In-Silico Molecular Docking Study of Flavonoids Against Prostaglandin Synthetase Enzyme

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***Abstract*—Inflammation is a physiological process and a self-controlled immune response to agents like infections, irritants, and injured cells. Inflammation is linked to a wide range of acute and chronic disorders, including rheumatoid arthritis, multiple sclerosis, chronic asthma, cardiovascular disease, allergies, atherosclerosis, and cancer. Molecular docking has gained considerable importance in the investigation of ligand protein interactions for the prediction of improved therapeutic efficacy. The present study focuses on a molecular docking analysis performed using Molegro Virtual Docker software, with binding affinity expressed as the MolDock score. Molecular docking is a computational technique used to explore ligand protein interactions and to evaluate the corresponding binding energies. Protein structures of prostaglandin synthetase were retrieved from the Protein Data Bank and docked with selected flavonoids and a standard compound. Two-dimensional and three-dimensional interaction analyses were carried out to examine hydrogen bonding, electrostatic interactions, and van der Waals forces. The observed interactions suggest potential inhibition of prostaglandin synthetase enzyme activity, which may contribute to the expected therapeutic effect.**

***Index Terms*—Molecular docking, Flavonoids, MolDock Software, Prostaglandin synthetase enzyme.**

I. INTRODUCTION

Inflammation is a physiological process and a self-controlled immune response to agents like infections, irritants, and injured cells (Karbab et al., 2020; Maleki et al., 2019). Inflammation is linked to a wide range of acute and chronic disorders, including rheumatoid arthritis, multiple sclerosis, chronic asthma, cardiovascular disease, allergies, atherosclerosis, and cancer. Pro-inflammatory cytokines and bacterial lipopolysaccharide (LPS) stimulate the expression of cyclooxygenases-1 (COX-1) and −2 (COX-2) in inflammatory cells such as macrophages and mast cells. NSAIDs, such as paracetamol, diclofenac, and celecoxib, are routinely prescribed to alleviate pain, fever, and inflammation (Mićović et al., 2022). However, chronic use of NSAIDs has been linked to a variety of negative effects, including gastroenteropathy (hepatorenal toxicity, metabolic disorders (Peng et al., 2022), and a decrease in the host's resistance to infections during medication (Hussain et al., 2022; Karbab et al., 2020).NSAIDs' mode of action is mostly observed in their inhibitory effect on the enzyme cyclooxygenase (COX), of which COX-1 and COX-2 are the two most frequent enzymes that play a part in the inflammation process. COX-1 is an enzyme that exists at all times and improves the physiological role of prostaglandins (PGs), such as keeping the stomach lining healthy and maintaining regular blood flow. In contrast, COX-2 is only produced in response to an inflammatory stimulation. In the search for anti-inflammatory drugs, NSAIDs are regarded to be a primary target in inhibiting the COX enzyme.

II. MATERIAL AND METHODS

The structure of Prostaglandin synthetase was retrieved from the protein drug bank whereas the structure of flavonoid and standard compound was constructed by using the chem draw furthermore, the protein drug bank was retrieved for the further study.

Protein Drug Bank of Indomethacin, Protein Data Bank of Flavonoid, Molecular docking.

The Molecular docking analysis is used for the identification of interactions between the microsomal prostaglandin synthetase and flavonoids. Molecular docking analysis was performed using Molegro virtual docker software. Binding score was depicted in MolDock score. MolDock score for our compound was -85.10. Figure 1, 2 & 3 was depicted hydrogen bond, electrostatic bond and hydrophobic interactions of compound with receptor microsomal Prostaglandin E Synthase-1 (mPGES-1) bound to DG-031 (PDB: 6VL4). Figure 4 was representing 2D interaction of compound with mPGES-1 receptor. SER A: 10, SER A: 90, PHE A: 16, LEU A: 13, LEU A: 17 was exhibited van der Waal interactions shown in green color in fig.4. In case of standard indomethacin, Fig 5. Van der Waal interactions were found with residues PHE A: 91, LEU A: 17 helped to stabilize ligand at binding site. PHE A: 87 amino acid was shown pi alkyl interactions with compound purple in colour.

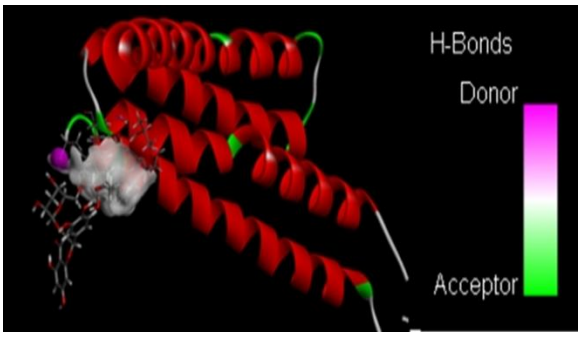


Figure 1: Hydrogen bond receptor interactions with microsomal Prostaglandin E Synthase-1 (mPGES-1) bound to DG-031 (PDB: 6VL4)

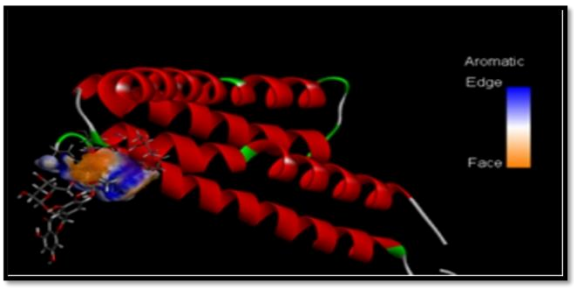


Figure 2: Electrostatic interactions with receptor microsomal Prostaglandin E Synthase-1 (mPGES-1) bound to DG-031 (PDB: 6VL4)

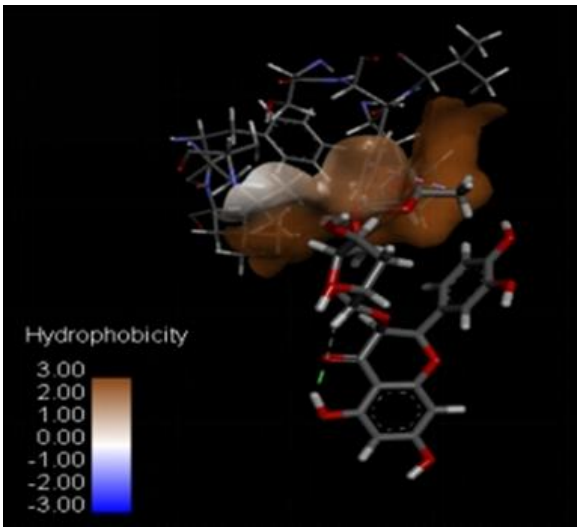
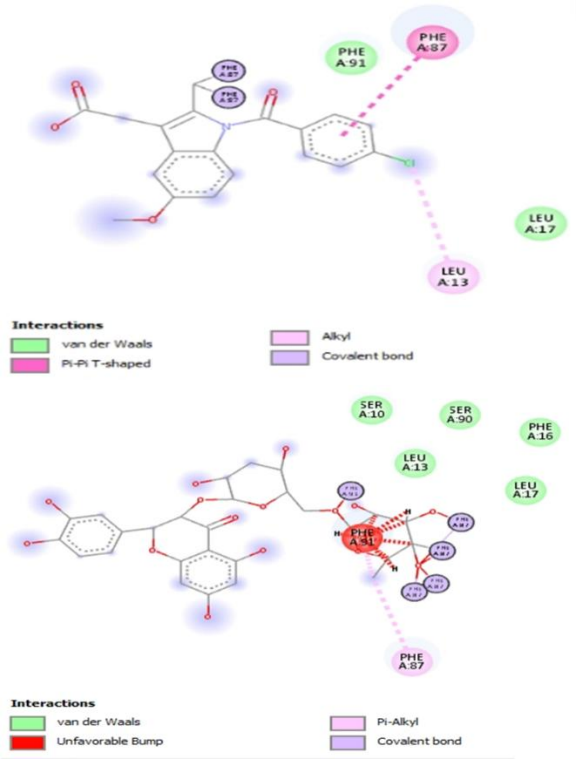


Figure 3: Hydrophobic interactions with receptor microsomal Prostaglandin E Synthase-1 (mPGES-1) bound to DG-031 (PDB: 6VL4)



III. RESULT AND DISCUSSION

Molecular docking analysis was performed using Molegro virtual docker software. Binding score was depicted in MolDock score. MolDock score for our compound was -85.105 indicating moderate to strong affinity and for standard indomethacin it was -83.27

MolDock score that indicated slightly less affinity than the compound towards receptor PDB: 6VL4. Figure 1, 2 & 3 was depicted hydrogen bond, electrostatic bond and hydrophobic interactions of compound with receptor microsomal Prostaglandin E Synthase-1 (mPGES-1) bound to DG-031 (PDB: 6VL4). Figure 4 was representing 2D interaction of compound with mPGES-1 receptor. SER A: 10, SER A: 90, PHE A: 16, LEU A: 13, LEU A: 17 was exhibited van der Waal interactions shown in green color in fig.4. By stabilizing through weak non-covalent interactions, these interactions imply that the ligand is well-accommodated in the binding pocket. In case of standard indomethacin, Fig 5. Van der Waal interactions were found with residues PHE A: 91, LEU A: 17 helped to stabilize ligand at binding site. PHE A: 87 amino acid was shown pi alkyl interactions with compound purple in color. Aromatic rings of compound were produced hydrophobic interactions with PHE 87, which may lead to strong ligand binding. Whereas indomethacin showed Pi-Pi T-shaped Interaction with PHE A: 87. But the fig 4 was also supporting the steric hindrance of compound with PHE A: 91 that has possibility to destabilize affinity. Reduction of steric hindrance by optimizing compound near this region can increase the binding stability of compound with receptor. And in standard drug indomethacin alkyl interaction was found with LEU A: 13 residues at binding site. According to the docking data of compound, the ligand and mPGES-1 interact favourably through hydrogen bonding, Pi-Alkyl, and Van der Waals interactions. To improve stability and fit, steric hindrance with PHE 91 A must be optimized. While in case of standard indomethacin, van der Waals, covalent, and Pi-Pi stacking confirmed good binding interactions with mPGES-1 (6VL4).

IV. CONCLUSION

The molecular docking has taken more attention in the analysis of drug receptor interaction& target identification. The current article emphasizes on the virtual analysis of drug, hydrophobic interaction with receptor prostaglandin synthase, electrostatic interaction between the receptor prostaglandin synthase furthermore from the result & discussion it was revealed that the moldock score of the flavonoid had more affinity towards receptor site while in standard indomethacin drug had less affinity towards the receptor site. So, our drug may have good binding affinity towards the enzyme & it may produce the desired therapeutic effect.

V. ACKNOWLEDGEMENT

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