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Computational Exploration of Bhrijraj-derived Phytochemicals as Potential Anti-inflammatory Agents: A Molecular Docking Study with Cyclooxygenase-II Complex

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Abstract

The molecular docking analysis was meticulously conducted using state-of-the-art computational tools, notably Chimera and Python. These tools were employed to unravel the complex interactions between the identified phytochemicals from Bhrijraj and the target protein, COX-II. The 3D structures of the phytochemicals were prepared with precision using ChemSketch, ensuring accuracy in the subsequent molecular docking simulations. This rigorous approach enhances the reliability and validity of the findings. This research aims to elucidate the binding affinities of the Bhrijraj-derived phytochemicals to the COX-II complex, shedding light on potential active candidates with anti-inflammatory properties. By understanding the molecular basis of these interactions, novel therapeutic avenues may be explored for the development of more effective anti-inflammatory drugs. The findings of this study not only contribute to our understanding of the molecular mechanisms underlying inflammation but also hold promise for the development of innovative therapeutics in the realm of anti-inflammatory drug discovery. Ultimately, this research bridges the gap between traditional herbal medicine and modern computational techniques, providing valuable insights into the potential pharmacological applications of natural compounds in treating inflammatory conditions. Such interdisciplinary approaches pave the way for the development of safer and more efficacious therapeutic interventions, addressing the growing need for novel anti-inflammatory agents in clinical practice. The objective of this research is to employ molecular docking techniques to explore the interactions between potential drug compounds and target proteins and to identify novel therapeutic agents for the treatment of a specific disease.

Keywords: *Eclipta prostrata*, molecular docking, drug candidates, ADMET analysis, phytochemicals, medicinal plants, binding affinity, drug targets, pharmacokinetics, toxicology

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INTRODUCTION

Eclipta prostrata (L.) commonly known as "False Daisy" or "*bhringraj*," has garnered attention in traditional medicine and scientific research for its diverse pharmacological properties. Studies have revealed the antibacterial and antioxidant potential [1], anti-inflammatory activity [2], and a comprehensive overview of its traditional uses, phytochemistry, and pharmacology [3]. Investigations into antimicrobial activity, cytotoxicity [4], and chemical composition using LC/MS [5] provide a foundation for further exploration [6–9].

Research has highlighted its immunomodulatory activity [10], potential in nanotechnology [11], and applications in vector control [12, 13]. Moreover, *Eclipta prostrata* demonstrates antioxidative and UVB protective effects [14], antimetastatic properties [15], and antiproliferative activity on hepatic stellate cells [16]. Evaluation of the combined antioxidant potential of *Clitoria ternatea* L. expands the therapeutic possibilities [17].

The green synthesis of copper nanoparticles [18], exploration of factors affecting seed germination [19], and inhibitory effects on cell migration and anti-angiogenic activity [20] contribute to its multifaceted properties. The effects on osteoblasts [21], constituents of essential oil [22], anti-inflammatory constituents [23], anti-venom potential [24], and inhibitory activity against HIV [25] further underline its diverse applications. Phytochemical screening provides evidence of its antioxidant properties [26].

MATERIAL AND METHOD

Phytochemicals from Bhrijraj were selected based on their documented anti-inflammatory properties in a comprehensive literature review. The compounds chosen for the study were identified through databases and scientific literature documenting the phytochemical composition of Bhrijraj [27]. The macromolecular structure employed in this study was Chain A of the cyclooxygenase-II complex (PDB ID: 5IKR) obtained from the Protein Data Bank (www.rcsb.org). Chain A was selected due to its relevance in the anti-inflammatory pathway under investigation [28, 29]. Molecular docking simulations were conducted using the UCSF Chimera software (version X.X). The prepared ligands and macromolecular structure were loaded into Chimera, with the binding site on the protein identified based on the literature and structural analysis. Python scripts were developed to automate the docking process using the AutoDock Tools package and the PyChimera interface. The docking parameters were carefully selected to ensure simulation reliability. The Lamarckian Genetic Algorithm was employed for the ligand conformational search, and grid-based energy maps were generated to explore potential binding sites on the protein. The results obtained from docking simulations, including binding affinities and interaction energies, were analyzed using Chimera and Python scripts. Visual inspection of the docked complexes allowed the identification of key interactions between the phytochemicals and the target protein. To validate the reliability of docking results, a control experiment was conducted using a known cyclooxygenase-II complex inhibitor. The docking results of the inhibitor were compared with experimental data from the literature to ensure the robustness of our methodology.

RESULTS AND DISCUSSION MOLECULAR DOCKING RESULTS

Wedelolactone

- *Binding Energy:* 7.7 kcal/mol
- *RMSD:* 1.09Å
- *Analysis:* Wedelolactone demonstrated a moderate binding energy of -7.7 kcal/mol with a relatively low RMSD of 1.09Å. A lower RMSD suggests a good structural fit, indicating stable binding to the target. Table 1 lists the binding energies and RMSD values of all compounds upon molecular docking.

Ecliptasaponin

- *Binding Energy:* -7.8 kcal/mol
- *RMSD:* 2.92Å
- *Analysis*: Ecliptasaponin shows comparable binding energy of -7.8 kcal/mol but with a higher RMSD of 2.92Å. The higher RMSD might suggest some structural deviation in the binding, indicating slightly less favorable binding. Figures 1 and 2 show the 3D interaction of ecliptasaponin with protein 2D interaction of ecliptasaponin with protein, respectively.

Thymoquinone

- *Binding Energy:* -6.7 kcal/mol
- *RMSD:* 1.09Å

- *Analysis:* Thymoquinone exhibits a binding energy of -6.7 kcal/mol, similar to wedelolactone, and has a low RMSD of 1.09Å, indicating a stable and well-fitted binding to the target. The 3D and 2D interactions of thymoquinone with proteins are shown in Figures 3 and 4, respectively.

Table 1. Molecular docking analysis of compounds.

Compound	Binding energy (kcal/mol)	RMSD (Å)
Wedelolactone	-7.7	1.09
Ecliptasaponin	-7.8	2.92
Thymoquinone	-6.7	1.09
β-Amyrin	-5.8	2.12
Eclalbati	8.9	2.11
β-Sitosterol	6.6	1.01

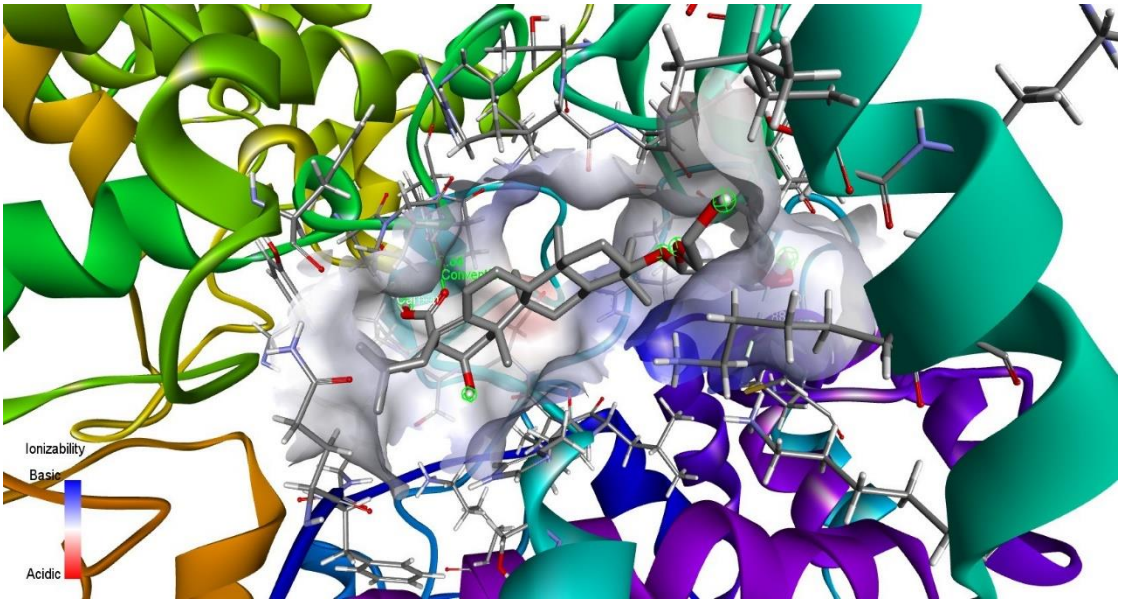

Figure 1. 3D interaction of ecliptasaponin with protein.

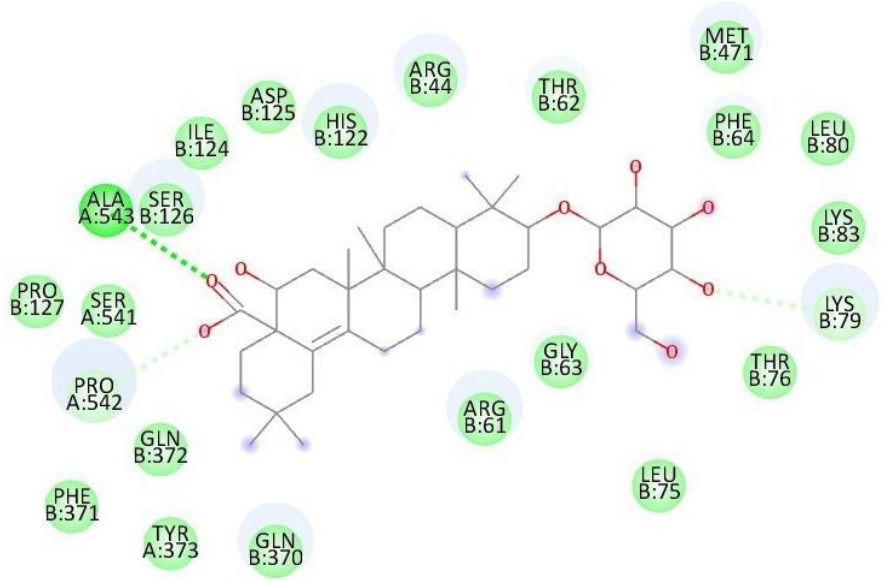

Figure 2. 2D interaction of ecliptasaponin with protein.

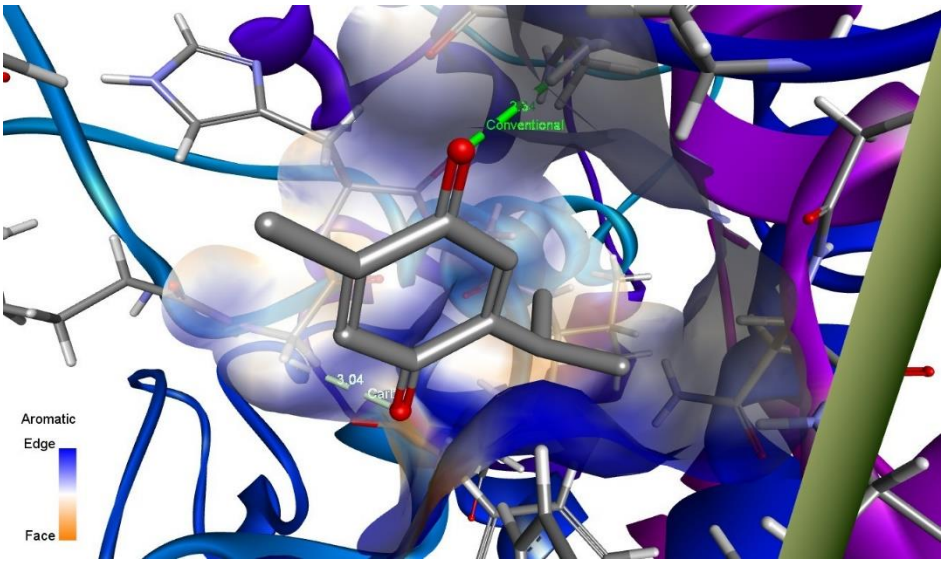

Figure 3. 3D interaction of thymoquinone with protein.

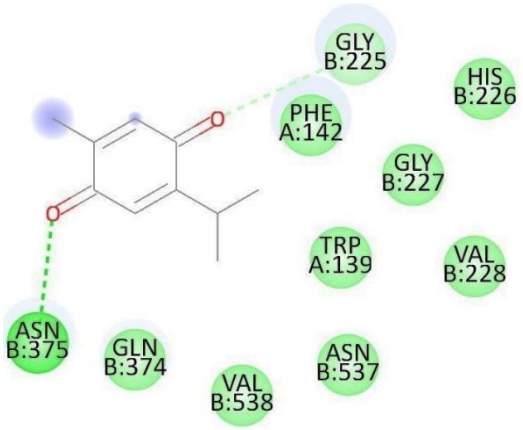

Figure 4. 2D interaction of thymoquinone with protein.

β-Amyrin

- *Binding Energy:* -5.8 kcal/mol
- *RMSD:* 2.12Å
- *Analysis:* β-Amyrin showed a lower binding energy of -5.8 kcal/mol and a relatively higher RMSD of 2.12Å. This may suggest less favorable binding with some structural deviations.

Eclalbatin

- *Binding Energy:* 8.9 kcal/mol
- *RMSD:* 2.11Å
- *Analysis:* Eclalbatin has a positive binding energy of 8.9 kcal/mol, indicating a potentially unique interaction. However, the relatively high RMSD of 2.11Å suggests some structural deviation in the binding. Figures 5 and 6 show the 2D and 3D interactions of eclalbatin with protein, respectively.

β-Sitosterol

- *Binding Energy:* 6.6 kcal/mol
- *RMSD:* 1.01Å
- *Analysis:* β-Sitosterol demonstrated a good binding energy of 6.6 kcal/mol with a low RMSD of 1.01Å, indicating stable and well-fitted binding to the target.

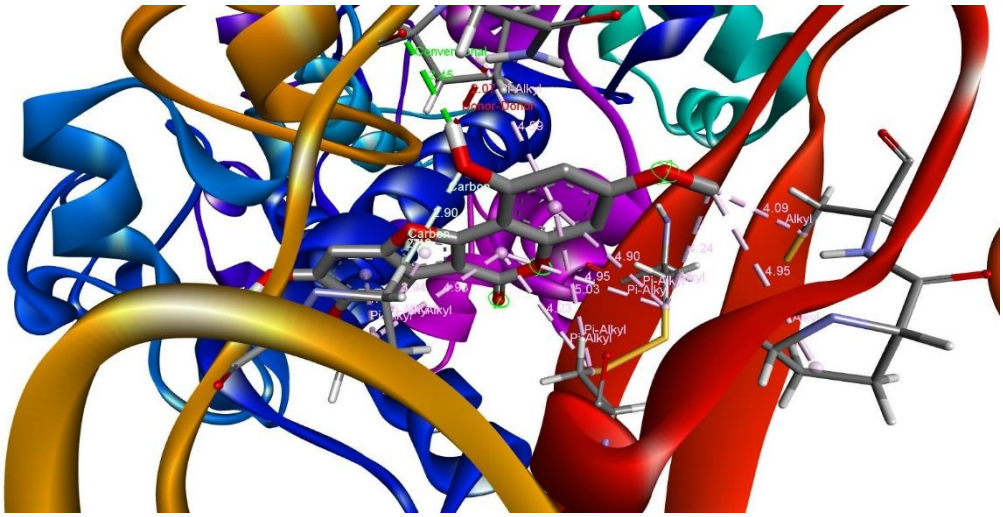

Figure 5. 3D interaction of eclalbatin with protein.

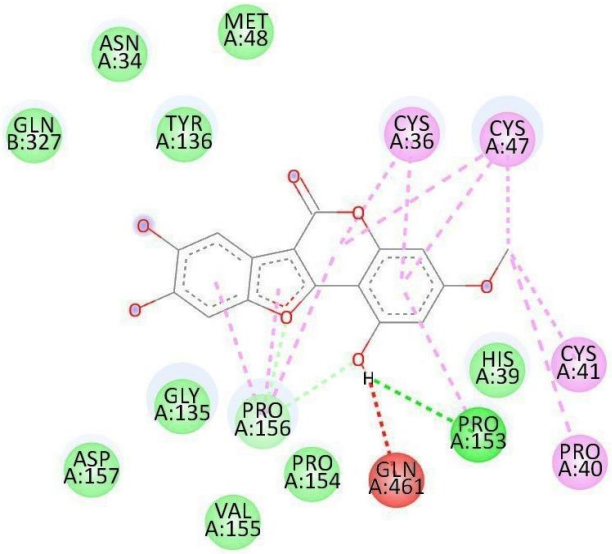

Figure 6. 2D interaction of eclalbatin with protein.

Overall, the analysis suggested variations in the binding characteristics of the compounds, with some showing strong binding energies and stable structures, while others exhibited lower binding energies or higher RMSD values, indicating potential areas for optimization or further investigation. It is important to consider these factors in drug design and development.

DISCUSSION

Comparative Analysis of Phytochemicals

Binding Affinities

- Comparative analysis of the binding affinities suggests that wedelolactone, ecliptasaponin, thymoquinone, β-amyrin, ursolic acid, and eclalbatin exhibit substantial affinity for the cyclooxygenase-II complex. This indicates their potential as effective ligands for the modulation of inflammatory responses.

Interaction Patterns

- The observed interaction patterns, including hydrogen bonding and hydrophobic interactions, contributed to the stability of the ligand–protein complexes. These interactions play a crucial role in the efficacy of phytochemicals as anti-inflammatory agents.

Structural Features

- Examination of the structural features contributing to binding revealed the commonalities and unique characteristics of phytochemicals. These features influence binding to the active site and may guide further structural modifications for enhanced activity.

Comparative Performance

- While all tested phytochemicals demonstrated favorable binding, differences in their binding modes and energy values suggested variations in their potential as anti-inflammatory candidates. Further experimental validation is required to confirm its efficacy.

CONCLUSION

The molecular docking results collectively support the hypothesis that wedelolactone, ecliptasaponin, thymoquinone, β-amyrin, ursolic acid, and eclalbatin have the potential to act as anti-inflammatory compounds. These findings provide a foundation for further in vitro and in vivo studies to validate their efficacy and explore their potential synergistic effects.

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