Computational Evaluation of Mimosa pudica Phytoconstituents for Parkinson's Disease: A Network Pharmacology and Molecular Docking Approach

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A B S T R A C T

This study explores the therapeutic potential of phytoconstituents derived from Mimosa pudica in the treatment of Parkinson's disease (PD) using an integrative computational approach. Seventeen bioactive compounds were identified through database and literature mining and subsequently screened using pharmacokinetic and ADMET analysis to evaluate their drug-likeness and oral bioavailability. Network pharmacology revealed 261 common gene targets shared between PD and Mimosa pudica constituents. Protein-protein interaction (PPI) network analysis identified key hub targets, including SRC, AKT1, DRD2, HSP90AA1, and BCL2, which are implicated in neurodegeneration and dopaminergic signalling. Molecular docking showed high binding affinities, particularly for Myricetin-3-O-beta-D-xylopyranoside, which interacted strongly with multiple targets, including HSP90 and DRD2, suggesting potential neuroprotective and dopamine-regulating effects. These findings support Mimosa pudica as a promising source of lead compounds for PD therapeutics and demonstrate the value of in silico tools in herbal drug discovery.

Keywords:

Parkinson's disease; Mimosa pudica; network pharmacology; molecular docking; myricetin-3-O-beta-D-xylopyranoside; phytoconstituents; neuroprotection; dopaminergic synapse; HSP90; DRD

1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder primarily characterised by the loss of dopaminergic neurons in the substantia nigra, a brain region critical for motor control. (1,2) First described by James Parkinson in 1817 as "shaking palsy," PD is now recognised as the second most common neurodegenerative disease after Alzheimer's disease, with prevalence increasing with age. (3) Its cardinal motor symptoms include tremors, bradykinesia (slowness of movement), rigidity, and postural instability, while non-motor symptoms often include cognitive decline, mood disorders, sleep disturbances, and autonomic dysfunction. (4)

The pathophysiology of PD is multifaceted, involving not only dopamine depletion but also the misfolding and aggregation of alpha-synuclein protein, forming Lewy bodies that contribute to neuronal dysfunction. (5) Genetic, environmental, and age-related factors are key contributors, with certain gene mutations (e.g., SNCA, LRRK2) and exposure to neurotoxins (e.g., pesticides) being linked to increased risk. (6) Epidemiologically, more than 10 million individuals worldwide are affected by PD, with a higher prevalence observed in men and those over 60 years of age. (7)

Current pharmacological therapies, including levodopa, dopamine agonists, MAO-B inhibitors, and COMT inhibitors, provide symptomatic relief but are often associated with significant side effects and do not halt disease progression. (8) Long-term use of these drugs can lead to motor fluctuations, dyskinesia, hallucinations, and various systemic complications. (9)

Given these limitations, interest in plant-derived compounds as alternative or complementary therapies is increasing. (10) Mimosa pudica, commonly known as the "touch-me-not" plant, is traditionally recognised for its neuroprotective, antioxidant, and anti-inflammatory properties. (11) Recent studies have indicated that its phytoconstituents, particularly myricetin-3-O-beta-D-xylopyranoside, may play a role in neuroprotection by modulating oxidative stress and dopamine regulation. (12)

Advancements in computational biology have facilitated drug discovery using techniques such as network pharmacology and molecular docking. (13) Network pharmacology integrates systems biology and bioinformatics to explore the multi-target actions of phytochemicals, while molecular docking predicts the binding affinity between ligands and their protein targets.

(14) These tools offer a cost-effective approach to screening plant-based compounds for their therapeutic potential against complex diseases like PD.(15)

This study applies an integrative computational methodology combining phytochemical screening, ADMET analysis, network pharmacology, and molecular docking to explore the potential of Mimosa pudica-derived compounds in targeting key proteins involved in Parkinson's disease. (16) Through this approach, the research aims to identify bioactive candidates that could contribute to the development of safer, more effective treatments. (17)

2. Materials and Methods

2.1 Screening of Phytoconstituents

Phytoconstituents of Mimosa pudica were identified through an extensive literature review and various databases, including Google Scholar and PubChem. The 3D structures and physicochemical properties of the compounds were retrieved using compound names, formulas, and CID/SID identifiers. Canonical SMILES notation was employed to further explore the pharmacokinetic properties of all active compounds.

2.2 Compound/Ligand Selection through Pharmacokinetic Properties and ADMET Analysis

Pharmacokinetic properties of the compounds were evaluated using SwissADME and MolSoft software. Screening was based on Lipinski's Rule of Five criteria, emphasising oral bioavailability (OB $\geq$ 30%), molecular weight (MW $<$ 500 Da), drug-likeness (DL $\geq$ 0.18), hydrogen bond donors ($<$ 5), octanol-water partition coefficient (log P $<$ 5), and hydrogen bond acceptors ($<$ 10). ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) properties were also predicted using SwissADME to assess key characteristics such as blood-brain barrier penetration and gastrointestinal absorption.

2.3 Network Pharmacology Profiling and Target Screening for Parkinson's Disease

Potential targets of active compounds were predicted using Swiss Target Prediction by inputting canonical SMILES and specifying species as Homo sapiens. Parkinson's disease-associated targets were retrieved from GeneCards. The common targets between compounds and Parkinson's were identified via Venn diagram analysis using bioinformatics tools.

2.4 Construction of Compound-Target Network

A compound-target interaction network was constructed using Cytoscape v3.10.3, where nodes represent compounds and targets, and edges represent interactions. Network Analyser was used to assess the network's topology, filtering nodes by degree (number of connections) to highlight key interactions.

2.5 Protein-Protein Interaction (PPI) Network and Hub Gene Identification

The protein-protein interaction network of 262 common targets was obtained from the STRING database specifying Homo sapiens as the organism. Visualisation and analysis were performed in Cytoscape v3.10.3, and hub genes were identified using the CytoHubba plugin based on node degree, indicating key target proteins with high connectivity.

2.6 Construction of Target-Compound-Pathway Network

KEGG pathway data for the top hub genes were retrieved from GeneCodis, and a target-compound-pathway network was constructed to elucidate the mechanisms of active compounds within relevant biological pathways.

2.7 Gene Ontology (GO) and KEGG Pathway Analysis

GO annotation and KEGG pathway enrichment analysis were performed using GeneCodis for Homo sapiens. Gene functions were classified into biological processes (BP), cellular components (CC), and molecular functions (MF). The top 20 enriched GO terms and KEGG pathways were selected based on a significance cutoff ($p < 0.05$) and visualised via Shiny GO using bar and lollipop plots.

2.8 Molecular Docking

3D structures of active compounds were downloaded from PubChem in SDF format and optimised. In contrast, protein structures of potential targets were obtained from RCSB PDB (selected based on resolution, completeness, and human origin). Proteins were prepared by removing water molecules and ligands using UCSF Chimaera. Ligands and proteins were further processed using AutoDock Tools v1.5.6 for charging, hydrogenation, and normalisation to generate PDBQT files. Molecular docking simulations were performed using AutoDock Vina to predict binding interactions, utilising its automated grid and fast processing capabilities.

3. Result and Discussion

3.1 Phytochemical Screening and Drug-Likeness Analysis

A total of 17 phytoconstituents from Mimosa pudica were selected through literature and database screening. Among them, 12 compounds passed ADMET screening and Lipinski's Rule of Five, indicating favourable pharmacokinetic profiles and potential oral bioavailability. These included Myricetin-3-O-beta-D-xylopyranoside, Quercetin derivatives, Luteolin, and Diplotrin B, among others. Most compounds exhibited high gastrointestinal absorption and blood-brain barrier permeability, essential characteristics for CNS-targeted therapeutics.

Figure 2. Drug Likeness

	A	B
1	**COMPOUND**	**DRUG LIKELINESS**
2	Co-careldopa	1.01
3	Norepinephrine	0.98
4	Quercetin 3-O-beta-D-xylopyranoside	0.93
5	myricetin-3-O-beta-D-xylopyranoside	0.74
6	Myricetin-3-O-arabinofuranoside	0.65
7	Quercetin-3-o-alpha-d-arabinofuranoside	0.6
8	Quercetin	0.52
9	5,3'-di-O-methylluteolin	0.42
10	Luteolin	0.38
11	7,3',4'-trihydroxy-3,8-dimethoxyflavone	0.16
12	Diplotrin B	0.13
13	Diplotasin	-0.05
14	2'-hydroxy-3,7,8,4',5'-pentamethoxyflavone	-0.18
15	Diplotrin A	-0.18
16	Diplotrin C	-0.27
17	Hernancorizin	-0.29
18	10H-phenothiazine	-1.08

3.2 Network Pharmacology and Target Prediction

SwissTargetPrediction identified 313 potential targets for the selected compounds. From GeneCards, 11,548 Parkinson's disease-associated targets were retrieved. After deduplication and intersection, 261 common targets were identified, suggesting a strong therapeutic overlap between Mimosa pudica constituents and Parkinson's disease pathology.

3.3 Compound-Target and Protein-Protein Interaction (PPI) Network

A compound-target interaction network constructed using Cytoscape showed multiple compounds targeting several Parkinson 's-related genes, supporting a multi-target mechanism. PPI analysis using the STRING database and CytoHubba plugin identified key hub genes, including SRC, ESR1, AKT1, CASP3, BCL2, EGFR, HSP90AA1, HSP90AB1, DRD2, and PRKCA. These proteins are known to play critical roles in cell survival, apoptosis, inflammation, and dopaminergic signalling.

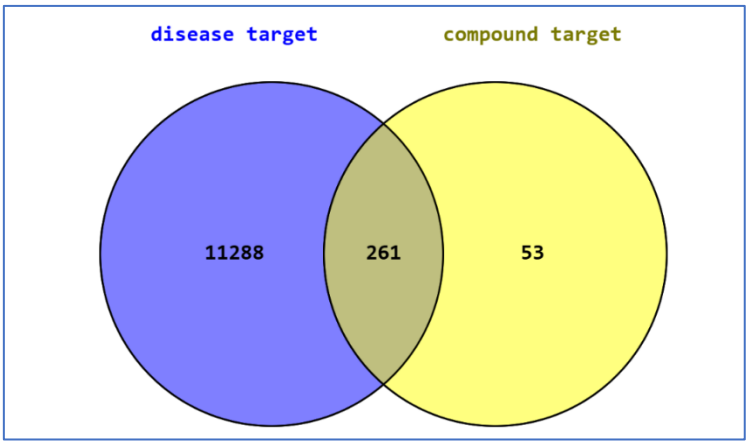


Figure 3. Venn Diagram of Disease Target and Compound Target

3.4 KEGG Pathway and Gene Ontology Enrichment

Enrichment analysis using GeneCodis and Shiny GO revealed significant involvement of the identified targets in several neuro-relevant pathways. The top enriched KEGG pathways included:

- Neuroactive ligand-receptor interaction (49 genes)
- Glutamatergic and dopaminergic synapse
- Calcium signalling pathway
- EGFR tyrosine kinase inhibitor resistance
- Nitrogen metabolism (highest relative enrichment)

These pathways are critically involved in neuronal communication, synaptic transmission, neuroinflammation, and PD pathogenesis.

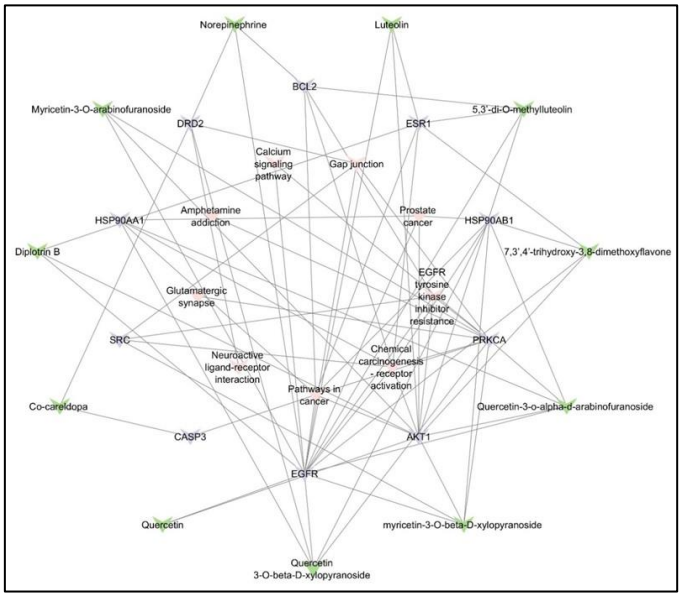
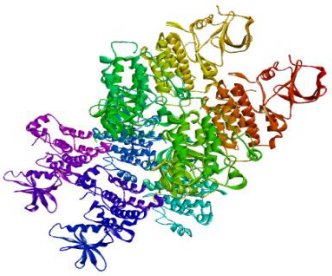
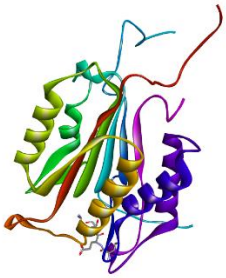
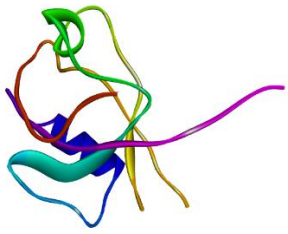


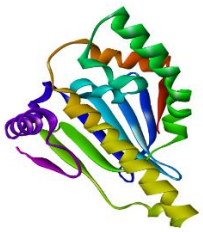
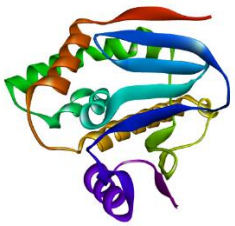
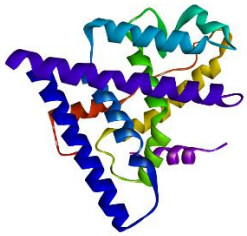
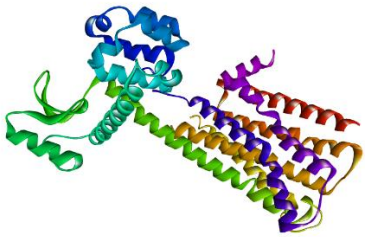
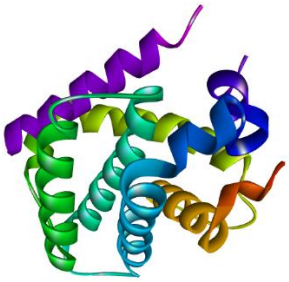
Figure 5. Enrichment Analyses of Targeted Genes (KEGG Pathways)

3.5 Molecular Docking Analysis

Molecular docking using AutoDock Vina showed that Myricetin-3-O-beta-D-xylopyranoside exhibited the strongest binding affinities among all compounds. The highest affinities (most negative ΔG values) were observed for:

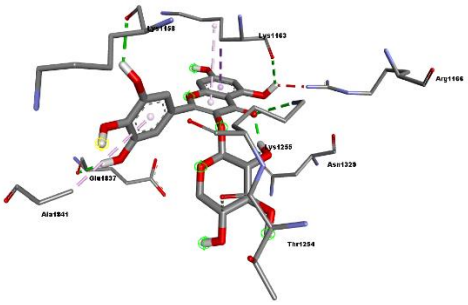
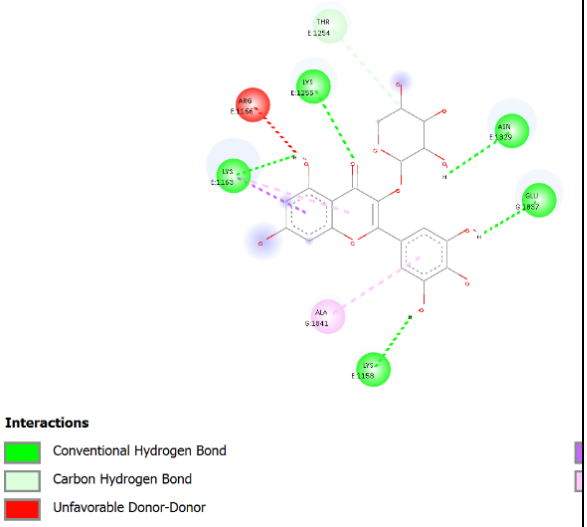
- HSP90AA1 (−10.4 kcal/mol)
- HSP90AB1 (−10.0 kcal/mol)
- SRC (−10.0 kcal/mol)
- DRD2 (−8.1 kcal/mol)
- BCL2, ESR1, AKT1, CASP3 (−6.7 to −7.5 kcal/mol)

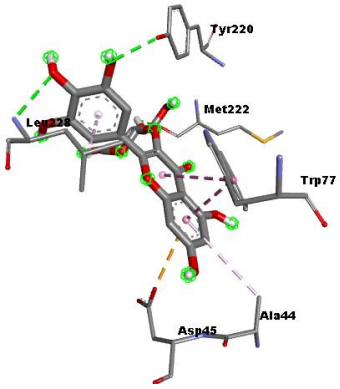
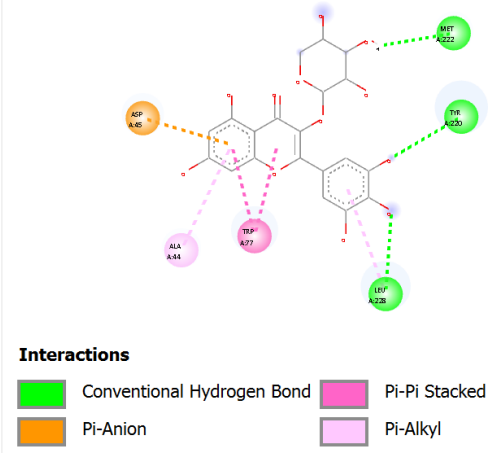
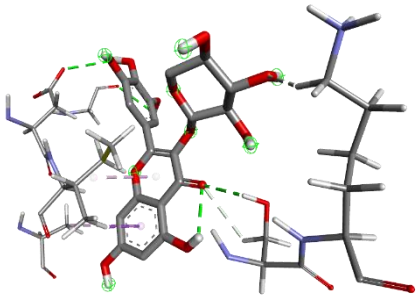
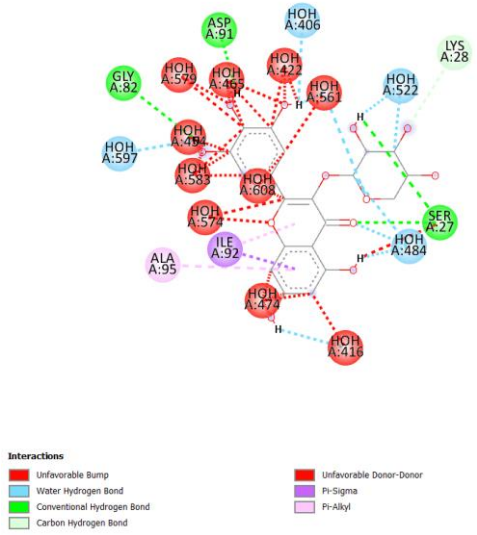
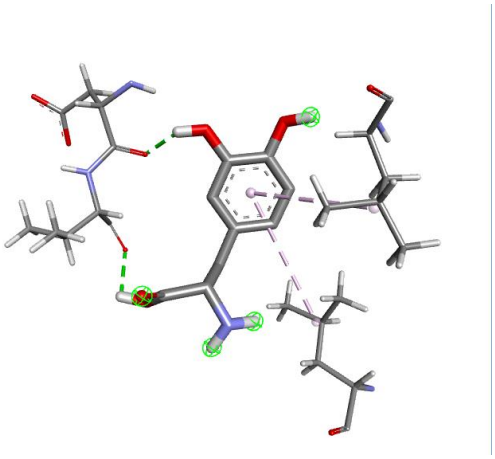
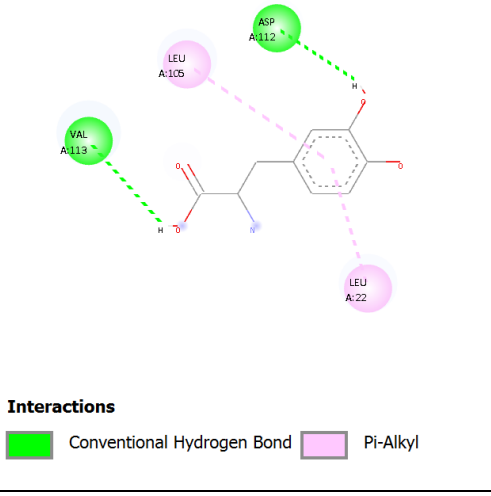
Sr no.	Compound	Target	Target PDB ID	Target Protein Structure	Binding affinity
1.	myricetin-3-O-beta-D-xylopyranoside	SRC	6E6E		-10
2.	myricetin-3-O-beta-D-xylopyranoside	CASB 3	2CNN		-6.7
3	myricetin-3-O-beta-D-xylopyranoside	PRKCA	2GZV		-6.9

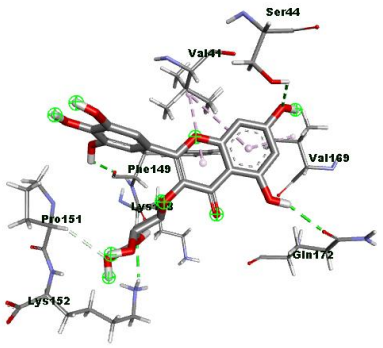
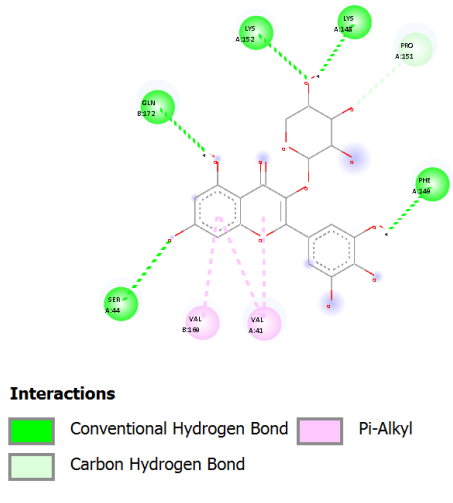
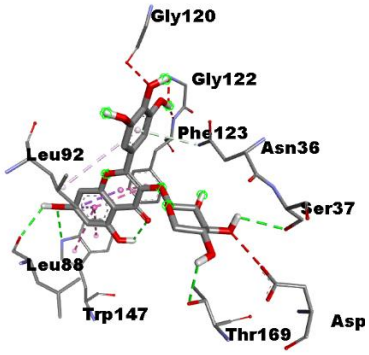
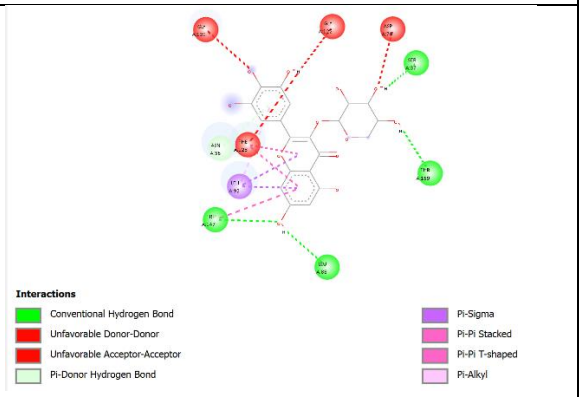
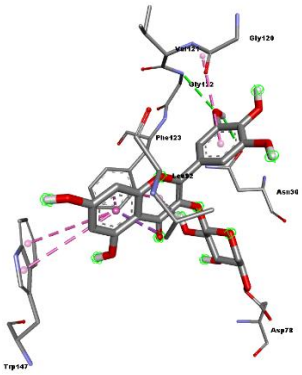
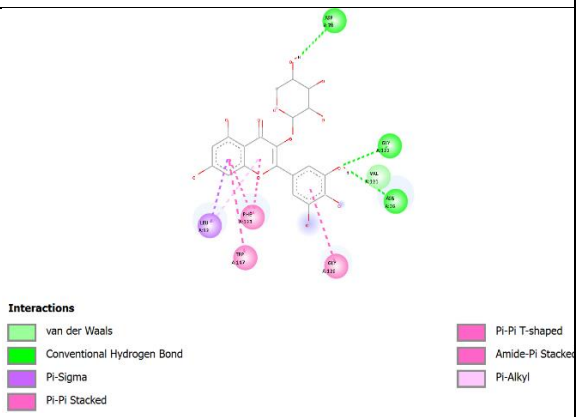
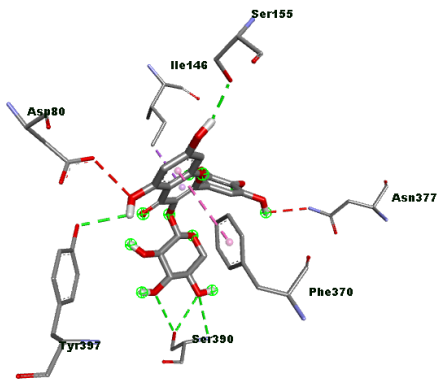
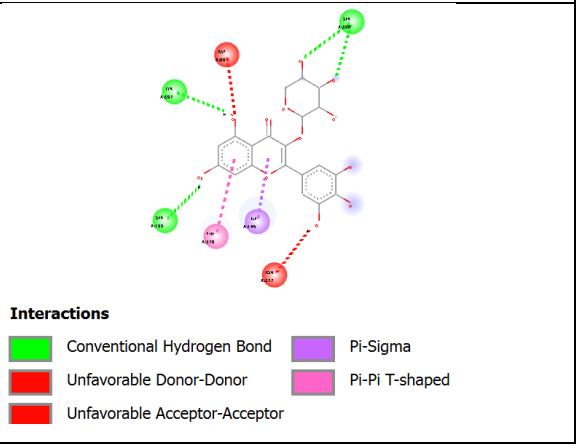
4	myricetin-3-O-beta-D-xylopyranoside	HSBA B1	6N8Y		-10
5.	myricetin-3-O-beta-D-xylopyranoside	HSP90 AA1	3O0I		-10.4
6.	myricetin-3-O-beta-D-xylopyranoside	ESR 1	1SJ0		-7.5
7.	myricetin-3-O-beta-D-xylopyranoside	DRD 2	6CM4		-8.1
8.	myricetin-3-O-beta-D-xylopyranoside	BCL 2	5UUP		-7.5

9.	myricetin-3-O-beta-D-xylopyranoside	AKT 1	8R5K		-7.3

Table No. 3 The Binding Affinity Of Compounds and Core Targets

Protein	3D	2D
SRC		

ESR1		
AKT1		
CASP3		

BCL2		
HSP90 AA1		
HSP90 AB1		
DRD2		

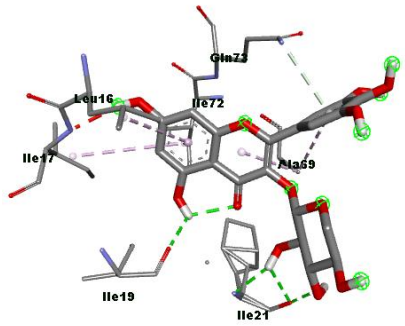
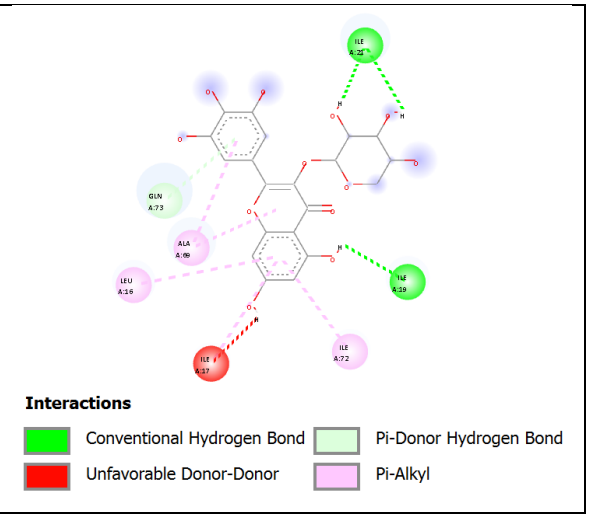
PRKCA		

Table No. 4 3D & 2D structure of Target

The strong binding of Myricetin-3-O-beta-D-xylopyranoside to HSP90 proteins suggests a role in inhibiting alpha-synuclein aggregation, while interaction with DRD2 supports potential restoration of dopaminergic activity.

Binding Affinity Analysis: Binding affinity values (in kcal/mol) indicate the strength of interaction between the ligand (myricetin-3-O-beta-D-xylopyranoside) and the target proteins. More negative binding affinity values indicate stronger binding. The highest binding affinity (most negative value) was observed for: HSP90AB1 (-10.4 kcal/mol), HSP90AA1 (-10 kcal/mol), SRC (-10 kcal/mol). These results suggest that myricetin-3-O-beta-D-xylopyranoside has the strongest interactions with HSP90 proteins and SRC kinase. DRD2 (Dopamine Receptor D2) – Binding Affinity: -8.1 kcal/mol. Dopamine receptors (especially D2 receptors) are crucial for motor function and cognition. In Parkinson's disease, dopamine levels are reduced, leading to impaired DRD2 signalling. Strong binding to DRD2 suggests that myricetin-3-O-beta-D-xylopyranoside might influence dopamine receptor activity, which could help restore dopamine signalling and improve motor symptoms. AKT1 (Protein Kinase B) – Binding Affinity: -7.3 kcal/mol. AKT1 is a key player in neuronal survival and neuroprotection. Reduced AKT1 activity has been linked to dopaminergic neuron degeneration in PD. Strong binding suggests that myricetin-3-O-beta-D-xylopyranoside could enhance AKT1 activity, promoting cell survival and neuroprotection. HSP90 (HSP90AA1 & HSP90AB1) – Binding Affinity: -10.4 and -10 kcal/mol. HSP90 is involved in protein folding and degradation. Misfolded proteins like alpha-synuclein contribute to PD pathology (Lewy bodies). Inhibiting HSP90 can reduce toxic protein aggregation, which is a therapeutic strategy for PD.

4. Conclusion

This study highlights the promising therapeutic potential of Mimosa pudica phytoconstituents in the treatment of Parkinson's disease (PD) through a comprehensive in silico approach integrating network pharmacology and molecular docking. Among the seventeen identified compounds, Myricetin-3-O-beta-D-xylopyranoside emerged as a standout candidate, exhibiting strong binding affinity toward key PD-related targets such as HSP90AA1, HSP90AB1, SRC, and DRD2. The network pharmacology analysis further revealed that these compounds interact with crucial genes involved in dopaminergic signalling, neuroinflammation, and apoptosis, aligning with known PD pathophysiology. KEGG and GO enrichment analyses supported the involvement of these targets in critical neurological pathways, such as dopaminergic synapse and calcium signalling. Overall, the findings underscore the potential of Mimosa pudica as a source of neuroprotective agents and provide a rational basis for further experimental validation and drug development. Future in vitro and in vivo studies are warranted to confirm these computational predictions and explore the pharmacodynamic and pharmacokinetic profiles of the key bioactive compounds.

5. Statements & Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to the study's conception and design. Tejas R. Ghadge and Shraddha M. Desai performed material preparation, data collection, and analysis. Tejas R. Ghadge wrote the first draft of the manuscript, and all authors, Shraddha M. Desai, Sanika S. Kawade, Yashoda M. Dahale, Rinku Choudhary, and Tejas R. Ghadge, commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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