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Biophysical Chemistry 274 (2021) 106607
https://doi.org/10.1016/j.bpc.2021.106607

Anti-obesity, Antioxidant and In Silico Evaluation of Justicia carnea Bioactive Compounds as Potential Inhibitors of an Enzyme Linked with Obesity: Insights from Kinetics, Semi-empirical Quantum Mechanics and Molecular Docking Analysis

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Abstract: Obesity is a global health problem characterized by excessive fat deposition in adipose tissues and can be managed by targeting pancreatic lipase (PL) activity. In the present study, we investigated the in vitro antioxidant and anti-obesity potentials of methanolic leaf extract of Justicia carnea(MEJC) using lipase inhibition kinetics model. In silico evaluations of MEJC bioactive compounds as potential drug-like agents and inhibitors of PL were also investigated using SwissADME prediction tool, semi-empirical quantum mechanics(SQM), molecular electrostatic potential(MEP) and molecular docking analysis. Gas chromatography-mass spectrometry (GC–MS) revealed presence of campesterol, stigmasterol, beta-amyrin etc. MEJC scavenged reactive species and inhibited PL activity via a mixed inhibition pattern (Ki = 107.69 μg/mL; Kii = 398.00 μg/mL) with IC50 > orlistat's IC50. Molecular docking of GC–MS identified compounds with porcine PL showed compounds 8,10,12 and 14 having high PL-binding affinity and similar binding pose with orlistat. Hydrophobic interactions and van der Waals forces were predominantly involved in the ligands' interactions with some key catalytic site amino acid residues (Ser-153,His-264). Compounds 10,12,13 and 14 indicated high drug-likeness, bioavailability, electronegativity, ELUMO-EHOMO energy gaps and MEP. Our findings show that MEJC is a rich natural source of antioxidant and anti-obesity agents which could be optimized for development of new anti-obesity drugs.

Keywords: Justicia carnea, Antioxidant activity, Lipase inhibitor, Obesity therapy, Semi-empirical calculations, Molecular docking