Exploring the Use of Polyprenylated Benzophenones in Enhancing Efficacy of BETA-Lactam Antibiotics Through Molecular Docking in AutoDock Vina

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This study investigated the inhibitory potential of 41 polyprenylated benzophenones (PPBs) from Garcinia species against TEM52 ß-lactamase, aiming to identify a potential non-competitive inhibitor to combat antibiotic resistance. Forty-one PPBs were retrieved from PubChem after excluding known toxic analogues, and nine control ligands (substrates and clinical inhibitors) were included. The TEM52 structure was prepared in AutoDock Tools 1.5.7 and visualized in UCSF ChimeraX; the active site cavity was located using “Find Cavities” and validated through docking of penicillin controls. Fifty independent docking runs per ligand were performed with AutoDock Vina (exhaustiveness = 32; num_modes = 20; energy_range = 5 kcal/mol) on a receptor refined by water removal, Kollman charge addition, rotatable bond optimization, and polar hydrogen addition. Both Oblongifolin A and Plukenetione A bound to the active site. Oblongifolin A achieved the highest binding affinity (–10.7 kcal/mol), while Plukenetione A had a score of –8.8 kcal/mol. Despite its lower docking score, Plukenetione A exhibited superior ADMET properties: water solubility –4.45 log mol/L, Caco-2 permeability 1.455 log Papp, 100 % human intestinal absorption, total clearance 0.352 log mL/min/kg, negative Ames mutagenicity, and no hERG I/II liabilities; VDss –0.212 log L/kg and zero fraction unbound were slightly outside ideal ranges. Plukenetione A complies with Lipinski’s rule-of-five, reinforcing its suitability for oral administration. Additionally, Oblongifolin A with ß-Lactam antibiotic could be an intravenous candidate to combat systemic infections or sepsis. Plukenetione A’s favorable ADMET and statistically high binding affinity, warrant in-vitro research and potetntially in-vivo efficacy studies.

Awards Won: