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STRUCTURE-BASED DRUG DESIGN FOR PARKINSON'S DISEASE: MOLECULAR DOCKING ANALYSIS OF NOVEL COMPOUNDS

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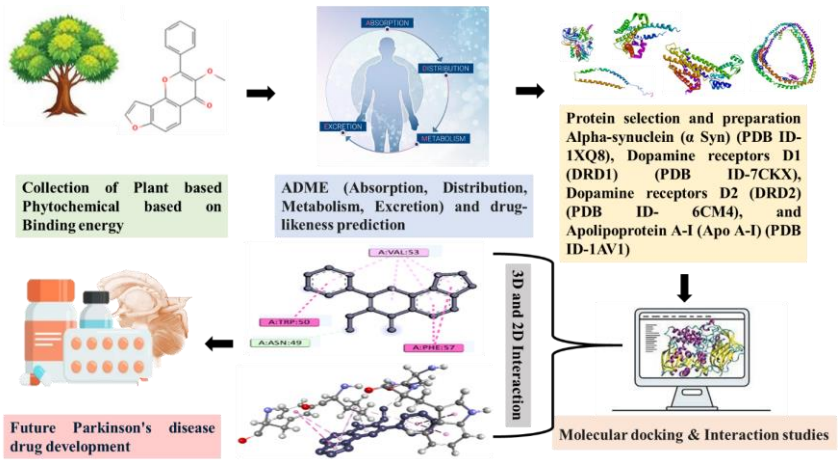
ABSTRACT

Parkinson's disease is a progressive neurodegenerative condition characterized by dopaminergic neuron destruction and misfolded proteins. Current treatments focus on motor symptoms, but do not target neuronal degeneration. Recent studies suggest a connection between lipid metabolism and neurodegenerative disorders. Targets include monoamine oxidase-B, alpha-synuclein, dopamine receptors, and ApoA-I. Plant-derived molecules, including flavonoids and polyphenols, have potential for drug discovery and therapeutic development. In this study, 12 phytoconstituents were docked against different proteins, and their binding affinities, types, and active amino acid residues were analyzed. The top three compounds with the lowest binding energy were identified. The study examined ten phytoconstituents and two medications for their pharmacokinetics, drug-likeness, and toxicity profiles. It predicted inhibitory effects on Parkinson's disease using in silico approaches. All 12 substances adhered to Lipinski's rule of five for oral availability. The study compared natural and synthetic PD adjuvant drugs, finding natural substances with higher binding energies than current market medications.

KEYWORDS: Parkinson's disease, molecular docking, neurodegenerative, pharmacokinetics, drug-likeness, lipinski's rule.

Graphical Abstract



1. INTRODUCTION

Parkinson's disease (PD) is a chronic, progressive neurodegenerative condition characterized by the selective destruction of Lipinski's rule dopaminergic neurons in the substantia nigra and the buildup of misfolded proteins, including alpha-synuclein (Beitz, 2014). Current treatments predominantly focus on alleviating motor symptoms but do not target the fundamental mechanisms of neuronal degeneration, underscoring the urgent necessity for innovative disease-modifying therapeutics (Kalia & Lang, 2015). Recent studies have revealed a possible connection between lipid metabolism and neurodegenerative disorders, such as Parkinson's disease. Recent advances in molecular neurobiology have identified several critical targets implicated in PD pathogenesis. Among them, monoamine oxidase-B (MAO-B) is a key enzyme responsible for dopamine catabolism; its inhibition increases synaptic dopamine levels and reduces oxidative stress, making it a validated therapeutic target (Tan et al., 2022). Likewise, alpha-synuclein, a neuronal protein prone to pathological aggregation, plays a central role in Lewy body formation. Inhibiting its aggregation can help slow or prevent neurodegeneration (Chen et al., 2022). In addition, dopamine receptors (D1 and D2-like families) are crucial for mediating dopaminergic signaling (Hassan and Thakar, 1988). Compounds that modulate these receptors can mimic or enhance dopaminergic activity, offering symptomatic relief. Apolipoprotein A-I (Apo A-I), a principal constituent of high-density lipoprotein (HDL), has been identified as a potential therapeutic target owing to its neuroprotective, anti-inflammatory, and antioxidant characteristics (Jiang et al., 2022). Research indicates that ApoA-I may affect alpha-synuclein aggregation, regulate neuroinflammation, and safeguard against oxidative stress, all of which are characteristics of Parkinson's disease pathology (Ohgita et al., 2023). Plant-derived molecules have long been a valuable source of bioactive compounds for drug discovery, offering structural diversity and a wide range of pharmacological activities. In the context of Parkinson's disease (PD), plant-based molecules have gained increasing attention due to their antioxidant, anti-inflammatory, neuroprotective, and anti-apoptotic properties—all of which are relevant to the pathogenesis of PD (Chaachouay & Zidane, 2024). Natural phytochemicals such as flavonoids, alkaloids, terpenoids, and polyphenols have shown potential in modulating key targets involved in PD (Kumari et al., 2023). Structure-based drug design (SBDD), especially using molecular docking approaches, provides a robust computational method to find and refine small compounds that can engage with certain protein targets. Through the simulation of binding interactions between markers and prospective ligands, researchers can forecast their capacity to augment markers' functionality or replicate their protective effects within the central nervous system (Ferreira et al., 2015). This study examines the molecular docking analysis of new drugs aimed at ApoA-I to identify possible neuroprotective treatments for Parkinson's disease. This study aims to find lead compounds that may influence MAO-B, alpha-synuclein, dopamine receptors, and ApoA-I function and aid in the formulation of novel therapeutic methods against Parkinson's disease by computational modeling, binding affinity assessment, and interaction profiling.

2. MATERIALS AND METHODS

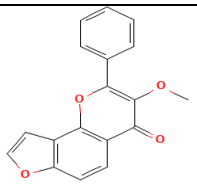
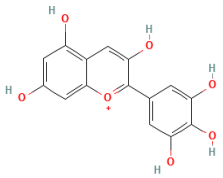
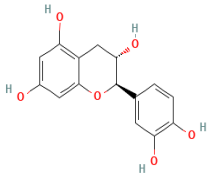
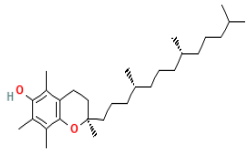
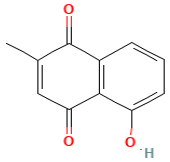
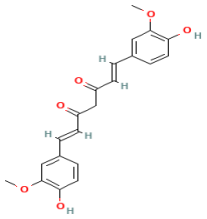
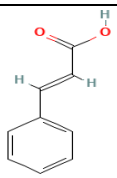
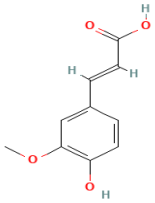
2.1 Ligand collection and preparation

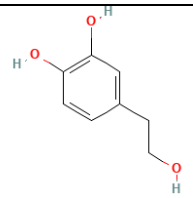
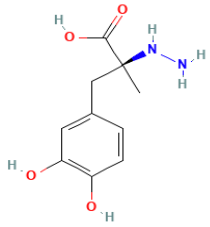
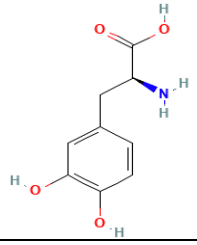
Based on the findings of ten prior molecular docking investigations, ten phytoconstituents with lower binding energies docked in different software applications with different PDB IDs were chosen for possible use in Parkinson's disease therapies (Table1). They are karanjin, hydroxytyrosol, curcumin, (+)-catechin, delphinidin, alpha tocopherol, ferulic acid, cinnamic acid, beta ocimene, and plumbagin. Chosen from online medical software, Parkinson's disease treatments include the traditional meds carbidopa and levodopa. Table 2 shows the physicochemical characteristics, including classification, PubChem CID, molecular formula, molecular weight, smile ID, and structure derived from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/).

Table 1: Collection of Phytochemical based on Binding energy.

S. No.	Phytochemicals	Binding energy	Software	Reference
1	Karanjin	-8.39	Autodock	(Gnanaraj et al., 2022)
2	Hydroxytyrosol	− 6.89	Glide docking	(Pathania et al., 2021)
3	Curcumin	-9.1	Autodock vina	(Ali et al., 2022)
4	(+)-Catechin	−9.4	Maestro 2017 (Schrödinger)	(Baessa et al., 2019)
5	Delphinidin	-8.90	Glide docking	(Bhowmik et al., 2024)
6	Alpha Tocopherol	-373.83	Patch dock	(Poornima & Sumath (2022)
7	Ferulic acid	–7.0991	Molecular docking analysis (MOE)	(Akhtar 2021)
8	Cinnamic acid	-6.26	AutoDock4.2	(Karan et al.,2019)
9	Beta Ocimene	-8.29	(Schrodinger	(Raju et al.,2021)
10	Plumbagin	-8.04	Autodock 4.2	(Shruti & Bharadvaja 2024)
11	Levodopa	NA	NA	https://www.webmd.com/parkinsons-disease/drug-treatments
12	Carbidopa	NA	NA	https://www.webmd.com/parkinsons-disease/drug-treatments

Table 2: Phytochemicals classification, Pubchem CID, molecular formula, molecular weight, smile ID and structure.

S. No.	Phytochemicals	Classification	Pubchem CID	Molecular Formula	Smile ID	Structure
1	Karanjin	Flavonoid	100633	$C_{18}H_{12}O4$	COC1=C(OC2=C(C1=O)C=CC3=C2C=CO3)C4=CC=CC=C4	
2	Delphinidin	Polyphenol	128853	$C_{15}H_{11}O7^{+}$	C1=C(C=C(C(=C1O)O)O)C2=[O+]C3=CC(=CC(=C3C=C2O)O)O	
3	(+)-Catechin	Flavonoid	9064	$C_{15}H_{14}O_6$	C1[C@@H]([C@H](OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)O	
4	Alpha Tocopherol	Phenolic	14985	$C_{29}H5_0O_2$	CC1=C(C2=C(CC[C@@](O2)(C)CCC[C@H](C)CCC[C@H](C)CCCC(C)C)C(=C1O)C)C	
5	Plumbagin	Quinones	10205	$C_{11}H_8O_3$	CC1=CC(=O)C2=C(C1=O)C=CC=C2O	
6	Curcumin	Polyphenol	969516	$C_{21}H_{20}O_6$	COC1=C(C=CC(=C1)/C=C/C(=O)CC(=O)/C=C/C2=CC(=C(C=C2)O)OC)O	
7	Cinnamic Acid	Monocarboxylic acid	444539	$C_9H_8O_2$	C1=CC=C(C=C1)/C=C/C(=O)O	
8	beta-Ocimene	Monoterpenes	18756	$C_{10}H_{16}$	CC(=CCC=C(C)C=C)C	
9	Ferulic acid	Phenols	445858	$C_{10}H_{10}O_4$	COC1=C(C=CC(=C1)/C=C/C(=O)O)O	

10	Hydroxytyrosol	Catechols	82755	$C_8H_{10}O_3$	C1=CC(=C(C=C1CCO)O)O	
11	Carbidopa	Standard drug	34359	$C_{10}H_{14}N_2O_4$	C[C@](CC1=CC(=C(C=C1)O)O)(C(=O)O)NN	
12	Levodopa	Standard drug	6047	$C_9H_{11}NO_4$	C1=CC(=C(C=C1C[C@@H](C(=O)O)N)O)O	

2.2 Protein preparation

The crystal structure of the MAO-B (PDB ID-1OJA), Alpha-synuclein (PDB ID-1XQ8), Dopamine receptors D1 (PDB ID-7CKX), Dopamine receptors D2 (PDB ID-6CM4), Apolipoprotein A-I (apo A-I) (PDB ID-1AV1) was retrieved or extracted from PDB databank https://www.rcsb.org/ (Figure 1, 2, 3, 4, 5). The protein was saved in .pdb format and visualized under the Discovery Studio visualizer (2022). For its optimization, the Pyrx software was used for molecular docking. The water molecules and hetatoms were deleted.

Fig. 1: Monoamine oxidase B (MAO-B) Chain –A (PDB ID-1OJA).

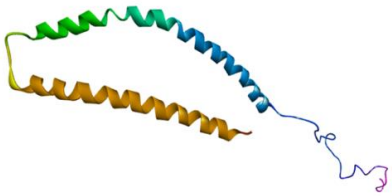


Fig. 2: Alpha-synuclein (αSyn) Chain -A (PDB ID-1XQ8).

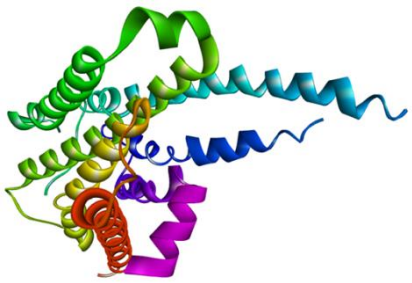


Fig. 3: Dopamine receptors D1 (DRD1) Chain-R (PDB ID-7CKX).

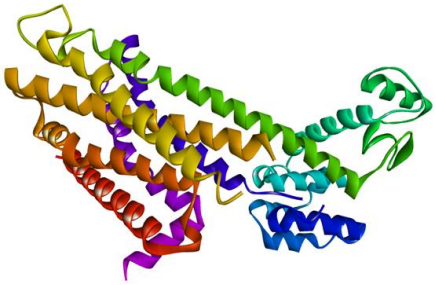


Fig 4: Dopamine receptors D2 (DRD2) Chain-A (PDB ID- 6CM4).

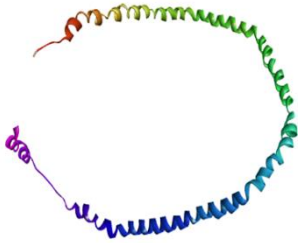


Fig. 5: Apolipoprotein A-I (apo A-I) Chain-A (PDB ID-1AV1).

2.3 ADME and drug-likeness prediction

The free web program SwissADME, developed by the Swiss Institute of Bioinformatics and freely accessible at (www.swissadme.ch), was used to conduct ADME screening and drug-likeness assessment. The screening approach was utilized for compounds exhibiting high-ranking binding energy values, along with the physicochemical properties and computational descriptors of the analyzed substances. Number of heavy atoms, number of aromatic heavy atoms, number of rotatable bonds, number of hydrogen bond acceptors, number of hydrogen bond donors, radar map. Anticipated ADME (pharmacokinetic) properties for the screened substances include gastrointestinal absorption, blood-brain barrier permeability, P-glycoprotein substrate status, and inhibition of CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4. Additionally, Log Kp values, along with the Lipinski, Ghose, Veber, Egan, and Muegge rules of five (RO5), and bioavailability scores were employed to assess drug-likeness suitability.

2.4 Swiss Target Prediction Analysis

Computational approaches offer valuable insights into drug-like properties of substances, potentially reducing costs, reducing resources, and speeding up procedures. In this study, the Swiss ADME online tool was used to predict targeted proteins for phytoconstituents and reference medications.

2.5 Molecular docking & Interaction studies

PubChem database (https://pubchem.ncbi.nlm.nih.gov/) yielded the three-dimensional structures of the ligands and drugs. PDB files of the targeted protein MAO-B (PDB ID-1OJA), Alpha-synuclein (PDB ID-1XQ8), Dopamine receptors D1 (PDB ID-7CKX), Dopamine receptors D2 (PDB ID-6CM4), Apolipoprotein A-I (apo A-I) (PDB ID-1AV1) was given by the Protein Data Bank (https://www.rcsb.org/). Molecular docking was done using PyRx software. The molecular interaction inside the binding pocket of the target proteins for the best-docked complexes was then seen using Biovia discovery studio visualizer.

3. RESULTS AND DISCUSSION

3.1 ADME and drug-likeness prediction

The computed ADMET properties (gastrointestinal (GI) absorption; blood-brain barrier (BBB) permeation; inhibition of the cytochrome P450 system; permeability glycoprotein (P-gp) substrate) of these compounds are presented in **Table 3.** According to the results, all the compounds showed high gastrointestinal absorption, except for compounds 14985 and 18756. BBB permeation potential was predicted for compounds 10205, 444539, 18756, and 445858. Compounds 100633, 128853, 9064 &14985, showed potential to be a substrate of P-gp. The potential to inhibit cytochrome P450 (CYP) isoforms was observed for compounds 100633 (for 5 isoforms); 969516 (for 2 isoforms); 128853 & 10205 (for 1 isoform). Compounds 9064, 14985, 444539, 18756, 445858, 6047 & 82755 were predicted to show no inhibitory activity against any of the CYP isoforms. The Brain or Intestinal Estimated Permeation Method (BOILED-Egg) accurately predicts pharmacokinetic parameters like absorption, cutaneous permeation, distribution, metabolism, biotransformation, and excretion, with a molecule's descent indicating passive absorption **Fig6.**

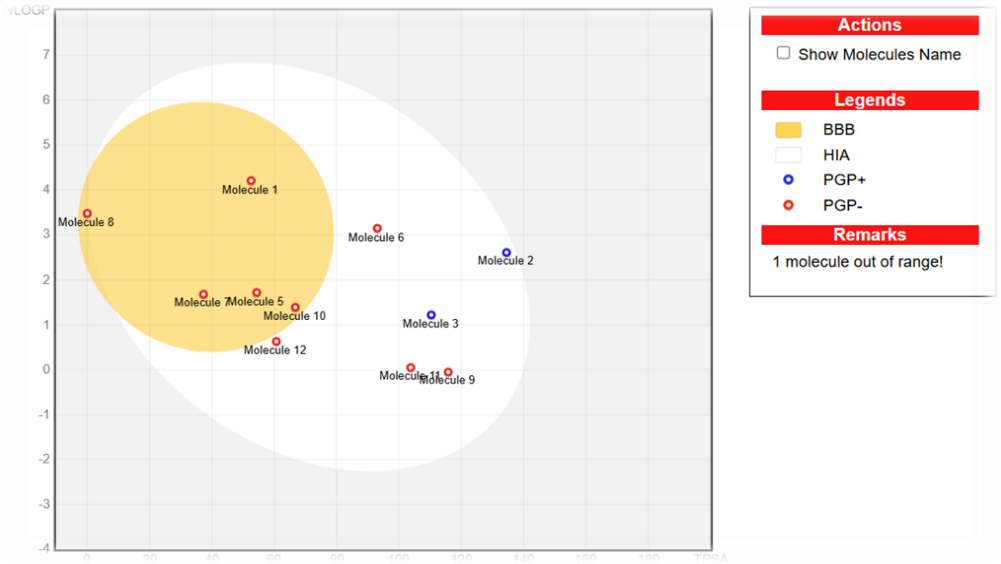


Fig. 6: The BOILED-Egg construction outlines the absorption and brain penetration of various compounds & drugs with the white region representing the most likely gastrointestinal tract absorption and the yellow region representing brain penetration.

Table 3: ADME (pharmacokinetic) parameters of the phytochemicals and reference drugs.

S. No.	Phytochemicals Pubchem ID	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log Kp [cm/s]
1	100633	High	No	Yes	Yes	Yes	Yes	Yes	Yes	-5.41 cm/s
2	128853	High	No	Yes	Yes	No	No	No	No	-7.86 cm/s
3	9064	High	No	Yes	No	No	No	No	No	-7.82 cm/s
4	14985	Low	No	Yes	No	No	No	No	No	-1.33 cm/s
5	10205	High	Yes	No	Yes	No	No	No	No	-5.82 cm/s
6	969516	High	No	No	No	No	Yes	No	Yes	-6.28 cm/s
7	444539	High	Yes	No	No	No	No	No	No	-5.69 cm/s
8	18756	Low	Yes	No	No	No	No	No	No	-4.11 cm/s
9	34359 (Standard drug)	High	No	No	No	No	No	No	No	-9.22 cm/s
10	445858	High	Yes	No	No	No	No	No	No	-6.41 cm/s
11	6047 (Standard drug)	High	No	No	No	No	No	No	No	-9.45 cm/s
12	82755	High	No	No	No	No	No	No	No	-7.75 cm/s

3.2 Physicochemical properties of phytochemicals

In the present study, the MWs of all selected phytoconstituents including reference drugs were found to be less than 500, thus favoring rapid GI absorption. The Num. rotatable bonds of all selected phytoconstituents including reference drugs were found to be less than 10 except Alpha Tocopherol (14985), thus favoring rapid Num. of rotatable bonds. Num. H-bond donors of all selected phytoconstituents including reference drugs were found to be less than 10 and all the phytoconstituents have less than 5 Num. H-bond acceptors except for Delphinidin, (+)-Catechin, Curcumin and standard drug Carbidopa and all phytoconstituents have 40 to 130 Molar refreactivity (MR) including reference drug except Alpha Tocopherol.

Table 4: Physicochemicals properties of phytochemicals.

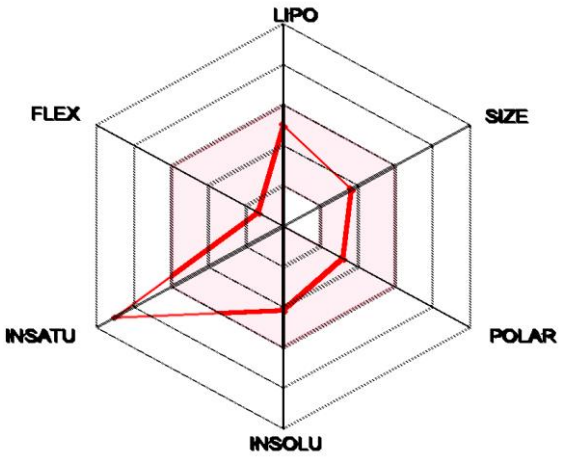
S. No.	Pubchem CID	Molecular Weight (g/mol)	No. heavy atoms	No. aromatic heavy atoms	No rotatable bonds	No. H-bond acceptors	No. H-bond donors	Molar Refractivity
1	100633	292.3	22	19	2	4	0	84.18
2	128853	303.24	22	16	1	7	6	78.20
3	9064	290.27	21	12	1	6	5	74.33
4	14985	430.7	31	6	12	2	1	139.27
5	10205	188.18	14	6	0	3	1	51.07
6	969516	368.4	27	12	8	6	2	102.80
7	444539	148.16	11	6	2	2	1	43.11
8	18756	136.23	10	0	3	0	0	48.76
9	445858	194.18	14	6	3	4	2	51.63
10	82755	154.16	11	6	2	3	3	41.42
11	34359 (Standard drug)	226.23	16	6	4	6	5	57.19
12	6047 (Standard drug)	197.19	14	6	3	5	4	49.55

3.3 Pharmacokinetic parameters and drug-likeness

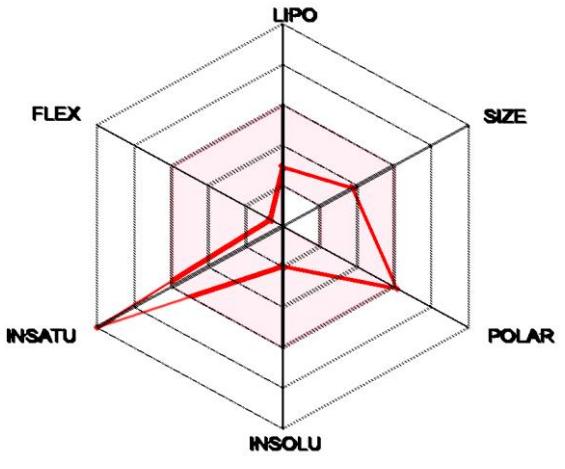
The computed drug-likeness, properties of the selected compounds are presented in **Table5**. According to the results, compounds 100633, 9064, and 969516 follow the all five filters (Lipinski, Ghose, Veber, Egan, and Muegge) used. The other compounds showed violation of at least one of the drug-likeness filters. The computed Abbot Bioavailability score 0.55 for compound 100633, 128853, 9064, 14985, 10205, 969516, 18756, 6047, 82755, except for compound 444539, 445858 (0.85) & 34359, (0.56).

Table 5: Physicochemicals and drugs pharmacokinetic parameters and drug-likeness.

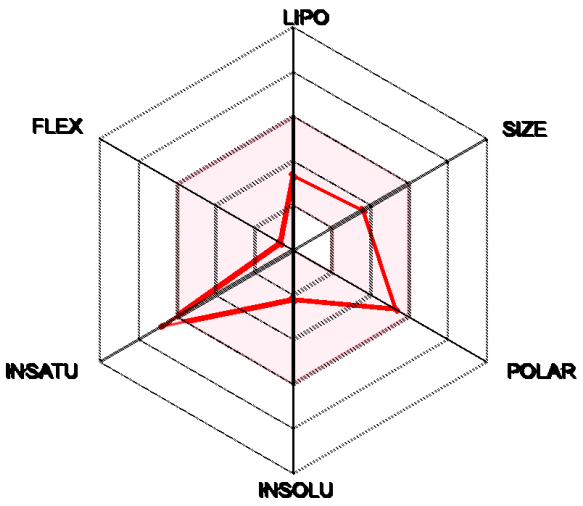
S. No.	Phytochemicals Pubchem ID	Lipinski	Ghose	Veber	Egan	Muegge	Bioavailability Score
1	100633	Yes	Yes	Yes	Yes	Yes	0.55
2	128853	Yes	Yes	Yes	No	No	0.55
3	9064	Yes	Yes	Yes	Yes	Yes	0.55
4	14985	Yes	No	No	No	No	0.55
5	10205	Yes	Yes	Yes	Yes	No	0.55
6	969516	Yes	Yes	Yes	Yes	Yes	0.55
7	444539	Yes	No	Yes	Yes	No	0.85
8	18756	Yes	No	Yes	Yes	No	0.55
9	34359 (Standard drug)	Yes	Yes	Yes	Yes	No	0.56
10	445858	Yes	Yes	Yes	Yes	No	0.85
11	6047 (Standard drug)	Yes	Yes	Yes	Yes	No	0.55
12	82755	Yes	No	Yes	Yes	No	0.55



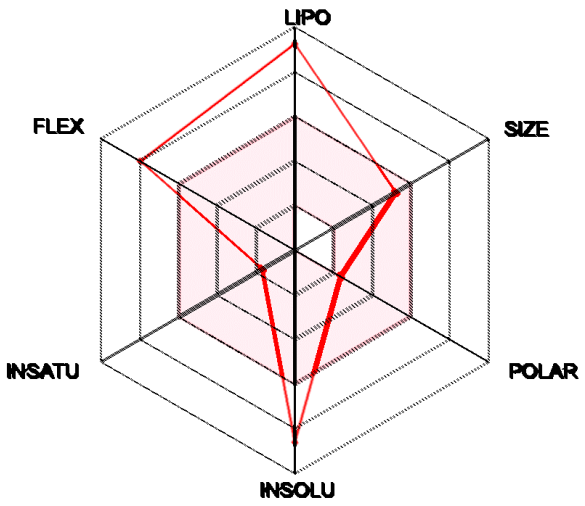
Karanjin



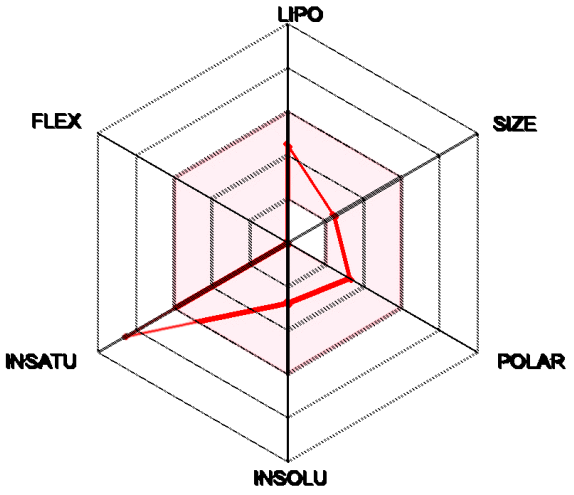
Delphinidin



(+)-Catechin



Alpha-tocopherol



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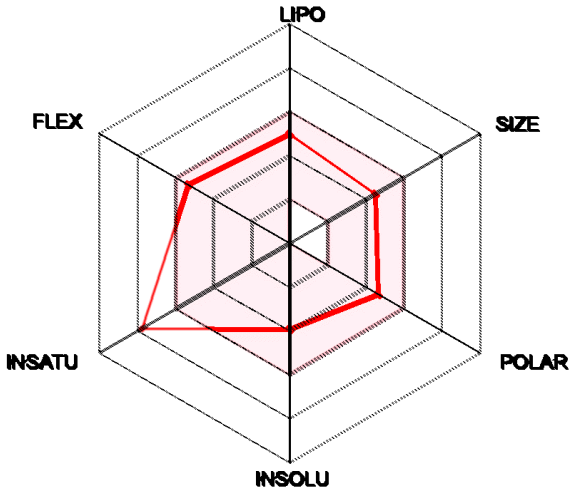

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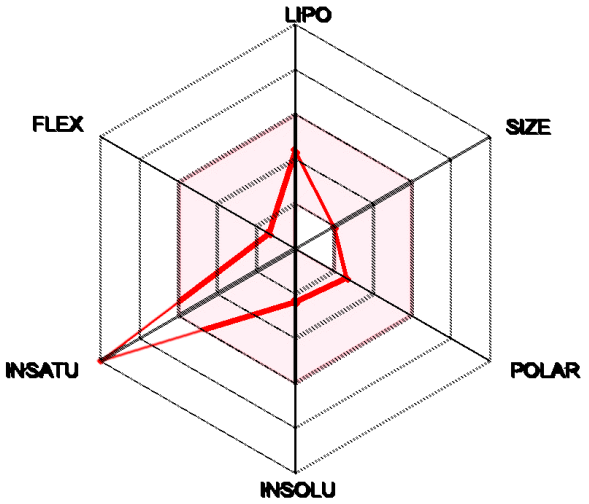

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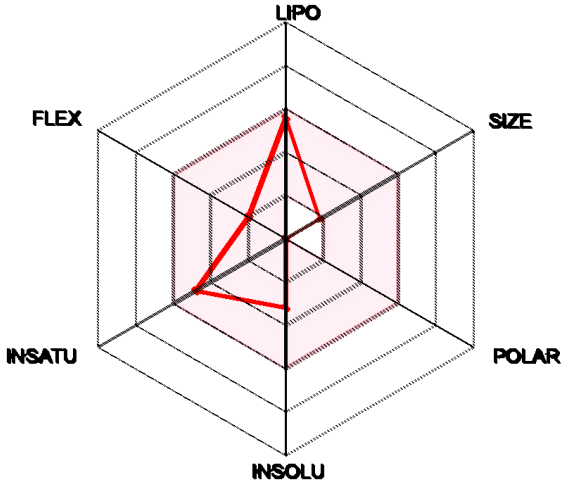

beta-Ocimene

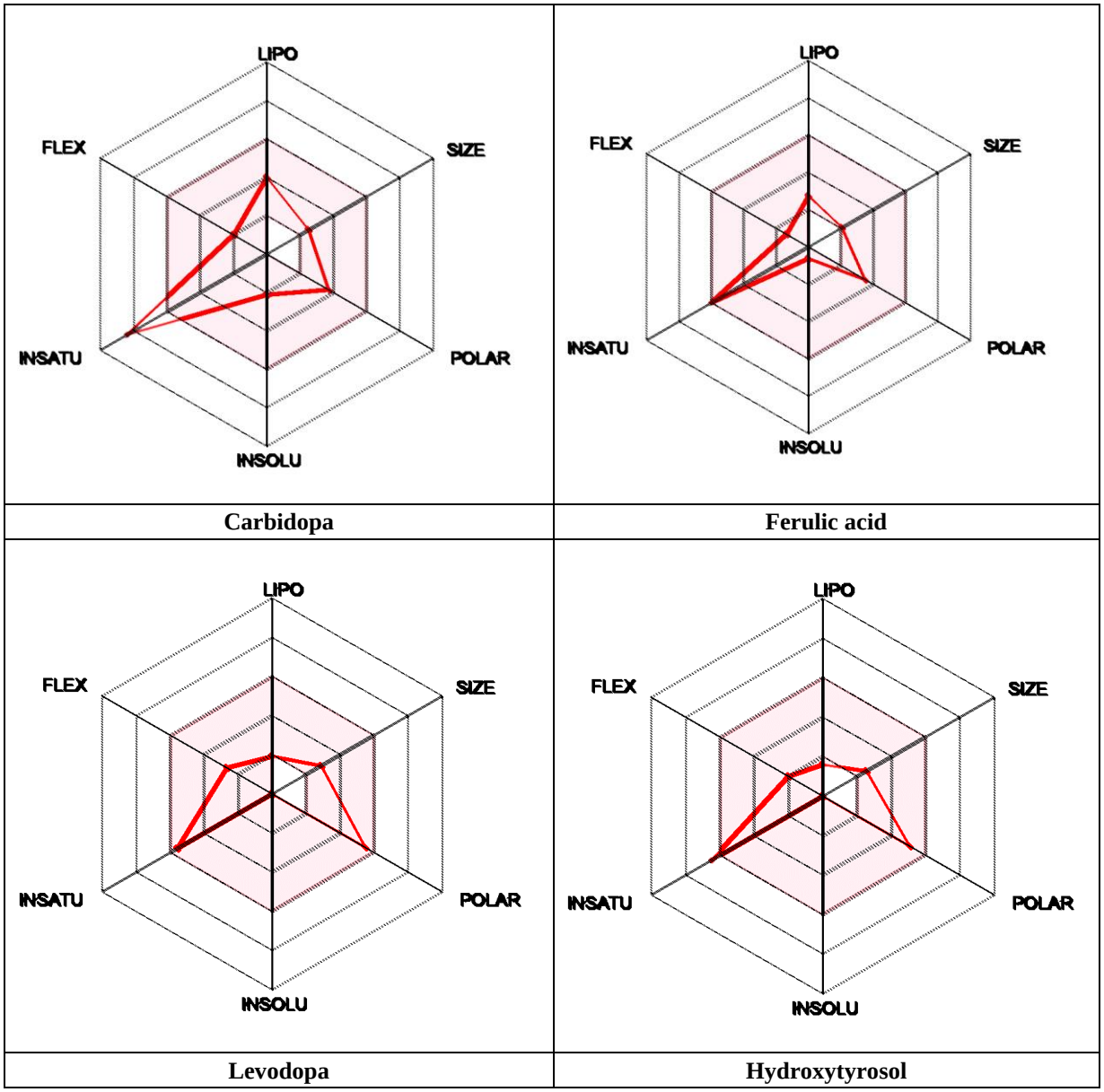

Fig 7: The Bioavailability Radar provides a preliminary assessment of the drug-likeness of various compounds & drugs, with the pink area indicating the optimal range for each property.

3.4 Swiss Target Prediction Analysis

The Swiss Target Prediction analysis revealed diverse target profiles for the selected phytoconstituents and standard drugs. The compounds exhibited a wide range of protein target classes, indicating their multi-target interaction potential. Karanjin, Delphinidin, Alpha-tocopherol, Curcumin, and Plumbagin displayed a broad spectrum of target classes, such as: Family A G protein-coupled receptors, Kinases, Nuclear receptors, Enzymes (oxidoreductases, lyases, hydrolases), and Ion channels and transporters. Each of these compounds showed a relatively even distribution among different classes, indicating polypharmacological properties. Cinnamic acid had a high specificity (66.7%) toward Family A GPCRs, suggesting a more targeted interaction profile, while other targets like enzymes and transporters were minimal. Beta-ocimene interacted predominantly with nuclear receptors (42.9%) and also showed significant affinity towards secreted proteins and oxidoreductases, implying its potential regulatory role. Ferulic acid showed strong interactions with lysases (60%), followed by oxidoreductases and phosphatases, highlighting its enzyme-specific action likely contributing to its antioxidant activity. Carbidopa and Levodopa, both standard dopaminergic drugs, demonstrated broad interactions, including oxidoreductases, kinases, ion channels, and receptors, validating their known multi-pathway involvement in neurotransmission and Parkinson's disease therapy. Notably, (+)-Catechin and Hydroxytyrosol showed no predicted active targets, which could indicate: Either a lack of structural similarity with known bioactives in the Swiss Target Prediction database or their mechanism of action may involve non-protein or less-characterized targets. This predictive analysis underscores the therapeutic versatility of the phytoconstituents, supporting their potential in

multi-target drug development. The variation in target classes across compounds provides valuable insights for further *in vitro* and *in vivo* validation.

The proportion of bioactivity displayed by selected phytoconstituents compared to the reference medication is shown in Fig 8 (Israr et al., 2024).

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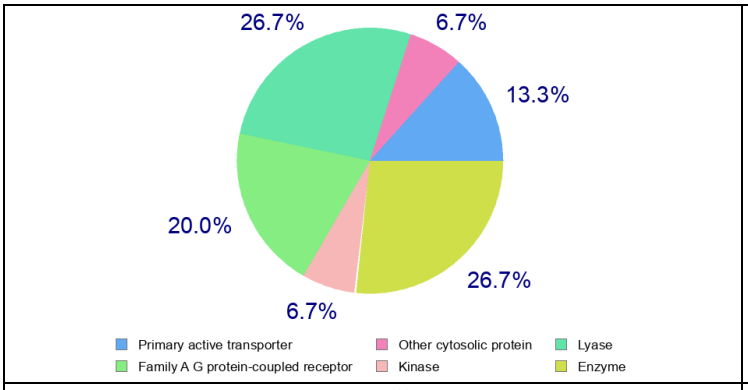
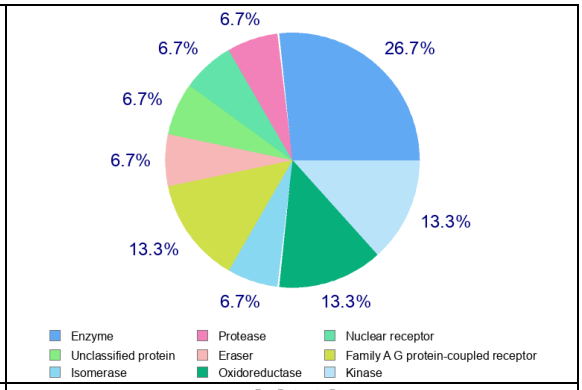
<tr><td> 
</td><td> 
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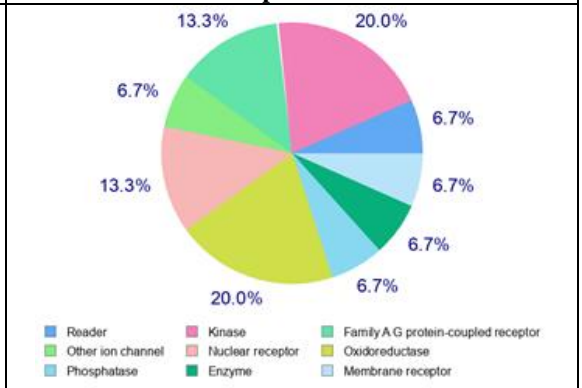
No target predicted.</td><td> 
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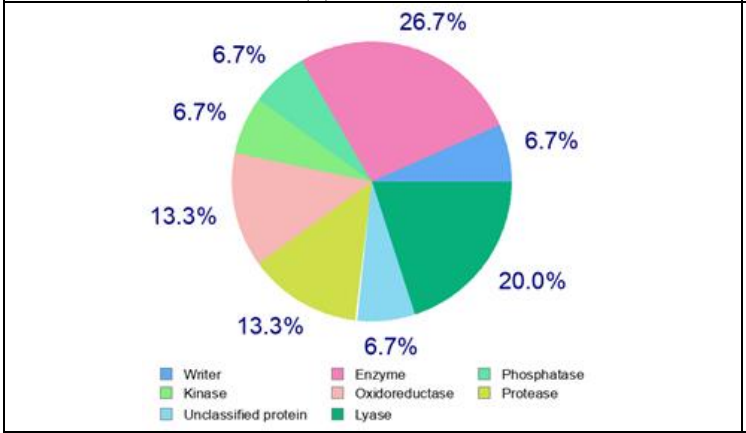
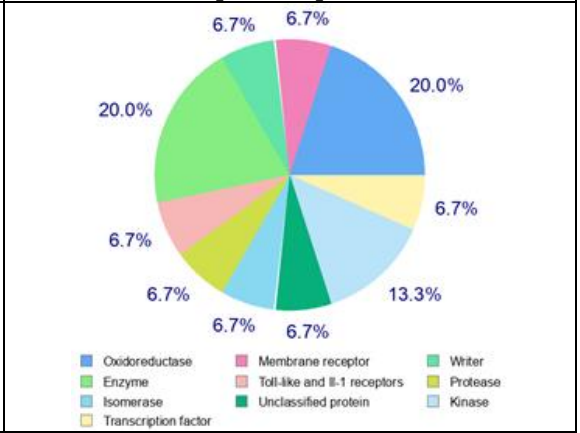
<tr><td> 
</td><td> 
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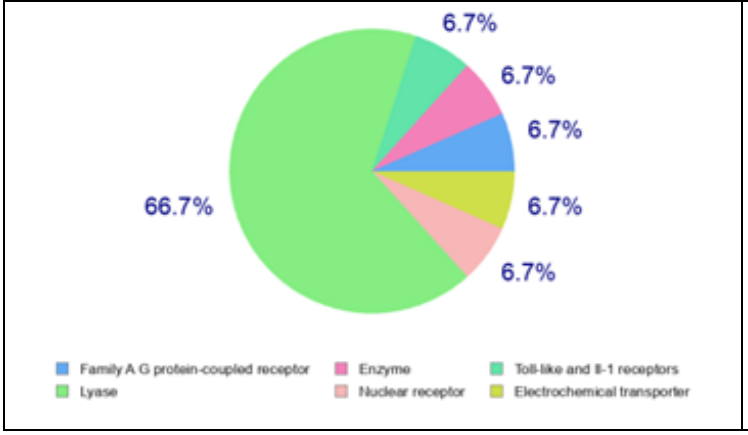
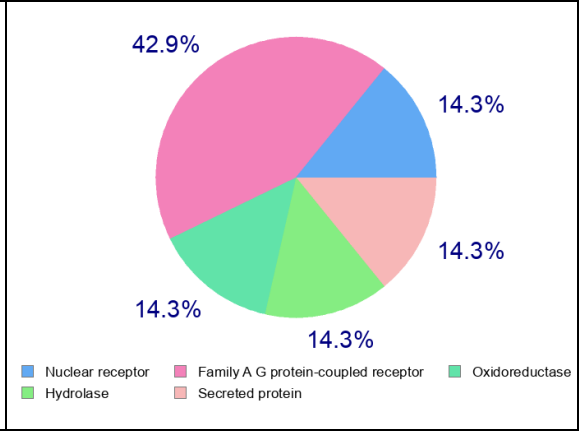
<tr><td>Plumbagin</td><td>Curcumin</td></tr>
<tr><td> 
</td><td> 
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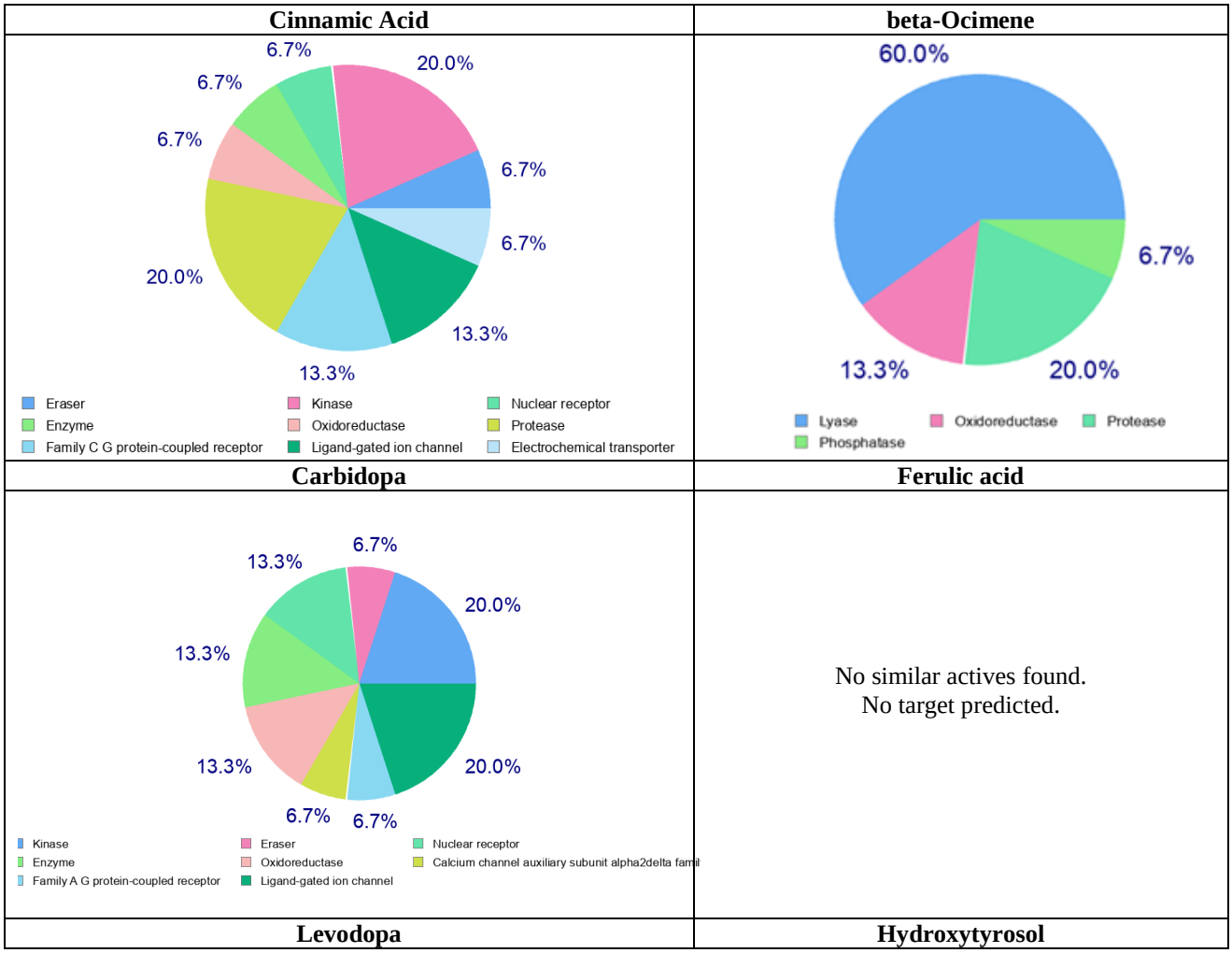


Fig 8: Swiss target prediction of phytochemicals and reference drugs.

3.5 Molecular docking & Interaction studies

Molecular docking is the most extensively used method for the calculation of protein-ligand interactions. It is an efficient method to predict the potential ligand interactions. In the present study, the native plant secondary metabolites (ligands) have been identified as potent protein monoamine oxidase B (PDB ID-1OJA), alpha-synuclein (PDB ID-1XQ8), dopamine receptors D1 (PDB ID-7CKX), dopamine receptors D2 (PDB ID-6CM4), and apolipoprotein A-I (apo A-I) (PDB ID-1AV1) inhibitors. Pyrx uses (genetic algorithm) binding free energy assessment to assign the best binding conformation. Further, the activity of docked ligand molecules was compared to that of standard drugs, which were controls. In total, 12 compounds were docked against different proteins (PDB ID-1OJA, 1XQ8, 7CKX, 6CM4, 1AV1). To identify the binding affinities, binding types, and active amino acid residues of the phytoconstituents & drugs under investigation in the target protein, molecular docking research was conducted. Predicting the binding affinities of 10 specific phytoconstituents with 2 drugs of Parkinson's biomarkers. The phytoconstituents under research demonstrated binding energies that ranged from -10.9 to -3.7 kcal/mol, which have been summarized in **Table 6**. The binding affinity of the top 3 compounds that have the lowest binding energy—**PDB ID-1OJA**-Karanjin-10.9, (+)-Catechin-9.7 & Delphinidin-9.6; **PDB ID-1XQ8**-(+)-Catechin-6.5, Delphinidin-6.3 & Karanjin-6.2; **PDB ID-7CKX**-Delphinidin-9, (+)-Catechin-9 & Curcumin-7.4; **PDB ID**-6CM4-Alpha Tocopherol-9.2, (+)-Catechin-9.1 & Karanjin-9; **PDB ID-1AV1**-Karanjin-6.2, Delphinidin-5.4 & (+)-Catechin-5.2—and the rest of the docking & interaction results are presented in **Tables 6 & 7** and **Fig 9&10.**

Table 6: Molecular docking results of monoamine oxidase B (PDB ID-1OJA), alpha-synuclein (PDB ID-1XQ8), dopamine receptors D1 (PDB ID-7CKX), dopamine receptors D2 (PDB ID-6CM4), and apolipoprotein A-I (apo A-I) (PDB ID-1AV1) protein with selected phytochemicals & drugs.

S.No.	Phytochemicals	Binding affinity				
		(PDB ID-1OJA)	(PDB ID-1XQ8)	(PDB ID-7CKX)	(PDB ID-6CM4)	(PDB ID-1AV1)
1	Karanjin	**-10.9**	-6.2	-7.2	-9	**-6.2**
2	(+)-Catechin	-9.7	**-6.5**	**-9**	**-9.1**	-5.2
3	Delphinidin	-9.6	-6.3	**-9**	-8.8	-5.4
4	Curcumin	-9.4	-5	-7.4	-7.6	-4.7
5	Plumbagin	-9	-5.1	-7.3	-7.5	-4.8
6	Alpha Tocopherol	-8.9	-5.2	-6.7	-9.2	-5.1
7	Cinnamic Acid	-7.9	-4.8	-6.1	-7.1	-4.5
8	Levodopa (Drug)	-7.7	-4.8	-6.6	-7.2	-4.2
9	Ferulic acid	-7.6	-5.1	-6.6	-6.7	-4.3
10	Carbidopa (Drug)	-7.5	-5	-7.1	-6.5	-4.3
11	beta-Ocimene	-7.3	-3.7	-5.8	-6.2	-4.4
12	Hydroxytyrosol	-6.7	-4.5	-6.2	-6.6	-4

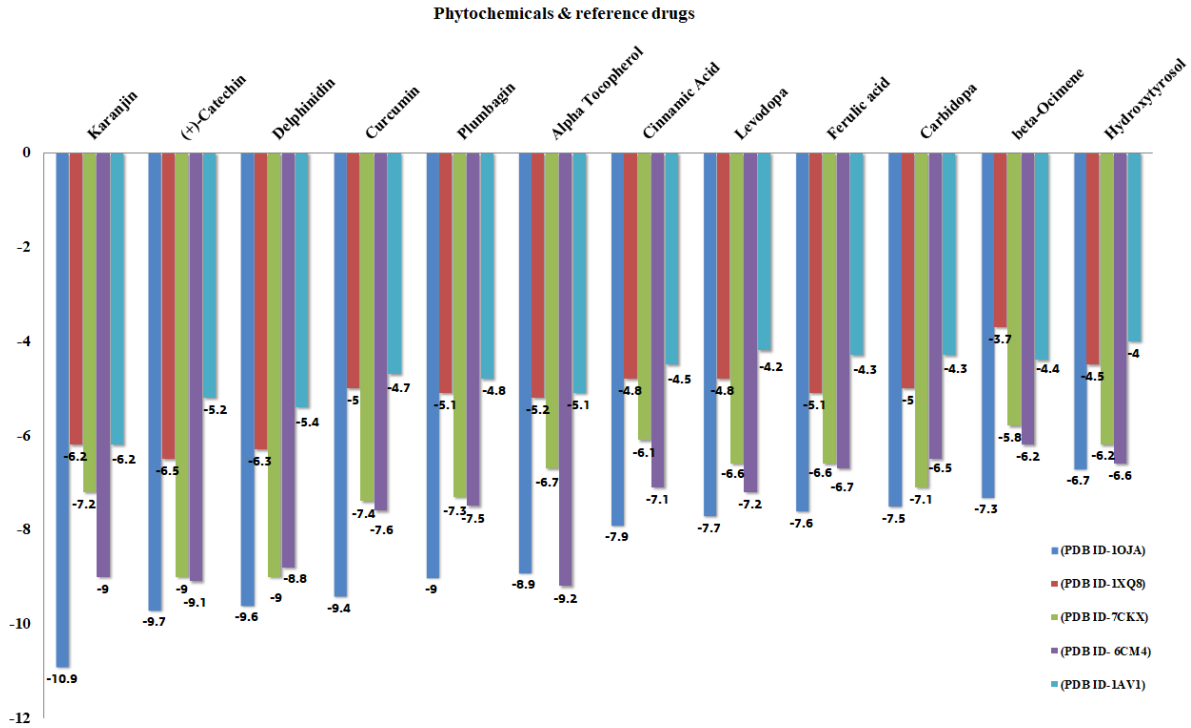


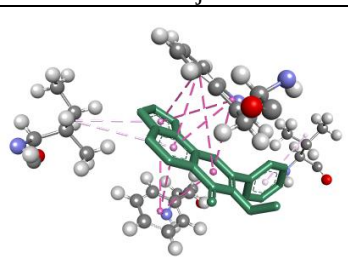
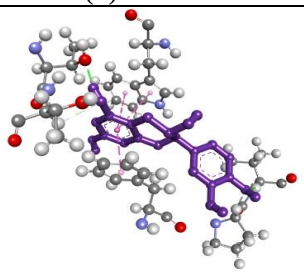
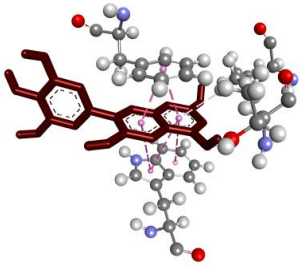
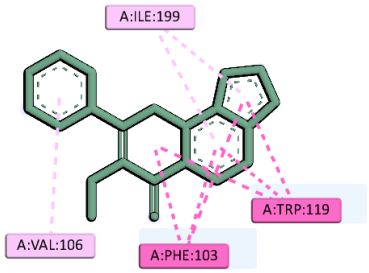
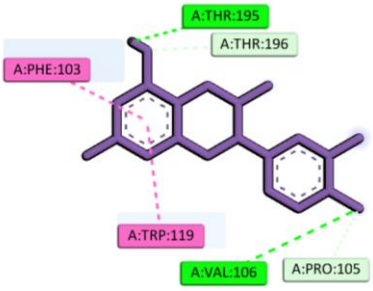
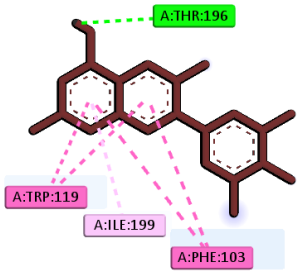
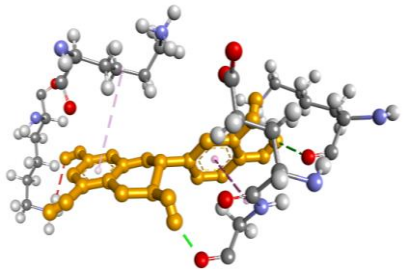
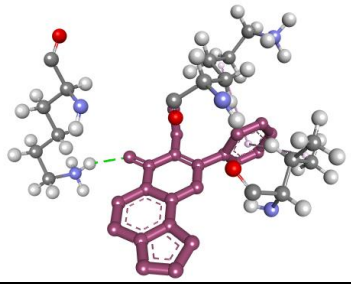
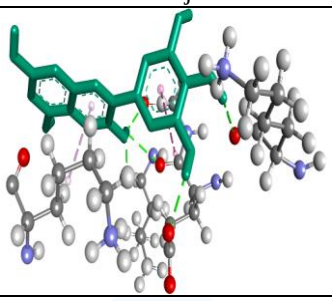
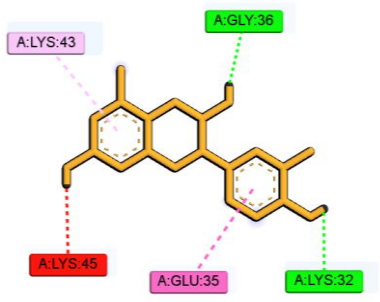
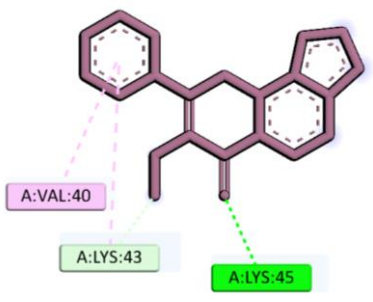
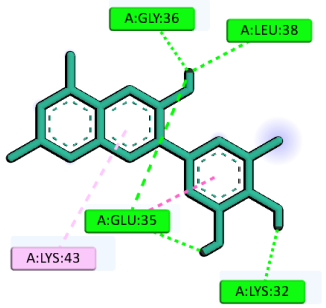
Fig 9: Graphical representation of the Molecular Binding affinity of phytochemicals and reference drugs through PyRx software.

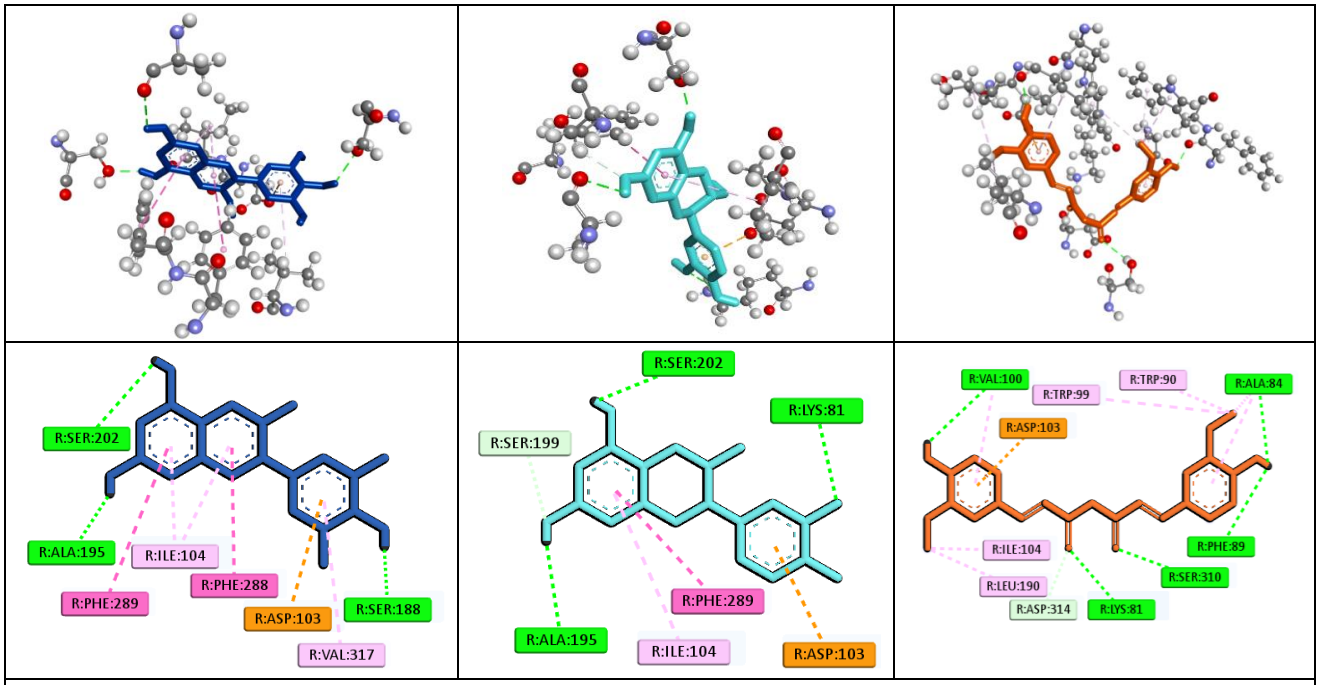
Table 7: Analysis of the binding interactions between PDB ID-1OJA, 1XQ8, 7CKX, 6CM4, and 1AV1 and several phytochemicals with the lowest binding affinities.

S.No.	Target marker	Phytochemical	Hydrogen bond interaction	Hydrophobic Bond interaction
1	MAO-B (PDB ID-1OJA)	Karanjin	-	PHE103, PHE103, TRP119, TRP119, TRP119, TRP119, TRP119, PHE103, TRP119, ILE199,

				ILE199, VAL106
		(+)-Catechin	VAL106, THR195, PRO105, THR196	PHE103, TRP119, TRP119
		Delphinidin	THR196	PHE103, PHE103, TRP119, TRP119, TRP119, ILE199
2	Alpha-synuclein (PDB ID-1XQ8)	(+)-Catechin	LYS32, GLY36	GLU35, LYS43
		Delphinidin	LYS32, GLU35, GLU35, GLY36, LEU38	GLU35, LYS43
		Karanjin	LYS45, LYS43	VAL40, LYS43
3	Dopamine receptors D1 (PDB ID-7CKX)	Delphinidin	SER188, SER202, ALA195	PHE288, PHE289, ILE104, ILE104, VAL317
		(+)-Catechin	LYS81, SER202, ALA195, SER199	PHE289, ILE104
		Curcumin	LYS81, SER310, VAL100, ALA84, PHE89, ASP314	ALA84, ILE104, LEU190, TRP90, TRP90, TRP99, VAL100, ALA84
4	Dopamine receptors D2 (PDB ID-6CM4)	Alpha Tocopherol	-	TRP386, TRP386, CYS118, CYS118, TRP100, PHE198, TRP386, PHE389, PHE389, PHE390, LEU94
		(+)-Catechin	THR119, THR119, VAL190, HIS393	HIS393, PHE189, TRP386, PHE389, PHE390
		Karanjin	HIS393, HIS393	PHE389, PHE389
5	Apolipoprotein A-I (apo A-I) (PDB ID-1AV1)	Karanjin	ASN49	PHE57, PHE57, TRP50, UNK1,

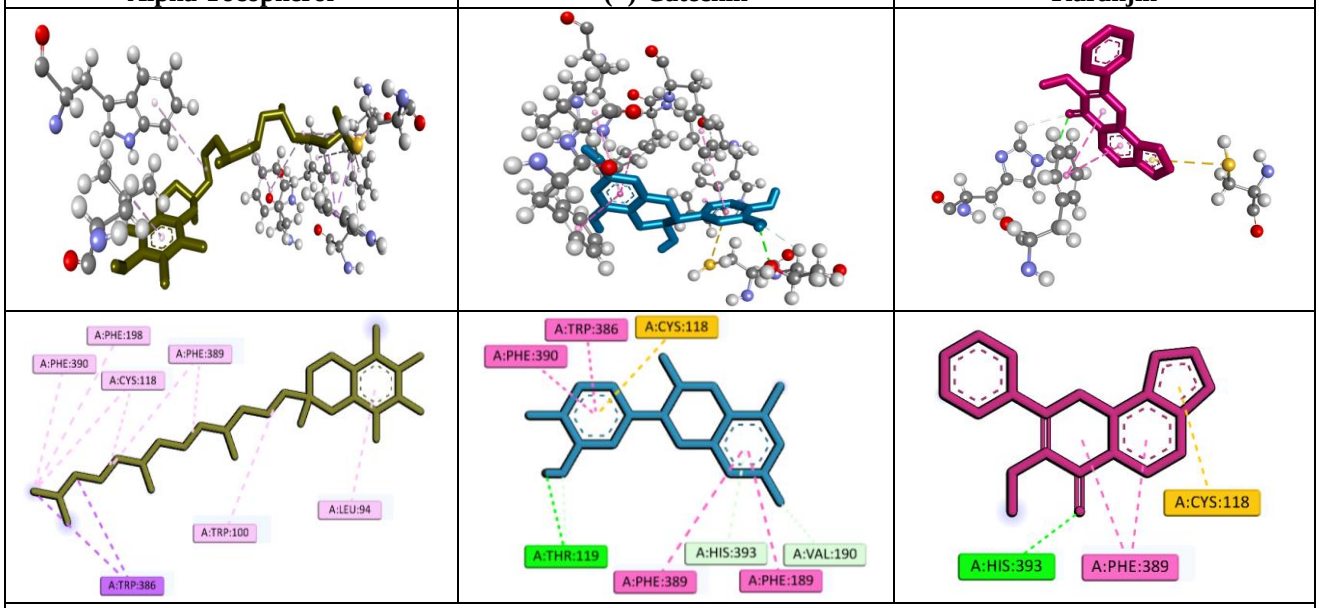
				VAL53, VAL53, VAL53, VAL53
		Delphinidin	ARG116	ARG123, ARG123, VAL119, ARG123
		(+)-Catechin	ARG116, ARG116	VAL119, ARG123, ARG123

Monoamine oxidase B (MAO-B) Chain –A (PDB ID-1OJA)		
Karanjin	(+)-Catechin	Delphinidin
		
		
Alpha-synuclein (α-syn) Chain -A (PDB ID-1XQ8)		
(+)-Catechin	Delphinidin	Karanjin
		
		
Dopamine receptors D1 (PDB ID-7CKX)		
Delphinidin	**(+)-Catechin**	**Curcumin**



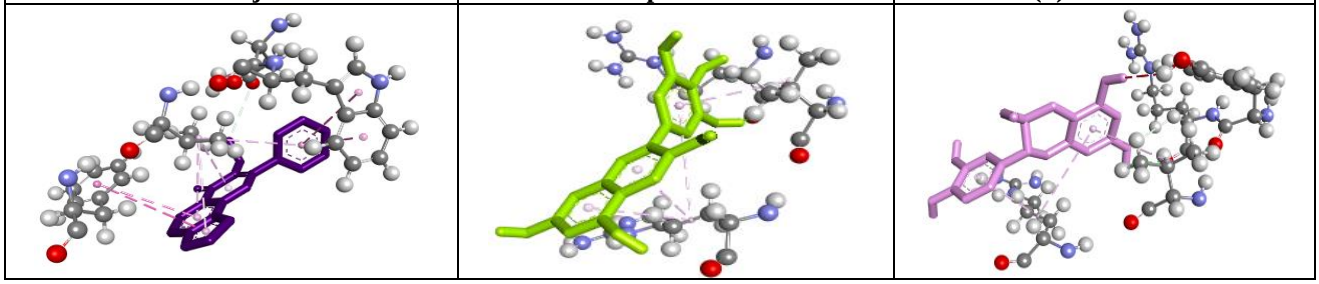
Dopamine receptors D2 (PDB ID-6CM4)

Alpha Tocopherol	(+)-Catechin	Karanjin



Apolipoprotein A-I (apo A-I) Chain-A (PDB ID- 1AV1)

Karanjin	Delphinidin	(+)-Catechin



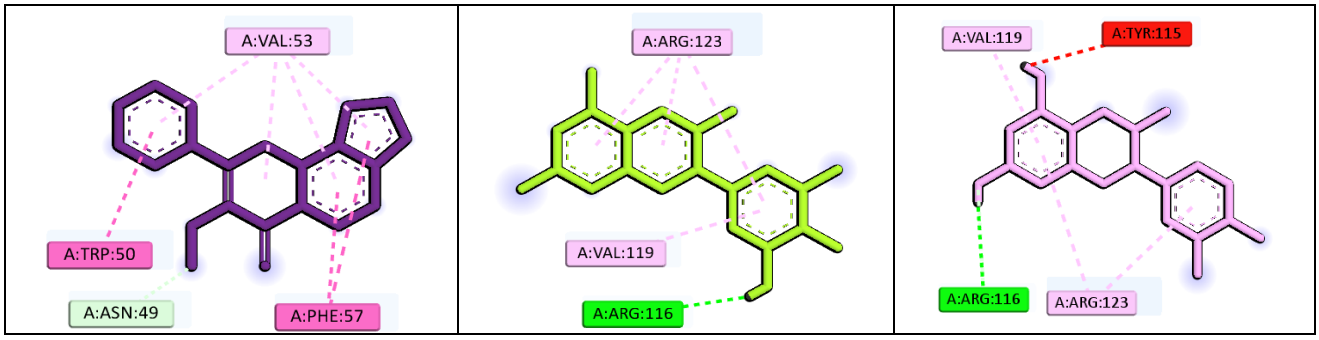


Fig. 10: Showing 3D & 2D interaction of MAO-B (PDB ID-1OJA), alpha-synuclein (PDB ID-1XQ8), dopamine receptors D1 (PDB ID-7CKX), dopamine receptors D2 (PDB ID-6CM4), and apolipoprotein A-I (apo A-I) (PDB1) with respective phytochemicals that have the lowest binding energy.

CONCLUSION

In conclusion, ten phytoconstituents and two medications were examined for their pharmacokinetics, drug-likeness, and toxicity profiles. Two medications from the Webmed database and ten phytoconstituents found from various plants through a literature review were predicted to have inhibitory effects on Parkinson's disease using in silico approaches. For oral availability, all 12 adhere to Lipinski's rule of five, which is appropriate for substances that are natural. Parkinson's disease is a neurological condition that impacts motor function and the dopamine system. Although there is no known cure for Parkinson's disease, patients can have their quality of life enhanced with symptomatic medication. This study has compared both the natural and synthetic PD adjuvant drugs that are conventionally prescribed. This in-silico method has proved beneficial in comparing, predicting, and determining the better natural compound with excellent binding affinity. The molecular docking and ligand interaction evaluate the binding affinity between the various phytochemicals & drugs and the MAO-B (PDB ID-1OJA), α-syn (PDB ID-1XQ8), DRD1 (PDB ID-7CKX), DRD2 (PDB ID-6CM4), and Apo A-I (PDB ID-1AV1) targets, respectively. This research has concluded that natural substances exhibited higher binding energies than medication currently on the market.

Conflict of interest

The authors declare that there is no conflict of interests.

REFERENCES

1. Akhtar, M. F. (2021). Anti-Parkinson’s evaluation of Brassica juncea leaf extract and underlying mechanism of its phytochemicals. *Frontiers in bioscience-Landmark*.
2. Ali, R., Alam, A., K. Rajput, S., & Ahmad, R. (2022). Pharmacotherapeutics and molecular docking studies of alpha-synuclein modulators as promising therapeutics for Parkinson’s disease. BIOCELL, 46(12): 2681–2694. https://doi.org/10.32604/biocell.2022.021224
3. Baessa, M., Rodrigues, M. J., Pereira, C., Santos, T., da Rosa Neng, N., Nogueira, J. M. F., ... & Custódio, L. (2019). A comparative study of the in vitro enzyme inhibitory and antioxidant activities of Butea monosperma (Lam.) Taub. and Sesbania grandiflora (L.) Poiret from Pakistan: New sources of natural products for public health problems. South African Journal of Botany, 120: 146-156.
4. Beitz JM. Parkinson's disease: a review. Front Biosci (Schol Ed)., 2014 Jan 1; 6(1): 65-74. doi: 10.2741/s415. PMID: 24389262.
5. Bhowmik, R., Kumar, S., Manaithiya, A., Mohan, C. G., Mathew, B., Parkkila, S., & Aspatwar, A. (2024). Elucidating the molecular mechanism of phytochemicals against Parkinson’s disease through an integrated systems biology and molecular modeling approach. *bioRxiv*, 2024-05.
6. Chaachouay N, Zidane L. Plant-derived natural products: a source for drug discovery and development. Drugs and Drug Candidates, 2024 Feb 19; 3(1): 184-207.
7. Chen R, Gu X, Wang X. α-Synuclein in Parkinson's disease and advances in detection. Clin Chim Acta. 2022 Apr 1; 529: 76-86. doi: 10.1016/j.cca.2022.02.006. Epub 2022 Feb 14. PMID: 35176268.
8. Ferreira LG, Dos Santos RN, Oliva G, Andricopulo AD. Molecular docking and structure-based drug design strategies. Molecules, 2015 Jul 22; 20(7): 13384-421. doi: 10.3390/molecules200713384. PMID: 26205061; PMCID: PMC6332083.
9. Gnanaraj, C., Sekar, M., Fuloria, S., Swain, S. S., Gan, S. H., Chidambaram, K., Rani, N. N. I. M., Balan, T., Stephenie, S., Lum, P. T., Jeyabalan, S., Begum, M. Y., Chandramohan, V., Thangavelu, L., Subramaniyan, V., & Fuloria, N. K. (2022). In Silico Molecular Docking Analysis of Karanjin against Alzheimer's and Parkinson's Diseases as a Potential Natural Lead Molecule for New Drug Design, Development and Therapy. Molecules (Basel, Switzerland), 27(9): 2834. https://doi.org/10.3390/molecules27092834
10. Hassan MN, Thakar JH. Dopamine receptors in Parkinson's disease. Prog Neuropsychopharmacol Biol Psychiatry, 1988; 12(2-3): 173-82. doi: 10.1016/0278-5846(88)90035-8. PMID: 3290993.
11. Shruti & Bharadvaja N In silico approach to identify key active plant derived natural compounds in

parkinson's disease. (2024). *Letters in Applied NanoBioScience*, *13*(2): 78. https://doi.org/10.33263/LIANBS132.078
12. Israr J, Ahamad T, Alam S, Misra S, Gupta D, Ahmad R, Arshad M, Khan MF, Maurya P, AlShammari L, Ali A. Bioactive Compounds from Achyranthes Aspera L. Extract: A UHPLC Profile and In Silico Study for Mouth Cancer. Chemistry Select, 2024 Oct; 9(38): e202402092.
13. Israr J, Fatima N, Alam S and Fatima A. In-silico analysis of phytochemicals from ginkgo biloba and aegle marmelos against allergic conjunctivitisijpsr, 2025; 16(2): 403-416.
14. Israr J, Khan MA, Misra S, Gupta D, Singh N, Ahmad R, Siddiqui S. In silico Screening and in vitro Cytotoxicity Study of Achyranthes aspera Phytochemicals Against Oral Cancer: A Possible Step towards the Development of Anti-cancer Agents. Comb Chem High Throughput Screen. 2024 Jul 11. doi: 10.2174/0113862073289916240503051643. Epub ahead of print. PMID: 38994626.
15. Jankovic, J., & Tan, E. K. (2020). Parkinson's disease: etiopathogenesis and treatment. *Journal of Neurology, Neurosurgery & Psychiatry*, *91*(8): 795-808.
16. Jiang H, Bai X. Apolipoprotein A-I mimetic peptides (ApoAI MP) improve oxidative stress and inflammatory responses in Parkinson's disease mice. Front Pharmacol., 2022 Aug 19; 13: 966232. doi: 10.3389/fphar.2022.966232. PMID: 36059954; PMCID: PMC9437339.
17. Kalia LV, Lang AE. Parkinson's disease. Lancet., 2015 Aug 29; 386(9996): 896-912. doi: 10.1016/S0140-6736(14)61393-3. Epub 2015 Apr 19. PMID: 25904081.
18. Karan S Kariat, Shravan Kumar Gunda, Naga Harini P, Mahmood Shaik (2019). "Modelling and Docking Studies on Natural Compounds against Parkinson's Disease", International Journal of Pharmaceutical and Phytopharmacological Research, 9(1): 1-10.
19. Kumari N, Anand S, Shah K, Chauhan NS, Sethiya NK, Singhal M. Emerging Role of Plant-Based Bioactive Compounds as Therapeutics in Parkinson's Disease. Molecules, 2023 Nov 14; 28(22): 7588. doi: 10.3390/molecules28227588. PMID: 38005310; PMCID: PMC10673433.
20. M Ganga Raju, Veena Yadav, NVL Suvarchala Reddy V, Natural Compounds AS D2 Receptor Agonist, M4 Receptor Antagonist and ACHE Modulator: Mechanistic and in Silico Modelling Studies, J Res Med Dent Sci., 2021; 9(6): 1-6.
21. Mettai, M.; Daoud, I.; Melkemi, N. In Silico Approaches for the Study of New Anti-Parkinson's Agents. Chem. Proc. 2023, 14, 55. https://doi.org/10.3390/ ecsoc-27-16067
22. Ohgita T, Kono H, Namba N, Saito H. Physicochemical mechanisms of aggregation and fibril formation of α-synuclein and apolipoprotein A-I. Biophys Physicobiol., 2023 Dec 29; 21(1): e210005. doi: 10.2142/biophysico.bppb-v21.0005. PMID: 38803339; PMCID: PMC11128303.
23. Pathania, A., Kumar, R., & Sandhir, R. (2021). Hydroxytyrosol as anti-parkinsonian molecule: Assessment using in-silico and MPTP-induced Parkinson's disease model. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*, *139*: 111525. https://doi.org/10.1016/j.biopha.2021.111525
24. Poornima, S. I., & Sumathy, V. J. H. (2022). In Silico Interaction Studies of Various Antioxidant Molecules with MAO-B Protein–A Potent Secondary Drug Target in Parkinson's Disease. *Indian Journal of Science and Technology*, *15*(19): 923-926.
25. Radhakrishnan, D. M., & Goyal, V. (2018). Parkinson's disease: A review. *Neurology India*, *66*(Suppl 1): S26-S35.
26. Tan YY, Jenner P, Chen SD. Monoamine Oxidase-B Inhibitors for the Treatment of Parkinson's Disease: Past, Present, and Future. J Parkinsons Dis., 2022; 12(2): 477-493. doi: 10.3233/JPD-212976. PMID: 34957948; PMCID: PMC8925102.
27. Whyte, S. K. (2007). The innate immune response of finfish–a review of current knowledge. Fish & shellfish immunology, 23(6): 1127-1151.