Unveiling KIF15 Inhibition Through Molecular Docking and 100 ns Dynamics of a Natural Ligand

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Abstract

KIF15 is a spindle-associated kinesin protein that plays a central role in mitotic progression, making it an attractive target in cancer research. In the present study, we evaluated the interaction and dynamic stability of 1,2-benzenedicarboxylic acid, DI—a phytochemical from *Clidemia hirta*—against KIF15 (PDB ID: 4BN2) using a 100 ns all-atom molecular dynamics simulation. Throughout the trajectory, the ligand-bound complex (4BN2-ZEN) remained structurally stable, reflected by a lower RMSD (0.27 ± 0.05 nm) compared to the apo and standard inhibitor systems. Residue-level fluctuations were minimal, and compactness indicators such as radius of gyration and SASA showed steady patterns with no major conformational disturbances. PCA and free-energy landscape analysis revealed that the protein–ligand complex occupied a stable conformational basin with restricted motion. MM-PBSA calculations further supported strong ligand binding, with a binding free energy of −109.63 ± 5.97 kJ/mol, nearly double the affinity of the standard inhibitor. These findings suggest that the phytocompound from *Clidemia hirta* may serve as a promising natural molecule for targeting KIF15 in cancer-related studies.

Keywords: KIF15, 1,2-Benzenedicarboxylic acid (DI), *Clidemia hirta*, Molecular Dynamics Simulation, MM-PBSA Binding Energy