Letters in Applied NanoBioScience
Open-Access Journal (ISSN: 2284-6808)

Article
Volume 13, Issue 2, 2024, 78
https://doi.org/10.33263/LIANBS132.078

In Silico Approach to Identify Key Active Plant Derived Natural Compounds in Parkinson's Disease

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Received: 15.04.2023; Accepted: 28.05.2023; Published: 30.06.2024

Abstract: Parkinson's disease is a condition that is characterized by loss of memory, dopamine level, oxidative stress, and several other comprehensible impairments. DJ-1 protein plays a vital role in treating this disease due to its chaperone activity. *Plumbago zeylanica* has been reported in past studies to protect neurons and motor activity in neurodegenerative diseases. The present study deals with different selected phytochemicals of the plant since they have vast medicinal and therapeutic activities. Computational studies of six compounds were carried out with the targeted protein with PDB ID: 4ZGG via molecular docking. A potential inhibitory effect was noticed with the six selected compounds, but Plumbagin showed the best binding energy when docking was used. The results were further validated using the online server patchDock. Ligands were passed through different filters, and an ADMET analysis was performed. The target was also validated via the Ramachandran plot. Additionally, the best-docked compound with the best binding energy was compared with the conventional drug of this disease i.e., Levodopa, and the phytocompound was found to be more effective than it. This study thus provides purposeful insights that Plumbagin could be a promising candidate to combat this disease.

Keywords: DJ- protein; 4ZGG; Levodopa; molecular docking; Parkinson’s disease; plumbagin

1. Introduction

Parkinson's disease is one of the most severe, chronic, and common neurodegenerative diseases prevailing in the aged population of the Western world. The disease has no specific pharmacological treatment despite millions of dollars being spent alone to allocate the resources for its treatment [1]. However, the symptomatic treatment or the fundamental therapy for this disease is L-dopa, yet associated with many complications [2]. This disease is primarily a neurodegenerative disorder, causing a loss in dopamine levels in the subtantia nigra and locus coeruleus. The disorder is mainly characterized by decreased dopamine levels, postural imbalance, weakness, muscle control, bradykinesia, and tremors [3]. This degeneration or deterioration in the motor nerves is typically caused due to a disability in the nigrostriatal system. Neuromelanin which is present in substantia nigra pars compacta, has drastic loss due to dopamine depletion. The significant aggregation of some proteins like α-synuclein, ubiquitin, etc., causes mutations in the individual, which is significantly less, as only 10% of the population has the Mendelian disorder behind this disease. This mutation ultimately leads to many other autosomal dominant (LRRK2) autosomal recessive (DJ-1 protein and PARKIN) Parkinson's disease [4]. Moreover, first and foremost, this disease's onset was initially noticed in patients suffering from the influenza virus. Hence, such environmental factors are also

associated with this disease apart from genetic disorders, which are viral infections, toxins, and other heavy metals found in the environment. Other causes are high consumption of coffee, cigarette smokers, etc., which have shown non-motor symptoms like sleeping misbalance, depression, anxiety, constipation, etc. The DJ-1 protein or the protein deglycase, also known as the PARK7 gene, is of familial form and is found in idiopathic and aging patients [3],[5]. This protein not only contributes to the reduction of the α-synuclein aggregation but also PD pathogenesis. The inhibition of this protein is targeted in this paper as it has the ability to control oxidative stress and the ubiquitin E3 ligase activity as well, which in turn reduces synuclein aggregation. Today the world is focusing more on therapeutic approach to cure various chronic diseases. So, this paper focuses on the phytocompounds of one of the most medicinally important plant *Plumbago zeylanica*, this plant is part of Plumbaginaceae family [6]. It is one of the oldest herbaceous plants used in aryurveda to treat various diseases and possesses several therapeutic activities. The chitrak (*Plumbago zeylanica*) plant has recently been used in various research due to its anti-inflammatory, antidepressant, anti-viral, antioxidant, anti-tumor, central nervous system stimulatory mechanism, etc. [7]. The pharmaceutical activities of this plant could be beneficial in fighting this disease. So, an in-silico approach has been carried out to screen various bioactive compounds or phytocompounds of *Plumbago zeylanica*, such as Napthoquinone, coumarins, saponins, alkaloids, flavonoids, tannins, and other phenolic compounds [8]. These phytochemicals have the ability to suppress the mechanism of action of NF-KappaB cells and inhibit or repress the IKappaB-α cells [9]. Also, in one of the studies, an experiment was conducted on rats to show this plant's stimulatory mechanism of the central nervous system, which is the main cause of the misbalance of motor nerves in Parkinson's disease [10]. According to previous studies, scientists also proved the therapeutic potential of this plant in treating depression, which is also one of the main causes of this disease. In the study, the antidepressant activity of this plant was explored in the stressed and the un-stressed mice [11]. The former studies have also proved that *Plumbago zeylanica* compounds are neuroprotective through both in vitro and in vivo experiments [12]. Today, the only solution to synthetic drugs' insidious and devitalizing effect is herbs [13]. *Plumbago zeylanica* is one such plant that is widely used all over the world for traditional purposes [14]. It contains a variety of important phytocompounds and many other chemical constituents [15]. The mechanism of action or these compounds' biological activities depends on their structure and other chemical properties [16]. The residents found different kinds of alkaloids, flavonoids, tannins, steroids, fats, and many other phytoconstituents in different parts of the plant, like roots, stems, and leaves [17]. Literature has also reported earlier the pharmacological importance of this plant-producing chitranone, maritinone, Plumbagin, flavonoids, sitosterol, lupeol, forms of zeylinone, glucose, and amino acids. Many other bioactive compounds were isolated, but this study focuses mainly on the compounds that exhibit anti-inflammatory effects, like Plumbagin, elliptionone, vanillic acid, napthalenone, isoshinanolone, and catechol. These compounds also possess several other pharmacological actions like anti-diabetic, anti-malarial, anti-microbial, anti-tumor, and anti-cancer. Moreover, the antioxidants and anti-inflammatory phytocompounds are among the most potent ones for chronic diseases due to the overproduction of oxidants and inflammation, ultimately leading to the pathogenesis of neurodegenerative diseases [18, 19]. They have various other health benefits, such as cofactors and inhibitors of biochemical reactions, [20] being present as a substrate for enzymatic reactions, and scavengers of reactive chemicals acting as ligands that agonize cell surface. Various studies have previously reported that the intake of herbal compounds has significantly

enhanced cell survival performance, boosted mental performance, and increased antioxidant and anti-inflammation activity [21]. Due to its medicinal importance and various therapeutic properties, this plant is now used to treat different diseases through herbal formulation [22]. Advanced researchers have also increased the utilization of particular plants in treating neurodegenerative diseases [23]. This study suggests the potential of phytocompounds in inhibiting inflammation and oxidation through a computational approach, thereby providing an idea for novel drug design compared to the standard drug for chronic diseases [24].

In the present study, the screening of the phytocompounds has been done to find the novel therapeutic agent from *Plumbago zeylanica* that could show better potency against the main protease of Parkinson's disease [6]. Six compounds were chosen for docking: Plumbagin (among the most essential compounds as it exhibits various ayurveda properties), napthalenone, elliptinone, isoshinanolone, catechol, and vanillic acid. After preliminary investigation, the best-docked compound was compared with the conventional drug, Levodopa, currently used in treating this disease [25]. It is the only symptomatic cure, but for long-term use, it may be toxic and might boost the disease. Hence, the effectiveness of the phytocompounds against the conventional drug was examined via docking simulation, which will provide distinction to other investigators.

2. Materials and Methods

2.1. Selection and optimization of protein.

The crystal structure of the DJ-1 protein (PDB id: 4ZGG) was retrieved or extracted from PDB databank (https://www.rcsb.org/) (Figure 1). The protein was saved in .pdb format and visualized under the Discovery Studio visualizer. For its optimization, the Autodock 4.2 tool was used for molecular docking. The water molecules and hetatms were deleted, polar hydrogen was added, non-polar hydrogen was removed, and kollman charges were added.

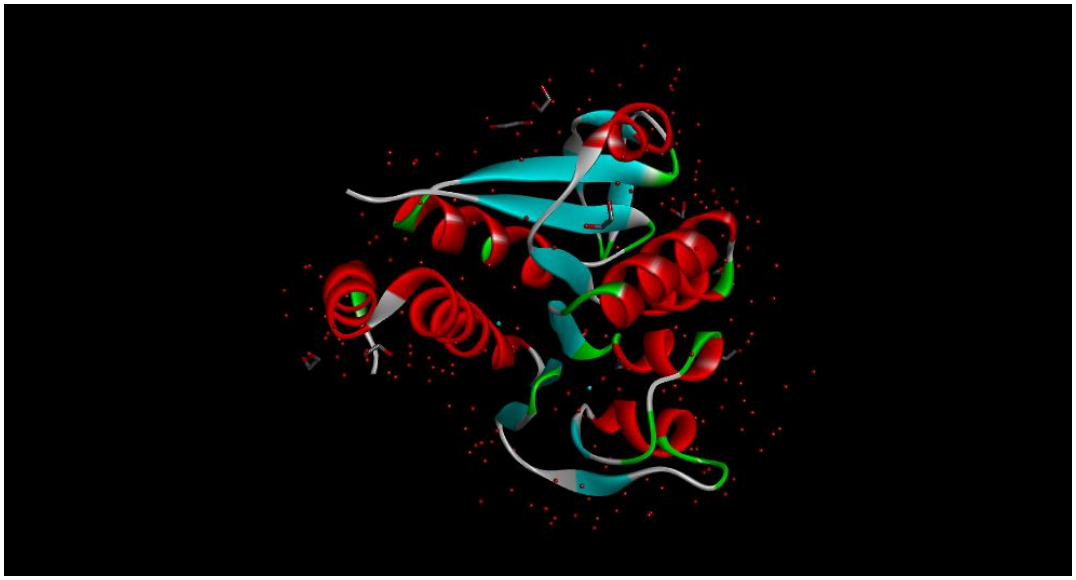


Figure 1. Crystal structure of DJ-1 protein.

2.2. Ligand preparation.

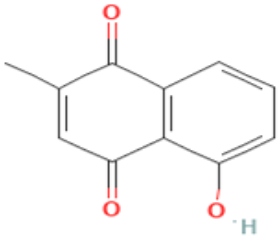
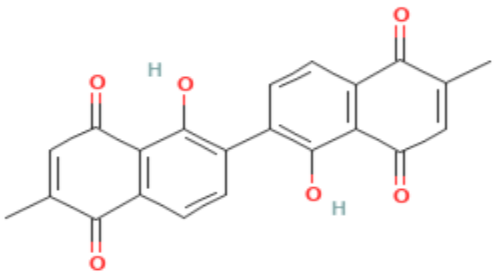
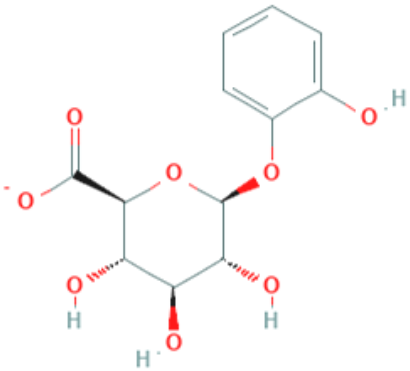
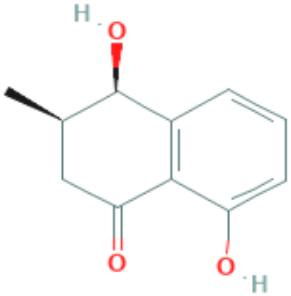
The 6 phytocompounds from *Plumbago zeylanica* were extracted by studying different research papers, and specifically, those compounds were chosen that show the property of anti-

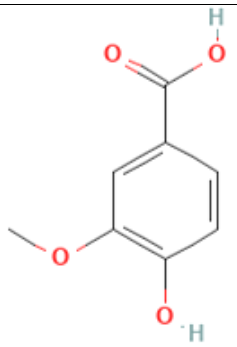
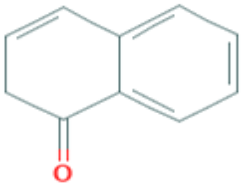
inflammation. These compounds were retrieved from the database, namely PubChem (https://pubchem.ncbi.nlm.nih.gov/) in .sdf format and later converted into .pdb format with the help of manual software, i.e., Open Babel GUI. Visualization can be done in the Discovery Studio visualizer. The 7th compound was also retrieved using the same server but in 2D format. So, for this to be converted into a 3D format, manual software was used, i.e., Chimera 1.10.2.

2.3. Lipinski's rule of five

All 6 compounds along with the conventional drug, were used to gather the information about drug-likeliness properties in which the rule of five is considered. The drug has to fulfill this rule in order to increase the efficacy of the drug being proposed. The 5 physiochemical properties are the molecular weight of the compound, no. of (hydrogen) H-bond acceptor and H-bond donor, LogP value (lipophilicity), and molar refractivity. The online tool used was (http://www.scfbio-iitd.res.in/). The compound's chemical structures and PubChem ID are mentioned in (Table 1).

Table 1. Different phytocompounds of *Plumbago zeylanica*, along with their ID and chemical structures.

S.No	PubChem ID	Compound's name	Chemical structures
1	10205	5-hydroxy-2-methylnaphthalene-1,4-dione	
2	146680	5-hydroxy-6-(1-hydroxy-6-methyl-5,8-dioxonaphthalen-2-yl)-2-methylnaphthalene-1,4-dione	
3	122198215	(2S,3S,4S,5R,6S)-3,4,5-trihydroxy-6-(2-hydroxyphenoxy)oxane-2-carboxylate	
4	443777	(3R,4R)-4,8-dihydroxy-3-methyl-3,4-dihydro-2H-naphthalen-1-one	

S.No	PubChem ID	Compound's name	Chemical structures
5	8468	4-hydroxy-3-methoxybenzoic acid	
6	12446728	2H-naphthalen-1-one	

2.4. Manual docking procedure.

For target and ligand interactions, the Autodock 4.2 tool was used as it is the most effective and accurate way to find out the binding interaction on the basis of Gibbs (free) energy. The default parameters were considered, and the Lamarckian genetic algorithm was carried out to generate the best-docked pose among the 6 phytocompounds. The grid was set to default, i.e., 60×60×60 with a spacing of 0.375 Å to cover the active site of the protein. Lastly, the DLG (docking log file) file was studied, and a comparison was made between the 6 phytocompounds with the standard drug.

2.5. Visualization of the docked compounds.

The ligand and protein interaction was visualized using discovery studio visualize, which is the freely available tool to analyze and view molecular structures in both 2D and 3D form. Hence, a schematic diagram was generated, which shows the number of hydrogen bonds associated with it as well as the amino acid residues surrounding the binding pocket.

2.6. Validation of the results.

For validation purposes, all 6 compounds were re-docked using an online web-based tool, i.e., PatchDock (https://bioinfo3d.cs.tau.ac.il/PatchDock/). It is the geometry-based algorithm for molecular docking. The compounds and the standard drug were docked to determine the docking score.

2.7. Further validation of the best result.

Ramachandran plot further validated our result, which is used to show the participating molecules during the interaction, such as ligand ion chains. It also gives information about the allowed and disallowed regions present in the protein so that the ligand can get locked with it.

2.8. ADMET analysis and its property characterization.

The analysis of ADME parameters of the 6 compounds was determined using a web-based tool, i.e., SWISSADME (http://www.swissadme.ch/).

2.9. Different drug-likeliness filters.

Different drug-likeliness filters were also used for screening purposes to prove these novel compounds' efficacy (Figure 2).

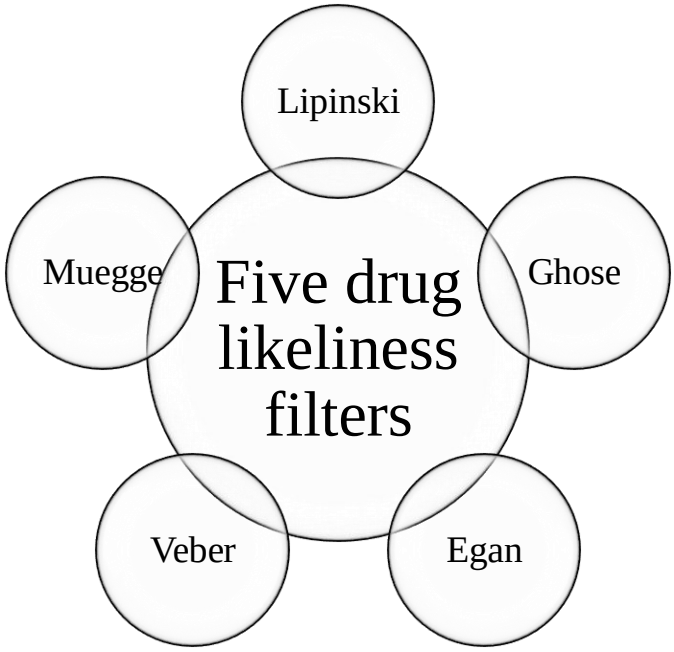


Figure 2. Different filters were used while screening different phytocompounds extracted from *Plumbago zeylanica.*

3. Results and Discussion

3.1. Lipinski's rule of five.

Before docking, all 6 compounds were passed through Lipinski's rule of five. Different physiochemical properties that were considered are molecular weight, LogP value, molar refractivity, hydrogen bond donor, and acceptor. The criterion of these properties is as follows: molecular weight (MW) should be ≤500 daltons, hydrogen bond donor (HBD) atoms should be ≤5, hydrogen bond acceptor (HBA) should be ≤10, LogP value should be ≤5 and lastly molar refractivity (MR) should be between the range of 40 to 130. All compounds fulfilled these 5 parameters; hence, these compounds can be used for docking simulation. (Table 2)

Table 2. Lipinski's rule of five analyses of all 6 compounds with different parameters.

S.No.	Pubchem ID	Compound name	HBA	HBD	LogP value	MW	MR
1	10205	5-hydroxy-2-methylnaphthalene-1,4-dione (PLUMBAGIN)	3	1	1.71	188	50.5
2	146680	5-hydroxy-6-(1-hydroxy-6-methyl-5,8-dioxonaphthalen-2-yl)-2-methylnaphthalene-1,4-dione (ELLIPTINONE)	6	2	3.41	374	100
3	122198215	(2S,3S,4S,5R,6S)-3,4,5-trihydroxy-6-(2-hydroxyphenoxy)oxane-2-carboxylate (CATECHOL)	2	2	1.09	110	50.77

S.No.	Pubchem ID	Compound name	HBA	HBD	LogP value	MW	MR
4	443777	(3R,4R)-4,8-dihydroxy-3-methyl-3,4-dihydro-2H-naphthalen-1-one (ISOSHINANOLONE)	3	2	1.64	192	51.17
5	8468	4-hydroxy-3-methoxybenzoic acid (VANILLIC ACID)	4	2	1.09	168	41.61
6	12446728	2H-naphthalen-1-one (NAPTHALENONE)	1	0	2.28	144	44.42

3.2. Docking simulations results

The target protein DJ-1 with PDB ID 4ZGG was docked with all 6 compounds with the help of manual and most precise software, Autodock 4.2. The binding energy, amino acid residues, and no hydrogen molecules associated are shown in (Table 3).

Table 3 Docking results of DJ-1 protein with ligands of *Plumbago zeylanica*

S.No.	Compound's chemical name	DOCKING PARAMETERS		
		Binding energy (kcal/mol)	No. of H bonds	Amino acid residues
1	Plumbagin	-8.04	4	VAL8, VAL71, VAL25, PRO22, ALA6, ILE168, ALA6, ARG27, ILE31, ALA29, VAL33,VAL169
2	Elliptinone	-6.43	3	GLU163, ALA167, GLU170, ALA171, VAL146, LYS148
3	Catechol	-6.23	4	GLY65, LYS62, PRO66, TYR67, ILE91, GLU95, GLN95, ARG98
4	Isoshinanolone	-6.07	4	ARG27, VAL33, VAL23, VAL25, ILE31, ALA29, ALA6, PRO22, VAL8, ALA165, VAL169, ILE168, VAL71
5	Napthalenone	-5.96	1	PRO22, ARG27, VAL71, VAL8, VAL33, VAL25, ALA165, ILE168, VAL169, ILE31, ALA6
6	Vanillic acid	-5.14	3	ILE31, ARG28, ARG27, VAL33, VAL25, VAL23, VAL8, PRO22, VAL71, PHE164, ALA155, ILE168, VAL169, ALA29

The docking results after performing manual docking showed the binding energies with the compounds Plumbagin, Elliptinone, Catechol, Isoshinanolone, Napthalenone, and Vanillic acid are -8.04, -6.43, -6.23, -6.07, -5.96 and -5.14 respectively. All these compounds have exhibited good results against the protein; Plumbagin showed the best binding energy among these compounds. Green dotted lines represent H-bonding (Figures 3-8).

Based on online results, Plumbagin has shown the best efficacy against the selected novel compounds, i.e., -8.04, and thus could be a potent inhibitor in Parkinson's disease. For this, we need to validate the results.

Additionally, we have compared the best-docked results with the proposed drug Levodopa for Parkinson's disease and found that Plumbagin showed better results than the conventional drug. Hence, we can say that the implementation of a therapeutic approach in treating diseases rather than conventional or standard drugs.

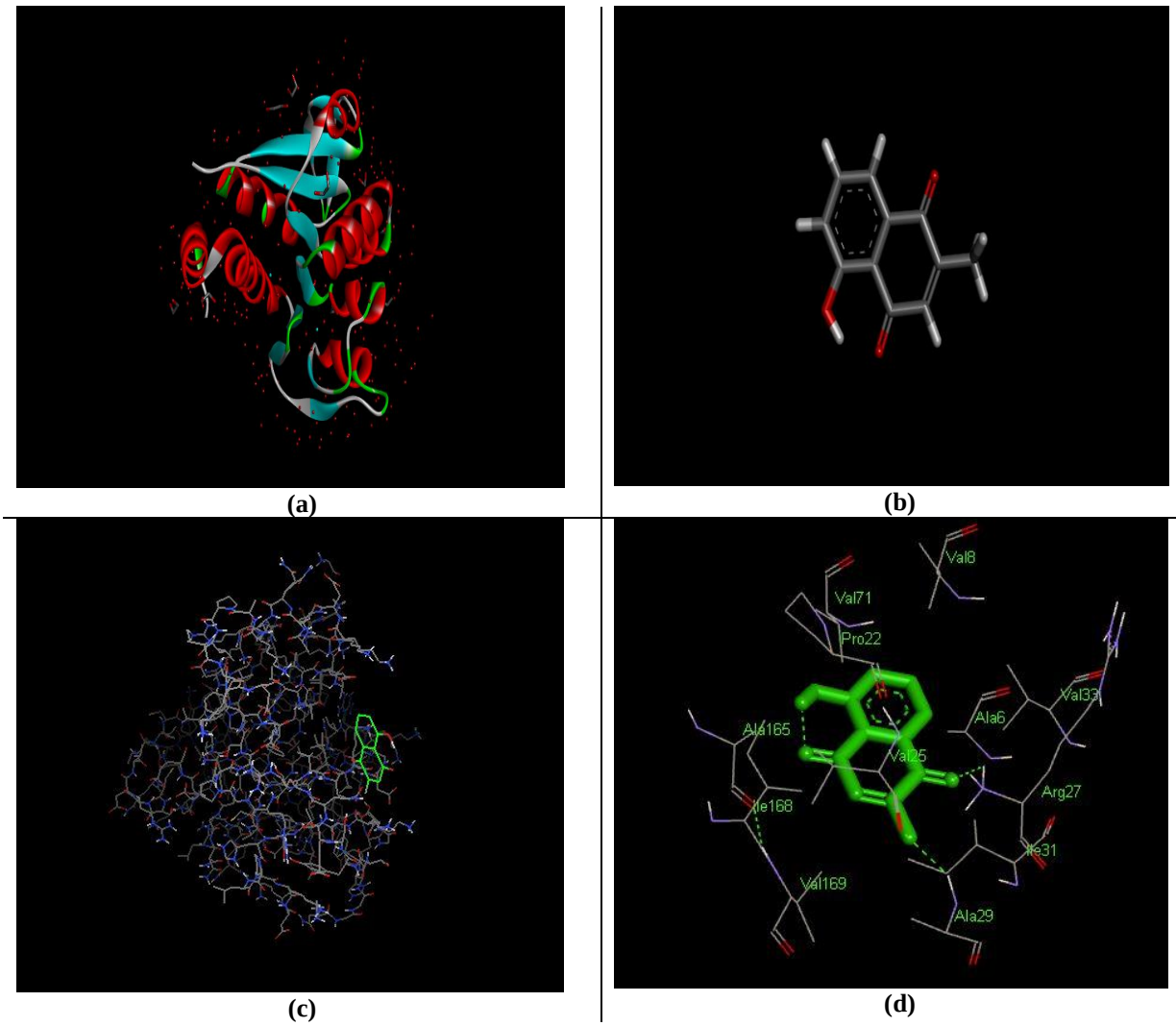
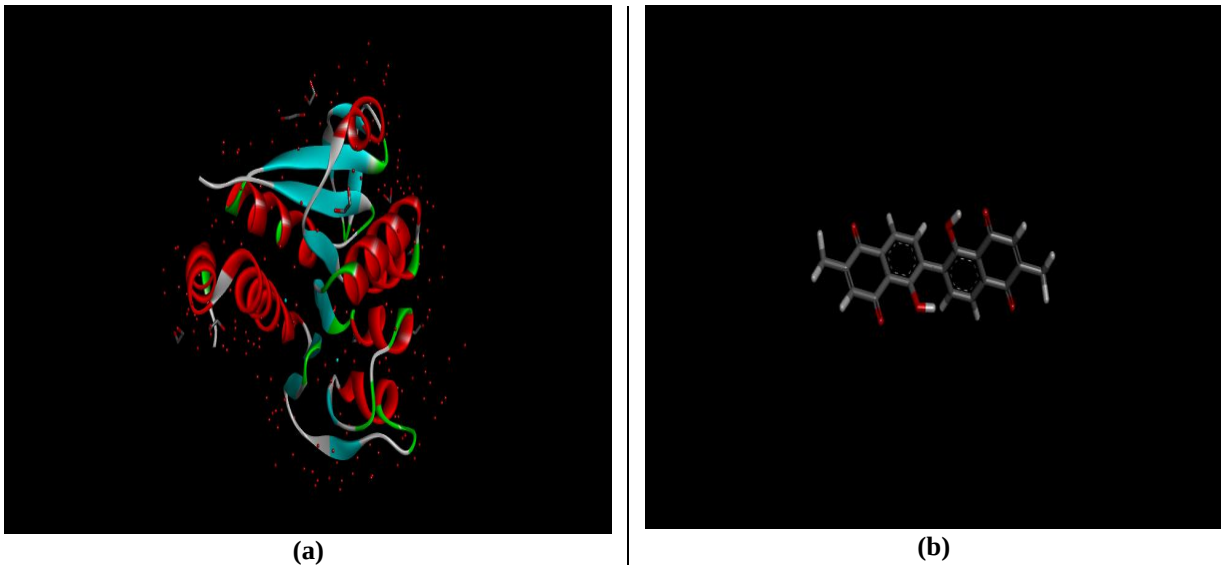
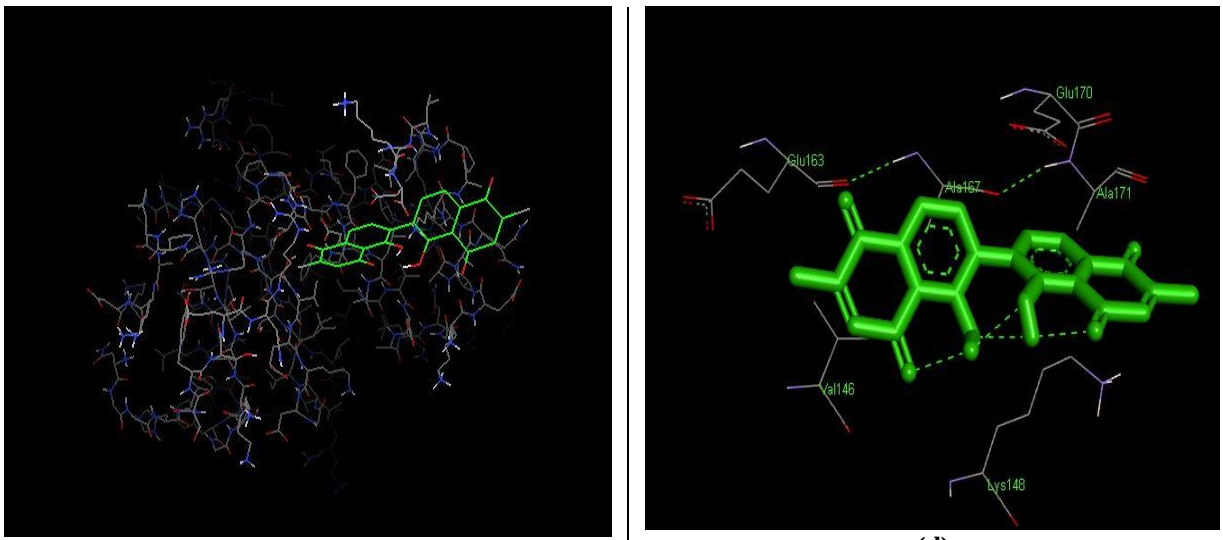


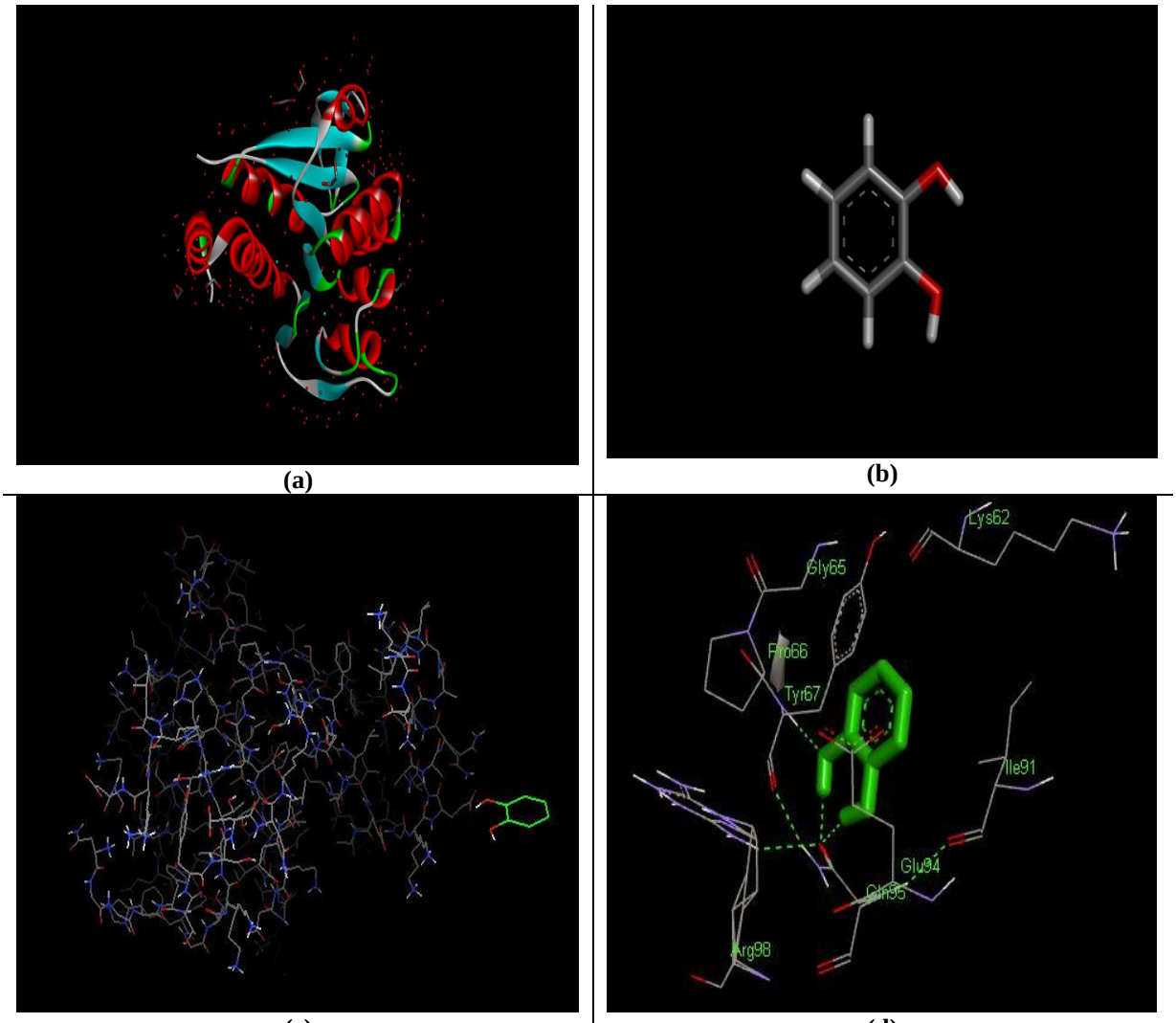
Figure 3. Molecular docking analysis between 4ZGG and Plumbagin. (**a**) Receptor protein - 4ZGG; (**b**) ligand-Plumbagin; (**c**) Protein-ligand interaction; (**d**) Docking results.





(c) (d)

Figure 4. Molecular docking analysis between 4ZGG and Elliptinone. (**a**) Receptor protein - 4ZGG; (**b**) Ligand-Elliptinone; (**c**) Protein-ligand interaction; (**d**) Docking results.



(a) (b)

(c) (d)

Figure 5. Molecular docking analysis between 4ZGG and Catechol. (**a**) Receptor protein - 4ZGG; (**b**) Ligand - Catechol; (**c**) Protein-ligand interaction; (**d**) Docking results.

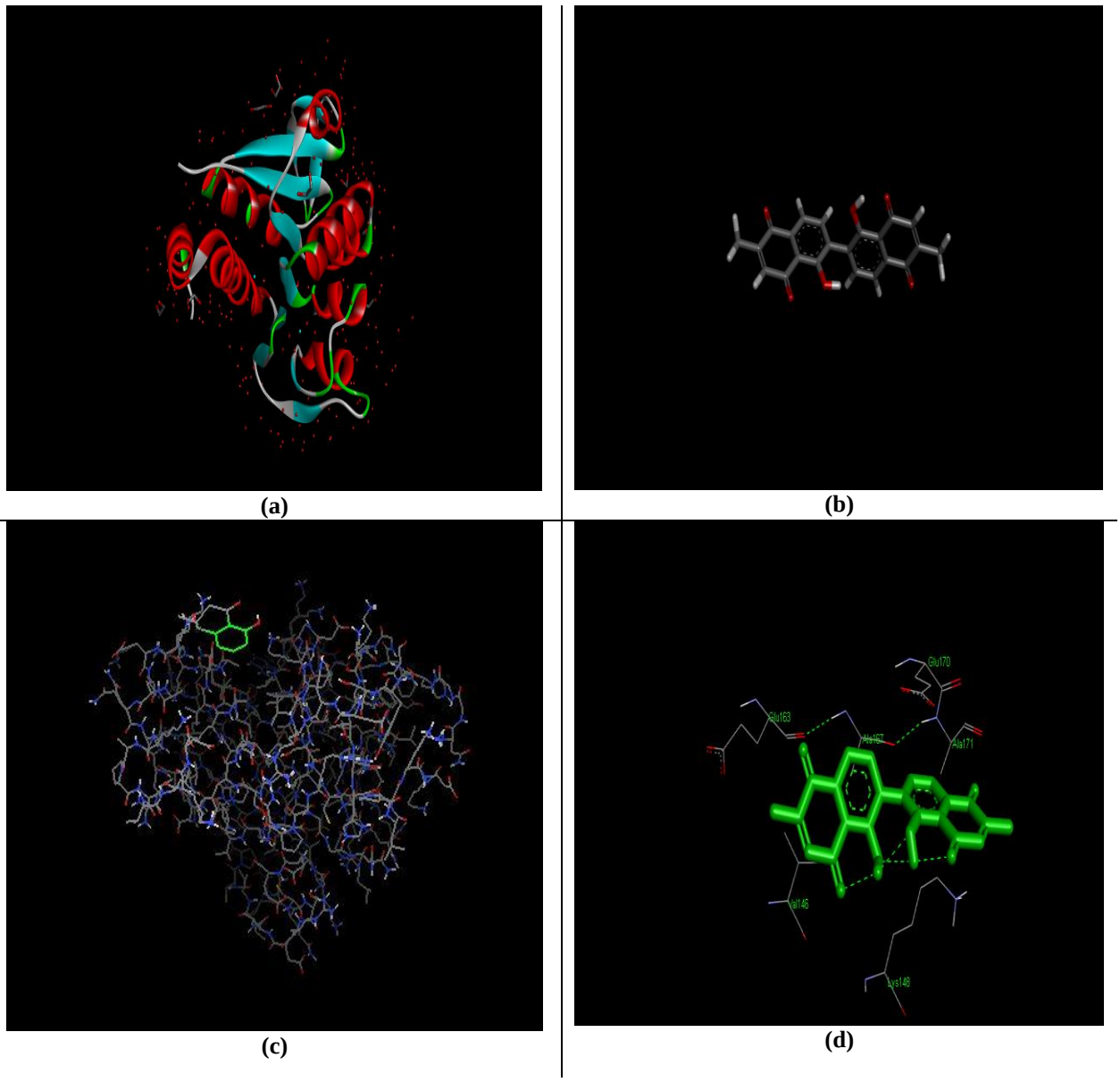
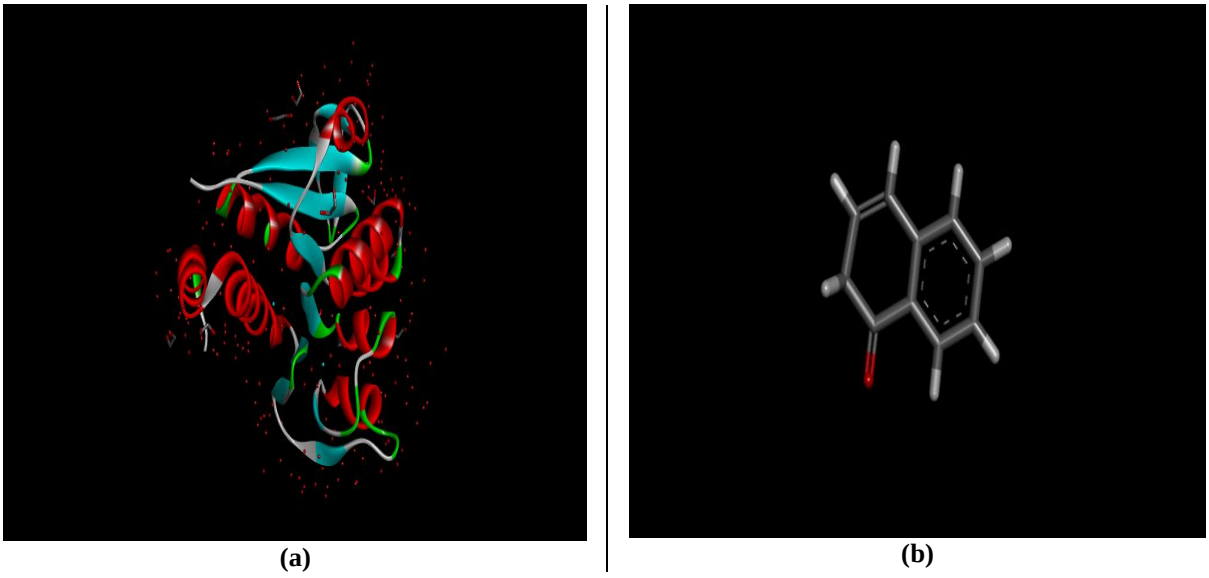
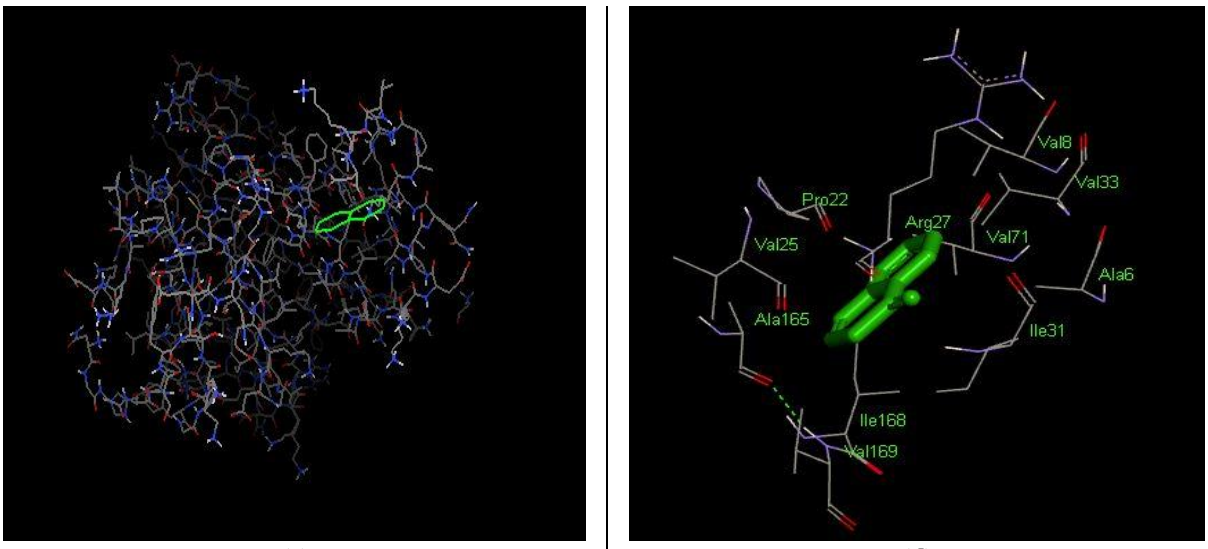


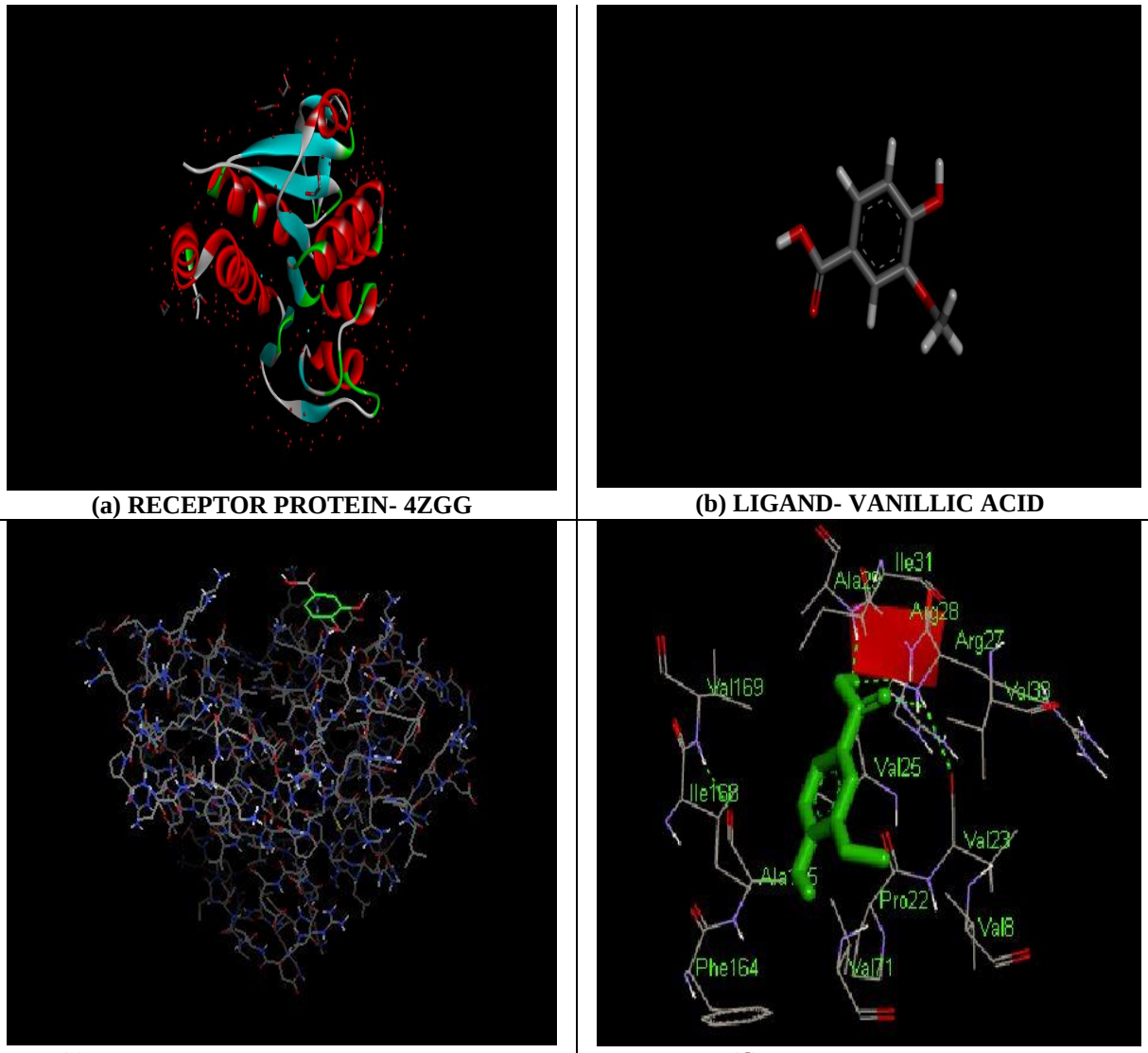
Figure 6. Molecular docking analysis between 4ZGG and Isoshinanolone. (**a**) Receptor protein - 4ZGG; (**b**) Ligand- Isoshinanolone; (c) Protein-ligand interaction; (d) Docking results.





(c) **(d)**

Figure 7. Molecular docking analysis between 4ZGG and napthalenone. (**a**) Receptor protein - 4ZGG; (**b**) Ligand- Napthalenone; (**c**) Protein-ligand interaction; (**d**) Docking results.



(a) RECEPTOR PROTEIN- 4ZGG **(b) LIGAND- VANILLIC ACID**

(c) PROTEIN-LIGAND INTERACTION **(d) DOCKING RESULTS**

Figure 8. Molecular docking analysis between 4ZGG and vanillic acid. (**a**) Receptor protein - 4ZGG; (**b**) Ligand-Vanillic acid; (**c**) Protein-ligand interaction; (**d**) Docking results.

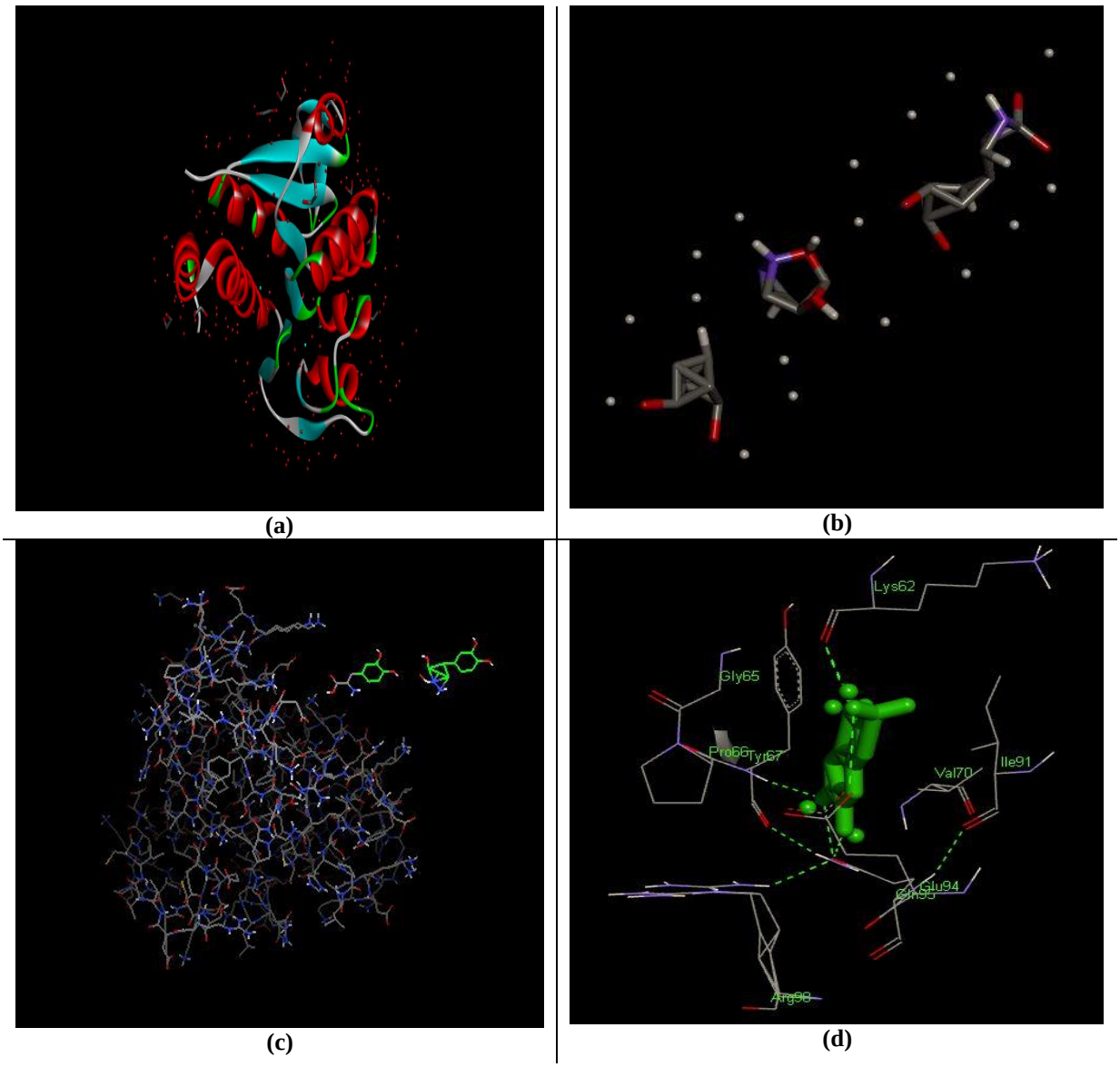


Figure 9. Molecular docking analysis between 4ZGG and conventional drug Levodopa. (**a**) Receptor protein - 4ZGG; (**b**) Ligand- Levodopa; (**c**) Protein-ligand interaction; (**d**) Docking results.

The binding energy of Levodopa after docking with the target protein 4ZGG was found to be -7.38 (Table 4).

Table 4. Docking result of Levodopa (conventional drug) with 4ZGG protein.

S.NO	COMPOUND	BINDING ENERGY	NO. OF HYDROGEN	AMINO ACID RESIDUES
1	Levodopa	-7.38	6	GLY65, LYS62, PRO66, TYR67, VAL70, ILE91, GLU94, GLN95, ARG98

3.3. Validation of the results.

An online docking server (PatchDock) was used to validate the results. Again, Plumbagin has shown the maximum docking score compared to other selected therapeutic compounds and conventional drugs (Table 5).

Table 5. PatchDock results of 6 phytocompounds and 1 conventional drug.

S. No	COMPOUND NAME	DOCKING SCORE
1	PLUMBAGIN	4130
2	ELLIPTINONE	3940

S. No	COMPOUND NAME	DOCKING SCORE
3	CATECHOL	2600
4	ISOSHINANOLONE	2400
5	NAPTHALENONE	2238
6	VANILLIC ACID	2227
7	LEVODOPA (standard drug)	3866

The above table shows that Plumbagin has the best docking score compared to the other 5 novel compounds and standard drugs.

3.4. Validation of the macromolecule by Ramachandran plot

An online server, PDBsumgenerate, was used to generate the plot statistics and determine the percentage of amino acid residues in the favored protein region. Over 90% of the allowed region is considered the quality model protein. Our validated results found that 98.1% of the residues were in the most favored region, 1.2% were in the additional favored region, and only 0.6% were in the disallowed region (Figure 10, Figure 11).

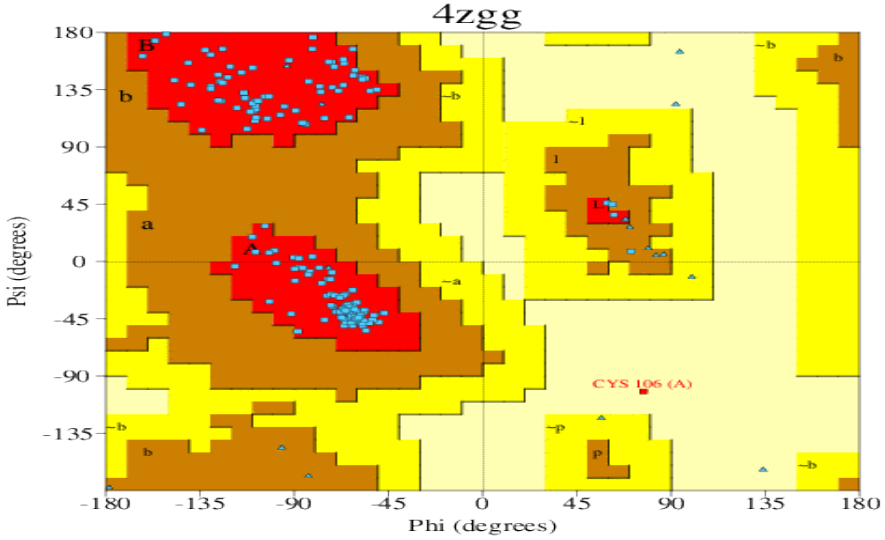


Figure 10. Ramachandran plot of 4ZGG having 98% amino acid in the allowed region.

PROCHECK statistics

1. Ramachandran Plot statistics

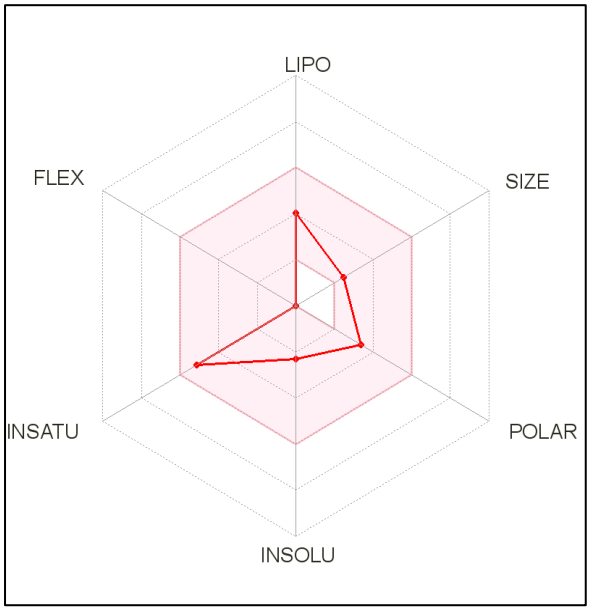
		No. of residues	%-tage
Most favoured regions	[A,B,L]	158	98.1%
Additional allowed regions	[a,b,l,p]	2	1.2%
Generously allowed regions	[~a,~b,~l,~p]	0	0.0%
Disallowed regions	[XX]	1	0.6%*
Non-glycine and non-proline residues		161	100.0%
End-residues (excl. Gly and Pro)		1	
Glycine residues		19	
Proline residues		9	
Total number of residues		190	

Based on an analysis of **118** structures of resolution of at least **2.0** Angstroms and *R*-factor no greater than **20.0** a good quality model would be expected to have over **90%** in the most favoured regions [A,B,L].

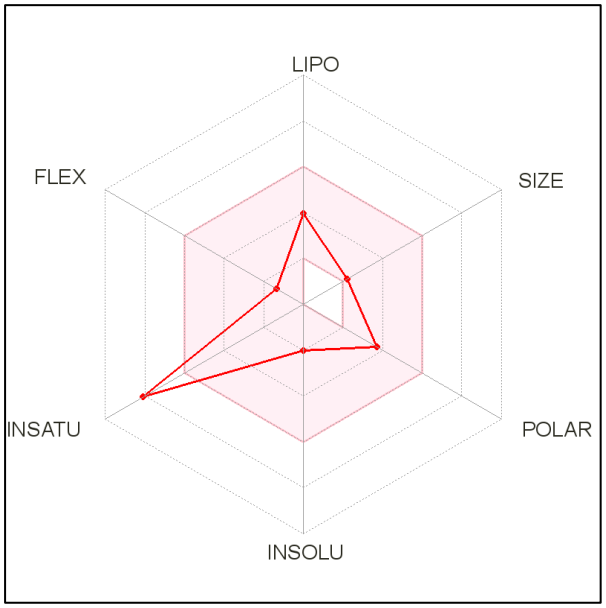
Figure 11. Ramachandran plot statistics of 4ZGG protein showing the percentage of residues in different regions.

3.5. Results of ADMET analysis.

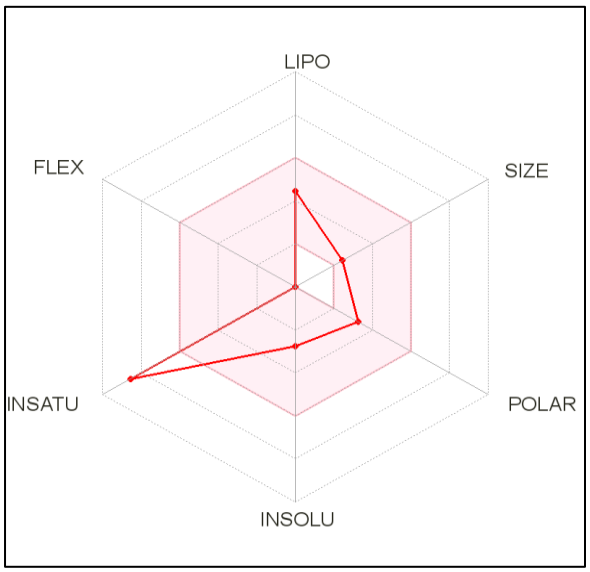
The patchDock results were again validated via ADME analysis with the help of the web-based tool SWISSADME. All 6 compounds of the preferred plant were predicted and have shown better efficacy than any conventional drug. Results proved that more or less pharmacokinetics and drug-likeliness properties were in the range. Here, ADME stands for absorption, distribution, metabolism, and excretion. LIPO (Lipophility): -0.7 <XLOGP3<+5.0. SIZE: 150 g/mol<TPSA< 130Å2. INSOLU (Insolubility): 0<LogS (ESOL) < fraction Csp3 < Number of rotatable bonds <9 (Figure 12).



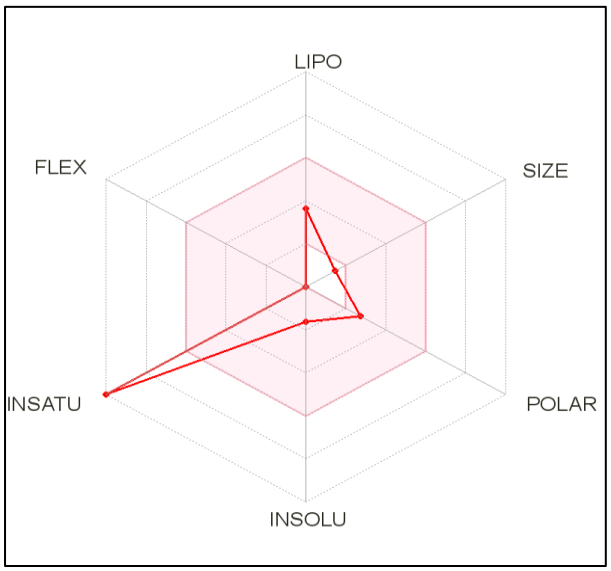
(a) PLUMBAGIN



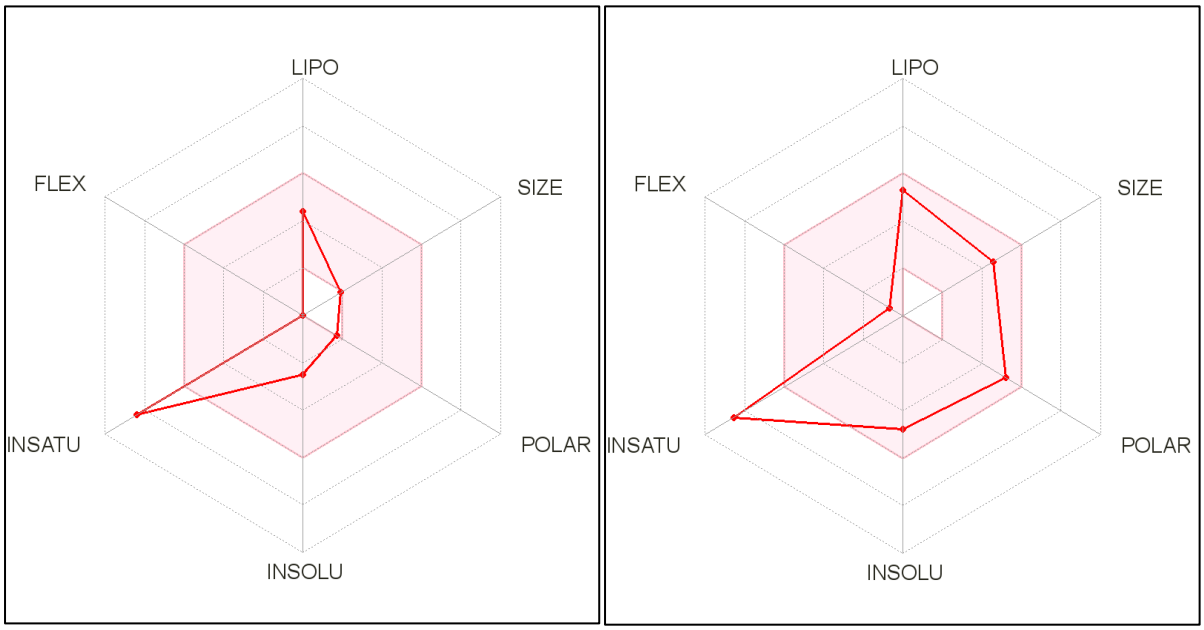
(**b**) ELLIPTINONE



(c) CATECHOL



(**d**) ISOSHINANOLONE



(e) NAPTHALENONE **(f)** VANILLIC ACID

Figure 12. (a, b, c, d, e and f) It represents the ADME parameters of compounds and shows better results than the standard drug. The colored region in the figures shows the space for the oral bioavailability of drugs.

3.6. Results of phytocompounds passing through different filters-

The different ligands were also passed through different filters, namely, Lipinski's, Ghose, Veber, and Egan, to ensure the drug-likeliness properties of the compounds. The compounds showed zero violations, suggesting they could later be used in drug discovery (Table 6).

Table 6. Table representing the different compounds passed through drug-likeness filters.

S. No	Compound	Lipinski's	Ghose	Veber	Egan
1	Isoshinanolone	yes	yes	yes	yes
2	Vanillic acid	yes	yes	yes	yes
3	Plumbagin	yes	yes	yes	yes
4	Catechol	yes	No(1violation)	yes	yes
5	Napthalenone	yes	No(1violation)	yes	yes
6	Elliptinone	yes	yes	yes	yes

In chronic diseases, Parkinson's is considered one of the major brain disorders that has not had a significant cure till now. There had been a major discussion and conflicts between therapeutic and conventional treatments. With time, it has been researched and proven that phytochemicals have built a holistic approach to several diseases without side effects [26]. *Plumbago zeylanica* is one of the prime examples of rasayana (ayurveda branch), which possesses different properties like an antidepressant, anti-inflammation, antioxidant, and neuroprotection [27]. Modern medicines of neuroprotection are rare and not very effective when exposed clinically; therefore, scientists rely on treatment as they are cost-effective and have higher efficacy, too [28],[29]. The aerial part and roots of the plant contain several microelements; macro elements contain different bioactive compounds like Plumbagin, Elliptinone, chitranone, and many more [30]. The main feature of this disease is chronic inflammation; studies reported that extracts of Plumbago suppressed the NF- Kappa activation in tumor cells and hence showed anti-inflammatory activity in both rats and patients [9,30]. Another study was conducted using in vivo experimental models, which showed that this plant suppressed the paw edema of rats, revealing antioxidant and anti-inflammatory activity against

many inflammatory diseases [31]. It also reduced the production of cytokines, TNF α, 1β before inflammation, etc. The current choice of drug for Parkinson's is L-dopa, but it has some adverse effects; in one of the studies, it was revealed that the roots of this plant not only uplifted the dopamine in the striatum but also amplified ambulatory and anti-parkinsonian activity [32,33]. This study also helped find an alternative to synthetic medicine. In another study, diene-conjugate and β-glucuronidase tests were taken into consideration to govern the activity of inflammation. The results revealed that the extracts of this plant are effective against inflammation and showed better results against salicylic acid (an anti-inflammatory agent), too. Hence, this signifies that this plant could play a potent role in neurodegenerative diseases. In another study, similar findings revealed that *Plumbago zeylanica* significantly reduced the stimulation of NF-Kappa B cells. Results indicated that this plant is credited with various therapeutic activities like central nervous system stimulation and neuroprotection. [34],[35] These studies provided insights to work against the disease-causing agent, as neurodegenerative diseases are the biggest social and economic problem. Also, recently, the potential of this plant has been revealed in Alzheimer's disease. Hence, we tried to explore more about the therapeutic properties of this plant in Parkinson's disease via the in-silico approach.

4. Conclusions

Previous reports indicated that *Plumbago zeylanica* is an effective inhibitor against neurodegenerative diseases through in vitro and in vivo methods. Recent studies also found that Plumbagin, a derivative of this plant, has shown great results against Alzheimer's. So, we explored the therapeutic properties of this plant in Parkinson's disease, which is also a neurodegenerative disorder, via molecular docking. We contended that the Plumbagin compound derived from *Plumbago zeylanica* has shown the best binding efficacy against the over-expresser DJ-1 protein of Parkinson's. We have selected a total of 6 compounds that have the medical and Ayurveda properties against the 4ZGG protein. This best-docked compound was more effective than the standard drug (Levodopa) as these are naturally derived compounds and do not exhibit any side effects. In conclusion, Plumbagin could be used as a potent inhibitor for further developing new drugs for Parkinson's disease. Further in-vivo and in-vitro studies are needed to examine its potential at its best to be used as a drug against the disease in further pre-clinical and clinical studies.

Funding

This research received no external funding.

Acknowledgments

The author would like to thank the Department of Biotechnology, Delhi Technological University, for their constant support. The author would like to thank Dr. Navneeta Bharadvaja, Plant Biotechnology Laboratory, Department of Biotechnology, Delhi Technological University, India, for her valuable suggestions to shape the outline of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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