organic Chemistry

ABSTRACT

Background

Urolithiasis remains a significant global health problem characterised by recurrent pain, renal dysfunction, and high relapse rates. Existing therapies are limited by adverse effects and cost, underscoring the need for safer alternatives. Plant-derived bioactive compounds are gaining attention for their litholytic, nephroprotective, and antioxidant properties. This study investigated the anti-urolithiasis potential of *Mirabilis jalapa* (Marvel of Peru), *Brassica oleracea* (Cabbage), and *Calliandra haematocephala* (Red Powder Puff) leaves using an ethylene glycol-induced urolithiasis rat model, complemented with molecular docking against the calcium oxalate crystal nucleation protein (6TQK).

Materials and Methods

Ethical clearance for animal use was obtained from the University of Medical Sciences Animal Research Ethics Committee. Methanol/ethyl acetate leaf extracts were subjected to phytochemical screening, antimicrobial testing, antioxidant assays (DPPH, $ABTS^{+}$, FRAP, OH^{-}), and membrane stabilization studies. Wistar rats were induced with urolithiasis and treated with the extracts. Biochemical parameters (creatinine, urea, electrolytes) and renal histology were evaluated, while expression of urolithiasis-related genes (CD44, OPN, IL-1β, HO-1) was determined by RT-PCR. HPLC and GC-MS were employed to identify bioactive compounds. Molecular docking was conducted using AutoDock Vina in PyRx, with Tamsulosin HCl as reference, while ADMETlab 2.0 predicted pharmacokinetics and toxicity. Statistical analysis was performed using One-Way ANOVA and Tukey's post hoc test.

Results

Phytochemical screening confirmed the presence of key metabolites, with HPLC detecting gallic acid, quercetin, and caffeine. GC-MS revealed major compounds including 9-octadecenamide (46.89%, *M. jalapa*), α-D-mannofuranoside (0.312%, *B. oleracea*), and 4H-pyran-4-one-2,3-dihydro-3,5-dihydroxy (0.309%, *C. haematocephala*). The extracts displayed strong antimicrobial activity, notably against *E. coli* (22 mm) and *S. aureus* (18 mm). *B. oleracea* and *C. haematocephala* showed excellent membrane stabilization, while *M. jalapa* leaf extract exhibited high antioxidant capacity. Treated rats demonstrated significant reductions in creatinine and urea levels (*B. oleracea*: 0.68±0.02, 0.59±0.1; *C. haematocephala*: 0.66±0.1, 0.53±0.02; $p<0.05$) at 50 and 100 mg/kg respectively. Histology revealed preserved kidney architecture, and gene expression analysis showed modulation of urolithiasis-related genes, with *C. haematocephala*

downregulating α-Feto and CD44. Docking studies identified five lead compounds from *M. jalapa* with higher binding affinities to 6TQK than Tamsulosin HCl (−6.4 kcal/mol): Gorgost-5-en-3-ol (−8.5), 9,19-cyclolanostan (−8.1), Obtusifoliol (−7.8), Ergosta-8,24-dien-3-ol (−7.7), and Cholest-5-ene (−7.3). These compounds demonstrated favourable hydrogen bonding and stable ligand–protein interactions. ADMET profiling indicated drug-likeness, oral bioavailability, and safety, with no significant toxicity or mutagenicity predicted (>500 mg/kg).

Conclusion

The study demonstrates that *M. jalapa* and *C. haematocephala* possess strong anti-urolithiasis properties through nephroprotection, antioxidant activity, gene modulation, and molecular targeting. These findings validated their potential as safe, plant-derived therapeutic agents and highlight their translational relevance as leads for novel phytotherapeutics in urolithiasis management.

Keywords*: Urolithiasis, Gallic acid, Gorgost-5-en-3-ol, Paraoxonase gene, ADMET analysis*