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Research Article

Identification of Potential Anti-Inflammatory Phytochemicals from Leucas Aspera Using A Computer-Aided Drug Design Approach

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Background: Leucas aspera is a medicinal plant traditionally used for the treatment of inflammatory disorders. The present study aimed to evaluate selected phytochemicals from Leucas aspera as potential anti-inflammatory agents using a computer-aided drug design approach. Methods: Eight phytochemicals, namely ursolic acid, oleanolic acid, apigenin, chrysoeriol, catechin, β-sitosterol, acacetin, and β-caryophyllene, were screened against the anti-inflammatory target protein Microsomal Prostaglandin E synthesis-1 (mPGES-1, PDB ID: 5IKR) using molecular docking. Docking studies were performed using AutoDock Vina integrated in PyRx. Protein–ligand interactions were analyzed using Discovery Studio Visualizer. Drug-likeness and pharmacokinetic properties were evaluated using SwissADME. The crystal structure of mPGES-1 (PDB ID: 5IKR) was retrieved from the Protein Data Bank and used as the molecular target for docking studies. Results: Ursolic acid exhibited the highest binding affinity (-9.4 kcal/mol), followed by oleanolic acid (-9.0 kcal/mol) and apigenin (-9.0 kcal/mol). Apigenin, acacetin, catechin, and chrysoeriol demonstrated favorable pharmacokinetic properties with high gastrointestinal absorption and no Lipinski rule violations. Interaction analysis revealed hydrogen bond formation with key amino acid residues including SER143, ASN144, CYS47, ARG376, HIS226, ARG456, LEU171, and GLN372. SwissADME analysis revealed favorable drug-likeness and pharmacokinetic profiles for selected compounds. Conclusion: The study identified ursolic acid, oleanolic acid, and apigenin as promising phytoconstituents with potential anti-inflammatory activity. Further in vitro and in vivo studies are required to validate these findings.

Keywords: Leucas aspera, molecular docking, anti-inflammatory activity, SwissADME, phytochemicals, AutoDock Vina, mPGES-1, Computer-Aided Drug Design.

INTRODUCTION

Inflammation is a protective biological response to tissue injury, infection, and other harmful stimuli[10,11]. Chronic inflammation contributes to numerous diseases including arthritis, cardiovascular disorders, and autoimmune diseases[12,13]. Although several anti-inflammatory drugs are available, long-term use may result in adverse effects. Medicinal plants represent an important source of bioactive compounds with therapeutic potential[4,5]. Leucas aspera (Willd.) Link, belonging to the family Lamiaceae, has been traditionally used for the treatment of inflammation, fever, skin disorders, and other ailments[7,9]. Previous phytochemical investigations have reported the presence of flavonoids, terpenoids, sterols, and phenolic compounds in the plant[5,8,9]. Computer-aided drug design (CADD) techniques, particularly molecular docking, provide an efficient approach for identifying potential drug candidates by predicting ligand–protein interactions[20,22,29]. Therefore, the present study was undertaken to evaluate selected phytochemicals from Leucas aspera against an anti-inflammatory target protein using molecular docking and pharmacokinetic analysis. Microsomal prostaglandin E synthase-1 (mPGES-1) is a terminal enzyme involved in prostaglandin E2 biosynthesis and plays a crucial role in inflammatory responses[26,28].

Selective inhibition of mPGES-1 has emerged as a promising strategy for development safer anti-inflammatory agents. Recent advances in computer-aided drug design (CADD) have accelerated the identification of bioactive compounds through virtual screening molecular docking, and pharmacokinetics prediction.

MATERIALS AND METHODS

1. Selection of Phytochemicals

Eight phytochemicals reported from *Leucas aspera* were selected:

1. Ursolic acid
2. Oleanolic acid
3. Apigenin
4. Chrysoeriol
5. Catechin
6. β-Sitosterol
7. Acacetin
8. β-Caryophyllene

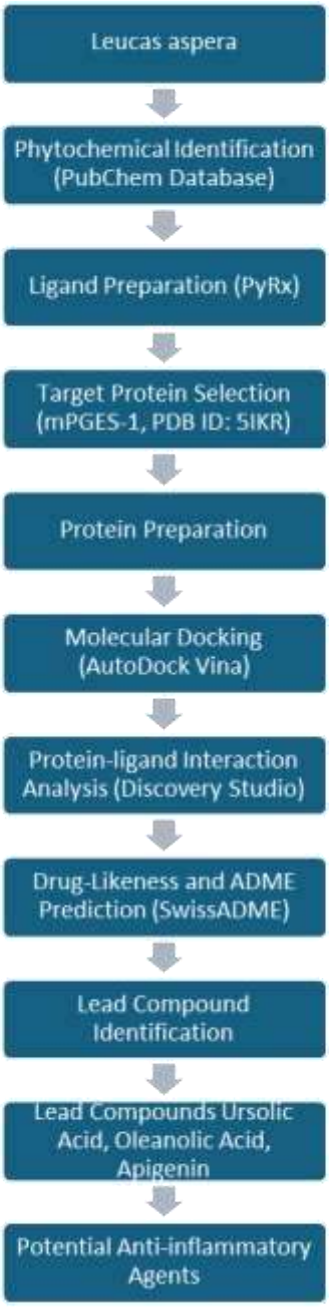

Figure 1. Workflow of the computer-aided drug design (CADD) approach employed for the identification of potential anti-inflammatory phytochemicals from *Leucas aspera* targeting mPGES-1 (PDB ID: 5IKR).

2. Ligand Preparation

The three-dimensional structure of the selected phytochemicals were obtained from PubChem database in SDF format. Energy minimization and conversion into PDBQT format were performed using PyRx software.

3. Protein Preparation

The crystal structure of the anti-inflammatory target protein (PDB ID: 5IKR) was retrieved from the Protein Data Bank. Water molecules and unwanted heteroatoms were removed before docking.

4. Molecular Docking

Molecular docking was performed using AutoDock Vina implemented in PyRx 0.8[1,3]. The crystal structure of mPGES-1 (PDB ID: 5IKR) was used as the target protein. The docking search was defined with grid center coordinates X=20.9683, Y=20.1647, and Z=33.7710 and dimensions of 59.2686 Å × 66.4320 Å × 77.6215 Å. All selected phytochemicals were docked using the same grid parameters. The binding conformations were ranked according to binding affinity, and the pose with the lowest binding energy was selected for further analysis. Binding affinity values were recorded in kcal/mol.

5. Interaction Analysis

Protein-ligand interactions were visualized and analyzed using Discovery Studio Visualizer to identify hydrogen bonds and hydrophobic interactions.

6. Drug-Likeness and Pharmacokinetics Evaluation

Drug-likeness properties and ADME parameters were predicted using SwissADME[2,32,33].

Result and Discussion

1. Molecular Docking Analysis

The docking results demonstrated varying binding affinities among the selected phytochemicals.

Table 1. Molecular Docking Results

Rank	Compound	Binding Affinity (kcal/mol)
1	Ursolic acid	-9.4
2	Oleanolic acid	-9.0
3	Apigenin	-9.0
4	Chrysoeriol	-8.6
5	Catechin	-8.6
6	β-Sitosterol	-8.6
7	Acacetin	-8.4
8	β-Caryophyllene	-6.8

Among all compounds evaluated, ursolic acid demonstrated the strongest binding affinity, indicating a greatest tendency to interact with the active site of the target protein.

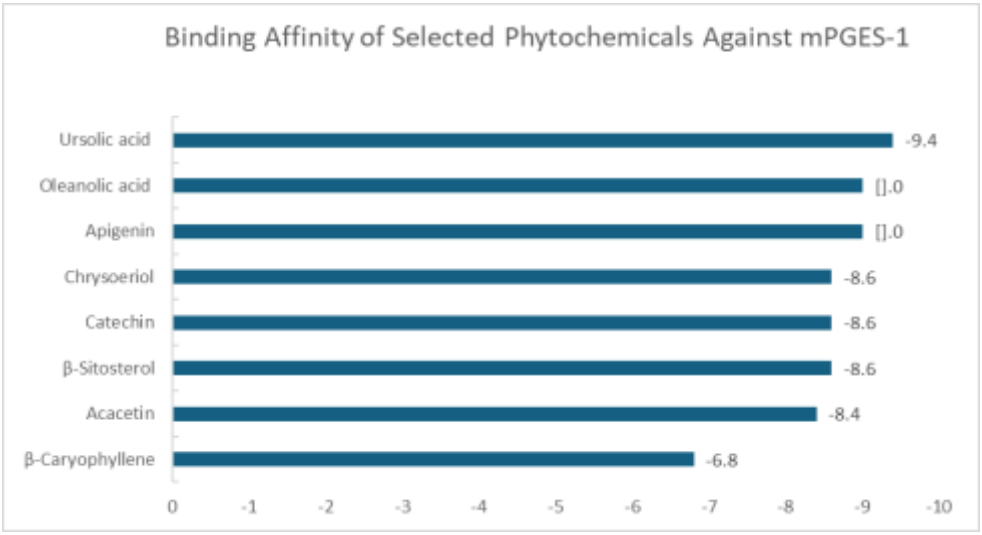

Figure 2. Comparison of molecular docking binding affinities of selected phytochemicals from Leucas aspera against mPGES-1 (PDB ID: 5IKR).

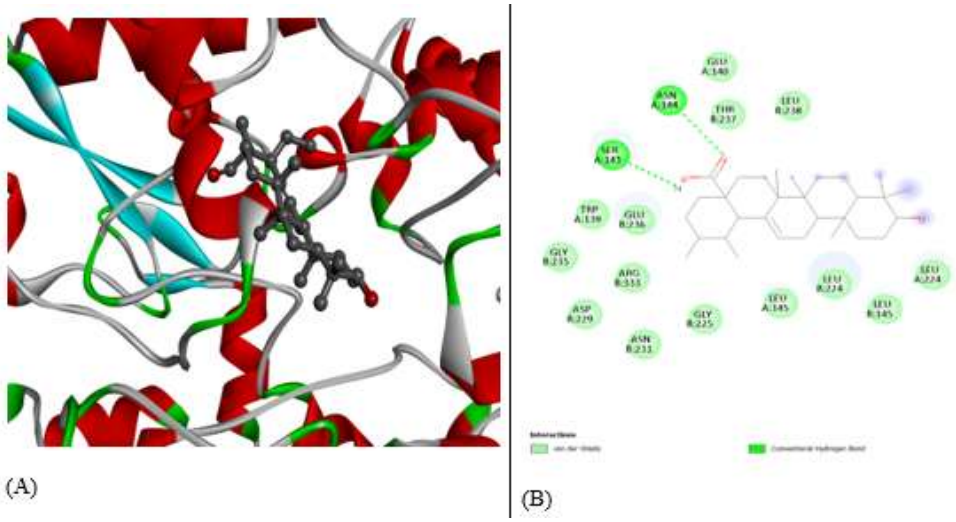

Figure 3. Molecular docking interaction of ursolic acid with 5IKR. (A) Three-dimensional binding pose of Ursolic acid within the active site of microsomal prostaglandin E synthase-1(mPGES-1; PDB ID: 5IKR). (B) Two-dimensional protein-ligand interaction diagram showing the binding interaction of ursolic acid with residue in the active site.

2. Protein-Ligand Interaction analysis

Table 2. Protein-Ligand Interaction Analysis

Compound	H-Bond Residues
Ursolic acid	SER143, ASN144
Oleanolic acid	ARG456, LEU171
Apigenin	CYS47
Chrysoeriol	ARG376, HIS226
Catechin	ARG376, HIS226
β-Sitosterol	ARG376, HIS226
Acacetin	CYS47
β-Caryophyllene	GLN372

Hydrogen bonding and hydrophobic interactions contributed to ligand stabilization within the binding pocket.

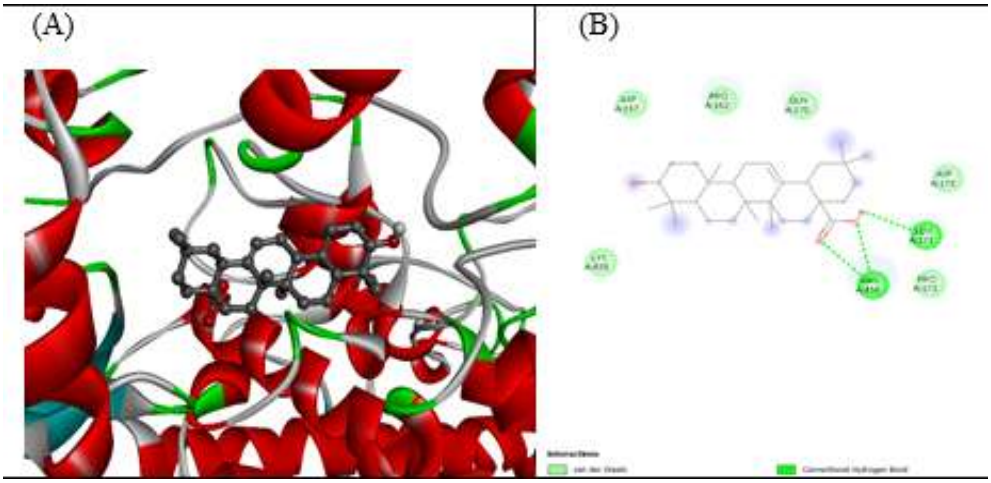

Figure 4. Molecular docking interaction of Oleanolic acid with 5IKR. (A) Three-dimensional binding pose of Oleanolic acid within the active site of microsomal prostaglandin E synthesis-1 (mPGES-1; PDB ID: 5IKR), illustrating its accommodation within the receptor binding pocket. (B) 2D protein-ligand interaction diagram of oleanolic acid docking with 5IKR showing interactions with ARG456 and LEU171 residues.

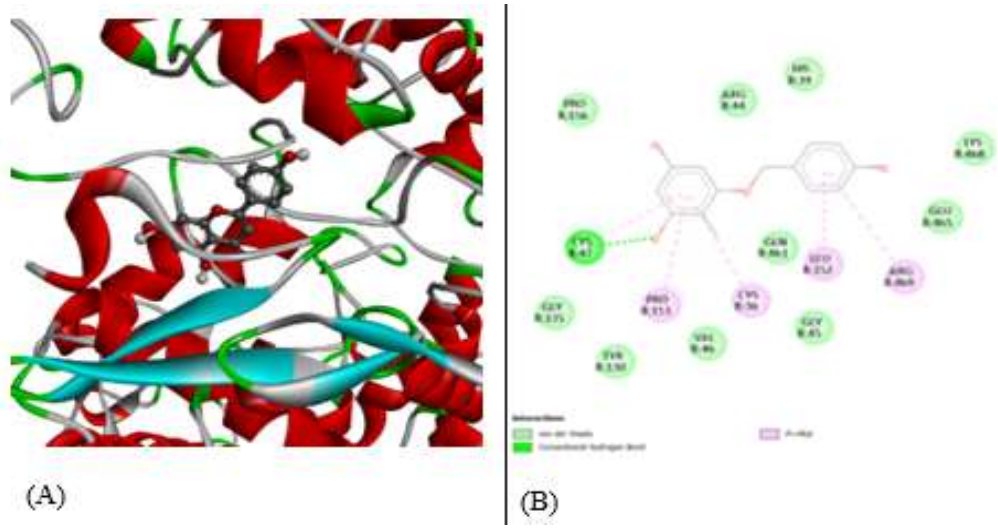

Figure 5. Molecular docking interaction of apigenin with 5IKR. (A) Three-dimensional binding pose of apigenin within the active site of microsomal prostaglandin E synthesis-1 (mPGES-1; PDB ID: 5IKR), illustrating its accommodation within the receptor binding pocket. (B) 2D protein-ligand interaction diagram of apigenin docking with 5IKR showing hydrogen bond interaction with CYS47 residue.

3. SwissADME Analysis

Table 3. SwissADME Properties

Compound	Molecular weight	LogP	GI Absorption	Lipinski Violations	Bioavailability Score
Ursolic acid	456.70g/mol	6.43	Low	1	0.85
Oleanolic acid	456.70g/mol	6.60	Low	1	0.85
Apigenin	270.24g/mol	1.53	High	0	0.55
Chrysoeriol	300.26g/mol	1.45	High	0	0.55
Catechin	290.27g/mol	0.70	High	0	0.55
β-Sitosterol	414.71g/mol	7.78	Low	1	0.55
Acacetin	284.26g/mol	1.87	High	0	0.55
β-Caryophyllene	204.35g/mol	4.48	Low	1	0.55

DISCUSSION

The observed docking scores indicate that triterpenoids such as ursolic acid and oleanolic acid possess strong binding affinity toward the selected anti-inflammatory target. Previous studies have reported significant anti-inflammatory effects of these compounds through inhibition of inflammatory mediators and signaling pathways. Apigenin, a well-known flavonoid, has also demonstrated anti-inflammatory activity through modulation of NF-kB and cytokine production[18,19,34,37]. The present findings are consistent with previous reports and further support the therapeutic potential of phytochemicals present in Leucas aspera[7,9,40]. Ursolic acid exhibited the highest binding affinity (−9.4 kcal/mol), suggesting stronger interaction with the active site of mPGES-1 compared with the other phytochemicals investigated. The interaction analysis revealed hydrogen bond formation with SER143 and ASN144 residues, which may contribute to stabilization of the protein–ligand complex. Oleanolic acid and apigenin also demonstrated favorable binding energies and interaction profiles, indicating their potential as promising anti-inflammatory lead compounds.

LIMITATIONS

The present investigation is limited to computational predictions and does not include experimental validation. Therefore, in vitro and in vivo studies are required to confirm the anti-inflammatory activity of the identified lead compounds.

FUTURE PERSPECTIVES

Although molecular docking provides valuable insights into protein-ligand interactions, molecular dynamics (MD) simulations are recommended to further evaluate the stability and conformational behaviour of protein-ligand complexes under physiological conditions. Furthermore, in vitro and in vivo studies are necessary to validate the anti-inflammatory efficacy and safety of the identified lead compounds[20,21,30].

CONCLUSION

The present study employed molecular docking and pharmacokinetic analysis to evaluate the anti-inflammatory potential of phytochemicals from Leucas aspera against Microsomal Prostaglandin E Synthase-1 (mPGES-1; PDB ID: 5IKR). Among the screened compounds, ursolic acid (-9.4 kcal/mol), oleanolic acid (-9.0 kcal/mol), and apigenin (-9.0 kcal/mol) demonstrated the most favourable binding affinities toward the target protein. SwissADME analysis further revealed promising pharmacokinetic characteristics and drug-likeness profiles for these compounds. Among all the compounds investigated, ursolic acid exhibited the highest binding affinity and may represent the most promising lead candidate for further development. These findings suggest that phytochemicals from Leucas aspera may serve as potential anti-inflammatory lead molecules for future drug development. However, further molecular dynamics simulations and experimental validation through in vitro and in vivo studies are required to confirm their therapeutic efficacy and safety.

Conflict of Interest

The authors declare no conflict of interest.

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