عنوان مقاله:

In Depth Computational Screening of Novel Indane-۱, ۳-Dione Derivatives as Potential Anti-Tubercular Agents

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خلاصه مقاله:

Mycobacterium TB poses a significant challenge by developing resistance to currently available medications, making it a serious global health concern. Therefore, it is imperative to create novel medications that exhibit efficacy against diverse strains of Tuberculosis. Isoniazid (INH) is a primary anti-tubercular medication that works against Mycobacterium TB by blocking the activity of a specific enzyme called InhA, which is responsible for reducing a compound called ۲-trans-enoyl-acyl carrier protein. The aim of this study was to pinpoint novel inhibitors of the enoyl-acyl carrier protein (ACP) reductase InhA. This work specifically examines the use of in silico techniques molecular docking and molecular dynamic simulation to study designed substituted Indane-۱, ۳ dione derivatives (۱-۱۵). The In silico ADMET screening was conducted using the SwissADME and admet SAR online ADME prediction tool server and passes Lipinski's rule of five as well as pharmacokinetic features like skin permeability and molar refractivity lies with in limit which shows none of noticeable signs of toxicity. The stability of the docked complex was assessed by conducting a Molecular Dynamics (MD) simulation using Schrodinger Desmond over ۱۰۰ ns. Most of the residues in the root mean square fluctuation (RMSF) fell between the range of ۰.۵-۴ Å and radius of gyration ranges between ۱۸.۱ to ۱۸.۴ Å throughout the ۱۰۰ ns simulation reflects maintaining stability of protein complex during the catalytic activity. Most of compounds shows higher GI absorption and inhibits CYP-۳A۴, CYP-۲D۶, CYP promiscuity shows range from ۰.۵-۰.۹. Compound ۱۱ have highest docking score of -۱۰.۳۸ kcal/mol and shows excellent hydrophobic and hydrophilic interactions with most of amino acid residues. Moreover, compound ۱۱ were found to be safe for acute inhalation and cutaneous sensitization. Thus, the obtained results suggest that compound ۱۱, ۲-[(trifluoromethyl) phenyl] methylidene-۱H-indene-۱, ۳(۲H)-dione appear to be good candidates for drugs with a potential leading structure for further development.

کلمات کلیدی:

Indane ۱,۳ dione, Molecular docking, Molecular Dynamics, In silico ADMET