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Natural plant products as potential Cyclooxygenase-2 (COX-2) inhibitors: An *in-silico* drug discovery study

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Natural plant products have gained widespread recognition for their medicinal properties and have been used in traditional medicine for centuries. In recent years, there has been an increase in interest in exploring natural plant products as a potential source of new drug candidates for various diseases, particularly inflammation-related conditions. Cyclooxygenase-2 (COX-2) is a crucial enzyme involved in inflammation and is considered as a prime target for the development of anti-inflammatory drugs. In this study, we employed computational methods to investigate the potential of selected natural plant products as COX-2 inhibitors. A comprehensive screening of a database of natural plant products was conducted using molecular docking and molecular dynamics (MD) simulation techniques to identify potential COX-2 inhibitors. Molecular docking is a computational approach that predicts the binding affinity of ligand molecules to a target protein, while molecular dynamics is a computational simulation method used to study the behaviour and movement of molecules over time. Docking studies were carried out using a crystal structure of COX-2 as the receptor, and the binding free energies of the docked compounds were calculated. The results revealed that the selected natural plant products exhibited promising binding affinities to COX-2, suggesting their potential as COX-2 inhibitors. The binding energies in kilocalories per mole (kcal/mol) of the five ligands with the COX-2 protein can be arranged in descending order as; Tubulosine (-9.82), Dicentrine (-9.34), Celecoxib (-9.02), Crebanine (-8.87), and Cycleanine (-8.10), with 3,5'-dihydroxythalifaboramine exhibiting a binding energy of -7.38 kcal/mol. MD simulations were performed on protein-ligand complexes for 50 ns using CHARMM36 force field and the mean radius of gyration (Rg), root mean square deviation (RMSD) and root mean square fluctuation (RMSF) were calculated. The results of MD simulation analysis indicated the stability of the protein-ligand complex throughout the simulation time. These studied compounds belonged to diverse classes of natural products, including terpenoids, alkaloids, and phenolic compounds, which are known for their anti-inflammatory properties. Additionally, some of the identified compounds exhibited binding affinities to COX-2 that were comparable to or even better than known COX-2 inhibitors such as celecoxib, a selective COX-2 inhibitor, which is a currently prescribed drug for inflammation-related conditions. The MD analysis results along with docking results highlights the potential of natural plant products as a valuable source of COX-2 inhibitors, which could serve as a starting point for further experimental investigations and the development of novel anti-inflammatory drugs. The findings of this study contribute to the significance of natural plant products in drug discovery and provide insights into their potential as promising candidates for the treatment of inflammation-related diseases.

Keywords: Anti-inflammatory, Cyclooxygenase-2, Natural plant products, Molecular docking, Molecular dynamics