Title: Unveiling the renal therapeutic potential of *Nypa fruticans* leaves: An integrated experimental and *in silico* approach

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Abastact : Chronic kidney disease (CKD) is a progressive, irreversible disorder associated with renal dysfunction, inflammation, and oxidative stress. Given the limitations of current therapies, this study assessed the renal curative effects of *Nypa fruticans* ethyl acetate leaf extract (EaNFL) in a gentamicin-induced nephrotoxicity rat model. GC–MS and HPLC analyses identified 23 bioactive compounds in EaNFL, including rosmarinic acid, quercetin, and (−)-epicatechin, which were selected based on ADMET profiling, Lipinski's rule, and DFT analysis. These compounds were further investigated through computational studies against two renal targets: the AT1 receptor (PDB ID: 4YAY) and SGLT2 (PDB ID: 7VSI). Treatment with EaNFL, particularly at 400 mg/kg body weight and in combination therapy, significantly improved renal function and normalized biochemical and hematological parameters, likely due to its potent antioxidant and anti-inflammatory properties. Histopathological data supported these findings, showing reduced tubular necrosis, glomerular damage, and inflammation, especially in the high-dose groups. DFT analysis revealed that rosmarinic acid had the highest HOMO–LUMO energy gap ($\Delta E = 0.1314$ eV), suggesting high chemical reactivity and potential biological compatibility. Molecular docking identified quercetin, rosmarinic acid, and (−)-epicatechin as the top binders, with rosmarinic acid showing the strongest affinity and forming a stable complex, as confirmed by 100 ns MDS. Taken together, the *in vivo* and *in silico* results indicate that EaNFL offers renoprotective benefits by targeting the RAAS and glucose transport pathways while also mitigating oxidative stress and inflammation. These findings demonstrate its therapeutic potential and warrant further investigation into its bioactive constituents and potential clinical use in renal treatment..

Keywords: *Nypa fruticans* ,Renocurative, Histopathology, Creatinine, Molecular dynamics simulation

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