STM JOURNALS

International Journal of
Genetic Modifications and
Recombinations Research
https://journals.stmjournals.com/ijgmr/

Volume 1, Issue 1, 2023
January—June
DOI (Journal): 10.37591/IJGMR

Research IJGMR

Pharmacological Management of Parkinson's Disease: Current Therapies and Emerging Treatments

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Abstract

Objective*: Parkinson's disease, behind Alzheimer's, is the second most common neurodegenerative ailment and a major cause of neurological morbidity worldwide. Clinical diagnosis is made, and current management is limited to symptomatic treatments, with levodopa remaining the cornerstone of pharmaceutical therapy. In certain patient groups, deep brain stimulation of specific basal ganglia targets can provide significant clinical relief. There are currently no proven disease-modifying medicines in clinical use that can halt or reverse the underlying neurodegenerative process.* ***Methods:*** *For this study, proteins of interest were retrieved from the PDB and then subjected to docking analysis using BioVia. The ligands' and standard medications' binding affinity with each target protein was compared and assessed. Also, only 4 substances were choosen for SWISS-ADME final results.* ***Results:*** *The docking result revealed that the ligands selected have the best binding affinity with all the three target proteins.* ***Conclusion:*** *The ligands could potentially be used to treat Parkinson's Disease in the future approaches for studying the urge ligands in vitro and in vivo analysis in order to create novel parkinson's inhibitors.*

Keywords: Parkinson's Disease, Phytocompounds, Molecular docking, SWISS-ADMET analysis, Levodopa

INTRODUCTION:

With an estimated lifetime risk of about 3-7%, idiopathic Parkinson's disease ranks as the second most common neurodegenerative condition after Alzheimer's disease In 1990 and Between 2016, the incidence of Parkinson disease increased from around the world from 2.5 million people to 6.1 million.With age being the most significant risk factor for the condition, and in the setting of an increasingly ageing population, the prevalence of Parkinson's disease is expected to climb further. The buildup of misfolded aggregates of alpha-synuclein-containing Lewy bodies throughout the brain is a pathological characteristic of PD, as is neurodegeneration in the SNpc [1]. This results in a dopaminergic state in the disease's primary motor signs. Nonetheless, there has been a growing awareness and interest in the disease's non-motor manifestations, such as anosmia, constipation, REM, SBD, and NCD, some of which may predate the motor aspects by several decades. Likewise, neuropathological studies have revealed that Lewy Body deposition originates in lower brainstem regions and olfactory bulbs before reaching the midbrain [2].

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Received Date: April 13, 2023
Accepted Date: May 04, 2023
Published Date: May 18, 2023

Citation: Sheilina Choudhary. Pharmacological Management of Parkinson's Disease: Current Therapies and Emerging Treatments. International Journal of Genetic Modifications and Recombinations Research. 2023;1(1): 27–39p.

Although current medications can alleviate symptoms for a time, only a few therapies can prevent progressive loss of dopamine neurons. Several years before motor impairment manifests, Lewy body accumulates in peripheral tissues, implying that disease-modifying therapy should

begin earlier during the premotor stage. Long-term lifestyle, food, and nutraceutical supplementation may be possible disease-modifying strategies. In preclinical studies, diet can lessen the incidence of Parkinson's disease, and phytochemicals, the principal bioactive elements of herbs and plant foods, influence several pathogenic variables and exert neuroprotective effects [1, 2].

The elderly with PD experience a range of symptoms and issues, including both motor and nonmotor problems. Among these are ICDs, which refer to conditions like hypersexuality, pathological gambling, excessive shopping, and binge eating disorder, affecting around 13.6% of individuals with PD. DRA utilization is considered a significant risk factor for the emergence of ICDs. ICDs were linked with amantadine, and although to a lesser extent, high dosages of levodopa as well. Depending on the severity of the behavior(s), ICDs can adversely affect the social, occupational, and familial aspects of both patients and their families' livesIt is recommended to routinely monitor Parkinson's disease patients who are prescribed DRA, high doses of levodopa, and/or amantadine for the development of ICDs throughout the course of their treatment, both during the initiation and maintenance phases [3]. To improve the effectiveness of ICD therapy, it is often recommended to first reduce the dosage or completely stop taking the medication that is causing the problematic behavior, particularly dopamine receptor agonists (DRA). This initial step has shown to be a successful approach in managing the condition. Because there is a risk of exacerbating motor symptoms or inducing dopamine agonist withdrawal syndrome (DAWS), it is crucial to adjust the medication dosage carefully while closely monitoring the patient. This cautious approach is necessary to ensure that the patient's symptoms are managed effectively and that they do not experience any adverse effects during the medication adjustment process [3]. In patients with Parkinson's disease and impulse control disorders (ICD) who tapered or stopped taking dopamine receptor agonists (DRA), almost 30% experienced dopamine agonist withdrawal syndrome (DAWS). This suggests that careful consideration and monitoring are required when reducing or discontinuing DRA in these patients to minimize the risk of DAWS [3].

In order to maintain balance between ICD and DAWS, the lowest dose of DRA must be taken because other dopaminergic or psychotropic medications do not ease it. Amantadine, naloxone, cognitive behaviour therapy, deep brain stimulation, and psychopharmacotherapy are examples of further low-evidence treatments for ICD management that have produced varying effects [4]. Medical professionals must be knowledgeable of the psychosocial effects of Parkinson's disease, including ICD, in addition to the detection and treatment of motor symptoms.

The current research project involves testing the inhibitory potential of phytocompounds derived from the Uncaria rhynchophylla Jacks plant species against alpha-synuclein protein [4]. This evaluation will be conducted through a molecular docking approach, which involves using computational techniques to simulate the interaction between the phytocompounds and the protein of interest to predict their potential inhibitory effects.

The plant species Uncaria rhynchophylla Jacks belongs to the class Magnoliopsida, which is commonly known as dicotyledons. This is one of the two primary classes of flowering plants, also known as angiosperms, which are characterized by the presence of two embryonic seed leaves, or cotyledons, in their seeds, The other main class of flowering plants is known as Monocotyledons (Liliopsida) [5]. Uncaria rhynchophylla Jacks has been found to have neuroprotective properties, indicating that it may be able to shield the brain from damage or harm. The neuroprotective effect of Uncaria rhynchophylla Jacks is associated with its ability to increase cerebral blood flow and its anti-inflammatory properties. Moreover, the plant contains chemical compounds that have been shown to safeguard dopamine-producing neurons from damage, which is a crucial factor in the pathogenesis of Parkinson's disease, where these neurons are progressively destroyed [5].

Studies on Uncaria rhynchophylla Jacks have shown that it can be a natural treatment for Parkinson’s disease [6]. The plant's ability to enhance cerebral blood flow, exhibit antioxidant

properties, and protect dopamine-producing neurons from damage make it a promising candidate for further research as a natural therapy for this condition.:

Neuroprotective Properties

Uncaria rhynchophylla Jacks has been demonstrated to possess neuroprotective properties that can safeguard dopamine-producing neurons, which could potentially help slow down or prevent the progression of Parkinson's disease. This suggests that the plant may have therapeutic benefits in the management of this condition.

Anti-inflammatory Properties

Chronic inflammation in the brain is linked to Parkinson's disease, and Uncaria rhynchophylla Jacks has been found to possess anti-inflammatory properties that could potentially help reduce inflammation in the brain and protect neurons [6]. This suggests that the plant may have therapeutic benefits in the management of Parkinson's disease, particularly by targeting the underlying neuroinflammatory processes.

Antioxidant Effects

Oxidative stress and neuronal damage are closely associated with Parkinson's disease, and studies have demonstrated that Uncaria rhynchophylla Jacks has strong antioxidant properties that could potentially help protect neurons from harm. This suggests that the plant may have therapeutic benefits in the management of Parkinson's disease by counteracting the damaging effects of oxidative stress on neurons.

Dopamine Regulating Effects

Studies have reported that Uncaria rhynchophylla Jacks possesses dopamine-regulating properties that could potentially help increase dopamine levels in the brain and alleviate symptoms of Parkinson's disease [6]. This suggests that the plant may have therapeutic benefits in the management of this condition by targeting the underlying dopaminergic dysregulation that is central to the disease pathology.

This is a neurological condition that can result in involuntary movements, stiffness, and difficulties with balance and coordination. Symptoms normally appear gradually and progress over time [7]. As the condition progresses, individuals may experience difficulties with walking and speaking. Parkinson's disease can also lead to changes in mental and behavioral functioning, sleep disturbances, depression, memory impairment, and fatigue. Nonmotor symptoms and associated consequences, including neuropsychiatric and neurobehavioral issues, autonomic dysfunction, and sensory disturbances, are regarded as significant features of Parkinson's disease. Psychosis, delirium, and compulsive/impulsive spectrum disorders, such as dopamine dysregulation syndrome (DDS) and punding, are frequently observed in individuals with Parkinson's disease. (https://www.researchgate.net/publication/307558599_Introduction_to_Parkinson_disease_PD_and_its_complications).

Through this manuscript, I'm trying to acknowledge people more about Parkinson's disease, various phytochemicals used in its treatment and are proven to be helpful to treat Parkinson's. The study's main objective is to acess the anti-parkinson's and inhibitory effects of the 10 selected phytocompounds on the three target proteins of parkinson's disease [8]. Also to study the pharmacological as well as theraputic efficiency and the result obtained for the studies will be compared to those commonly used drugs which are approved by FDA.

PHYTOCHEMICALS

Phytochemicals act as antioxidants, protect mitochondrial function and balance, prevent intrinsic apoptosis and neuroinflammation, stimulate cellular signaling pathways triggering anti-apoptotic survival-pro-life genes like Bcl-2 protein family and damaged neurotrophic factors mitochond Drya,

α-synuclein They also facilitate the disassembly of aggregates [9]. Phytochemicals prevent α-synuclein oligomerization and aggregation, and dissolve preformed α-synuclein aggregates [10].

Most abundant and well-known classes of phytochemicals which are proven to be helpful in treating PD are shown in Table 1:

Table 1. Phytocompounds and its source

S.N.	Phytocompound	Plant from which it's obtained
1.	Oleic Acid	Justicia adhatoda L.
2.	Ginsenoside	Panax ginseng L.
3.	Rhynchophylline	Uncaria rhynchophylla Jacks
4.	Asiaticoside	Cantella asiatica urban
5.	Resveratrol	Vitis vinifera L.
6.	Thymol	Driganum ehrenbergii
7.	Caffein	Coffea arabica L.
8.	Curcumin	Curcuma longa L.
9.	Queretin	Morus alba L.
10.	Winthanones	Withania somnifera(L) Dunal

METHODS

Protein Extraction and Purification:

The three-dimensional (3D) structure of the protein alpha-synuclein was resolved using X-ray diffraction method with a resolution factor of 2.16 Å. The structures were obtained from the PDB Research Collaboratory for Structural Bioinformatics (RCSB PDB) (https://www.rcsb.org/) in pdb format. The missing residues were replaced using BIOVIA, which purifies the protein by eliminating the water molecules hetatm and adding polar hydrogen to the retained Chain A, while the rest of the chains are eliminated [11]. This purified protein is then stored in pdb file format, which was utilised to obtain the 2-dimensional structure and Ramachandran plot using PDBsum (https://www.rcsb.org/) and the Hydrophobicity plot from BIOVIA Discovery Studio programme.

Ligand Retrieval and Purification:

A total of 15 phytocompounds of different plant specimens were selected from IMPAAT (https://cb.imsc.res.in/imppat/) which has potential anti-parkinson's activity based on their antioxidant, anti-mutagenic, anti-hepatotoxic, anti-inflammatory, anti-aging, and chemopreventive properties. The canonical SMILES, PubChem CID, and the two-dimensional(2D) models of them Amentaflavon and Baiclein were retrieved in SDF format via the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) and all the structures were converted to PDB format with the help of Open Babel software (http://openbabel.org/).

Molecular Docking

After the retrieval of protein and ligand, molecular docking was executed using PyRx. PyRx works primarily as a virtual molecular screening tool, tasked with mapping libraries of small molecules to macromolecules to identify copper compounds with specific biological activities. The 15 phytocompounds and two standard drugs were added as ligands, and the two purified proteins were uploaded as macromolecules [12]. The added ligands were energy minimized and were all converted into .pdbqt format. All the ligands were docked with target proteins discretely and were evaluated based on binding affinity [13]. The strength of protein–ligand binding is known as binding affinity. The negative values for binding affinity (or binding free energy) indicate that the ligand is predicted to bind to a target macromolecule. The more negative the numerical values for the binding affinity, the better the predicted binding between a ligand and a macromolecule [14, 15]. Therefore, the ligand

with the least binding affinity along with zero RMSD value was selected for each protein and was visualized in BIOVIA Discovery Studio software. RMRMSD value is utilized to evaluate the docked conformation compared to other docked conformations or the reference conformation. Based on binding affinity the inhibitory activity of ligands and standard drugs will be compared.

Here, 15 phytocompounds and two standard drugs were uploaded as ligands and two target proteins I.e., 5F1T and 1xq8. The ligands loaded were with minimum energy and were converted to .pdbqt format and the grid was generated for targeted protein which is as follows. The grid for center is shown in the table2 and the values obtained for grid dimensions are as follows: X=15 Å Y=15 Å and Z=15 Å. This was similar foe all the three points.

Table 2. PDB ID of selected proteins and their specifications

PDB id of Protein	X	Y	Z
1xq8	237	87	-11
5f1t	44	16	58

Visualization

The top three ligands with the lowest binding affinity for each protein were chosen, and the best model of each ligand was saved in PyRx in pdb file format. The three-dimensional (3D) structure and non-bond interaction were observed using BIOVIA Discovery Studio software, and the 3D model was retrieved in png file format.

Physiochemical Studies (ADMET Analysis)

The pharmacokinetics were evaluated in ADMET (https://admetmesh.scbdd.com/) using Lipinski's rule of five (RO5). Pharmacodynamic properties were predicted by the parameters such as physiochemical properties, absorption, distribution, metabolism, medical chemistry, toxicity and excretion. The highest three docked ligand having the least binding affinity for each protein were evaluated ADMET analysis was performed using ADMETlab 2.0 (https://admetmesh.scbdd.com/). Table 3 shows Drugs used in PD treatment and their specifications.

Table 3. Drugs used in PD treatment and their specifications

Drug	Formula	No. Of H-Bond acceptors	No. Of H-Bond donors	No. Of Heavy atoms	Gastro-Intestinal absorption	Blood Brain Barrier Permeant	Lipinski
Levodopa	C19H25N3O8	11	9	30	Low	No	No
Apomorphine	C17H17NO2	3	2	20	High	Yes	Yes
Amantadine	C10H17N	1	1	11	High	Yes	Yes
Ropinirole	C16H24N2O	2	1	19	High	Yes	Yes

RESULTS

A key challenge for future development of disease-modifying therapies is reliance on current diagnostic criteria, which primarily assess physical symptoms and can detect Parkinson's disease (PD) when approximately 60-70 % in specific tissues already damaged only Being This highlights the urgent need for validated diagnostic biomarkers that can detect the onset of PD progression earlier than current standards allow.

A total of 16 phytocompounds were chosen, out of which only 10 were selected based on docking result. The two-dimensional chemical structure of the following is shown in Figure 1. To test these compounds' inhibitory efficacy against the target proteins, two standard medicines, Amentoflavone and Baicalein, were obtained, as shown in Fig:1. Also, resveratrol and amentoflavone are the two phytocompounds found to have best binding affinity with all the three proteins selected.

Protein retrieval and purification;

The Three-Dimensional (3D) crystal structure of the three target proteins which was retrieved from PDB. After that the proteins 5f1t, 5fIw and 1xq8 were purified in the BIOVIA Discovery software which is subjected to its structure analysis which is seen in Figures 2, 3 and 4 respectively. In structural analysis Ramachandran plot, Secondary Structure and hydropathy plot are analysed.

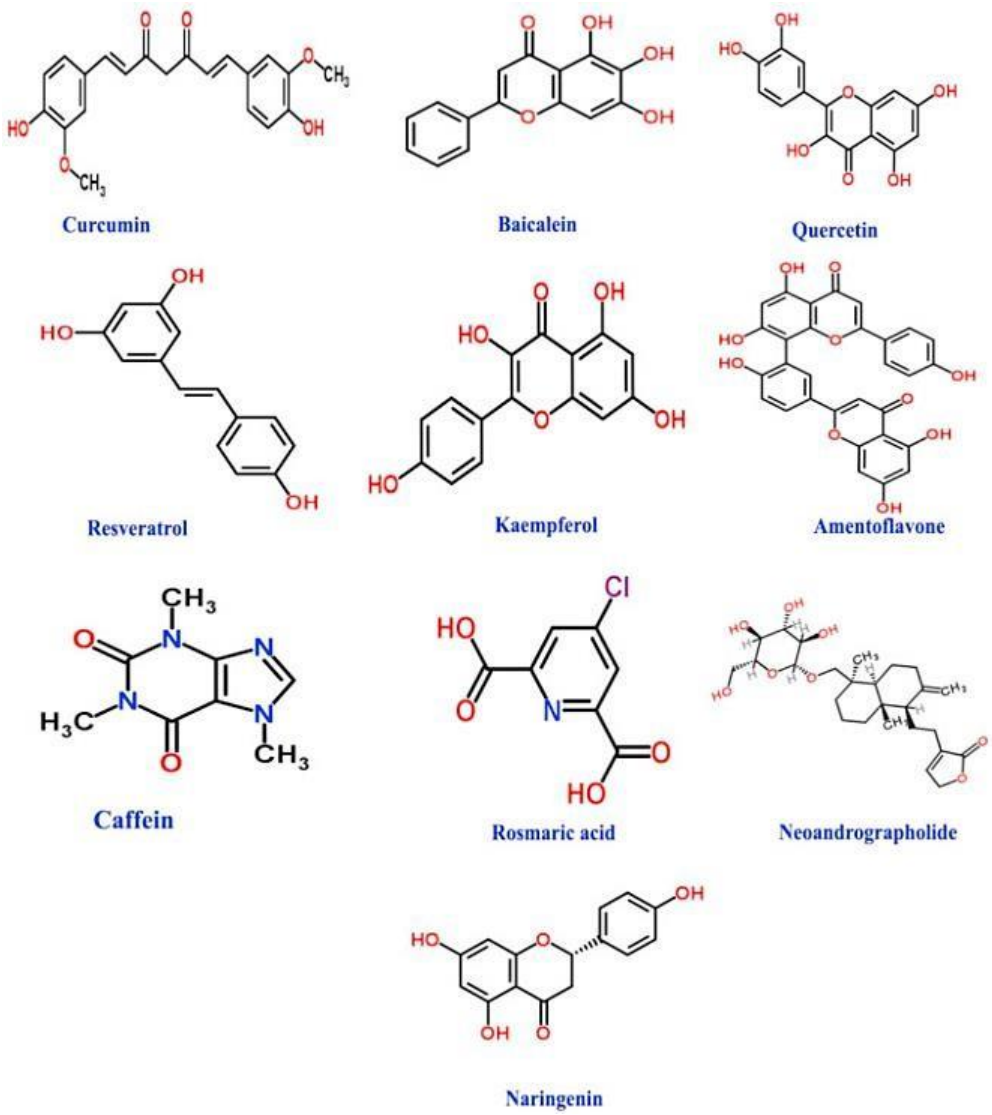


Figure 1. Chemical structure of top 10 phytocompounds and standard drugs.

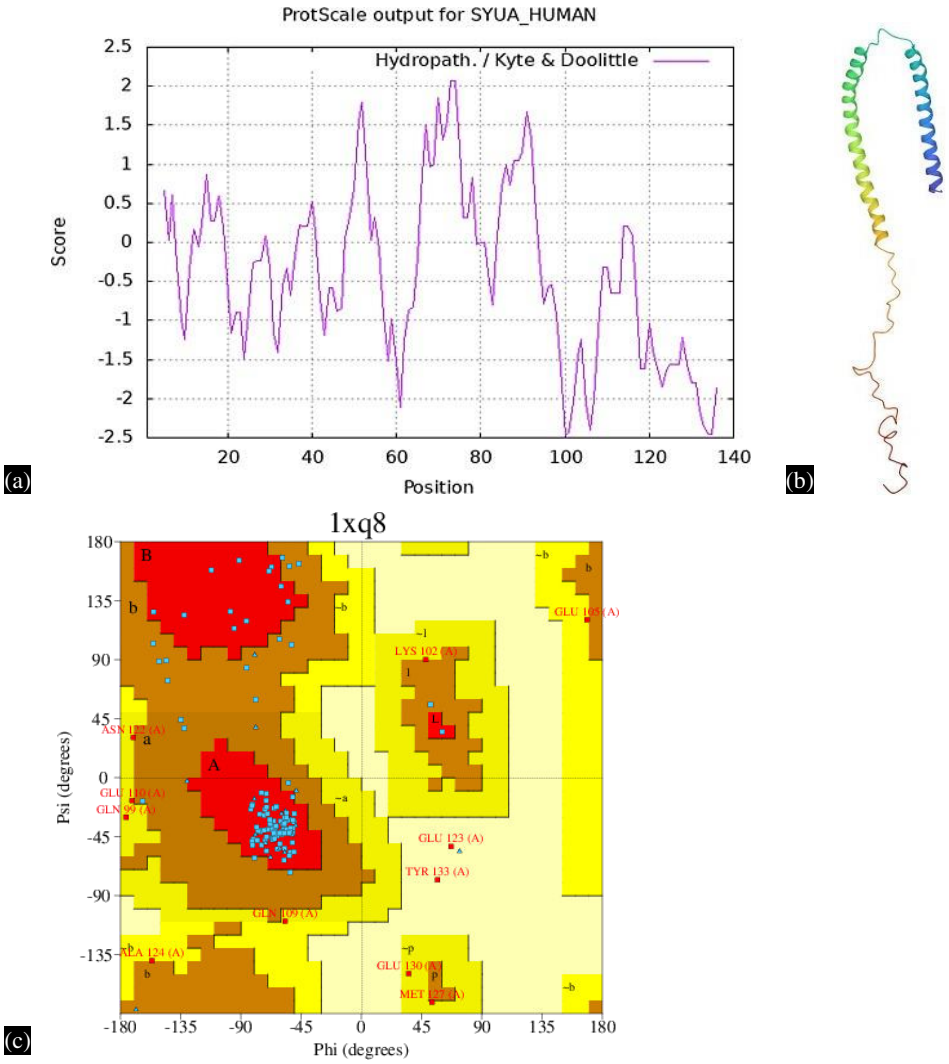
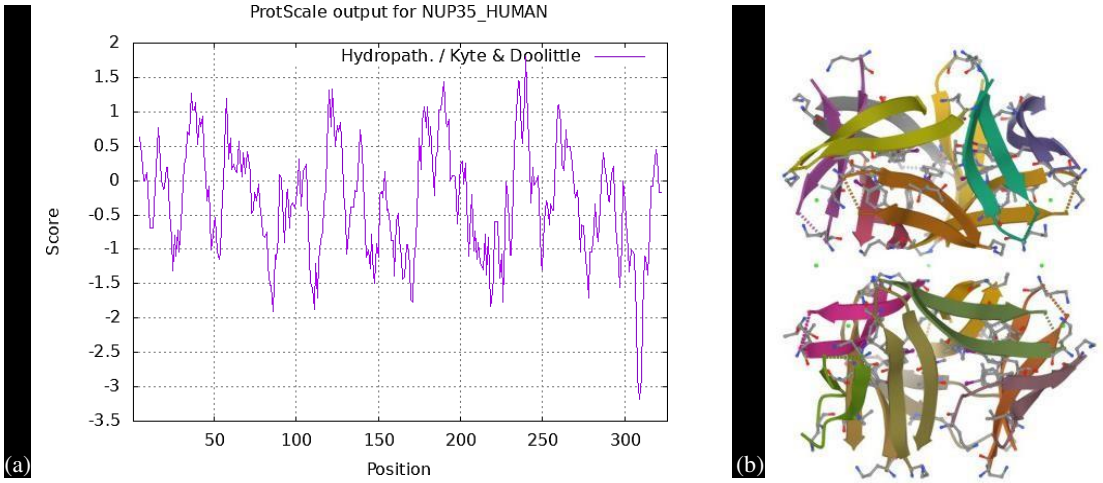


Figure 2. Structural analyses of 1xq8 (a) Hydropathy plot (b) Structure (c) Ramachandran plot.



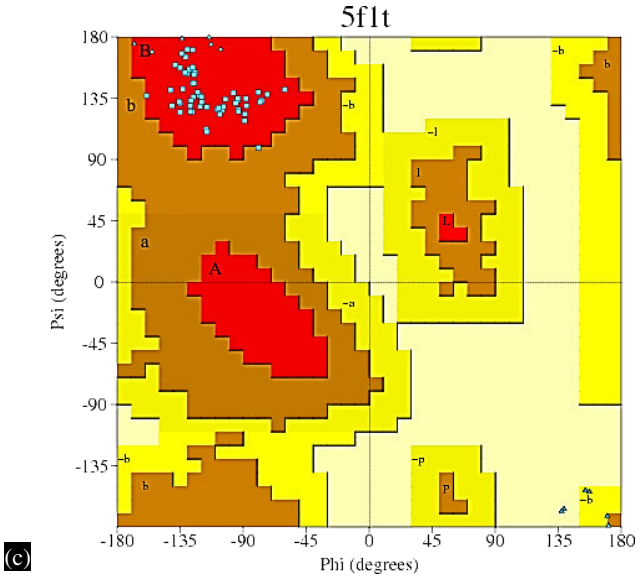
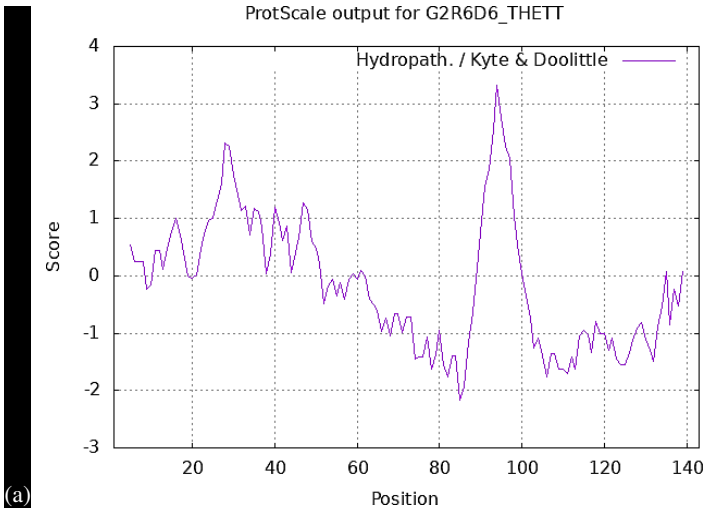
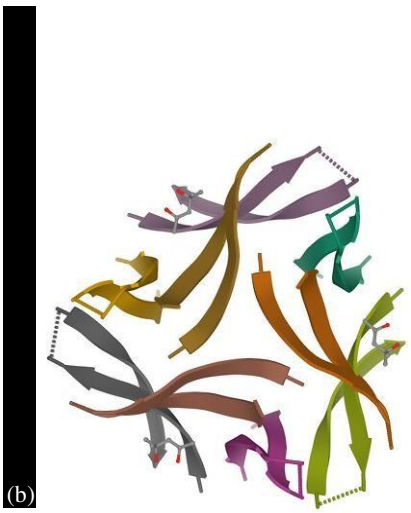


Figure 3. Structural analysis of 5F1T (a) Hydropathy plot (b) Structure (c) Ramachandran plot.





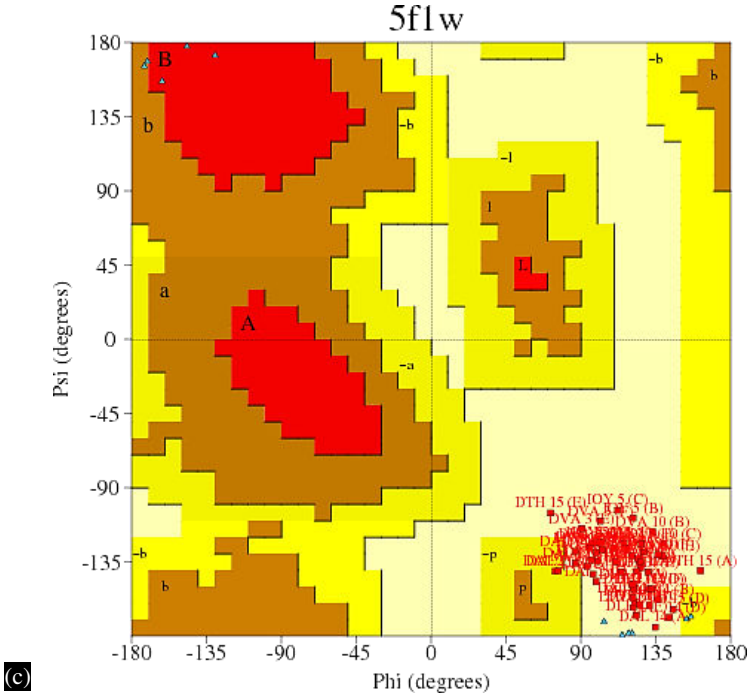


Figure 4. Structural analysis of 5F1W (a) Hydropathy plot (b) Structure (c) Ramachandran plot.

Molecular Docking

Fifteen ligands were docked in the PyRx software against the proteins 1xq8, 5f1t, and 5f1w for this docking study. The conformation with the lowest binding affinity and zero root mean square deviation (RMSD) was selected as the compound's optimal docking orientation upon the docking. Once the docking was completed the RMSD as well as binding affinity were recorded. Out of all the fifteen phytocompounds, the common phytocompounds for all the three target proteins that had lower binding affinity than 7 and above were selected along with these 10 phytocompounds the standard drugs were also docked with each protein and their binding affinity was recorded (Tables 4–8).

Table 4. Absorption of Phytocompounds

Ligand	HIA	Log S(ESOL)	Solubility
Oleic acid	61%	-5.41	1.09-03 mg/ml
Rhynchophylline	2.7-5.5%	-3.51	1.19-01 mg/ml
Ginsenoside	0.1-3.7%	-7.71	8.60-06 mg/ml
Asiaticoside	9.4%	-5.19	6.20-03 mg/ml
Resveratrol	2.0-2.2%	-3.62	5.51-02 mg/ml
Thymol	2-3%	-3.19	9.74-02 mg/ml
Caffein	95%	-1.48	6.50+00 mg/ml
Cucurmin	60-66%	-3.94	4.22-02 mg/ml
Quercetin	14%	-3.16	2.11-01 mg/ml
Withanones	2.5-5%	-4.55	1.33-02 mg/ml

Table 5. Medicinal Chemistry of Phytochemicals

Ligand	LIPINSKI	Pain Alert	SYN. ACC
Oleic acid	Accepted	0	3.07
Rhynchophylline	Accepted	0	4.78
Ginsenoside	Accepted	0	5.98
Asiaticoside	Accepted	0	10.00
Resveratrol	Accepted	0	2.02

Thymol	Accepted	0	1.00
Caffein	Accepted	0	2.03
Cucurmin	Accepted	0	2.97
Quercetin	Accepted	0	3.23
Withanones	Accepted	0	6.38

Table 6. Physiochemical Properties of Phytochemicals

Ligand	Molecular Weight	No. of Hydrogen Acceptors	No. of Aromatic Hydrogen Atoms
Oleic acid	282.46	20	0
Rhynchophylline	384.47	28	6
Ginsenoside	444.74	32	0
Asiaticoside	959.12	67	0
Resveratrol	228.24	17	12
Thymol	150.22	11	6
Caffein	194.19	14	9
Cucurmin	368.38	27	12
Quercetin	302.24	22	16
Withanones	470.60	34	0

Table 7. Distribution of Phytochemicals

Ligand	Blood Brain Barrier	Skin Permeation
Oleic acid	No	-2.60
Rhynchophylline	Yes	-7.01
Ginsenoside	No	-2.95
Asiaticoside	No	-12.08
Resveratrol	Yes	-5.47
Thymol	Yes	-4.87
Caffein	No	-7.53
Cucurmin	No	-6.28
Quercetin	No	-7.05
Withanones	No	-7.01

Table 8. Toxicity and Excretion of Phytochemicals

Ligand	CYP1A2	CYP2C19	CYP2C9	CYP2D6
Oleic acid	Yes	No	Yes	No
Rhynchophylline	No	No	No	Yes
Ginsenoside	No	No	No	No
Asiaticoside	No	No	No	No
Resveratrol	Yes	No	Yes	No
Thymol	Yes	No	No	No
Caffein	No	No	No	No
Cucurmin	No	No	Yes	No
Quercetin	Yes	No	No	Yes
Withanones	No	No	No	No

ADMET Analysis

DISCUSSION

Millions of people worldwide are impacted by Parkinson's disease, which is a degenerative

neurological condition. Parkinson's disease is characterized by a progressive loss of dopamine neurons in the brain. This can cause manifestations such as vibration, rigidity, navigation and structural difficulties. Along with these motor symptoms, the condition can also cause non-motor symptoms such as depression, anxiety, and cognitive impairment.

Although there is no known cure for Parkinson's disease at present, there are various treatments available that can assist in managing symptoms and improve the patient's overall quality of life. Therapies like physical therapy and speech therapy, along with medication that boosts dopamine levels in the brain, can help improve mobility and communication abilities in individuals with Parkinson's disease.

For many years, Uncaria rhynchophylla Jacks has been utilized as a traditional medicinal plant in China, Japan, and Korea to treat a range of health problems. Uncaria rhynchophylla Jacks, which is also called Gou Teng, is recognized for its beneficial properties including neuroprotection, anti-inflammatory, and antioxidant effects.The potential of Uncaria rhynchophylla Jacks as a treatment for various neurological disorders, including Parkinson's and Alzheimer's disease, has been investigated through research.

Studies have demonstrated that Uncaria rhynchophylla Jacks may safeguard dopamine-producing neurons in the brain, lower inflammation and oxidative stress, and regulate dopamine levels in the brain. Proteins 1wq8, 5f1w, and 5f1t are recognized as key contributors to the onset of Parkinson's disease. Uncaria rhynchophylla Jacks has been researched for its potential to target these proteins, making it a promising natural treatment option for the neurological condition.

A synthesis of qualitative studies that considered the experiences of Parkinson's disease patients was desperately needed. This was required to improve the quality of care provided by healthcare providers. The critical evaluation of studies highlighted methodological limitations of existing literature, specifically the absence of reference to theoretical saturation and a lack of information around minor issues. The current study gives significant theoretically saturated data from the analysis as well as trust in the outcomes produced, particularly in the minor themes (codes). The review successfully achieved its objectives, which focused on the effects of social identity and meaningful activities on hope and well-being, as well as identifying the factors and techniques that contribute to an individual's well-being. The review also aimed to develop a hope enablement paradigm that could be applied to various chronic neurological disorders and other chronic illnesses. Evidence from studies on stroke, spinal cord injury, multiple sclerosis, schizophrenia, and juvenile idiopathic arthritis supported most components of the model, indicating its potential universal relevance.

Parkinson's disease is associated with the enzyme MAO-B, which is responsible for breaking down dopamine, a neurotransmitter that plays a crucial role in regulating movement, motivation, and reward. Studies have shown that people with Parkinson's disease may have increased levels of MAO-B in the brain. Such an increase could lead to synergy between neurons that produce dopamine, an important neurotransmitter that regulates movement, motivation and reward. The loss of neurons that produce dopamine is a distinguishing characteristic of Parkinson's disease, and it is the cause of several typical symptoms of the disease, such as difficulties in movement, rigidity, and tremors. MAO-B inhibitors are commonly used to treat Parkinson's disease by reducing the activity of the MAO-B enzyme, which can lead to increased dopamine levels in the brain. This can help alleviate symptoms of the disease and slow down its progression.

As per the results section, it has been found that among the phytocompounds studied, resveratrol and amentaflavone have demonstrated the highest binding affinity with all three target proteins. To put it in other words, Japanese knotweed (Polygonum cuspidatum) is a source of resveratrol, while amentoflavone is extracted from the leaves of Ginkgo biloba. Resveratrol is extracted from the plant

Polygonum cuspidatum, which is known to be a rich source of this phyto-compound. This plant is often used as a source of resveratrol supplements, as it has potent antioxidant and anti-inflammatory properties. Resveratrol is also being studied for its potential role in preventing or treating a variety of diseases, including cancer, cardiovascular disease, and neurodegenerative disorders.

The therapeutic properties of the Ginkgo biloba tree have been used for centuries in traditional Chinese medicine, and its leaves are a popular herbal supplement. The leaves contain a variety of biologically active chemicals, including amentaflavone, which is considered to be one of the major molecules responsible for the plant's therapeutic effects.

Yes, amentaflavone has been studied for its potential health benefits, which include its antioxidant, anti-inflammatory, and neuroprotective effects. It has been suggested that amentaflavone may be helpful in the treatment of various neurological disorders, including Alzheimer's and Parkinson's disease. Further research is necessary to comprehensively determine its effects on such disorders, but it has the potential to be a treatment option for anxiety and depression.

CONCLUSION

Parkinson’s disease (PD) is a debilitating neurological disorder characterized primarily by decreased levels of dopamine in the brain. Dopamine, a neurotransmitter essential for functions such as movement, motivation and memory, is reduced in PD due to dopaminergic cell death This lack of dopamine is responsible for PD-related neurological defects and may also contribute to mood moderate decline seen in some individuals with disease. Parkinson's disease often goes undetected in its early stages due to a significant time delay between the initial damage to dopaminergic cells and the appearance of clinical symptoms. Therefore, it is critical to identify dependable molecular biomarkers that can differentiate PD from other disorders, track its development, or indicate a positive therapeutic response.

In Parkinson's disease, certain neurons in the brain gradually deteriorate or die. Parkinson's disease is characterized by the gradual loss or degeneration of nerve cells in the brain, which leads to a decrease in the production of dopamine, a neurotransmitter that is essential for normal brain function. As dopamine levels decrease, abnormal brain activity occurs, resulting in symptoms such as impaired mobility and other manifestations of Parkinson's disease.

Scientists have identified specific genetic mutations associated with Parkinson's disease, although these cases are rare, except in cases where the condition affects multiple family members.

Scientists have identified specific genetic mutations that can increase a person’s chances of developing Parkinson’s disease. However, the individual risk associated with these genetic markers is generally low, except in exceptional cases where Parkinson's disease affects many people. Common top 10 ligands listed in Table were run through ADMET analysis, in which all the ligands were examined for their physiochemical properties. The results obtained tell us that these ligands could potentially be used to treat Parkinson's disease in the future approaches for studying the urge ligands *in vitro* and *in vivo* analysis to create novel Parkinson’s inhibitors.

Acknowledgement

I would like to express my sincere thanks and gratitude to my bioinformatics teacher Ms. Samiksha for her vital support and providing guidance in completing this project.

ABBREVIATIONS:

Abbreviated form	Full Form
ADMET	Absorption, distribution, metabolism, excretion and toxicity
DAWS	Dopamine agonist withdrawal syndrome
DDS	Dopamine dysregulation syndrome
DRA	Dopamine receptor agonists
ICD	Impulse control disorder

MSA	Muscular system atrophy
NCD	Neurocognitive dysfunction
PD	Parkinson's Disease
REM	Rapid eye movement
SBD	Sleep behavior disorder
SNpc	Substantial Nigra pars compacta

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